Comorbidity between substance use and mental health in Australia:

Relationships of alcohol, tobacco and cannabis use with other substance use and mental disorders

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A thesis submitted in accordance with the requirements for Admission to the degree of Doctor of Philosophy

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DECLARATION

I hereby declare that this submission is my own work and that, to the best of my knowledge, it contains no material previously published nor written by another person, nor material which to a substantial extent has been accepted for the award of any other degree or diploma at the University of New South Wales (UNSW) or any other institute of higher learning, except where due acknowledgement is made in the thesis. Any contribution made to the research by others, with whom I have worked at UNSW or elsewhere, is explicitly acknowledged in the thesis.

I also declare that the intellectual content of this thesis is the product of my own work, except to the extent that assistance from others in the project’s design and conception or in style, presentation and linguistic expression is acknowledged.

Louisa Degenhardt August, 2001
ABSTRACT

Research into the comorbidity (or co-occurrence) of mental disorders is a relatively recent phenomenon. Much of this research has been conducted in clinical samples, which are prone to a range of biases that mean that the patterns observed are not representative of the general population. Although population-level research has previously been carried out, this thesis provides the first examination of comorbidity in the Australian population.

This thesis examined the comorbidity of substance use and mental disorders among Australian adults. The major empirical work involved an examination of the patterns of homotypic comorbidity (other substance use disorders) and heterotypic comorbidity (mood disorders, anxiety disorders, and psychosis) of alcohol, tobacco and cannabis in the 1997 Australian National Survey of Mental Health and Well-Being (NSMHWB). These drugs were chosen as they are the most commonly used psychoactive substances in the Australian population. The NSMHWB involved a structured diagnostic interview of mental disorders with a representative sample of Australian adults.

Three questions were addressed using this data: (1) What patterns of comorbidity exist between tobacco, alcohol and cannabis use, and other substance use and mental disorders?; (2) Are these patterns of comorbidity explained by common factors?; and (3) Does comorbidity affect the likelihood that mental health treatment has been sought?

Similar patterns of homotypic comorbidity were observed for all three substances, and they were not explained by the other factors examined (gender, age, education, relationship status, employment and neuroticism). Cannabis dependence was the most strongly associated with other substance use disorders.

Heterotypic comorbidity differed between alcohol, tobacco and cannabis use. Tobacco use predicted increased rates of all three groups of mental disorders (mood, anxiety and psychotic disorders). In the case of alcohol, only alcohol dependence was related to increased rates of all groups of mental disorders; alcohol use and abuse were not associated with heterotypic comorbidity. Any level of cannabis involvement was related to a similarly
increased risk of mood and anxiety disorders. Cannabis use was linearly related to the risk of screening positively for psychosis. Common factors did not change the patterns of heterotypic comorbidity of tobacco and alcohol use. However, alcohol, tobacco and other drug use appeared to explain the higher rates of mood and anxiety disorders among cannabis users. Treatment seeking was much more likely among alcohol, tobacco and cannabis users when they had comorbid mental disorders. It was moderately increased when they had comorbid substance use disorders.

The second piece of empirical work provided a more detailed examination of comorbid substance use problems among persons with psychosis. This topic was selected due to the limited epidemiological research on this issue, and the relatively large burden of disability that psychosis places upon the individual and the community. NSMHWB data were used to examine the prevalence of comorbid substance use disorders among persons who were likely to have met criteria for psychosis (as assessed by a screener used in the NSMHWB). Multiple regression analyses were used to test possible explanations for the higher rates of substance use disorders observed among persons reporting higher numbers of psychotic symptoms. The odds of alcohol dependence and regular tobacco use increased 1.5 times, and the odds of cannabis dependence increased twice, with each additional psychotic symptom reported, after adjusting for other substance use disorders, other mental disorders and demographic characteristics.

Given the debate about the reasons for the association between cannabis use and psychosis, the final study used mathematical modelling to test four hypotheses about relationships between cannabis use and psychosis. Specifically, it examined trends in psychosis that would be predicted given the marked increases in the prevalence of cannabis use that have occurred in Australia over the past thirty years. The results suggested that a causal relationship - in which cannabis use caused psychosis among persons who would not otherwise have developed the disorder - is unlikely to explain the association. There was a better fit to the data provided by the other hypotheses examined, namely, that (a) cannabis use precipitates psychosis among vulnerable individuals; (b) cannabis use increases the risk of relapse among persons with psychosis; and (c) persons with psychosis are more likely to become regular cannabis users (without any effect upon the disorder).
This thesis has demonstrated that in Australian adults there is significant comorbidity between alcohol, tobacco and cannabis use and other substance use and mental disorders. These patterns differ across the three substances. Some types of heterotypic comorbidity (e.g. between cannabis use and mood/anxiety disorders) are explained by common factors. The limited range of common factors tested here did not explain homotypic comorbidity. This thesis also suggested that mathematical modelling is a useful approach to consider when examining the plausibility of different relationships between risk factors and mental disorders.

A number of hypotheses regarding comorbidity could not be tested using NSMHWB data, such as common genetic and other environmental factors. These can best be tested in research with samples of twins, and using longitudinal designs that assess a wide range of social and environmental factors. The findings of this thesis also have implications for treatment, because persons with comorbid disorders are more likely to seek treatment. There is an absence of validated treatments for persons with comorbid substance use and mental disorders, and more research is needed on this issue.
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LIST OF ABBREVIATIONS

Δ9-THC  delta-9-tetrahydrocannabinol
95%CI  95% confidence interval
ABS  Australian Bureau of Statistics
APA  American Psychiatric Association
ASI  Addiction Severity Index
BDI  Beck Depression Inventory
BSI  Brief Symptom Inventory
CBT  cognitive behavioural therapy
CIDI  Composite International Diagnostic Interview
DALY  Disability Adjusted Life Years
DIS  Diagnostic Interview Schedule
DSM  APA Diagnostic and Statistical Manual of Mental Disorders
ECA  US Epidemiological Catchment Area study
GABA  gamma-aminobutyric acid
GAD  Generalised Anxiety Disorder
HMO  a US Health Maintenance Organisation
ICD  WHO International Classification of Diseases
LEAD  Longitudinal, Expert, All Data diagnoses
LPS  Australian Low Prevalence Study
NCS  US National Comorbidity Survey
NDHS  Australian National Drug Strategy Household Survey
NHSDA  US National Household Survey on Drug Abuse
NIMH  US National Institute of Mental Health
NLAES  US National Longitudinal Alcohol Epidemiologic Survey
NRT  nicotine replacement therapy
NSMHWB  Australian National Survey of Mental Health and Well-Being
OCD  Obsessive-Compulsive Disorder
OR  odds ratio
PS  Psychosis Screener used in the NSMHWB
PSE  Psychiatric State Examination
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>PTSD</td>
<td>Post-Traumatic Stress Disorder</td>
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<tr>
<td>SADS</td>
<td>Schedule for Affective Disorders and Schizophrenia</td>
</tr>
<tr>
<td>SDS</td>
<td>Severity of Dependence Scale</td>
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<tr>
<td>SES</td>
<td>socioeconomic status</td>
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<tr>
<td>SSRI</td>
<td>serotonin-selective reuptake inhibitor</td>
</tr>
<tr>
<td>VTA</td>
<td>ventral tegmental area</td>
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<td>WHO</td>
<td>World Health Organization</td>
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1 **INTRODUCTION**

Comorbidity can be defined as the co-occurrence of two or more mental health problems. It has emerged as a major clinical, public health and research issue over the past few decades, due in part to changes in psychiatric nomenclature, in which there is a greater focus upon elucidating any number of mental health problems with which an individual might present, rather than diagnosing one problem to the exclusion of others.

Currently, mental health problems are conceptualised as patterns of behaviour or thought that are associated with: significant disability, distress, loss of individual freedom, or adverse events such as death; and which arise from dysfunction within the individual (Neugebauer, 1999). These problems can encompass a wide range of behaviours including substance use, mood disturbances, anxiety, and disturbances in thought and perception.

According to current classification systems in psychology and psychiatry, mental disorders are diagnosed according to operationalised diagnostic criteria, and the diagnosis of one disorder does not necessarily preclude the diagnosis of another (American Psychiatric Association, 1994; World Health Organization, 1993). In some cases, more than one mental disorder is diagnosed – such comorbidity is examined in this thesis.

This thesis examines the patterns of comorbidity of the most prevalent forms of substance use in the general population: alcohol, tobacco and cannabis. It examines comorbidity with other substance use disorders; comorbidity with the two most common forms of mental disorders, mood and anxiety disorders; and comorbidity with the most disabling mental disorders, namely psychoses.

Comorbidity is an important issue on many levels. It is acknowledged, but rarely addressed. It has implications for the aetiology of mental disorders, and hence efforts directed towards prevention; and it has implications for both treatment and prognosis. The traditional separation of mental health and substance use treatment services has also hindered efforts to deal with comorbidity between substance use and mental disorders.
1.1 Chapter Aims

This Chapter provides a summary of the history of psychiatric nomenclature and epidemiological research into mental health over the past century. It also examines how researchers have estimated the prevalence of psychiatric problems in the community over this time, and presents some of the resulting issues. This context gives a background to the population-level data on mental disorders that feature prominently in the examination of comorbidity in this thesis, the 1997 Australian National Survey of Mental Health and Well-Being.

The aims of this Chapter are to:

1. Give an overview of the development of psychiatric nomenclature over the past century, to help understand why comorbidity is an issue;
2. Give an overview of psychiatric epidemiology, its importance to the field of mental health, and the development of research in this field over the past century, to highlight the development and current state of research into mental health;
3. Briefly define the concept of comorbidity;
4. Outline the issues surrounding research into comorbidity and the importance of using general population samples to examine comorbidity;
5. Give a brief introduction to the Australian National Survey of Mental Health and Well-Being (NSMHWB);
1.2 The History of Psychiatric Nomenclature

How should we classify mental health problems? This question is difficult to answer and has been an important one in the history of psychiatric nomenclature. Typically, classification of physical diseases is based upon aetiology (Kendell, 1993). Such a practice has been more difficult for the classification of mental health, primarily because relatively little has been known about the (physical or other) causes of these problems. As a result, there has been a dramatic change in the way that mental health has been classified, as theorists attempt to produce a system that is (a) consistent with evidence about these disorders; and (b) contends with a great deal of dissatisfaction about the way in which disorders are currently conceptualised and grouped.

Several major stages may be observed in the development of psychiatric nomenclature over the past century (Kendell, 1993; Shorter, 1997). One of the most important theorists of psychiatric classification at the end of the 19th century and early decades of the 20th century was Emil Kraepelin (Shorter, 1997). Kraepelin’s system of classifying mental disorders was revolutionary in that he moved from classifying disorders on the basis of their symptoms and aetiology, to concentrating upon their course and outcome (Schneck, 1960; Shorter, 1997). Kraepelin felt that given the limited knowledge of the aetiology and mechanisms of mental disorders, it was fruitless to attempt to classify mental disorders on an aetiological basis.

Kraepelin’s classification system aimed to provide meaningful classifications of diseases for both clinicians and for patients and their families (Shorter, 1997). In the sixth edition of his textbook on psychiatric illness (in 1899), Kraepelin grouped disorders into 13 classes in a hierarchical pyramid, which posited categorical and mutually exclusive disease entities. Kraepelin’s model was a medical one, in that psychiatric illness was approached in the same manner as a physical disease, in contrast to other “biopsychosocial” approaches of the time (Shorter, 1997). Two of the most important groupings of Kraepelin’s system were his division of psychotic illnesses into those with and without an affective (mood) component: “dementia praecox” (later called schizophrenia by Bleuler) and “manic-depressive illness”.

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3
Kraeplin felt that the disorders in these two groups were the outcome of a unique disease process. The fact that this was the case could be validated by the difference in prognosis: those with manic-depressive illness were likely to improve, while those with dementia praecox probably would not.

One of the other major figures in psychiatric nomenclature of the early decades of the 20th century was Adolf Meyer. Meyer was arguably one of the most influential psychiatrists in the US during the early 20th century (Alexander & Selesnick, 1966; Schneck, 1960; Shorter, 1997). Meyer initially used Kraeplin’s hierarchical system, in particular the concepts of dementia praecox and manic-depression, but later rejected them and embraced what he called a “common sense” approach to classifying mental illness (Schneck, 1960), by moving from an approach based on the course and outcome of a disorder to one based upon the background and characteristics of the person who was experiencing it. He placed more emphasis on a patient’s biological, historical, social and psychological history than on a patient’s “constitutional forces” (Shorter, 1997). By the 1940s, Meyer advocated psychotherapy for schizophrenia and argued that it was a psychogenic disorder that was the product of maladjustment and poor adaptation (Schneck, 1960). He argued that mental illness was the result of “faulty reaction patterns”, and advocated a holistic approach to diagnosis. Some have argued, however, that there was no sound basis upon which to understand the individual patient in Meyer’s system (Alexander & Selesnick, 1966).

Meyer was instrumental in developing the first version of one of the world’s predominant classification system of mental health in psychology and psychiatry, the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders, or DSM-I (with subsequent versions called DSM-II, DSM-III, DSM-III-R, and DSM-IV) (American Psychiatric Association, 1952; 1968; 1980; 1987; 1994). DSM-I reflected dominant Meyerian concepts of mental health at the time (Kendell, 1993); it had little influence, since in the 1950s and 1960s, many held diagnostic categories in general in low regard, due in large part to a great lack of diagnostic reliability and validity (Kendell, 1989). There was also little consistent meaning attached to the same diagnosis in different parts of the world, as evidenced by comparative studies of diagnoses in the UK and the US that revealed tremendous differences in the diagnoses arrived at by psychiatrists in the two countries (Cooper et al. (1972); World Health Organization (1973); cited in Kendell (1993)).
Other theorists took a different approach to mental health, avoiding diagnostic categories altogether. Sigmund Freud developed a theory in which mental health problems were at the extremes of a dimensional distribution along which each person could vary: these dimensions largely included such concepts as “hysteria” and “neurosis” (Alexander & Selesnick, 1966; Schneck, 1960; Shorter, 1997). Theorists such as Carl Rogers argued against any use of diagnostic categories. These theoretical models were based largely upon observations of clients in institutions and both outpatient and inpatient settings.

During the 1960s, the contrast of dimensional versus categorical models of psychiatric disorder continued. Two British schools of thought debated over whether anxiety, “neurotic depression”, and severe psychotic depression were best conceptualised as a continuum (the Maudsley school, led by Aubrey Lewis), or as distinct clinical syndromes (the Newcastle school, led by Martin Roth) (Akiskal, 1995). Hans Eysenck developed validated measures of his dimensional model of neurosis (Kendell, 1993). Other researchers such as David Goldberg in the UK developed symptom measures of “psychological distress”, which were designed for use in general health care settings (Goldberg, 1972).

One of the most significant developments in psychiatric nomenclature in the past hundred years was the development of DSM-III, which was published in 1980 (American Psychiatric Association, 1980). DSM-III was developed in response to increasing evidence that psychiatric diagnoses (such as those in DSM-II) were unreliable and had little validity, particularly since they meant different things in different countries of the world (Kendell, 1993). DSM-III was the product of extensive debate, discussion and consultation. Field studies were conducted to establish diagnoses’ reliability; and it contained operationalised criteria for nearly all diagnoses, with the aim of ensuring that it would clarify who did and did not meet diagnostic criteria (American Psychiatric Association, 1980).

DSM-III was also a multiaxial classification system in which five different areas were recorded: clinical syndrome (Axis I), lifelong disorders or handicaps (Axis II), physical conditions (Axis III), psychosocial stressors (Axis IV), and social and occupational functioning (Axis V). DSM-III marked a move from less well-defined concepts, which often implied some sort of aetiology and had abounded in psychiatry (such as “hysteria” and “neurosis”), to terms that relied upon more objective symptomatology. A revised
diagnostic criteria for many disorders, the removal of some contentious disorders, and the
addition of other disorders.

The DSM-III system differs from Kraeplin’s exclusive approach to psychiatric diagnosis,
but it and subsequent editions (DSM-III-R and DSM-IV) have nevertheless been called
“neo-Kraeplinian” (Klerman, 1990; Wittchen, 1996), since they encompass some key
characteristics of Kraeplin’s approach, namely, structured and delimited diagnostic
categories, and a multilevel approach to profiling the patient (diagnostic Axes I – V).

In 1987, an APA task force began the process of reviewing literature and harmonising
classifications with the World Health Organization’s International Classification of
Diseases (ICD-10) system (World Health Organization, 1993). It consulted widely, and
reviewed each individual section of DSM-III-R. These revisions were published as DSM-
IV and remain the current classification system of the APA (American Psychiatric
Association, 1994). Because the process involved a considerable emphasis upon data
analysis, observation, and many field trials of the diagnostic criteria (e.g. Grant, 1996; Price,
Helzer, Cottler, & Robins, 1991; Woody, Cottler, & Cacciola, 1993) DSM-IV is perhaps the
most comprehensive and validated attempt to classify and operationalise current
conceptualisations of mental health. It still relies upon symptoms in its classifications of
mental disorders. Future research will doubtless improve such classification systems’ ability
to diagnose mental disorders on the basis of aetiology rather than symptomatology.

In the meantime, DSM-IV is perhaps the most widely used and well validated diagnostic
system for classifying mental health problems. Research continues to evaluate its validity
(e.g. Akiskal et al., 2000; Andrews, Slade, & Peters, 1999; Grant, 1996; Hasin, Paykin,
Meydan, & Grant, 2000; Hasin, Van Rossem, McCloud, & Endicott, 1997; Horton,
Compton, & Cottler, 2000; Kendler & Gardner, 1998; Langenbucher et al., 1997; Muthen,
1996; Schuckit et al., 1999; Topp & Darke, 1997; Winters, Latimer, & Stinchfield, 1999).
The present thesis examines DSM-IV substance use disorders (abuse and dependence),
mood disorders, anxiety disorders and psychotic disorders. Appendix A presents the DSM-
IV diagnostic criteria used to classify these disorders.
1.3 **Psychiatric Epidemiology**

Epidemiology has been defined as “the study of the occurrence (incidence and prevalence), distribution, and determinants of states of health in the general population” (p.13) (Dohrenwend, 1994). It is concerned with mapping the distribution of disease in the community and investigating associations between disease and its causative agents (Kessler, 2000). Psychiatric epidemiology is concerned with mapping the distribution of mental health indices as set out in classification systems of mental disorders. Such diagnostic systems are of obvious interest to the field of psychology, particularly clinical psychology, which is concerned with the sorts of behaviour set out in these systems. One question to ask, however, is why should psychologists be concerned with epidemiological approaches to these issues?

1.3.1 **The Importance of Psychiatric Epidemiology**

Psychiatric epidemiology is important to psychologists and other mental health professionals for clinical and theoretical reasons. Both will affect psychologists as practitioners and as researchers.

First, it is important to estimate the prevalence of mental disorders in a population because only a small proportion of those who have significant mental health problems will present for treatment (Link & Dohrenwend, 1980a; Robins & Regier, 1991). This is the case even for the more disabling disorders such as schizophrenia (Link & Dohrenwend, 1980a; Robins & Regier, 1991). Without assessing mental disorders in the general community, we cannot begin to know how common they really are, since relying on data sources such as hospital registers or treatment service records produce estimates that are far lower than the true prevalence. Additionally, not all persons who do present will be recognised and referred for specialist psychological treatment.
Second, different disorders differ in the likelihood that the sufferer will present their problems for treatment, so the most common disorders in treatment settings differ from the most common disorders in the general community. For example, research has shown that only a small proportion of persons with substance use disorders present for treatment for their substance use problems; persons with depression or anxiety disorders, in contrast, are more likely to seek help (Robins & Regier, 1991). If estimates of prevalence were taken purely from treatment settings, then estimates of substance use disorders would be considerably lower than those of mood and anxiety disorders, which would not accurately reflect their frequency in the general population (Kessler et al., 1994; Robins & Regier, 1991).

Third, treatment rates differ among different community groups (Dohrenwend, 1994). Hence, it is important to ask whether the characteristics of persons with mental health problems in treatment settings are representative of all those persons with mental health problems. It is likely that they are not: research has shown that treatment seeking for mental health problems differs according to particular characteristics, such as socio-economic status (Dohrenwend, 1994) and gender (Kessler et al., 1997d). Only by obtaining a representative sample of the whole population is it possible to understand the extent to which treatment is received among different groups in the community. All of these factors are critically important when considering how many people may need treatment for mental health problems; who is not currently receiving treatment; and what mental health problems these treatments might need to address.

As noted in the overview of the history of psychiatric nomenclature, early systems were based on observations of persons in very specific settings, notably inpatient settings. Given that treatment seeking differs across groups (Dohrenwend, 1994), it is possible that classification systems may be affected if only certain subsections of the community are studied and theories based solely on these unrepresentative populations. As will be outlined below, much of early 20th century research on “psychiatric epidemiology”, which provided the foundations for the classification of mental health by theorists of the time, was carried out with specific subpopulations. However, over the past century, changes in psychiatric epidemiological research have seen more emphasis upon studies of representative samples of the general population, with instruments that provide reliable and valid information.
1.3.2 THE HISTORY OF PSYCHIATRIC EPIDEMIOLOGY

Reviewers of the development of psychiatric epidemiology have discussed three "generations" of research on the population prevalence of mental disorders (Dohrenwend, 1994; Dohrenwend & Dohrenwend, 1965; Dohrenwend & Dohrenwend, 1982; Mezzich, 1994). These will be briefly outlined below.

1.3.2.1 "FIRST GENERATION" STUDIES

First generation studies were carried out in the early decades of the 20th century, until the beginning of World War II (Dohrenwend, 1995). It has been estimated that 16 studies were carried out in this time, which usually involved agency records and key informants. By relying on such information, prevalence estimates probably grossly underestimated the actual prevalence of disorders as they were then characterised (Dohrenwend, 1995). Median estimates of the prevalence of disorders were around 3.6% in studies that employed direct interviews. The validity of these findings is doubtful since inconsistent nomenclature was used, and there was little evaluation of instruments' ability to accurately classify known types of disorder (Dohrenwend, 1995).

1.3.2.2 "SECOND GENERATION" STUDIES

Second generation studies, conducted after World War II, were partly prompted by the work of psychologists during the war, in which there were considerable efforts made to develop assessment techniques for psychiatric screening of recruits in the armed forces (Regier & Kaelber, 1995). Estimates have been made that around 60 studies were carried out between 1945 and 1980, usually involving direct interviews with participants (Dohrenwend, 1995). Two different types of interviews were used. European and Asian research tended to be carried out by a psychiatrist or team of psychiatrists, with diagnoses made without a standardised interview. The second (US) approach was much more standardised and explicit. Interviews were conducted by either lay interviewers or professionals, but all cases were identified according to psychiatrists' evaluations of the
interview protocols. Examples of these studies were the Stirling County study and the Midtown study (Leighton, Harding, Macklin, Macmillan, & Leighton, 1963; Srole, Langner, Michael, Opler, & Rennie, 1962; cited in Dohrenwend, 1995). These studies classified persons according to psychiatric “caseness” or “impairment” rather than diagnostic types.

These decisions reflected the dissatisfaction that many clinicians felt with the then current classification system of DSM (as noted above). The validity of these studies was also limited since there was a lack of consensus about which symptoms should be assessed; what classification should be used; and in some cases there was little attempt to validate the scales used for assessment (Dohrenwend, 1995). In the case of brief screening scales, there was research supporting their reliability and internal consistency (Link & Dohrenwend, 1980b). However, it is less clear what construct they were measuring, since research has shown that these scales all correlate well with measures of “hopelessness”, “confused thinking” and “sadness” (Link & Dohrenwend, 1980b), and they did not discriminate between persons who did and did not have “diagnosable” mental disorders (Dohrenwend, 1995; Link & Dohrenwend, 1980b).

1.3.2.3 “THIRD GENERATION” STUDIES

In the late 1970s, US reviews of the state of research on mental health concluded that there was a great need to develop accurate, scientific estimates of: (a) the prevalence of mental disorders; and (b) the use of health services by persons with mental disorders (President’s Commission on Mental Health, 1978; Regier, 1992; Regier & Kaelber, 1995). To do so required an instrument that used reliable, valid, and operationalised diagnostic criteria to estimate the prevalence of mental disorders.

Anticipating this need, researchers at Washington University in the US, including Eli Robins (Feighner et al., 1972; Robins & Guze, 1970; Woodruff, Goodwin, & Guze, 1974), had developed operationalised criteria for 15 psychiatric usable by lay interviewers (Feighner et al., 1972). Subsequent research efforts developed operationalised instruments for epidemiological research on psychiatric disorders, such as the semi-structured Psychiatric State Examination (PSE) at Maudsley hospital in London (Wing, Cooper, &
Sartorius, 1974) and the Schedule for Affective Disorders and Schizophrenia (SADS) at
Yale University in the US (Endicott & Spitzer, 1978).

One result of the 1978 US President’s Commission on Mental Health was the decision to
conduct epidemiological research to estimate the prevalence of mental disorders in the
general community and the extent of health service use among persons with such disorders
(President’s Commission on Mental Health, 1978; Regier & Kaelber, 1995). This project
combined the best available scientific and research expertise to produce the assessment
measures, deal with sampling issues and undertake data analysis and collection (Regier &
Kaelber, 1995). The project was undertaken by the US National Institute of Mental Health
(NIMH), and the resulting study was the Epidemiological Catchment Area study (ECA).

The US Epidemiological Catchment Area study
The ECA aimed to provide estimates of the prevalence and incidence of the following
major DSM-III disorders: mood disorders, substance use disorders, anxiety disorders, and
psychotic disorders.

Researchers involved in the ECA decided to develop a diagnostic interview that
incorporated the newly defined DSM-III diagnostic criteria, since no such DSM-III-based
interview existed at that point (Regier & Kaelber, 1995). The resulting interview, based on
the Renard Diagnostic Interview (Helzer, Robins, Croughan, & Welner, 1981), was the
NIMH Diagnostic Interview Schedule (DIS) (Robins, Helzer, Croughan, & Ratcliff, 1981a;
Robins, Helzer, Croughan, Williams, & Spitzer, 1981b). This interview was highly
structured, designed to be administered by trained lay interviewers, and would identify
persons who met operationalised criteria for specific DSM-III mental disorders (Regier &
Kaelber, 1995). It was validated against existing diagnostic interviews, clinicians’ diagnoses,
and physicians’ diagnoses (Folstein et al., 1985; Helzer et al., 1985; Orvaschel et al., 1985).

In the ECA study, samples were taken from five “catchment area” sites with a total
population of at least 200,000 persons. They were chosen by the NIMH from applications
from the following institutions: Yale University, Johns Hopkins University, Washington
University, Duke University, and the University of California in Los Angeles, which
surveyed New Haven, Baltimore, St. Louis, Durham, and Los Angeles, respectively (Robins & Regier, 1991). Both community and institutional facilities (such as prisons, nursing homes, and psychiatric facilities) were sampled.

The ECA’s response rate was 76%, with an overall sample size of 19,640 (Robins & Regier, 1991). Sample sizes of approximately 3,000 household residents and 500 institutional residents per site had been targeted to ensure that risk factors for schizophrenia (which affects around 1% of the population) could be studied (Regier & Kaelber, 1995; Robins & Regier, 1991). The research groups were required by the NIMH to obtain representative samples of the population in the five sites (Holzer et al., 1985). The estimates obtained were weighted to project estimates for the entire United States (Robins & Regier, 1991). Lay interviewers, all trained at Washington University to ensure comparability of interview administration, conducted the interviews (Regier & Robins, 1991). Each site conducted its own survey and data collection.

The ECA has been called a “landmark study in psychiatric epidemiology” (p.81) (Kessler, 1994a) in that: (a) it was the largest general population survey of mental disorders carried out to that date; (b) it was the first to administer a structured diagnostic interview; and (c) it was the first to estimate total population prevalence estimates, since institutionalised and non-institutionalised samples were obtained (Kessler, 1994a).

The ECA stimulated a number of epidemiological surveys in other countries, which used similar sampling methods, the same DSM-III diagnostic criteria, and the same survey instrument (the DIS). Studies were carried out in Munich, Germany (Fichter et al., 1996; Wittchen, Essau, von Zerssen, Krieg, & Zaudig, 1992); Edmonton, Canada (Bland, Newman, & Orn, 1988); Christchurch, New Zealand (Oakley-Browne, Joyce, Wells, Bushnell, & Hornblow, 1989; Wells, Bushnell, Hornblow, Joyce, & Oakley-Browne, 1989); Shanghai, China (Wang et al., 1992); Korea (Lee, 1992); and Taiwan (Hwu, Yeh, & Chang, 1989).
The US National Comorbidity Study

The design of the ECA was improved upon by researchers who designed and conducted the US National Comorbidity Survey (NCS) in 1992 (Kessler, 1994a; Kessler, 1994b). The NCS extended the ECA in the following ways:

a. The NCS used DSM-III-R diagnostic criteria, with some allowance for comparisons with DSM-IV when it was released, in contrast to the DSM-III criteria used in the ECA;

b. The NCS was designed not only as a study of the prevalence of mental disorders, but also as a study of the risk factors for such disorders;

c. It was a nationally representative sample of US adults, as opposed to the five catchment areas that were used in the ECA; and

d. As the title suggests, one of the NCS’ primary aims was to explore the patterns of comorbidity between different mental disorders that had been observed in the ECA.

The NCS was designed to explore the prevalence, causes and consequences of comorbidity. The age range (18 to 54 years) used in the study was chosen because comorbidity was found to be most prevalent among this age group in the ECA (Kessler, 1994a; Kessler, 1994b). The NCS was a national survey: participants were selected from the non-institutionalised civil population in the 48 contiguous US States, with an additional sample of students from university campus housing. Institutional samples were not selected since the inclusion of such samples in the ECA had not been found to make a substantial difference to prevalence rates of mental disorders (Robins & Regier, 1991). Experienced field interviewers were used in the data collection to ensure that interviews were conducted by competent staff. A special feature of the NCS was that non-responders to initial interviews were re-targeted for interview to ensure that prevalence estimates were not affected by non-response rates. This was because research had suggested that those who refused to participate in surveys had higher rates of mental disorders (Kessler, 1994a).

The NCS had a response rate of 83%, with a final sample size of 8,098. The psychiatric diagnoses assessed were DSM-III-R diagnoses of anxiety disorders, mood disorders, substance use disorders and psychotic disorders. The diagnostic interview was the
Composite International Diagnostic Interview (CIDI), which was designed for administration by trained interviewers who are not clinicians (Kessler et al., 1994). It was administered by staff at the Survey Research Centre at the University of Michigan between September 1990 and February 1992 (Kessler et al., 1994).

Other epidemiological studies

Since the conduct of the ECA and NCS, a number of epidemiological studies have been carried out using DSM-III-R or DSM-IV criteria with representative samples of persons from countries such as the US (Grant & Pickering, 1998), Canada (Ross, 1995), and the Netherlands (Bijl, Ravelli, & van Zessen, 1998).

The UK conducted the National Psychiatric Morbidity Survey (Jenkins et al., 1997a; Jenkins et al., 1997b), using an adapted DIS interview for assessing ICD-10 substance dependence. Unfortunately, it did not assess mental health using a standardised instrument designed to provide diagnoses of mental disorders, instead using symptom and screening measures (Farrell et al., 1998).

These studies were consistent in that they found mental disorders to be common in the adult population, and to be associated with disability and social disadvantage. Chapters Two and Three will outline some of the major findings of these epidemiological studies.

Specifically, Chapter Two will outline the findings on the prevalence of substance use disorders, which are among the most commonly occurring mental disorders in the general population (Kessler et al., 1994; Robins & Regier, 1991). Chapter Three will discuss three other groups of disorders. Two of these are the other most commonly occurring groups of mental disorders: anxiety disorders (such as phobias and panic); and mood disorders (such as major depression and bipolar disorder). The third, psychotic disorders (such as schizophrenia), occur less frequently, but have been associated with greater disability and social disadvantage, and a more chronic course than many of the other mental disorders.
The state of Australian research

There has been no previous examination of the prevalence of DSM or ICD classified mental disorders in the Australian general population using a structured diagnostic interview; it is not necessarily appropriate to assume that the patterns in one country are the same in another. Some prevalence studies that have been carried out used symptom inventories rather than structured diagnostic interviews involving standardised diagnostic criteria, and they were also limited to cities or communities such as Canberra (Henderson, Duncan-Jones, Byrne, Scott, & Adcock, 1979), Prahran (Krupinski & Stoller, 1971), Botany Bay (Andrews, Schonell, & Tennant, 1977), and Heyfield (Krupinski et al., 1967).

To address this issue, researchers planned and conducted the Australian National Survey of Mental Health and Well-Being (NSMHWB) in 1997. It involved a modified version of the CIDI (which is a more recent version of the DIS) and used DSM-IV criteria. It therefore provides the first nationally representative data on the mental health of Australian adults, using operationalised diagnostic criteria that provide estimates of the prevalence of mental disorders in the general population. The NSMHWB is discussed more fully in Chapter Five, and NSMHWB data are used in this thesis to examine the comorbidity of substance use and substance use disorders with other mental health problems.
1.4 COMORBIDITY

The issue of comorbidity between substance use disorders and other mental disorders has gained increasing prominence in psychiatry and psychology within the past few decades (Wittchen, 1996). This has accompanied a move away from less well-defined concepts of psychopathology to classification systems of increasing specificity (such as the changes occurring in successive DSM classification systems). It has also accompanied an increasing awareness of problems with strictly hierarchical diagnostic systems such as those originally developed by Kraepelin, in which diagnosis of one disorder precluded the diagnosis of others (Boyd et al., 1984; Klerman, 1990).

As noted in the beginning of this Chapter, comorbidity refers to the co-occurrence of two or more mental disorders. In classification systems such as DSM-IV, diagnosing one mental disorder does not necessarily preclude the diagnosis of another, so a co-occurrence of mental disorders may result.

1.4.1 WHY STUDY COMORBIDITY?

The study of comorbidity has been called “the premier challenge of the 1990s” (p.833) (Kendall & Clarkin, 1992). Comorbidity potentially has implications for many areas, particularly with respect to theories of aetiology, prevention and treatment of mental health problems. These implications are more fully discussed in Chapter Four.

1.4.1.1 IMPORTANCE FOR THEORY

One reason to examine comorbidity is a theoretical one. If mental health problems are more likely to occur among those with substance use disorders, this raises important questions about the aetiology of mental disorders (and vice versa). Several hypotheses exist concerning the reasons why comorbidity might occur, including that: (a) there is a
causal relationship between the two; (b) that common factors increase the likelihood of both disorders; and (c) that the relationship is spurious (artefactual), resulting from factors such as the methods with which the sample was selected (Caron & Rutter, 1991; Kessler, 1995; Mueser, Drake, & Wallach, 1998). Before we can begin to unravel the reasons behind any “comorbidity”, we need to carefully document the nature of any associations. This will give some insight into possible mechanisms underlying the association.

1.4.1.2 IMPORTANCE FOR TREATMENT

A second reason to study comorbidity is a clinical one. If people who are problematic substance users are more likely to have other mental health problems, this needs to be taken into account both in the assessment of a client, and in determining the most appropriate treatment.

Comorbidity is particularly relevant if co-occurring disorders predict a differential clinical outcome, which has been suggested by previous research (e.g. Carey, Carey, & Meisler, 1991; Haywood et al., 1995; Pristach & Smith, 1990; Rouillon, 1996). Attention to comorbid problems may also improve treatment outcome. This has been suggested in tobacco smoking cessation treatment among persons who are also depressed, which has simultaneously targeted depression (Hall et al., 1998).

1.4.2 WHY STUDY COMORBIDITY BETWEEN SUBSTANCE USE AND MENTAL HEALTH?

Previous epidemiological research in other countries has found that substance use problems are common in the community, as are mental health problems such as mood disorders and anxiety disorders (Kessler et al., 1994; Robins & Regier, 1991). Substance use disorders and mental disorders have each been found to cause significant burden (due to premature mortality and disability) (Murray & Lopez, 1997). In established market economies, five out of fifteen of the top causes of disability are mental health problems: unipolar depression, alcohol use, schizophrenia, self-inflicted injuries, and bipolar disorder (Neugebauer, 1999). If substance use disorders co-occur with other disorders, these major causes of burden are likely to negatively impact upon the sufferer and the community.
1.5 The Importance of Epidemiological Research on Comorbidity

It is critically important to study patterns of comorbidity between different mental disorders in general population samples. It is not possible to know that patterns observed in clinical samples will reflect those in the general community, because significant biases may be present (see Chapter Four). There is a variety of reasons why comorbidity might be more common in clinical samples. It is also likely that skewed patterns of comorbidity will exist because of factors such as areas of particular interest or expertise of clinicians in a given treatment centre, or alternatively, exclusionary policies of a treatment centre, or factors that may differentially influence a person’s decision to seek help.

These factors are impediments to making accurate decisions about treatment needs of the general population from clinical samples. It is also difficult to make advances in theories about comorbidity since we do not know whether comorbidity observed in clinical samples is due to sampling or referral biases. Only by studying representative samples of the general population can we ensure that our findings reflect general patterns of co-occurrence of different mental health problems in the community.

With this in mind, I turn now to consider the Australian NSMHWB. The nationally representative NSMHWB sample involved the assessment of DSM-IV substance use disorders, mood disorders, anxiety disorders, and it also screened for likely cases of psychosis. It therefore represents an excellent opportunity to examine patterns of comorbidity in the Australian adult population and to address theoretical and clinical issues concerning comorbidity between substance use and mental disorders.
1.6 OVERVIEW OF THE THESIS

This thesis examines population-level comorbidity between the level of involvement with substance use and mental health problems. The substances examined in this thesis include the most commonly used psychoactive substances in the general Australian population – alcohol, tobacco and cannabis (Australian Institute of Health and Welfare, 1999; Makkai & McAllister, 1998). As these substances are the most commonly used substances, associations with other mental health problems will have implications for a large number of persons in the community.

Comorbidity of two types will be examined in this thesis: comorbidity with other substance use and substance abuse/dependence; and comorbidity with mood disorders, anxiety disorders, and psychosis. The other substances examined included stimulants (including amphetamines and cocaine), opioids (including heroin) and sedatives (including tranquilisers) (Australian Institute of Health and Welfare, 1999; Makkai & McAllister, 1998). While opioid use is less frequent than sedative and stimulant use, problematic opioid use has a considerable negative impact upon the user and their family, as well as upon the community, to a much greater degree than is suggested by its small prevalence of use (Hall, Lynskey, & Degenhardt, 1999a; Mathers, Vos, & Stevenson, 1999).

The mental disorders examined in this thesis were chosen based upon two factors: first, their prevalence in previous epidemiological research; and second, the degree to which they adversely affect individual sufferers, their families, and the community. This led to the following three major groups being chosen: mood disorders, anxiety disorders, and psychotic disorders.

Mood disorders were examined because they are: among the most commonly occurring mental disorders in the community (Kessler et al., 1994; Robins & Regier, 1991); and they rank among the leading causes of disease and disability burden (Murray & Lopez, 1996; Neugebauer, 1999).
Anxiety disorders were selected because they are also among the most commonly occurring disorders (Kessler et al., 1994; Robins & Regier, 1991), and they also rank among the leading causes of disability (Murray & Lopez, 1996; Neugebauer, 1999).

Finally, psychotic disorders were chosen because although they are much less prevalent than anxiety and mood disorders (Jablensky, 1999; Kessler et al., 1994; Robins & Regier, 1991), they still rank among the leading causes of disability in the general population (Neugebauer, 1999). They are associated with significant adverse outcomes for the individual sufferer and their family (Eaton et al., 1992a; Eaton et al., 1992b; Hall et al., 1985; Mason, Harrison, Glazebrook, Medley, & Croudace, 1996b), and significant costs to the community (Hall et al., 1985; Knapp, 1997).

1.6.1 THESIS OUTLINE

This thesis focuses on the comorbidity between substance use disorders and other mental disorders in the general population. It aims: to describe the population patterns of comorbidity between these disorders; to examine some potential explanations for the existence of any comorbidity; and to look at the effect (if any) of comorbid mental health problems on treatment seeking.

Chapter Two outlines the definitions, epidemiology and theories concerning substance use and substance use disorders (including abuse of and dependence upon substances). Chapter Three does the same for mood, anxiety, and psychotic disorders. Chapter Four outlines the concept of comorbidity, research into comorbidity, and theories about why it might occur.

Chapter Five describes the background, design and conduct of NSMHWB. Chapter Six examines comorbidity of alcohol, while Chapter Seven examines tobacco, and Chapter Eight examines cannabis. Chapter Nine directly compares the patterns of comorbidity between alcohol, tobacco and cannabis use with other substance use and mental disorders.

Chapter Ten examines in greater detail the comorbidity between substance use and psychotic symptoms in the Australian population. Finally, Chapter Eleven models a
number of hypothetical relationships between cannabis use and psychosis using empirically derived parameters, and also using the existing literature on trends in the prevalence of both psychosis and cannabis use in the general population.

Chapter Twelve summarises the major findings of this thesis, and draws some conclusions about their implications for theories of substance use disorders and mental disorders; and suggests implications for comprehensive assessment and effective treatment.
2 SUBSTANCE USE AND SUBSTANCE USE DISORDERS

A large body of research has examined the prevalence of substance use and substance related problems in the general population. This research has consistently found that psychoactive substance use is common in most Western countries.

Psychoactive substance use is also related to substantial mortality and morbidity, which poses a major challenge to public health. Tobacco is among the leading causes of premature death in Australia, with 19,019 deaths attributed to tobacco use in 1998, and alcohol use estimated to have caused 3,271 deaths (Ridolfo & Stevenson, 2001). Illicit drugs were estimated to account for 1,023 deaths in 1998, most of which were due to opioid overdose. Estimates from the World Health Organization (WHO) revealed that in established market economies, the risk factors of alcohol use, tobacco use and illicit drug use accounted for 10.3%, 11.7% and 2.3%, respectively, of disability-adjusted life years (DALYs) in 1990 (Murray & Lopez, 1997).

Research on the prevalence and correlates of problematic substance use has been greatly assisted by the development of operationally defined diagnostic classification systems, as outlined in Chapter One. In particular, the continuing development and adoption of DSM classification systems in research has led to increasingly comparable research on the prevalence of these disorders in a number of countries.
2.1 CHAPTER AIMS

The aims of this Chapter are to:

1. Summarise research on the prevalence and correlates of substance use with an emphasis upon Australian research;
2. Give an overview of DSM-IV classifications of substance abuse and dependence;
3. Summarise research on the epidemiology of substance use disorders (abuse and dependence). As noted in Chapter One, a number of large-scale epidemiological surveys have been carried out around the world that have assessed substance use disorders and other mental disorders. The findings of these studies will be summarised with respect to the prevalence and correlates of substance use disorders;
4. Present a brief overview and description of the major theories that have been proposed to explain the development of substance use and substance use disorders. These theories fall into three broad categories: biological, psychological, and socio-cultural.

In short, the aims of this Chapter are to provide an overview of existing research into assessment, epidemiology and theoretical explanations of substance use and substance use disorders.
2.2 **SUBSTANCE USE**

In Australia, surveys of representative samples of the general population have been carried out since 1985 to assess the prevalence of the use of a range of psychoactive substances in the general population (Australian Institute of Health and Welfare, 1999; Makkai & McAllister, 1998). Alcohol has consistently been the most commonly used psychoactive substance in the general population, followed by tobacco, with cannabis the most commonly used illicit drug (Australian Institute of Health and Welfare, 1999; Makkai & McAllister, 1998).

### 2.2.1 PREVALENCE OF SUBSTANCE USE

The 1998 Australian National Drug Strategy Household Survey (NDSHS) estimated that around 9 in 10 persons aged 14 years and over had used alcohol at some point in their lives, with 83% having done so in the past year (Australian Institute of Health and Welfare, 1999). One in four persons aged 14 years and over (26%) reported use of tobacco within the past year, with two thirds (65%) reporting lifetime use (Australian Institute of Health and Welfare, 1999). Slightly more than one third (37%) of persons aged 14 years and over reported having used cannabis at some point in their lives, with 17% reporting usage within the past 12 months. Smaller proportions of Australian adults reported having used amphetamines (4%), cocaine (1%), heroin (0.7%), analgesics (5%) and tranquillisers (3%) within the past year (Australian Institute of Health and Welfare, 1999; Darke, Ross, Hanlon, Hall, & Degenhardt, 2000).

Clearly, in terms of the numbers of people reporting use of psychoactive substances, alcohol, tobacco and cannabis are those that are the most widespread, and therefore, those that potentially have the greatest public health significance.
2.2.2 EPIDEMIOLOGY OF SUBSTANCE USE

In general, males are more likely than females to use most psychoactive substances (Darke et al., 2000; Greenfield & O’Leary, 1999; Johnston, O’Malley, & Bachman, 2000a; Johnston, O’Malley, & Bachman, 2000b; Kandel, 1993). There are indications, however, that this gender difference in rates of use may be diminishing in more recent birth cohorts (Darke et al., 2000). This has been supported by research examining birth cohort trends in substance use, which found that while marked gender differences existed in the prevalence of substance among older birth cohorts, these differences became smaller in more recent birth cohorts (Degenhardt, Lynskey, & Hall, 2000).

Substance use (particularly illicit substance use, but also alcohol and tobacco use) is strongly associated with a person’s age. Young people are by far the most likely age group to report using psychoactive substances within the past year (Bachman, Wadsworth, O’Malley, Johnston, & Schulenberg, 1997; Darke et al., 2000; Makkai & McAllister, 1998). Recent use (for example, use within the past year) typically declines in adulthood, reflecting the adoption of roles such as child-rearing, marriage and employment (Bachman et al., 1997).

Some research has suggested that socio-economic factors may be related to alcohol and tobacco use. Tobacco use has been related to a number of indicators of lower socio-economic status, such as lower levels of education and a greater likelihood of being unemployed (Giovino, Henningfield, Tomar, Escobedo, & Slade, 1995; Kandel, Chen, Warner, Kessler, & Grant, 1997; Warner, Kessler, Hughes, Anthony, & Nelson, 1995; Whitlock et al., 1997). Research has also found that education is negatively related to involvement with alcohol use (Fillmore et al., 1998b). Individuals with heavier alcohol use have also been found to be more likely to be unemployed (Helzer, Burnam, & McEvoy, 1991).

Similarly, illicit substance use has been correlated with a number of sociodemographic factors. Low levels of education are typically found among samples of illicit drug users (Darke et al., 2000), and general population studies have found that lower education levels
are associated with reporting the use of illicit drugs (Australian Institute of Health and Welfare, 1999). Persons who have used illicit drugs such as cannabis, amphetamines, and heroin are more likely to be unemployed (Darke et al., 2000; Kandel, 1993; Kandel et al., 1997; Warner et al., 1995). They are also less likely to be married or in a defacto relationship than those who have not used illicit drugs (Darke et al., 2000; Kandel, 1993; Kandel et al., 1997; Warner et al., 1995).
2.3 Substance Abuse and Dependence

Most people who use psychoactive substances do so without experiencing any problems related to their use, but some do develop problems (Anthony, Warner, & Kessler, 1994). The conceptualisation and measurement of these problems has undergone considerable change over the past three decades, with the emergence of the concept of a substance “dependence syndrome”, influenced by Edwards and colleagues’ work on alcohol dependence (Edwards & Gross, 1976).

2.3.1 Definitions of Substance Abuse and Dependence

In 1977, Edwards and colleagues suggested that alcohol dependence could be thought of as a cluster of symptoms that were distinguishable from alcohol-related problems occurring in heavy drinkers (Edwards, Gross, Keller, Moser, & Room, 1977). Seven factors were regarded as major symptoms of alcohol dependence:

- Narrowing of the behavioural repertoire;
- Salience of drinking (alcohol use given priority over other activities);
- Subjective awareness of a compulsion (experiencing loss of control over alcohol use, or an inability to stop using);
- Increased tolerance (using more alcohol to get the same effects, or finding that the same amount of alcohol has less effect);
- Repeated alcohol withdrawal symptoms (such as fatigue, sweating, diarrhoea, anxiety, trouble sleeping, tremors, stomach ache, headache, hallucinations, fever);
- Relief or avoidance of withdrawal symptoms by further drinking; and
- Reinstatement of dependent drinking after abstinence.

The concept of a dependence syndrome has since been extended to other substances such as cannabis, tobacco, amphetamines, opioids and sedatives. Another category of
Problematic substance use has also been developed: the concept of substance abuse. This was developed in an attempt to classify persons who experienced clinically significant problems associated with their substance use, but who were not using the substance in a dependent manner. The most recent operationalisation of the substance abuse and dependence syndromes is DSM-IV (American Psychiatric Association, 1994), the criteria for which are summarised in Table 2.1. DSM-IV Substance Abuse criteria require a pattern of substance use that causes clinically significant distress or impairment, and indicated by at least one of the abuse criteria in Table 2.1 (American Psychiatric Association, 1994). DSM-IV Substance Dependence criteria require a cluster of three or more indicators (of a possible total of seven – see Table 2.1) that a person continues to use the substance despite significant substance related problems (American Psychiatric Association, 1994). These include: tolerance, withdrawal, indicators of impaired control over use, use despite problems and the reduction of activities not related to substance use.

Table 2.1: DSM-IV criteria for substance abuse and dependence

<table>
<thead>
<tr>
<th>Substance abuse</th>
</tr>
</thead>
<tbody>
<tr>
<td>A recurrent pattern of substance use that is causing clinically significant impairment in functioning as evidenced by at least one of the following:</td>
</tr>
<tr>
<td>• Failure to fulfil role obligations due to substance use;</td>
</tr>
<tr>
<td>• Use in hazardous situations;</td>
</tr>
<tr>
<td>• Legal, social or interpersonal problems resulting from substance use.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Substance dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of a substance continues despite a cluster of three or more of the following indicators of problems related to use:</td>
</tr>
<tr>
<td>• Tolerance to the effects of the substance;</td>
</tr>
<tr>
<td>• A withdrawal syndrome on ceasing or reducing use;</td>
</tr>
<tr>
<td>• Using the substance in larger amounts or for a longer period than intended;</td>
</tr>
<tr>
<td>• A persistent desire/ unsuccessful efforts to reduce/ cease substance use;</td>
</tr>
<tr>
<td>• A disproportionate amount of time spent obtaining, using and recovering from use;</td>
</tr>
<tr>
<td>• Social, recreational or occupational activities reduced/ given up due to substance use;</td>
</tr>
<tr>
<td>• Continued substance use despite knowledge of physical or psychological problems caused by such use.</td>
</tr>
</tbody>
</table>
2.3.2 Prevalence of Substance Abuse and Dependence

There has been less research on the epidemiology of substance use disorders in the general population than there has on substance use. Two of the most influential epidemiological surveys of substance use disorders were the US Epidemiological Catchment Area (ECA) study and the US National Comorbidity Study (NCS) (for details on these studies see Chapter One). These studies found that the most commonly used substances were also the most commonly misused substances (Anthony & Helzer, 1991; Anthony et al., 1994).

The ECA found that the lifetime prevalence of DSM-III alcohol abuse/dependence was 13.8% (Helzer et al., 1991). Approximately 6.8% of persons met criteria for DSM-III alcohol abuse/dependence within the past 12 months (Helzer et al., 1991). Approximately one in 23 persons (4.4%) met criteria for DSM-III cannabis abuse or dependence in their lifetime, 38% of whom experienced problems in the past year (Anthony & Helzer, 1991). This was followed by stimulant abuse/dependence (1.7%), sedative abuse/dependence (1.2%), and opioid abuse/dependence (0.7%) (Anthony & Helzer, 1991). Nicotine abuse and dependence were not assessed in the ECA.

The NCS found that approximately 14.1% of adults met criteria for alcohol dependence at some point in their lives, with another 9.4% meeting criteria for alcohol abuse (Anthony et al., 1994; Kessler et al., 1994). Within the past 12 months, 2.5% of persons met criteria for DSM-III-R alcohol abuse and 4.4% for dependence (Kessler et al., 1997b). Approximately one in four persons (24%) met criteria for nicotine dependence at some point in their lives while 7.5% met criteria for other drug dependence, and 4.4% for other drug abuse (Anthony et al., 1994; Kessler et al., 1994). Cannabis was the most common illicit drug of dependence (4.2% met lifetime dependence criteria), followed by cocaine (2.7%), stimulant (1.7%) and sedative (1.2%) dependence (Anthony et al., 1994). Lifetime dependence upon heroin was reported by 0.7% of the population (Anthony et al., 1994).

The findings of the ECA and NCS have been generally consistent with the patterns found in other studies where standardised instruments have been used to diagnose substance use disorders in general population samples (e.g. Bijl et al., 1998; Farrell et al., 1998; Grant &
Pickering, 1998; Oakley-Browne et al., 1989; Ross, 1995), where alcohol, tobacco and cannabis use disorders have been found to be the most prevalent substance use disorders.

Given these previous findings, and given what we know about the prevalence of substance use in Australia (Australian Institute of Health and Welfare, 1999; Makkai & McAllister, 1998), it seems likely that alcohol, tobacco and cannabis are the substances most commonly used in an abusive or dependent manner in the Australian population.

2.3.3 EPIDEMIOLOGY OF SUBSTANCE ABUSE AND DEPENDENCE

A range of factors have been consistently related to substance use disorders. Males are more likely to meet criteria for alcohol and other substance use disorders (Anthony & Helzer, 1991; Anthony et al., 1994; Grant, 1997; Helzer et al., 1991; Kandel et al., 1997). Substance use disorders also decline significantly with age, with young persons by far the most likely to meet criteria for all substance use disorders (Anthony & Helzer, 1991; Anthony et al., 1994; Grant, 1997; Helzer et al., 1991; Kandel et al., 1997).

As with illicit substance use, illicit substance use disorders have been found to be strongly associated with a number of indicators of social disadvantage. Persons meeting criteria for illicit substance use disorders have a higher likelihood of being unemployed than those who do not meet such criteria (Anthony & Helzer, 1991; Anthony et al., 1994). They are also more likely to have completed fewer years of education than are persons who do not meet criteria for substance use disorders (Anthony & Helzer, 1991; Kessler, Foster, Saunders, & Stang, 1995a). They are also less likely to be married or in a defacto relationship.

Alcohol and tobacco use disorders are also associated with these sociodemographic characteristics (Anthony et al., 1994). Persons with alcohol use problems are more likely than those who do not have such problems to be separated or divorced (Power, Rodgers, & Hope, 1999). Research has found that less educated persons have an increased risk of developing alcohol abuse and dependence (Crum, Bucholz, Helzer, & Anthony, 1992; Crum, Helzer, & Anthony, 1993). Individuals with heavier alcohol use, and those who meet criteria for alcohol use disorders, have been found to be more likely to be unemployed.
(Anthony et al., 1994; Helzer et al., 1991). Similarly, an association has been shown between tobacco dependence and lower education levels and socioeconomic status, and a lower likelihood of being currently employed (Anthony et al., 1994; Whitlock et al., 1997).
2.4 THEORIES OF PROBLEMATIC SUBSTANCE USE

A variety of different approaches have been taken to the question of which factors predispose people to problematic substance use. What follows is a summary of three major areas of explanation. The first is largely biological, and includes theories examining genetic liabilities to problematic substance use, as well as the neurobiological changes that characterise problematic use (and the maintenance of such use). The second approach is psychological, with explanations concentrating upon behavioural models of dependence and individual differences in liability to problematic use. The final approach is a socio-cultural one, with explanations concentrating upon the cultural and environmental factors known to increase the likelihood of problematic substance use.

2.4.1 BIOLOGICAL THEORIES

One area of investigation explores biological characteristics that underlie problematic substance use. These investigations are of two types: those which examine individual differences in propensity to develop problematic substance use due to genetic characteristics, and those which explain problematic substance use as the result of changes produced in the brain by chronic substance administration. Before presenting these two groups of investigations, it is useful to provide an overview of the neurotransmitters of the brain and the actions of psychoactive substances upon the brain.

2.4.1.1 NEUROTRANSMITTERS AND THE BRAIN

The three principle groups of neurotransmitters of the brain are monoamine neurotransmitters, amino acid neurotransmitters, and neuropeptide neurotransmitters (Grebb, 1995). The monamine neurotransmitters include the catecholamines (including dopamine, norepinephrine and epinephrine), serotonin, acetylcholine and histamine (Baraban & Coyle, 1995). Amino acid neurotransmitters include excitatory glutamate (an
excitatory amino acid) and γ-aminobutyric acid, or GABA (an inhibitory amino acid) (Javitt & Zukin, 1995). Neuropeptides are chains of two or more amino acids, and include corticotropin-releasing factor and growth hormone-releasing factor (Bissette & Nemeroff, 1995).

In terms of their importance for substance use and pharmacology, the most important group of neurotransmitters are the monoamines (Grebb, 1995). These neurotransmitters are affected by psychoactive substances, they are implicated in psychiatric disorders, and are the targets for pharmacological treatments of mental disorders.

2.4.1.2 MECHANISMS OF THE ACTIONS OF PSYCHOACTIVE SUBSTANCES ON THE BRAIN

While different psychoactive substances certainly act in different ways upon the brain (Altman et al., 1996; Koob & LeMoal, 1997; Markou, Kosten, & Koob, 1998; Nutt, 1997; Stahl, 1996), two major pathways in the brain have been implicated as final common pathways upon which most psychoactive substances act (Koob & LeMoal, 1997; Nutt, 1997). These are the mesolimbic-fronto cortical dopaminergic pathway (an anatomical pathway which extends from the ventral tegmental area (VTA) to the prefrontal cortex and nucleus accumbens) and the endogenous opioid receptor system (a biochemical pathway).

These two systems have been characterised as having two different functions (DiChiara & North, 1992). DiChiara and North (1992) hypothesised that the dopaminergic pathway is associated with the incentive, preparatory aspects of reward, which are experienced as thrill, urgency or craving. In contrast, the opioid system is associated with the satiation and consummatory aspects of reward, such as rest, blissfulness and sedation (DiChiara & North, 1992).

Dopamine reward system

The mesolimbic-fronto cortical dopamine system (containing the mesolimbic and mesocortical dopamine systems) is regarded as a critical pathway in brain reward (Nutt, 1997; Wise & Rompre, 1989). The mesolimbic dopamine system begins in the VTA
dopaminergic neurons, and extends to the ventral striatum (an area that includes the nucleus accumbens), the amygdala, and the septal nuclei (Altman et al., 1996). The mesocortical dopamine system also originates in the VTA, and extends to the prefrontal and cingulate cortices (Altman et al., 1996).

Dopamine has been implicated in the reinforcing effects of alcohol. Alcohol use directly stimulates dopamine release and also an indirectly increases in dopamine levels (Altman et al., 1996). The behavioural rewards of nicotine, and perhaps the basis of nicotine dependence, may also be linked to the release of dopamine in the mesolimbic pathway (Benowitz, 1998; Markou et al., 1998). Following administration of nicotine, increased dopamine is released in rats, and lesions in the mesolimbic dopamine pathway lead to reduced self-administration of nicotine (Altman et al., 1996).

Amphetamine drugs inhibit dopamine reuptake and increase dopamine release, and their reinforcing effects are thought to depend upon the dopaminergic system (Jaffe, 1995a). Cocaine's effects have also been related to an increase in dopamine function (Bergman, Kamien, & Spealman, 1990; Caine & Koob, 1994; Spealman, 1990; Spealman, Bargman, Madras, & Melia, 1991). Chronic treatment with opioids has also been found to be related to supersensitivity in the dopaminergic transmitter system. The dopaminergic system originating in the VTA is also thought to be important in the reinforcing properties of opioid drugs (Jaffe, 1995b).

Cannabis was long considered to be an atypical psychoactive drug because it did not appear to interact with the brain’s reward system. However, research has revealed that an active component of cannabis, delta-9-tetrahydrocannabinol (Δ⁹-THC), enhances brain-stimulation reward in rats at doses within the range of human use (Gardner, 1992). Studies have also revealed cannabinoid receptors are found in areas associated with brain reward, and that Δ⁹-THC increases dopamine levels (Adams & Martin, 1996; Gardner, 1992). These findings suggest that cannabis does in fact interact with the dopaminergic system.
Endogenous opioid system

There is also evidence suggesting that the brain’s endogenous opioid system may play an important role in substance use and misuse (Enoch & Goldman, 1999). Exogenous opioids such as heroin, morphine and codeine act as opioid receptor agonists, readily causing tolerance and dependence. Adaptation of opioid receptors occurs readily after chronic opioid use; it is seen in the need to use larger amounts to achieve pain relief or euphoria. Further, the opioid antagonist naloxone will induce withdrawal if administered to opioid dependent persons (Darke & Hall, 1997).

Research increasingly suggests that the opioid system may be involved in the rewarding effects of other psychoactive substances (Volpicelli & O’Brien, 1995). One form of therapy for alcohol dependence is the use of the opioid antagonist naltrexone (Gianoulakis, De Waele, & Thavundayil, 1996; Petrakis & Krystal, 1997). Naltrexone has been shown to block the reinforcing properties of alcohol, suggesting that the endogenous opioid system may play an important role in the rewarding effects of alcohol (Enoch & Goldman, 1999; Gianoulakis et al., 1996).

Recent research suggests that long-term tobacco smoking may cause changes in the responsivity of the endogenous opioid system (Krishnan-Sarin, Rosen, & O’Malley, 1999). Research has also found that doses of naloxone reverse the enhancement of brain reward caused by Δ9-THC, suggesting that some of its rewarding effects are mediated through the opioid system (Gardner, 1992).

Serotonergic neurotransmitters

Other neurotransmitters also play a role in the development and maintenance of problematic substance use. In particular, recent research has shown that the serotonergic system is affected by substance administration (Julien, 2001). For example, alcohol use has been associated with augmented serotonergic function in the nucleus accumbens and reduced serotonin transporter function may play a part in early onset alcohol dependence (Heinz et al., 1998a). Serotonin antagonists reduce alcohol self-administration in animals.
(Swift, Davidson, Whelihan, & Kuznetsov, 1996), and serotonin transporters are reduced among persons with alcohol use disorders (Heinz et al., 1998b; Tollefson, 1991).

Similarly, serotonin is responsible for some of the rewarding effects of cocaine and heroin, and serotonin function is altered by heavy or abusive use of these substances (Baumann & Rothman, 1998; King, Xiong, & Ellinwood, 1998; Kish et al., 2001; Macedo, Ribeiro, Morgadinho, & Abreu, 1998; Rocha et al., 1998a; Rocha et al., 1998b). Nicotine and Δ⁹-THC also increase the synaptic transmission of a number of other neurotransmitters, including serotonin (Adams & Martin, 1996; Benowitz, 1998).

### 2.4.1.3 Genetic Factors

One hypothesis to explain why some people seem more likely to develop problematic substance use is that they inherit an increased susceptibility (vulnerability) to the development of problematic substance use. The question of whether or not such vulnerability exists has been examined in family studies, adoption studies, and twin studies.

Family studies of alcohol use disorders (abuse and dependence) suggest that problematic alcohol use does cluster in families (Kendler, Davis, & Kessler, 1997a; Merikangas, 1990; Merikangas et al., 1998b). In one recent study, over one third (36%) of the relatives of persons with an alcohol use disorder were also diagnosed with an alcohol use disorder (abuse or dependence), compared to 15% of relatives of controls (Merikangas et al., 1998b). This relationship was stronger in a study that examined the rate of alcohol dependence among siblings: among subjects identified with alcohol dependence, 50% of male siblings met criteria for alcohol dependence, compared to 20% of male siblings of controls; for female siblings, the rates were 24% and 6% (Bierut et al., 1998). Clearly, alcohol use disorders are likely to occur among more than one family member.

Similar familial aggregation has been found for other substance use disorders (Bierut et al., 1998; Merikangas et al., 1998b). For example, among persons whose predominant problematic substance was cannabis, 13% of relatives also had a cannabis use disorder,
compared to 2.4% of controls' relatives; the comparative rates for opiates were 10% vs. 0.4%, and for cocaine, 7.5% vs. 0.8% (Merikangas et al., 1998b).

These studies suggest that substance use disorders are likely to cluster within families. However, family studies do not permit the separation of genetic and environmental influences. The clustering may occur simply because the siblings share the same environment rather than any underlying genetic cause. This possibility may be examined, however, in studies of adopted children, and studies of monozygotic and dizygotic twins.

Adoption studies examine rates of disorder among adoptees, given their biological and adoptive parents' disorder status. This allows evaluation of the genetic effects (biological parents' status) and environmental effects (adoptive parents' status) upon vulnerability to substance use disorders. Research suggests that there is a significant genetic factor that influences adoptees' vulnerability to alcohol use disorders (Bohman, Sigvardsson, & Cloninger, 1981; Cloninger, Bohman, & Sigvardsson, 1981; Goodwin, Schulsinger, Hermansen, Guze, & Winokur, 1973; Heath, 1995). In the Swedish adoption studies of Cloninger and colleagues, 23% of sons of biological fathers with a history of alcohol abuse (defined as at least one report to the Swedish Temperance Board) also met criteria for alcohol abuse, 26% of those with biological mothers with alcohol abuse also met criteria for alcohol abuse, and 33% with both biological parents meeting abuse criteria also met criteria for alcohol abuse, compared to 15% of those whose biological parents did not have such a history (Cloninger, Bohman, Sigvardsson, & von Knorring, 1985). Among females, having a biological mother with a history of alcohol abuse increased the risk of alcohol abuse, irrespective of whether biological fathers had such a history (Cloninger et al., 1985).

Among males without a lifetime history of alcohol abuse, 18% had a biological father who had a history of alcohol abuse. The proportions were significantly higher among males who did have a history of alcohol abuse themselves: 31% of those with mild alcohol abuse (one notification to the Temperance Board); 44% of those with moderate alcohol abuse (two or three notifications to the Temperance Board); and 22% of those with severe alcohol abuse (hospitalisation, treatment or 4 or more notifications) (Cloninger et al., 1981). Approximately 16% of female adoptees with a history of any alcohol abuse had biological
mothers with a history of alcohol abuse, compared to 3% of the mothers of females who did not have a history of alcohol abuse (Bohman et al., 1981).

Researchers have attempted to develop models of vulnerability to substance use disorders, in which vulnerability is the product of genetic and/ or environmental factors. Research with twins suggests that there is a significant genetic component (heritability) that increases the likelihood of dependence on a range of substances. For example, twin studies have produced estimates of the heritability of alcohol dependence ranging from 39% to 60% of the total variance (Heath, 1995; Heath & Martin, 1994; Kendler, Heath, Neale, Kessler, & Eaves, 1992a; Kendler, Neale, Heath, Kessler, & Eaves, 1994; Kendler, Prescott, Neale, & Pedersen, 1997b; Prescott & Kendler, 1999; True et al., 1999a). Similarly, the heritability of smoking persistence has been estimated at 53% (Heath & Martin, 1993), and heritability for nicotine dependence estimated at 60-70% (Kendler et al., 1999; True et al., 1999a). Research examining dependence upon other substances has revealed significant heritability estimates for cannabis abuse and dependence (ranging from 62-79%) (Kendler & Prescott, 1998a; Tsuang et al., 1998), and also for dependence upon heroin, sedatives, and stimulants (Kendler & Prescott, 1998b; Tsuang et al., 1996; Tsuang et al., 1998).

The exact nature of these genetic vulnerabilities is not known. Thus far, there have been no single candidate genes discovered which are directly related to substance abuse (Altman et al., 1996). It is likely that genetic influences involve multiple genes or the incomplete expression or function of several genes (Kendler, 1999; Schuckit, 1999). For example, there is evidence of a relationship between tobacco smoking and the genes involved in dopamine regulation (Lerman et al., 1999; Pomerleau & Kardia, 1999; Sabol et al., 1999). Variants of the genes involved in the brain’s cannabinoid system have been associated with cannabis, cocaine and heroin dependence (Comings et al., 1997). It is likely that knowledge in this area will rapidly increase given the mapping of the human genome, and given that there are numerous large scale twin studies in progress, which will allow study of the genetic correlates of problematic substance use.
While genetic researchers have examined whether some persons inherit a predisposition to developing problematic substance use, other researchers have focused upon the biological explanations of the maintenance of problematic substance use. One theory of substance dependence is based upon the concept of neuroadaptation (Koob & LeMoal, 2001; Koob & LeMoal, 1997). Neuroadaptation refers to changes in the brain occurring after repeated administration to oppose the acute effects of substance use. This may be of two types: within-system adaptations, where the changes occur at the site of action of the substance, and between-system adaptations which are changes in different mechanisms that are triggered by the substance. When substances are repeatedly administered, changes occur in the chemistry of the brain to oppose the substance's effects. When substance use is discontinued, the adaptations are no longer opposed; the brain's homeostasis is disrupted (Koob & LeMoal, 2001; Koob & LeMoal, 1997).

According to this hypothesis, neuroadaptation explains the development of tolerance to the effects of a substance and the experience of withdrawal when substance use abruptly stops (Koob, Caine, Parsons, Markou, & Weiss, 1997). While traditionally, models of substance dependence focused on physical withdrawal symptoms, more recent formulations have concentrated upon more motivational symptoms, such as dysphoria, depression, irritability and anxiety. It has been hypothesised that these negative motivational symptoms are manifestations of neurobiological changes that signal "not only... the beginning of the development of dependence, but may also contribute to vulnerability to relapse and may also have motivational significance" (p.53) (Koob & LeMoal, 1997). This approach hypothesises that after chronic substance use, changes occur in brain systems such as the dopamine reward system and the endogenous opioid system, which maintain substance use and make it difficult to cease use (Koob & LeMoal, 1997).

2.4.2 Psychological theories

Psychological approaches to the explanation of substance dependence have often been based on concepts which are common to those of other syndromes of behaviour that
involve compulsive or impulsive behaviours, such as obsessive-compulsive disorder or gambling (Miller, 1980). These theories emphasise impaired control over use and continued use despite problems with use. Among a variety of psychological approaches to the explanation of substance dependence, are theories based on: learning and conditioning (behavioural models), pre-existing behavioural tendencies (personality theories), and models of rational choice.

2.4.2.1 BEHAVIOURAL THEORIES

Behaviourist models of addiction focus on directly observable behaviour. One group concentrates upon the fact that behaviour is maintained (or made more likely) by the consequences (reinforcers) of such behaviour (West, 1989). Substance self-administration is then an example of instrumental behaviour because the activities of persons (or animals in an experiment) are instrumental in obtaining the consequences (the substance's effects).

Research with animal subjects has shown that when substances are available, substance-naïve animals will self-administer them, often to excess (Institute of Medicine, 1996). This finding has been replicated with many animal species and using a variety of routes of administration (Altman et al., 1996; Institute of Medicine, 1996). This observation has led to the development of the self-administration model of substance use whereby substances are used for their reinforcing effects. Substances might be reinforcing in two general ways: through the direct effects of substances upon some sort of reinforcement system in the brain; or through its effects upon other reinforcers (such as social or sexual reinforcers) or behaviour (such as increased attention) (Altman et al., 1996). Animal research models have controlled both the history of use (learning) and current environmental conditions of use (cues). Both of these factors are important in the development of persistent use or abuse of substances (Barrett & Witkin, 1986).

Another group of behaviourist theories focus upon classical conditioning to explain the development and persistence of addictive behaviour (Greeley & Westbrook, 1991; Heather & Greeley, 1990). According to cue exposure theory, cues for substance use are important in the development and maintenance of addictive behaviour (Drummond, Tiffany, Glautier,
A cue that has previously been present when substances were administered will be more likely to elicit a conditioned response (cue reactivity), which is thought to underlie craving. Cue reactivity may explain why someone who was dependent upon a substance but has been abstinent for some time experiences strong cravings when exposed to drug-related cues (Heather & Greeley, 1990).

The number of cues that may be associated with addictive behaviours is potentially infinite. Exteroceptive cues occur before the use of a substance, and may include the smell of an alcoholic drink, the sight of a needle, or the time of day when substances are typically taken. Interoceptive cues include the effects of substance on the brain’s receptors, mood cues such as depressed affect (e.g. (Greeley, Swift, & Heather, 1992), or cognitions such as beliefs about substance effects (Drummond et al., 1995). The response to these cues may be autonomic, behavioural or symbolic-expressive (Drummond et al., 1995). Autonomic responses include changes in heart rate, temperature and salivation. Symbolic-expressive responses include self-reported substance craving and urges to use substances. Behavioural responses include an increased likelihood to use substances (Drummond et al., 1995).

2.4.2.2 COGNITIVE THEORIES

One cognitive theory proposes that self-regulation is an important factor in the development of substance use problems. Self-regulation has been described as taking “planful action designed to change the course of one’s behaviour” (Miller & Brown, 1991), the “executive (i.e. non-automatic) capacity to plan, guide and monitor one’s behaviour flexibly, according to changing circumstances” (Diaz & Fruhauf, 1991). Self-regulation involves planning, accounting for social and physical factors as well as one’s own goals, and acting appropriately. Addictive behaviours are seen as the result of having an excessive reliance on external structures - in the case of substance dependence, excessive reliance on substance use - to maintain a physical and psychological balance.

Rational choice theories attempt to explain why some people voluntarily engage in self-destructive behaviour (Elster & Skog, 1999). One of the central elements of substance dependence is that the person has impaired control over their use of the substance. This
may manifest itself in continued use despite a wish to cut down or stop use, using greater amounts than intended, or using the substance for longer periods than intended (American Psychiatric Association, 1994).

Some argue that this represents a form of “weakness of will” – that addiction is an example of behaving “against one’s own better judgement” (Davidson, 1985; Pears, 1984). For such theorists, substance dependent persons have a choice of two options: they know that one option (not using the drug) is the superior option from a longer-term perspective, yet choose the other option. However, as Elster and Skog (1999) point out, the problem with the “weakness of will” explanation is that it is difficult to know whether such a person knew at the time of acceptance that when at a party, choosing to have a drink (for example) was the less preferred option. They may have made this considered decision before the party, and regretted accepting the drink after the party, but it is difficult to ascertain whether they thought so at the time they accepted the drink (Elster & Skog, 1999).

Other theorists argue that substance-dependent persons do make rational choices in their continued use of substances (Ainslie, 1992; Becker & Murphy, 1988; Herrnstein & Prelec, 1992). These theories centre on people’s ability to weigh present and future benefits: their ability to consider the immediate rewards associated with substance use, weighed against the longer-term benefits of abstention. With some differences, these hypotheses argue that present and future benefits are weighted and viewed in ways that make present benefits more likely to determine substance use (Ainslie, 1992; Becker & Murphy, 1988; Herrnstein & Prelec, 1992).

2.4.2.3 Personality theories

Some theorists argue that some people are more prone to addiction than others because they have an “addictive personality”. Hans Eysenck (1997) has discussed this theory in terms of a psychological resource model in which habitual substance use develops because the substances produce effects fulfilling certain purposes related to their personality profile. For these people, substance use – or more specifically, “addiction” – holds benefits even though negative consequences eventuate.
Three major independent personality dimensions are proposed: P (psychoticism), N (neuroticism), and E (extraversion) (Eysenck & Eysenck, 1985). The P dimension is an underlying propensity to functional psychosis, which lies along a continuum from “altruistic” to “schizophrenic”; those scoring highly may display the traits of aggression, coldness, egocentricity, impersonality and impulsivity (Eysenck, 1997). The N dimension is a propensity towards emotional lability: some of the traits of neurotic persons are moodiness, irritability and anxiety. The E dimension runs along a continuum from introversion to extraversion. Genetic factors have been shown to play a significant role in determining the major personality dimensions (Eley & Plomin, 1997; Eysenck, 1997).

There has been extensive examination of the relationship between substance dependence and these personality dimensions. Research on the link between E and substance dependence has revealed inconsistent findings; a review of 24 studies showed that ten studies found a negative relationship, two found a positive correlation, and twelve studies found no significant relationship (Francis, 1996).

By contrast, research suggests that persons dependent on alcohol, heroin, benzodiazepines, and nicotine have higher than normal N and P scores (Francis, 1996). In other words, persons who are more moody, irritable and anxious (have high N scores), and those who are more impulsive and aggressive (have high P scores) are also more likely to have substance use problems. For example, research has shown that persons with heavier alcohol use are likely to have higher scores on measures of neuroticism than those with less heavy use (Ogden, Dundas, & Bhat, 1989; Prescott, Neale, Corey, & Kendler, 1997; Rankin, Stockwell, & Hodgson, 1982; Sieber & Angst, 1990).

However, correlational studies alone do not enable statements to be made about the nature of the relationship between these personality traits and substance use problems. For example, persons who develop problematic substance use may become more irritable, moody or aggressive because of changes produced by their substance use, rather than reflecting a stable trait. Furthermore, research suggests that dimensions such as N may indicate a genetic vulnerability to psychopathology in general (Andrews, 1996; Andrews, Stewart, Allen, & Henderson, 1990), rather than a tendency to have an “addictive personality” per se.
2.4.3 SOCIAL AND ENVIRONMENTAL THEORIES

There are several social and environmental factors that have been strongly related to substance use and substance use disorders. These are in keeping with the findings of twin studies showing that while there is a strong genetic component accounting for vulnerability to substance dependence, there is also a substantial environmental component (e.g. (Kendler et al., 1999; Kendler & Prescott, 1998a; Kendler & Prescott, 1998b). A number of these factors will be outlined below.

There is abundant evidence that people who engage in antisocial behaviour are more likely to have or develop substance use problems. Adolescents with conduct disorders are significantly more likely to develop substance use disorders than those without such conduct problems (Cicchetti & Rogosch, 1999; Gittelman, Mannuzza, Shenker, & Bonagura, 1985). In general, it appears that the earlier, more varied and more serious a child’s antisocial behaviour, the more likely it will be continued into adulthood, with substance misuse considered one of these antisocial behaviours (Costello, Erkanli, Federman, & Angold, 1999; Robins, 1978). Furthermore, children or young people with anxiety or depressive symptoms are more likely to begin substance use at an earlier age, and more likely to develop substance use problems (Cicchetti & Rogosch, 1999; Costello et al., 1999; Henry et al., 1993; Loeber, Southamer-Lober, & White, 1999).

The peer environment also has a large influence on the substance use behaviours of individuals. Substance use usually begins with peers, and peer attitudes to substance use have been shown to be highly predictive of adolescent substance use (Fergusson & Horwood, 1997; Hoefler et al., 1999; Newcomb, Madaian, & Bentler, 1986). This may be because those who use substances are more likely to choose to spend time with other people who use such substances. There is, however, no direct evidence on the influence of peers on the development or maintenance of substance dependence (Institute of Medicine, 1996).

Families also have a strong effect upon the likelihood that people will develop substance use problems (Hawkins, Catalano, & Miller, 1992; Lynskey, Fergusson, & Horwood, 1998). This occurs in a number of ways. First, modelling of substance use by parents and other
family members has been shown to affect the chances of adolescents’ substance use behaviour. For example, parents’ substance use has been associated with the initiation and frequency of alcohol and cannabis use (Hawkins et al., 1992), while older brothers’ substance use and attitudes towards substance use have been associated with younger brothers’ substance use (Brook, Whiteman, Gordon, & Brook, 1988). Second, there is evidence that if parents hold permissive attitudes towards the use of specific substances by their children, their children will be more likely to use such substances (Hawkins et al., 1992). Third, the nature of family relationships has an effect upon the likelihood that adolescents will develop problematic substance use. The risk of substance misuse is higher if there is family discord; poor or inconsistent behavioural management by parents; or low levels of bonding within the family (Hawkins et al., 1992).

The socio-cultural background of a person will also affect the likelihood that they develop substance use problems. For example, people who come from lower socioeconomic backgrounds are more likely to have problematic use of a range of substances (Anthony et al., 1994; Hawkins et al., 1992). Those who have completed fewer years of education, or who have performed poorly in school, are also much more likely to have problematic substance use (Institute of Medicine, 1996; Lynskey & Hall, 2000). People who have grown up in an area in which there are high rates of crime, where substances are readily available, and who have associated with delinquent peers, are also much more likely to have substance misuse problems (Fergusson & Horwood, 1997; Hawkins et al., 1992; Institute of Medicine, 1996).
2.5 Conclusions

Substance use has been consistently linked to a number of social and demographic characteristics, with males, younger persons, unemployed persons, those with less education, those who are not married and those from lower socioeconomic backgrounds all more likely to report licit and illicit substance use. In general, these same factors have also been related to an increased risk of problematic substance use.

The neurobiological effects of chronic substance use are becoming more clearly described and better understood. There appear to be key pathways in the brain that are affected by substance use and that appear to be responsible for its rewarding effects. Research has revealed that changes in the brain’s neurotransmitter function occur after chronic substance use.

A multitude of theories has been proposed to explain why some people develop problematic substance use. Genetic factors appear to play a part: twin studies indicate these components have a significant role in developing dependence upon the most commonly used substances. There is also consistent evidence that a range of environmental factors will increase the likelihood of problematic substance use. These include economic disadvantage, family conflict, modelling of substance use or parents’ permissive attitudes towards substance use, as well as childhood conduct and emotional problems.

Psychological approaches to the explanation of substance misuse have attempted to explain some of the behavioural and cognitive phenomena thought to underlie problematic substance use. Some theories – such as those proposing a personality type more disposed to addiction, or those characterising the “rational” addict – have less importance for clinicians. However, research evaluating learning theories suggests that learning plays an important role in the development and maintenance of substance use problems. In the same way, learning-based treatments may be used to overcome these problems.
Clearly, there are a number of approaches to explaining why some people become problematic substance users. Each level of explanation – biological, psychological or socio-cultural – has been supported by empirical research. However, these different levels remain to be integrated into a more comprehensive model of addiction.

The next Chapter reviews the epidemiology and theoretical explanations of mood disorders, anxiety disorders, and psychotic disorders, whose patterns of comorbidity with substance use disorders are examined in this thesis. These disorders are defined, and the existing evidence on their prevalence in the general population is outlined. Current knowledge about the epidemiology of these disorders is summarised, as are the theories that have been proposed to explain these disorders.

As will become clear, there are strong similarities between the explanations of problematic substance use and these mental disorders. Chapter Four outlines the concept of comorbidity and reviews research on this issue.

These Chapters provide the background for Chapter Five, which outlines the design and conduct of the Australian National Survey of Mental Health and Well-Being. It also explains how this survey allows an exploration of the prevalence and epidemiology of substance use disorders, mood disorders, anxiety disorders and psychotic disorders in the Australian population, and the patterns of comorbidity between them.
3 Mental Disorders

This Chapter provides a general overview of the mental disorders whose patterns of comorbidity with alcohol, tobacco and cannabis use are examined in this thesis. It summarises what is known about the epidemiology of these disorders, and the theories that have been proposed to explain their occurrence.

As has been mentioned in Chapter One, the disorders examined in this thesis were chosen based upon two factors: the prevalence of the disorder based on previous epidemiological research; and the degree to which the problem affects an individual sufferer, their family, and the community. The three groups chosen were:

a) Mood disorders (including major depressive disorder, dysthymia, and bipolar disorder). They are among the most commonly occurring mental disorders in the community (Kessler et al., 1994; Robins & Regier, 1991). Many persons meeting criteria for a mood disorder will report significant amounts of disability, including reduced productivity at work, reduced social functioning, and days spent out of their normal daily roles (Ormel et al., 1994; Ustun, 1999). World Health Organization (WHO) estimates of the global burden of disease (due to disability and premature death) have placed depression and bipolar disorder among the leading causes of disease burden (Murray & Lopez, 1996). Mood disorders are strong predictors of suicide attempts (Adams & Overholser, 1992; Beautrais et al., 1996). Suicide represents a growing concern particularly among males, for whom rates of completed suicide are higher than females, and highest among middle aged males (Cantor, Neulingr, & De Leo, 1999). Youth suicide is a growing problem among young adults, in Australia and other countries (Cantor et al., 1999; Lynskey, Degenhardt, & Hall, 2000);

b) Anxiety disorders (including panic disorder and agoraphobia, social phobia, generalised anxiety disorder, post-traumatic stress disorder, and obsessive-compulsive disorder). Anxiety disorders are also among the most prevalent mental disorders in the general population (Kessler et al., 1994; Robins & Regier, 1991). The WHO calculated that anxiety disorders will also become one of the leading causes of disease burden over the next twenty years (Murray
Anxiety disorders have been ranked among the leading causes of disability in the general population (Murray & Lopez, 1996; Neugebauer, 1999), and have been argued to be one of the leading causes of economic loss in the general population (Greenberg et al., 1999).

c) Psychotic disorders (including schizophrenia and schizoaffective disorder). Although psychotic disorders (of which schizophrenia is the most common) occur less often than anxiety and mood disorders (Jablensky, 2000; Keith, Regier, & Rae, 1991; Kessler et al., 1994), they impose a considerable burden of disease (Murray & Lopez, 1996). A number of studies have produced estimates that around 75% of persons diagnosed with schizophrenia will have a recurrent illness, with moderate to severe negative effects upon functioning in social, occupational and personal spheres (Eaton et al., 1992a; Eaton et al., 1992b; Hall et al., 1985; Mason et al., 1996b). One Australian study estimated that the economic costs of schizophrenia were 50% of the size of those attributable to myocardial infarction (Hall et al., 1985). More recent work in the UK estimated that 5.4% of the total UK National Health Service costs were attributable to schizophrenia, with combined expenses of £2.6 billion (Knapp, 1997).
3.1 Chapter Aims

The aims of this Chapter are to:

1. Give an overview of DSM-IV classifications of the major mood, anxiety and psychotic disorders;
2. Summarise research on the epidemiology of these disorders as revealed in a number of large-scale epidemiological surveys;
3. Present a brief overview of the major theories that have previously been proposed to explain these groups of disorders.

In short, the present Chapter provides a description of the major mood, anxiety and psychotic disorders, summarises the epidemiology of these disorders, and outlines the theories of these disorders.
3.2 Mood Disorders

Depressive symptoms such as unhappiness or disappointment are a relatively common occurrence in everyday life, affecting perhaps one third of adults at any given point in time (Doris, Ebmeier, & Shajahan, 1999). Feelings of elation or elevated mood are also a common experience of life. D.T. Campbell argued that humans' affective experience is relatively grouped as “one-third pleasure, one-third pain, and one-third blah” (p.1121) (Campbell, 1975). Given that mood does typically change, “normal” or average mood states can thought of as not typically feeling particularly euphoric or sad, but that this can change given the circumstances, so that if something good happens, mood is lifted, whereas if something bad happens, mood is depressed (Goodwin & Jamison, 1990).

There is a difference between such normal variations in mood and situations in which mood changes become pervasive, disrupt everyday life, and interfere with an individual’s functioning. Some have referred to mood disorders as disturbances that “magnify human experiences to larger than life proportions. Among their symptoms are exaggerations of normal sadness and fatigue, joy and exuberance, sensuality and sexuality, irritability and rage, energy and creativity” (Goodwin & Jamison, 1990).

According to DSM-IV, the term “mood disorders” refers to disorders in which the dominant feature is a significant and pervasive disturbance of an individual’s mood, which adversely affects an individual’s ability to function in their everyday roles. This disturbance may be a flattening of mood or loss of interest in most areas of life; and/or it may involve an abnormally elevated or expansive mood. The major DSM-IV mood disorders are summarised in Table 3.1 (American Psychiatric Association, 1994). Details of diagnostic criteria for these disorders are presented in Appendix A.

According to the DSM-IV, a depressive episode is one in which there is a significant and pervasive flattening of mood or loss of interest in many activities in day-to-day life, which occurs over a period of at least two weeks. It is associated with symptoms such as appetite change, feelings of worthlessness or guilt, suicidal thoughts, fatigue, sleep problems and
problems making decisions (American Psychiatric Association, 1994). The mood disorders of major depression and dysthymia involve one or more depressive episodes, with the major difference between the two being the duration of the depressive episode (at least 2 weeks for major depression, and at least two years for dysthymia).

A manic episode, on the other hand, involves episodes of at least a week in which there is abnormally and persistently altered mood that is elevated, expansive or irritable (American Psychiatric Association, 1994). During this period symptoms may include grandiosity, distractibility, decreased need for sleep, and excessive motor agitation and goal-directed activity (American Psychiatric Association, 1994). Bipolar I disorder involves one or more manic episodes, while the individual may also have had one or more depressive episodes. Bipolar II disorder, on the other hand, involves one or more depressive episodes that have been accompanied by one or more hypomanic episodes (which are shorter and less severe than episodes of mania) (American Psychiatric Association, 1994).

Table 3.1: DSM-IV mood disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major depression</td>
<td>a period of at least 2 weeks of persistent depressed mood or loss of interest in most activities, accompanied by symptoms such as appetite change, sleeping difficulties, lowered energy, feelings of worthlessness, and suicidal ideation;</td>
</tr>
<tr>
<td>Dysthymia</td>
<td>a period of chronically depressed mood, which does not meet criteria for a major depressive episode, which occurs on most days for a period of at least 2 years;</td>
</tr>
<tr>
<td>Bipolar I disorder</td>
<td>this disorder involves one or more episodes of mania (periods of abnormally elevated, expansive or irritable mood lasting at least one week); the individual may also have experienced periods of depressed mood;</td>
</tr>
<tr>
<td>Bipolar II disorder</td>
<td>this disorder involves recurrent major depressive episodes, along with at least one hypomanic episode (periods of abnormally elevated, expansive or irritable mood lasting at least four days).</td>
</tr>
</tbody>
</table>
3.2.1 Epidemiology of Mood Disorders

Mood disorders are among the most common mental disorders in the general population (Doris et al., 1999; Kessler et al., 1994; Robins & Regier, 1991). For example, the US National Comorbidity Survey (NCS) found that around 10% of persons aged 15 to 54 years had met criteria for a major depressive episode within the past year, with around 1% meeting criteria for a manic episode and 2.5% for dysthymia (Kessler et al., 1994).

A consistent finding in epidemiological research on major depression has been that females are more likely than males to meet criteria for major depression (Bland, 1997; Blazer, Kessler, McGonagle, & Swartz, 1994; Doris et al., 1999; Robins & Regier, 1991). In contrast, the NCS findings suggested that bipolar disorders do not differ according to gender (Kessler, Rubinow, Holmes, Abelson, & Zhao, 1997a). Mood disorders tend to decline in prevalence among older age groups (Blazer et al., 1994; Henderson et al., 1998; Weissman, Livingston Bruce, Leaf, Florio, & Holzer, 1991).

A number of socio-economic indicators are related to the likelihood of meeting criteria for a mood disorder (Bland, 1997). Mood disorders are associated with lower socio-economic status (Blazer, 1995; Weissman et al., 1991), although there have been differences in the strength of this association in different epidemiological studies (Blazer, 1995). Less educated persons have been found to be more likely than more educated persons to meet criteria for major depression (Kessler, Zhao, Blazer, & Swartz, 1997e). Furthermore, those who were not employed are more likely than employed persons to meet criteria for depression (Blazer et al., 1994; Dooley, Catalano, & Wilson, 1994).

Marital status has been strongly related to the likelihood of meeting criteria for major depression and for bipolar disorder, with rates of depression highest among those who are separated, divorced or widowed (Blazer et al., 1994; Kessler et al., 1997e; Power et al., 1999; Weissman et al., 1991). The Epidemiological Catchment Area study (ECA) also found that separated and divorced persons had significantly higher rates of bipolar disorder (Weissman et al., 1991).
3.2.2 THEORIES OF MOOD DISORDERS

Several approaches have been used to explain the aetiology of mood disorders. Biological theories attempt to explain the neurobiological processes underlying the subjective experience of disrupted mood. Behavioural theories emphasise the way in which context plays an important causal role in establishing and maintaining dysfunctional affect; while cognitive hypotheses emphasise styles of thinking that intercede between context and resulting moods. There is evidence that environmental factors play an important role in precipitating these disorders.

3.2.2.1 BIOLOGICAL THEORIES

Biological theories aim to identify whether some persons have a biological predisposition to developing mood disorders, and attempt to characterise the biochemical changes occurring among persons with mood disorders.

Genetic liabilities

There is abundant evidence that some of the risk for developing mood disorders is familial and hence, may reflect genetic liabilities. The NCS found that in a general population sample, around one third (34%) of persons with DSM-III-R major depression had parents with a history of major depression, compared to 16% of the parents of those without a lifetime history of major depression. This relationship remained significant after controlling for a number of variables (Kendler et al., 1997a). Twin studies have suggested that this increased occurrence is due at least in part to a significant genetic vulnerability (Doris et al., 1999; Kendler et al., 1997a; Kendler, Kessler, Neale, Heath, & Eaves, 1993d; Roy, Neale, Pedersen, Mathe, & Kendler, 1995). Recent research estimated that 39% of the vulnerability to lifetime major depression was due to genetic factors in both males and females (Kendler & Prescott, 1999). Research has suggested an even stronger genetic element for bipolar disorder (Blazer, 1995; Craddock & Jones, 1999), with twin research suggesting that the lifetime risk of bipolar disorder in a monozygotic twin whose twin has bipolar disorder is 40-70% (Craddock & Jones, 1999). The prevalence in a first degree
relative is 5-10%, compared with 0.5-1.5% in the general population (Craddock & Jones, 1999).

Genetic and environmental factors interact in the development of major depression, with persons who have a genetic vulnerability being more likely than those without to develop major depression after experiencing a stressful life event (Kendler, 1998; Kendler et al., 1995a). Persons with such a genetic vulnerability may also be more likely to place themselves in an environment where stressful life events are more likely to occur (Kendler, Neale, Kessler, Heath, & Eaves, 1993a; Kendler, 1998). The response to stressful life events may be completely mediated by genetic factors such as neuroticism (Saudino, Pedersen, Lichtenstein, McClean, & Plomin, 1997).

**Neurotransmitter function**

Persons with mood disorders are likely to show significant changes in monoamine neurotransmitter function. Reduced serotonin function has been hypothesised to play a significant part in depression, since serotonin-depleting medications may cause depression, and antidepressant medications work by increasing levels of serotonin in the brain (Akiskal, 1995; Deakin, 1998a; Leonard, 1984; Leonard, 1996).

Petty and colleagues argued that disturbances in dopamine, norepinephrine and gamma-aminobutyric acid (GABA) function also play a part in mood disturbances (Petty, Davis, Kabel, & Kramer, 1996). Reduced norepinephrine function has been hypothesised to be involved in the pathogenesis of depression (Leonard, 1984). Norepinephrine reuptake inhibitors are also effective treatments for depression (Gorman & Kent, 1999); and there is recent evidence that depressed persons have reduced norepinephrine function (Lambert, Johansson, Agren, & Friberg, 2000). This is consistent with what is known of the neuroanatomy of the serotonergic and noradrenergic pathways, which are thought to project to systems involved with mood mediation, appetite, sleep and aggression (Akiskal, 1995; Goodwin, 2000).

Dopamine function has also been related to depression. Dopamine function is reduced among depressed persons (Lambert et al., 2000), reduced dopaminergic activity is
associated with psychomotor slowing (Shah, Ogilvie, Goodwin, & Ebmeier, 1997), and during recovery from depression there is increased transmission in the dopaminergic pathways extending to the basal ganglia and prefrontal cortex (Goodwin et al., 1993). Naranjo and colleagues argued in a recent review that the functioning of the brain’s dopaminergic reward system (as outline in Chapter Two) underlies the loss of pleasure and interest that is often seen in depressed persons (Naranjo, Tremblay, & Busto, 2001).

However, these systems cannot explain the entire picture, because there is a delay in the onset of antidepressants’ therapeutic effects (which increase levels of neurotransmitters such as serotonin and norepinephrine) (Julien, 2001). Rather, it is likely that there is a cascade of changes throughout other neurotransmitter systems which are induced by the monoamines, and it is these other systems that have a primary role in depression (Doris et al., 1999; Heninger, Delgado, & Charney, 1996). In recent years, for example, it has been argued that an important factor in the pathogenesis of depression is stress hormone dysregulation, which results in excess levels of cortisol (Doris et al., 1999; Holsboer, 2000; Holsboer & Barden, 1996).

3.2.2.2 PSYCHOLOGICAL THEORIES

Cognitive theories

There are a variety of cognitive theories that attempt to explain why some persons suffer from depression. Persons who have fewer personal resources (such as poor problem solving skills and a negative attributional style) are more likely to be depressed (Kupfer & Frank, 1997). Persons who are depressed are also more likely to have low self-esteem, which is thought to contribute to the development and maintenance of depression (Craig, 1990).

Other cognitive models of mood disorders have hypothesised that mood disorders are characterised by tendencies to process information in a way that maintains negative mood states (Mathews & MacLeod, 1994). One well-known model is the cognitive model of depression that was developed by Aaron Beck (Beck, Rush, Shaw, & Emery, 1979). According to Beck’s theory, negative patterns of thinking are the defining feature of depression: a cognitive triad of negative interpretations of the self, one’s experience, and
hopes for the future. Given these patterns, depressed mood is reinforced and worsened when the patient interprets information in a negative way. More recent evidence has revealed that such a manner of thinking is an attributional style of depressed persons, and is global, stable and internal (Akiskal, 1995).

One problem with such models is that the evidence to support them comes from persons who have already developed depressive disorders, i.e. they do not necessarily mean that the information processing characteristics of persons with mood disorders are related to their aetiology. Stronger evidence is provided by studies showing that cognitive therapy that changes such attributional styles produces significant improvements in mood for depressed persons (Balslev Jorgensen, Dam, & Bolwig, 1998). This indicates that at least the thinking style maintains depressed mood once it has become established.

**Behavioural theories**

Several more behaviourally based theories of depression exist. According to the learned helplessness model of depression, depressed persons have learned to be helpless because past situations have shown them that their actions did not result in favourable outcomes (Akiskal, 1995). This hypothesis is based upon animal research that has shown that dogs that were prevented from avoiding shocks later made no attempts to avoid shocks, even when escape was possible. In humans, this hypothesis proposes that past experiences of helplessness could lead to passivity, self-blame and a lack of hostility (Akiskal, 1995).

**Personality**

The idea that persons with certain personality traits are more liable to developing mood disturbances is not a new one. The trait for which the greatest amount of evidence exists to support a link with later major depression is the trait of neuroticism. As noted in Chapter Two (2.4.2.3 - Personality theories), persons who are more neurotic tend to have be more irritable, more anxious, and have greater mood lability than persons who are less neurotic.

Research has found that persons who are more neurotic are more likely to develop depression (Andrews et al., 1990; Eysenck, 1991; Kendler et al., 1993d; Mackinnon, Henderson, & Andrews, 1990; Martin, 1985; Roberts & Kendler, 1999). Some research...
also suggested that this link may be due to shared genetic contributions to both depressive symptoms and neuroticism (Andrews et al., 1990; Mackinnon et al., 1990), and this has been discussed in terms of cognitive processes related to neuroticism that may make depression more likely (Martin, 1985).

3.2.2.3 ENVIRONMENTAL FACTORS

Multiple factors have been implicated in the precipitation and/or maintenance of major depression. Particularly important precipitating factors that increase the risk of major depression are stressful life events, which increase the risk of experiencing a major depressive episode (Kendler et al., 1995a).

Other factors, such as the loss of a parent during childhood, have received mixed support as to whether they increase the risk of developing adult-onset depression (Tennant, 1988). Clearer evidence has been found for the role of child-parent interactions: a lack of parental care has been associated with increased risks of adult-onset depression (Parker, 1983). However, it has been argued that it is probably more important to view studies of childhood experience on a cumulative basis, with the hypothesis that greater experience of adversity in general, as opposed to any specific factor in particular, may be more appropriate when attempting to estimate the future risks of mood disorders such as depression in adulthood (Kessler, Davis, & Kendler, 1997c).

3.2.2.4 SUMMARY

Research has begun to delineate the biological, psychological and social-environmental factors that are predictive of mood disorders. With respect to major depression, there has also been some attempt to integrate these separate domains into a comprehensive aetiological model (Akiskal, 1995; Kendler et al., 1993d). Kendler and colleagues examined genetic, environmental, and personality factors: the best fitting model of liability to developing major depression included (in order of strength): stressful life events; genetic factors; previous major depression; and neuroticism (Kendler et al., 1993d). Reported parental warmth indirectly affected depression through its impact on these factors.
3.3 **Anxiety disorders**

Anxiety has been distinguished from fear. Fear has been described as a reaction to a specific stimulus that is perceived as threatening, and for which the focus is specific and the time course episodic, ceasing when the stimulus is removed (Maier & Watkins, 1998). Anxiety, by contrast, is a negative affect that has been defined as “the tense anticipation of a threatening but vague event; a feeling of uneasy suspense” (p.2) (Rachman, 1998). It has been described as a less distinct emotion, the reason for which is more difficult to identify, and which is more persistent (Rachman, 1998).

The term “anxiety disorder” refers to a range of psychological disorders in which the experience of excessive anxiety is a central feature. This excessive anxiety may constitute repeated episodes of intense fear, having fast onset with a relatively short duration (as in the case of panic disorder), or it may consist of a much more pervasive, persistent and less defined state of constant uneasiness and anxiety (such as generalised anxiety disorder). The DSM-IV has categorised seven types of anxiety disorder, which are listed in Table 3.2 (American Psychiatric Association, 1994). Details of diagnostic criteria for these disorders are presented in Appendix A.
Table 3.2: DSM-IV anxiety disorders

- Panic disorder: this involves recurrent unexpected panic attacks (sudden onset of intense fear and apprehension, perhaps with feelings of impending doom, accompanied by symptoms such as shortness of breath, heart palpitations, and a fear of losing control) about which there is persistent concern;
- Agoraphobia: involves anxiety about or avoidance of situations from which escape might be difficult or where help might not be available if a panic attack began;
- Social phobia: involves clinically significant anxiety due to exposure to social or performance situations, which may lead to avoidance of these situations;
- Specific phobia: involves clinically significant levels of anxiety caused by exposure to a specific object or situation, which may lead to avoidance of this object;
- Generalised anxiety disorder: at least 6 months where there was persistent anxiety and excessive worry;
- Obsessive-compulsive disorder: obsessions which cause significant anxiety or distress, and/ or compulsive behaviours which serve to reduce anxiety;
- Post-traumatic stress disorder: the re-experiencing of a traumatic event, which causes increased arousal and perhaps avoidance of things related to the event.

3.3.1 Epidemiology of Anxiety Disorders

Anxiety disorders are among the most commonly occurring disorders in the general population. The NCS estimated that around 17% of persons met criteria for a DSM-III-R anxiety disorder within the past year (Kessler et al., 1994). The most prevalent of these were simple phobia (termed specific phobia in DSM-IV) and social phobia, with 12-month rates of 8.8% and 7.8% respectively (Kessler et al., 1994). The NCS produced similar rates to the ECA of panic disorder (2.3%), agoraphobia (2.8%) and generalised anxiety disorder (GAD: 3.1%) (Kessler et al., 1994). The lifetime prevalence of post-traumatic stress disorder (PTSD) in the NCS was 7.8% (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995b). Obsessive-compulsive disorder (OCD) was not assessed in the NCS but was assessed in the ECA; 1.7% of persons had met criteria for this disorder within the past year (Karno & Golding, 1991).
Epidemiological research – much of which has been conducted in the US – has generally found that anxiety disorders are more common among females than males (Eaton, Dryman, & Weissman, 1991; Kessler et al., 1994; Magee, Eaton, Wittchen, McGonalge, & Kessler, 1996; Rouillon, 1996; Weissman et al., 1997). The ECA estimated that females had a two-fold greater likelihood of meeting lifetime criteria for simple (specific) phobias (Eaton et al., 1991), OCD (Karno & Golding, 1991), and GAD (Blazer, Hughes, George, Swartz, & Boyer, 1991). However, rates of DSM-III social phobia were no different among males and females (Eaton et al., 1991). An analysis of NCS data found that DSM-III-R agoraphobia and simple phobias were more than twice as likely among females than males (Magee et al., 1996). In contrast to the ECA, social phobia was also more common among females than males (1.4 times more likely) (Magee et al., 1996). PTSD was found to be more than twice as common among females than males in the NCS (Kessler et al., 1995b).

Anxiety disorders are more common among younger adults (Kessler et al., 1995b; Magee et al., 1996; Rouillon, 1996; Weissman et al., 1997). This has been found for both lifetime and 12-month diagnoses of phobias (Magee et al., 1996), leading to the suggestion that birth cohort effects may explain differences in lifetime rates (Magee et al., 1996). An analysis of age of onset among persons with social phobia, agoraphobia and simple phobia from the NCS found that the cumulative prevalence of anxiety disorders was higher at younger ages among more recent birth cohorts. (Magee et al., 1996). Among persons exposed to trauma, youth predicts a higher likelihood of developing PTSD (Brewin, Andrews, & Valentine, 2000).

Some research has found that persons who are separated or divorced are more likely to have an anxiety disorder (Rouillon, 1996). In an analysis of NCS data on the correlates of PTSD, Kessler and colleagues found that women who were divorced, separated or widowed were significantly more likely to meet lifetime criteria for PTSD (Kessler et al., 1995b); while those with social phobia were found to be more likely to never have married (Magee et al., 1996). Although clinical evidence suggested that persons with OCD may be more likely to have “marital maladjustment” (Rasmussen & Tsuang, 1984), such a relationship was not found in the ECA (Karno & Golding, 1991). No relationships were
found in the NCS between relationship status and agoraphobia or simple phobia (Magee et al., 1996).

Educational level has been associated with anxiety disorders (Kessler et al., 1995a; Rouillon, 1996). Persons meeting criteria for anxiety disorders were all found to have completed fewer years of education (Kessler et al., 1995b; Magee et al., 1996). A meta-analytic review concluded that low education was a significant risk factor for an increased likelihood of developing PTSD after exposure to trauma (Brewin et al., 2000). There is also some evidence that early onset anxiety disorders are related to lower educational attainment (Kessler et al., 1995a).

3.3.2 Theories of Anxiety Disorders

There are three major types of theories about anxiety disorders. The first attempts to explain anxiety in terms of biological dysfunctions. The second explains anxiety in terms of psychological processes such as learning and cognitions. The third - environmental factors - has also been the subject of some research.

3.3.2.1 Biological Theories

Genetic liabilities
There is an abundance of evidence that there is a significant genetic contribution to a range of anxiety disorders (MacDonald & Murray, 1994; Marks, 1986). Twin studies have suggested that there are significant genetic influences upon the likelihood of developing GAD (Kendler, Neale, Kessler, Heath, & Eaves, 1992b; Roy et al., 1995), panic disorder (Kendler et al., 1995b), OCD (Andrews et al., 1990), and phobias (Andrews et al., 1990; Kendler et al., 1995b).

Neurotransmitter function
As with mood disorders, there has been considerable discussion of alterations in neurotransmitter function among persons with anxiety disorders. It has been argued that
serotonergic projections to different areas of the brain are involved in responses to future threats (the dopaminergic structures extending to the frontal cortex and corpus striatum) and to acute events (the brain stem) (Deakin, 1998a; Deakin, 1998b). Dysfunctions in these two systems, it has been suggested, explain GAD and panic disorder, respectively (Deakin, 1998a; Deakin, 1998b). These hypotheses have been supported by evidence that serotonergic function is indeed altered among persons with GAD (Connor & Davidson, 1998; Deakin, 1998b). Indeed, evidence suggests that overactivity of the serotonergic system may be involved in many of the anxiety disorders (Eison, 1990; Petty et al., 1996).

Others have argued that disturbances in dopamine, norepinephrine and GABA function all play a part in anxiety disturbances (Petty et al., 1996). Given the wide range of problems for which serotonin reuptake inhibitors are effective, Petty and colleagues have argued that serotonin assists in returning the mind to its homeostatic set point (Petty et al., 1996).

3.3.2.2 Psychological theories

There is a significant environmental influence on the development of anxiety disorders, such as traumatic events in childhood (Rachman, 1998). Learning theories have attempted to account for the development of anxiety disorders in terms of responses to events.

Learning theories

The theory that learning underlies the development of anxiety problems has been discussed for many years, particularly for the specific phobias (Barlow, 1988; Barlow & Liebowitz, 1995; Fyer, 1998). Specific phobias have been shown to be resulting from direct negative experiences with the phobic stimulus, from vicarious experience, and from modelling of others' behaviour (Fyer, 1998). Nevertheless, not all persons with a phobia can remember a negative encounter; and a small number of stimuli are able to account for the majority of specific phobias. This has led to the hypothesis that it is not simply the case that phobias are evolutionarily predetermined – “innate” predispositions to develop fear of certain situations (Fyer, 1998; Seligman, 1971). This hypothesis has been supported by animal research (Mineka & Cook, 1986; Mineka & Cook, 1993) and human studies of blood injury phobias (Rachman, 1990).
Cognitive theories

Cognitive theories have been proposed for all of the anxiety disorders (Heinrichs & Hofmann, 2001; Mathews & Mackintosh, 1998; Rapee & Heimberg, 1997). In general, persons with anxiety disorders have been hypothesised to have specific patterns of information processing in which they allocate increased attentional resources to potential sources of threat. This hypothesis has been supported in a range of experimental situations (Heinrichs & Hofmann, 2001; Mathews & Mackintosh, 1998; Rapee & Heimberg, 1997). Advocates of this hypothesis argue that this reflects an evolutionarily primitive “threat evaluation system” which works at an automatic, preconscious level, and which is nonverbal (Mathews & Mackintosh, 1998). It has been suggested that the amygdala is involved in this system, and the output of the system when stimuli are perceived to be threatening is anxiety.

Personality

There is substantial evidence that persons who have higher levels of neuroticism are also more likely to meet criteria for an anxiety disorder at some point in their lives (Andrews et al., 1990; Bienvenu et al., 2001; Clark, Watson, & Mineka, 1994; Mackinnon et al., 1990). For example, recent research using data from the Baltimore ECA follow-up study found that persons with social phobia, specific phobia and panic disorder had significantly higher neuroticism scores than those without such disorders (Bienvenu et al., 2001). Research has also suggested that this link may be due to shared genetic contributions to both anxiety and neuroticism (Andrews et al., 1990; Mackinnon et al., 1990).

3.3.2.3 Environmental theories

PTSD is an anxiety disorder for which environmental factors (traumatic life events) are necessary by definition. They are not sufficient, however, because the majority of persons who are exposed to traumatic events do not develop PTSD. In the NCS, for example, only 8% of males and 20% of females who had ever been exposed to a traumatic event had actually developed PTSD (Kessler et al., 1995b). A range of social and individual factors predicted an increased risk of developing PTSD. These include: lower education, lower
socioeconomic status (SES), lower intelligence, a history of other mental health problems, childhood abuse and childhood adversity, lack of social support and other sources of life stress (Brewin et al., 2000).

Stressful life events have been implicated as aetiological factors in other anxiety disorders. The ECA found that persons who had experienced unexpected and very important negative events were significantly more likely to have developed DSM-III generalised anxiety disorder (Blazer et al., 1991). Stressful events have also been implicated in research examining other anxiety disorders (Barlow, 1988).
3.4 Psychotic Disorders

Reports of persons with psychosis have been discussed for thousands of years, with descriptions of cases dating back to the 15th century BC (Carpenter & Buchanan, 1995). The most common psychotic disorders are schizophrenia and schizoaffective disorder. Bleuler (1911) used the term “schizophrenia” – splitting of the mind – to describe what Kraepelin had termed “dementia praecox”. This name reflected Bleuler’s conceptualisation of schizophrenia as a disorder in which the brain’s normal associations were not present: the “fabric of thought and emotion” was torn (Andreasen, 1997).

The central feature of these disorders is a combination of characteristic symptoms that involve a range of cognitive and emotional dysfunctions that affect movement, perception, inferential thinking, language, communication, affect and attention (American Psychiatric Association, 1994; Carpenter & Buchanan, 1995). Table 3.3 summarises the criteria of the DSM-IV diagnosis of schizophrenia and schizoaffective disorder. Details of diagnostic criteria for these disorders are presented in Appendix A.
### Table 3.3: DSM-IV criteria for schizophrenia and schizoaffective disorder

<table>
<thead>
<tr>
<th>Schizophrenia</th>
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<tbody>
<tr>
<td>• Two or more of the following characteristic symptoms present for a significant proportion of one month:</td>
</tr>
<tr>
<td>o Delusions;</td>
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<tr>
<td>o Hallucinations;</td>
</tr>
<tr>
<td>o Disorganised speech (such as incoherence);</td>
</tr>
<tr>
<td>o Grossly disorganised or catatonic behaviour;</td>
</tr>
<tr>
<td>o Negative symptoms: flattened affect, alogia (decreased speech productivity), avolition (inability to initiate/persist in goal-directed activity);</td>
</tr>
<tr>
<td>• Markedly affected social or occupational functioning since the onset of symptoms;</td>
</tr>
<tr>
<td>• Continuous signs of the disturbance persist for at least 6 months;</td>
</tr>
<tr>
<td>• The disturbance is not due to substance use, a medical condition or a developmental disorder such as autism.</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>Schizoaffective disorder</th>
</tr>
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<tbody>
<tr>
<td>• Major depressive episode, manic episode, or a mixed episode, concurrently with symptoms that meet criteria for schizophrenia.</td>
</tr>
</tbody>
</table>

#### 3.4.1 Epidemiology of Psychotic Disorders

Population estimates of the lifetime prevalence of schizophrenia have ranged between 1 to 10 cases per 1000 persons (Jablensky, 2000; Keith et al., 1991). Males have an earlier age of onset than females (Jablensky, 2000; Jablensky, Sartorius, & Ernberg, 1991; Jones & Cannon, 1998), but the incidence of schizophrenia is higher in later life among females, so the lifetime prevalence is similar among males and females (Bijl et al., 1998; Jablensky, 1999; Jablensky, 2000; Jones & Cannon, 1998; Kendler, Gallagher, Abelson, & Kessler, 1996a). The peak periods of incidence of schizophrenia are in early to middle adulthood (Jablensky et al., 1991).
There is a great deal of disability associated with schizophrenia and other psychotic disorders (Jablensky et al., 1991; Murray & Lopez, 1996). This is reflected in a number of indicators of socioeconomic disadvantage and social isolation.

In analyses of NCS data on persons meeting criteria for nonaffective psychoses (schizophrenia, schizoaffective disorder, schizophreniform disorder, delusional disorder, and psychosis not otherwise specified), persons with psychosis were more likely to have completed many fewer years of education than those without psychosis (Kendler et al., 1996a). They were also more likely to have the lowest level of household income, and less likely to be currently employed than persons who did not meet criteria for nonaffective psychosis. This is consistent with the findings of a study by the WHO examining the incidence and course of schizophrenia in first-episode cases over a 2-year period in samples from 10 countries (Jablensky et al., 1991). This study also found high rates of unemployment, low education, and low income among persons with the disorder (Jablensky et al., 1991). In the NCS sample, persons with nonaffective psychosis were less likely to be married than those without the disorder (Kendler et al., 1996a). This finding was consistent with the low rates among the large clinical sample in the study by Jablensky and colleagues, although in the latter sample, rates of unmarried persons were higher (1991).

The WHO study found that the manifestations of schizophrenia were similar across all sites, as was the incidence rate. The course of the disorder, however, appeared more benign in developing countries that in developed countries (Jablensky et al., 1991). Given the different social factors working in the developing countries (less demand on the individual and greater emphasis upon community support), this has been interpreted as evidence that psychosocial factors affect the course rather than the aetiology of the disorder (Carpenter & Buchanan, 1995; Jablensky et al., 1991).

### 3.4.2 Theories of Psychotic Disorders

There is consensus that psychotic disorders are “biological” diseases, in that social factors probably do not play much part in their aetiology (Mueser et al., 1998; Wright & Woodruff,
The models describing psychosis, however, range from neurobiological to cognitive (Andreasen, 1997). There have been numerous attempts to elucidate the mechanisms by which schizophrenia may be characterised. Such explanations have ranged from theories of neurotransmitter function, to models of the cognitive phenomena that result from disturbances in neurotransmitter function.

Despite considerable research on the aetiology of schizophrenia and related psychotic disorders, the causes of these disorders are poorly understood (Wright & Woodruff, 1995). Some have criticised the “single disease” model of schizophrenia, which has been the basis for much of the thinking about this disorder (Carpenter & Buchanan, 1995). This paradigm conceives of schizophrenia as a disorder having a similar aetiology and pathophysiology for all persons diagnosed with the disorder. It assumes that research will eventually discover this underlying process. The symptoms of schizophrenia – dissociation between thought processes, emotions and behaviour – are believed to be the manifestations of this underlying disturbance.

Sceptics of this paradigm prefer to characterise psychotic disorders as a “clinical syndrome” (Carpenter & Buchanan, 1995). They have argued that this is more appropriate because it is unclear – and is perhaps unlikely – that the same aetiology is responsible for all cases of schizophrenia (as is the case with the variety of different aetiologies that underlie the syndrome of intellectual disability) (Carpenter & Buchanan, 1995).

There is debate over whether schizophrenia is a neurodevelopmental disorder or a neuropathological disorder. In other words, does the brain fail to develop as it should over the lifespan, or is it the case that the (developed) brain is damaged? Increasing evidence suggests it is probably the former, given that changes have been noted in the early developmental stages of the central nervous system (CNS) of persons who have developed psychoses (Wright & Woodruff, 1995). Also consistent with this hypothesis is evidence that significant differences in brain structure exist, similar to those found in schizophrenic persons, among persons who are at high risk of developing schizophrenia before they develop the disorder (Lawrie et al., 2001).
3.4.2.1 Biological theories

Genetic factors

There is strong evidence that genetics are a significant factor in the aetiology of psychotic disorders such as schizophrenia, with heritability estimates ranging from 0.63 to 0.87 (De Domenico et al., 1994; De Domenico et al., 1995; Jones & Cannon, 1998; Meltzer, 2000; Tsuang, 2000; Tsuang, Stone, & Faraone, 1999; Wright & Woodruff, 1995). Theorists have discussed this genetic influence as vulnerability to “schizophrenia spectrum” disorders rather than to “schizophrenia” specifically (De Domenico et al., 1995; Lichtermann, Karbe, & Maier, 2000; Wright & Woodruff, 1995).

Genetic influences upon the development of schizophrenia are probably complex in nature. They are unlikely to be due to functional abnormalities a single gene but rather, involve a number of susceptibility genes, each with risk-increasing alleles that are common in the population and which, individually, exert a limited effect on risk of the disorder (i.e. multiple genes of small effect rather than single genes of large effect) (Lichtermann et al., 2000; Wright & Woodruff, 1995).

Despite the fact that genetic factors probably play a large role in the aetiology of schizophrenia, they do not explain the syndrome. For example, twin studies have found that among monozygotic twins, 48% concordance rates exist for schizophrenia, compared to 4% among same-sex dizygotic twins (Onstad, Skre, Torgersen, & Kringlen, 1991). If genes were solely responsible for its aetiology, concordance rates would be 100%.

Neurotransmitter function

The so-called “dopamine hypothesis” of schizophrenia was at one point extremely popular. This hypothesis proposed that schizophrenia is caused by abnormal activity of the dopaminergic system of the brain (Seeman, 1987; Seeman, Corbett, & Van Tol, 1997a; Seeman & Kapur, 1997; Seeman & Kapur, 2000; Seeman, Tallerico, Corbett, Van Tol, & Kamboj, 1997b). The hypotheses was suggested by two sources of information: the fact that persons who used large amounts of amphetamine – a strong dopamine agonist – often developed symptoms similar to the positive symptoms of schizophrenia (Kahn, 1997); and
the fact that effective antipsychotic drugs reduce levels of dopamine in the brain (Julien, 2001).

More recently, this hypothesis has been modified. It is now argued that both the dopaminergic and the serotonergic systems are involved in schizophrenia (Iqbal & Van Praag, 1995; Julien, 2001; Kahn, 1997). The dopaminergic system is believed to be involved in the positive symptoms of schizophrenia; while the serotonergic system may be related to the negative symptoms of schizophrenia. The latter hypothesis would explain why negative symptoms were not effectively treated with traditional antipsychotics having a primarily dopaminergic action (Julien, 2001). It is supported by recent research that the newer antipsychotic drugs exert therapeutic effects on the negative symptoms of schizophrenia by acting upon serotonergic function (Julien, 2001; Kahn, 1997).

A range of other neurotransmitter systems has been implicated in schizophrenia, including the noradrenergic system and GABA neurons (Wright & Woodruff, 1995). It has also been proposed that the corticostriatal pathway of the excitatory amino acids is involved in the pathophysiology of schizophrenia (Wright & Woodruff, 1995). The glutamate hypothesis of schizophrenia is likely to gain more attention as researchers attempt to investigate more fully the underlying mechanisms of the cognitive dysfunction, which some researchers believe to be the underlying deficit of schizophrenia (Andreasen, 1999). Research has suggested that this cognitive dysfunction is not effectively targeted by the newer antipsychotic drugs that target both dopaminergic and serotonergic receptors (Julien, 2001).

3.4.2.2 PSYCHOLOGICAL THEORIES

Some authors have proposed that the disturbances in schizophrenia are due to a disruption of the normal relationship between stored material and current sensory input - that is, that it is a disturbance in the information processing system of the brain (Himle et al., 1999). The cognitive abnormalities observed in schizophrenia may result from a disturbance in the neural circuit involved in the prediction of subsequent sensory input. While it is certainly the case the cognitive dysfunction is an important symptom of schizophrenia, it is unlikely to be the cause of it (Andreasen, 1997; Carpenter & Buchanan, 1995).
The “stress-diathesis” model of schizophrenia proposes that persons who are vulnerable to schizophrenia (i.e. because of an increased genetic risk) may be at higher risk of developing the disorder if they experience a triggering event.

Theories regarding viral and immunological causes of schizophrenia have been discussed for over a hundred years. It is considered unlikely that there is a single acute cause, but rather, a less obvious mechanism, which is more difficult to precisely define (Carpenter & Buchanan, 1995; Wright & Woodruff, 1995). Factors implicated in causing schizophrenia include prenatal viral infections, maternal influenza, and nutritional deficiencies (Carpenter & Buchanan, 1995; Wright & Woodruff, 1995). A number of studies have also documented increased risks of the development of schizophrenia among persons who had a history of obstetric complications (Gunther-Genta, Bovet, & Hohlfeld, 1994; Wright & Woodruff, 1995). The evidence suggests that this may be due to neonatal hypoxia, and that cerebral damage may increase the risk of schizophrenia in later life (Murray, Lewis, & Reveley, 1985).
3.5 CONCLUSIONS

Based upon epidemiological research predominantly in the US, mood and anxiety disorders are among the most commonly occurring disorders in the general population, together with substance use disorders. Psychotic disorders such as schizophrenia are much less prevalent, but such disorders are likely to be chronic or recurring disorders that cause substantial disability to the individual, and account for significant costs in health care.

These mental disorders are all more likely to occur among younger persons. Mood and anxiety disorders are more common among females. Psychotic disorders do not appear to be distributed differentially among males and females, although males have an earlier age of onset than females. The evidence on the demographic correlates suggests that all of these disorders are associated with greater levels of social disadvantage, as evidenced by lower educational achievement, lower income, lower employment and relationship status.

Many theories have been proposed to explain why these mental disorders occur. On a neurobiological level, all three groups of disorders are characterised by disturbances in monoamine neurotransmitter function. There is increasing evidence that genetic liabilities play a significant role in the aetiology of all these disorders, although they do not account for the entire picture since significant non-genetic components are also observed. Some of the other hypotheses of these disorders may explain this non-genetic influence. These include models of the cognitive processes that may maintain and perhaps precipitate such disorders; learning processes such as modelling and conditioning; personality factors; and environmental factors that might “trigger” these disorders, particularly stressful life events.
4 COMORBIDITY

The central aim of this thesis is to examine two types of comorbidity: between different substance use disorders; and between substance use disorders and other mental disorders - mood disorders, anxiety disorders, and psychotic disorders.

Previous Chapters have reviewed the definitions, epidemiology and theoretical explanations for substance use disorders (Chapter Two) and other mental disorders (Chapter Three). Several common themes emerged in these reviews:

1. Both substance use disorders and other mental disorders (particularly mood and anxiety disorders) are prevalent in the general population;
2. The distribution of these disorders seems to be similar according to some demographic characteristics;
3. There have been many hypotheses put forward to explain both substance use disorders and other mental disorders, including biological, psychological and social-cultural; and
4. Some of these hypotheses overlap, such as genetic influences, neurotransmitter dysfunction, and a range of social variables.
4.1 CHAPTER AIMS

The aims of the present Chapter are to:

1. Define the concept of comorbidity;
2. Give an overview of clinical research on comorbidity between substance use disorders and other mental disorders;
3. Outline the problems with evidence on comorbidity in clinical populations, and explain the need for general population samples to provide unbiased estimates of comorbidity;
4. Present an overview of the theories of the mechanisms underlying comorbidity.

This Chapter does not review the evidence from general population studies of comorbidity between alcohol, cannabis and tobacco use and other mental disorders. This evidence is reviewed separately in the following three Chapters, since different research issues emerge for each of the three drug types. This Chapter is intended to give an overview of the definitions and explanations of comorbidity as a background for the following Chapters.

Chapter Six includes a review of the epidemiological research on comorbidity between alcohol use and mental health; Chapter Seven includes a review of literature on comorbidity between tobacco use and mental health; and Chapter Eight includes a review of the literature on comorbidity between cannabis use and mental health.
4.2 Definitions of Comorbidity

“Comorbidity” was defined by Feinstein as “any distinct clinical entity that has co-existed or that may occur during the clinical course of a patient who has the index disease under study” (p.456-7) (Feinstein, 1970). Within psychiatry, comorbidity is commonly used to refer to the overlap of two or more psychiatric disorders (Boyd et al., 1984).

More recent work in psychology has distinguished between two types of comorbidity. Homotypic comorbidity refers to the co-occurrence of mental disorders within a diagnostic grouping (Angold, Costello, & Erkanli, 1999). The co-occurrence of two different substance use disorders (e.g. cannabis and alcohol) is an example of homotypic comorbidity. Heterotypic comorbidity refers to the co-occurrence of two disorders from different diagnostic groupings (Angold et al., 1999). This might include, for example, the co-occurrence of a substance use disorder and an anxiety disorder.

This thesis will involve an examination of both homotypic and heterotypic patterns of comorbidity: between alcohol, cannabis and tobacco use, with:

1. Other substance use and substance use disorders (homotypic comorbidity);
2. Other mental health problems: mood disorders, anxiety disorders and psychotic disorders (heterotypic comorbidity).
4.3 REASONS FOR EXAMINING COMORBIDITY BETWEEN SUBSTANCE USE AND MENTAL HEALTH

There are several good reasons to examine links between substance use and mental health, as were outlined in Chapter One. The first is a theoretical one: if mental health problems are more likely to occur among those with substance use disorders, this raises important questions about the aetiology of mental disorders. There is a number of hypotheses about the mechanisms underlying comorbidity. However, the first step is to carefully document patterns of comorbidity before examining the reasons behind them.

The second is a matter of public health policy: if substance use disorders are associated with other mental health problems, this has implications for service provision. It means that treatment services for persons with problematic substance use may need to address comorbid mental health problems. This is particularly the case if co-occurring disorders predict a worse clinical outcome, which there is some evidence to suggest is the case. Persons with comorbid panic disorder and substance use disorders, for example, are more likely to have a chronic disorder, a greater chance of suicidal behaviour, and poorer social functioning (Rouillon, 1996). Persons with social phobia and alcohol use disorders may also have a worsened clinical outcome (Brunello et al., 2000), including an increased risk of suicide (Chignon, Cortes, Martin, & Chabannes, 1998). Persons with mood disorders and substance use disorders may have a greater chance of experiencing a recurring mood disorder (Feinman & Dunner, 1996; Kessing, 1999) and attempting suicide (Tondo et al., 1999).

Research with clinical samples of persons with schizophrenia has also found that those with substance use problems are more likely to experience symptom worsening or relapse (Carey et al., 1991; Salyers & Mueser, 2001), rehospitalisation (Haywood et al., 1995), homelessness or housing instability (Caton et al., 1994; Drake et al., 1991), poor compliance with medication (Pristach & Smith, 1990), poor response to antipsychotic medication (Bowers, Mazure, Nelson, & Jatlow, 1990; Lutz, 1976; Salyers & Mueser, 2001),
impaired social functioning (Salyers & Mueser, 2001), an increased burden upon the sufferer's family (Clark, 1994), and increased treatment costs (Bartels et al., 1993).

These findings suggest that comorbidity between substance use and mental health problems has implications both for assessment (determining whether comorbid problems exist) and for treatment for substance use problems (given that untreated comorbid mental disorders may adversely affect treatment outcome).
4.4 **CLINICAL STUDIES OF COMORBIDITY**

There is a large amount of clinical research documenting extensive comorbidity between problematic substance use and other mental health problems. This section provides an overview of clinical research on (a) comorbidity between different substance use disorders; and (b) comorbidity between alcohol, cannabis and tobacco use and mood, anxiety and psychotic disorders. As noted above, general population research is outlined in later Chapters.

### 4.4.1 COMORBID SUBSTANCE USE DISORDERS

In clinical samples of persons seeking treatment for problematic substance use, a substantial proportion will report the problematic use of more than one substance (Compton et al., 2000; Darke & Ross, 1997; Hays, Farabee, & Miller, 1998; Henningfield, Clayton, & Pollin, 1990).

Higher rates of tobacco use have also been reported in studies of outpatients receiving alcohol treatment who reported more problematic alcohol use (Hays et al., 1998; Henningfield et al., 1990), and among those meeting diagnostic criteria for alcohol dependence (compared to those who did not) (DiFranza & Guerrera, 1990). Alcohol-dependent inpatients also have more severe levels of nicotine dependence than controls (Marks, Hill, Pomerleau, Mudd, & Blow, 1997).

Tobacco use is also more common among patients who regularly use other drugs (Henningfield et al., 1990), and among patients who are problematic users of other drugs (DiFranza & Guerrera, 1990; Hays et al., 1998; Henningfield et al., 1990). Regular cannabis users are more likely to smoke tobacco, and to smoke it daily, than those who use cannabis less often (Henningfield et al., 1990).

Similarly, persons undergoing treatment for alcohol use disorders are likely to also meet criteria for other substance use disorders. A study by Schuckit and colleagues of a large
sample \((n = 2,945)\) of persons in treatment for alcohol dependence found that 81% of the sample had used cannabis more than 21 times in their lives; 57% had used cocaine more than 11 times; 45% had used amphetamines more than 11 times; and 32% and 38%, respectively, had used opiates and sedatives more than 11 times (Schuckit et al., 1997a).

Over half of the sample also met criteria for DSM-III-R drug dependence at some point in their lives. The most common drug of dependence was cannabis (34%), followed by cocaine (31%), amphetamines (17%), sedatives (12%) and opiates (9%) (Schuckit et al., 1997a). A recent study of persons in treatment for DSM-III-R drug dependence found that 64% also met lifetime criteria for DSM-III-R alcohol dependence (Compton et al., 2000).

A study of comorbidity among a sample of 222 heroin injectors (half of whom were in treatment for heroin dependence) found that 95% used tobacco in the past 6 months, 83% had used cannabis, 73% used alcohol and 59% had used benzodiazepines (Darke & Ross, 1997). In the sample, 49% met criteria for DSM-III-R dependence upon alcohol in the past year; 40% met criteria for cannabis dependence, and 24% and 16% met criteria for amphetamine and benzodiazepine dependence respectively (Darke & Ross, 1997).

### 4.4.2 Comorbid Mood Disorders

In clinical samples, persons with alcohol use and other drug use disorders are also likely to meet criteria for mood disorders such as major depression, bipolar disorder, and dysthymia (Hughes, Hatsukami, Mitchell, & D'Ahlgren, 1986; Kushner, Abrams, & Borchhardt, 2000; Mezzich, Ahn, Fabbra, & Pilkonis, 1990; Miller, Klamen, Hoffmann, & Flaherty, 1996; Pozzi, Bacigalupi, & Tempesta, 1997; Raimo & Schuckit, 1998; Schuckit et al., 1997b; Strakowski & DelBello, 2000; Strakowski et al., 1998; Swensden & Merikangas, 2000; Tomasson & Vaglum, 1995).

A study of 2,713 persons in treatment for alcohol use disorders by Schuckit and colleagues found that 42% met criteria for DSM-III-R major depression, 4% met criteria for bipolar disorder, and 4% met criteria for dysthymia (Schuckit et al., 1997b). These rates were significantly higher than among control participants (rates of 16%, 1% and 1%
respectively). In a review of research on comorbidity between alcohol dependence and mood disorders, Lynskey (1998) found that in studies that used standardised diagnostic criteria, and which had a sample size of at least 50 persons, between 26% and 67% of persons in treatment for alcohol use disorders also met criteria for depression.

There is substantial research documenting an association between other substance use problems and mood disorders (Miller et al., 1996; Strakowski & DelBello, 2000; Strakowski et al., 1998). One study reported a rate of lifetime DSM-III-R major depression of 44% among a sample of 6,355 persons in treatment for substance use disorders (Miller et al., 1996). A sample of patients in treatment for drug dependence found that 24% had met lifetime criteria for DSM-III-R major depression, with another 12% meeting criteria for DSM-III-R dysthymia (Compton et al., 2000).

Clinical research has also suggested an association between tobacco use and mood disorders. For example, in an Italian case-control study of patients with DSM-III-R bipolar disorder, researchers found that 63% of bipolar persons reported current smoking, and 51% reporting daily smoking; control participants had smoking rates of 45% (current) and 33% (daily) (Gonzalez-Pinto et al., 1998).

4.4.3 COMORBID ANXIETY DISORDERS

Populations of persons seeking treatment for anxiety disorders have high rates of tobacco use (Hughes et al., 1986; Pohl, Yeragani, Balon, Lycaki, & McBride, 1992). There is also clinical evidence of an association between problematic alcohol use and anxiety disorders. Research with a sample of 75 inpatient alcoholics, which used diagnostic criteria to assess anxiety disorders, found that 40% had met criteria for an anxiety disorder at some point in their lives (Chambless, Cherney, Caputo, & Rheinstein, 1987). This estimate was similar to a number of other studies using diagnostic criteria, which found that between 23% to 44% of persons in inpatient treatment for problematic alcohol use met lifetime criteria for an anxiety disorder (Bowen, Cipywyny, D'Arcy, & Keegan, 1984; Powell, Penick, Othmer, Bingham, & Rice, 1982; Weiss & Rosenberg, 1985).
Other studies that also assessed phobias (including social phobia) estimated that between 2% to 57% of samples of persons in treatment for alcohol dependence met lifetime criteria for an anxiety disorder (Mullaney & Trippett, 1979; Smail, Stockwell, Canter, & Hodgson, 1984; Weiss & Rosenberg, 1985). Research on persons seeking treatment for anxiety disorders has also found elevated rates of alcohol use disorders, ranging from 14% to 44% (Lepine & Pelissolo, 1998; Page & Andrews, 1996; Thyer & Curtis, 1986; Wittchen, 1991).

Schuckit and colleagues reported that elevated rates of anxiety disorders were found among alcohol dependent persons (Schuckit et al., 1997b). Around 5% of a sample of alcohol dependent persons in treatment met criteria for DSM-III-R panic disorder, 3% for agoraphobia, 4% met criteria for social phobia, and 3% for obsessive-compulsive disorder. These rates compared to rates of around 1% each for each disorder among control participants (Schuckit et al., 1997b).

Similarly, high rates of anxiety disorders have also been found among drug dependent patients. In one sample, approximately 39% of drug dependent patients met criteria for phobias, 10% for generalised anxiety disorder, and 3% for other anxiety disorders (Compton et al., 2000).

### 4.4.4 COMORBID PSYCHOTIC DISORDERS

In case-control studies, schizophrenic patients have been found to be more likely to have used substances such as amphetamines, cocaine and hallucinogens than other psychiatric patients or normal controls (Schneier & Siris, 1987; Smith & Hucker, 1994; Warner, Taylor, & Wright, 1994). The prevalence of substance use in schizophrenic patients has varied between studies but it is generally higher than comparable figures in the general population (Warner et al., 1994). These variations are probably due to differences in the sampling of patients, with younger newly incident cases reporting higher rates than older persons with chronic disorders. Studies have also differed in the criteria used to diagnose schizophrenia and in the way that substance use has been assessed (Mueser, Bellack, & Blanchard, 1992).
Research involving clinical samples of persons with psychotic disorders such as schizophrenia has found that this group are likely to also report problematic use of a range of substances (Batel, 2000; Mueser et al., 1998). Most of these samples have been from the US (e.g. Barbee, Clark, Crapanzo, Heintz, & Kehoe, 1989; Dixon, Haas, Weiden, Sweeney, & Frances, 1991a; Drake, Osher, & Wallach, 1989; Pristach & Smith, 1990) and the majority of these have involved inpatient samples.

Tobacco use has been found to be highly prevalent among such clinical samples (Barbee et al., 1989; Glassman, 1993; Goff, Henderson, & Amico, 1992; Masterson & O'Shea, 1984; McEvoy & Brown, 1999; O'Farrell, Connors, & Upper, 1983). For example, a recent study found that more than 80% of first-episode schizophrenic patients were tobacco smokers (McEvoy & Brown, 1999).

Research has found high rates of alcohol use disorders among persons with schizophrenia who are in contact with treatment services (Bartels, Drake, & McHugo, 1992; Drake et al., 1989; Fowler, Carr, Carter, & Lewin, 1998; Mueser et al., 1990). Estimates of the lifetime prevalence of alcohol abuse/dependence have ranged from between 21% (DeQuardo, Carpenter, & Tandon, 1994) and 55% (Pristach & Smith, 1990). One Australian study found a lifetime prevalence of alcohol abuse/dependence of 48% (Fowler et al., 1998).

Estimates of the lifetime rate of cannabis abuse/dependence have ranged between 14% (Ziedonis & Trudeau, 1997) and 42% (Mueser et al., 1990). Rates of lifetime abuse and dependence upon other illicit drugs such as heroin, cocaine and amphetamines have generally been lower than abuse/dependence rates for cannabis, but significantly higher than general population rates (Dixon et al., 1991a; Drake & Wallach, 1989; Fowler et al., 1998; Galanter, Egelko, DeLeon, Rohrs, & Franco, 1992; Mueser et al., 1992; Mueser et al., 1990).
4.5 THE NEED FOR GENERAL POPULATION SAMPLES TO EXAMINE COMORBIDITY

One reason why epidemiological research on comorbidity is so important is to distinguish between “artefactual” comorbidity and “true” comorbidity (Caron & Rutter, 1991). Artefactual comorbidity is comorbidity that arises because of the ways in which samples are selected or the behaviour is conceptualised, measured and classified. For example, artefactual comorbidity is made more likely if the criteria used to classify two disorders are the same or similar. True comorbidity refers to the actual co-occurrence of two separate conditions at a rate higher than expected by chance.

There are a number of reasons, related to sampling biases, which make artefactual comorbidity more likely in research in clinical populations. The first is Berkson’s bias (Berkson, 1946). This refers to the fact that if a person has two disorders at a given point in time, then they are more likely to receive treatment simply because there are two separate disorders for the person might seek help. Empirical work has demonstrated the existence of this bias (Roberts, Spitzer, Delmore, & Sackett, 1978).

The second reason has been called a clinical bias (Galbaut Du Fort, Newman, & Bland, 1993). This refers to the fact that persons who have two disorders may be more likely to seek treatment because they have two disorders. Again, this source of bias has been demonstrated empirically (Galbaut Du Fort et al., 1993).

Third, referral biases may exist, whereby some persons will be referred for treatment because of other background factors, such as having a family history of psychopathology. This may make it more likely that persons who are so referred will have a number of different mental health problems (Caron & Rutter, 1991).

Fourth, different treatment agencies may have criteria for patient selection that will affect the patterns of comorbidity found in that agency’s client population. For example, an agency treating persons with anxiety disorders may specialise in the treatment of persons...
with comorbid depressive disorders, or they may exclude potential clients who have a substance use disorder. A study of the patterns of comorbidity of these clients would probably find (unsurprisingly) that clients were highly likely to have problems with depression, but were unlikely to have co-occurring substance use problems.

Finally, and related to the fourth point, the type of agency in which comorbidity is studied will affect the patterns of comorbidity that are observed. It might be the case, for example, that more persons with anxiety disorders seek treatment than do persons with alcohol use disorders (Dohrenwend, 1995). This might mean, then, that persons with less severe anxiety (and other) problems seek treatment; and hence that the rates of alcohol use disorders, for example, might be lower (since comorbidity might not be strongly related to treatment seeking). In contrast, if few people with alcohol use disorders seek treatment, then comorbidity might be a bigger predictor of help seeking, so rates of anxiety disorders might be particularly high among clinical samples of persons with alcohol use disorders. Furthermore, systematic differences are likely to exist among those who present with different “primary” problems. For example, someone who presents for treatment of their anxiety disorder, but who also has problematic alcohol use, might well have less problematic or dependent alcohol use than someone who presents specifically for treatment of their alcohol dependence, who laso has problems with anxiety.

All these biases have probably contributed to the great variations in the prevalence estimates of comorbid disorders between different studies. For example, Lynskey’s (1998) review found estimates of comorbid major depression among alcohol dependent persons ranging from 26% to 67%. The clinical evidence on comorbidity between cannabis use disorders and schizophrenia has also produced widely varying estimates, ranging between 14% (Ziedonis & Trudeau, 1997) and 42% (Mueser et al., 1990).

Hence, while research with clinical populations provides important information about disorder patterns among persons in treatment, it may provide misleading information on how often disorders co-occur in the general population. Most critically, it cannot tell us about persons who have not come to the attention of treatment agencies. Such information is crucial if we are to: assess the treatment needs of the population in general who have substance use problems (whether or not they are currently in contact with treatment
services); investigate common factors that may explain the co-occurrence of different mental health problems; and estimate the public health significance of comorbid mental health problems in the general population.

In order to address these issues, studies must be directed at examining patterns of comorbidity in representative samples of the general population. In these samples, the biases that affect clinical samples do not exist, so observed patterns better reflect general patterns of comorbidity. General population patterns of comorbidity will therefore be much less affected by the above referral and sample selection biases, which might produce artefactual comorbidity in clinical samples.

Population-level research on the comorbidity between substance use disorders and mental health has largely been carried out in the US, such as in the ECA, the NCS and the NLAES, with some work carried out in Europe. The details of the research that has been conducted to date are reviewed separately for each of the three major drug classes: alcohol (Chapter Six), tobacco (Chapter Seven), and cannabis (Chapter Eight). An expanded review of research on comorbidity between substance use and psychosis is outlined in Chapter Ten.
4.6 EXPLANATIONS OF TRUE COMORBIDITY

There are several reasons why two disorders might co-occur - that is, be truly comorbid (Caron & Rutter, 1991; Kessler, 1995). These are: (1) that there is a direct causal relationship between the two, with the presence of one disorder making another more likely to develop; (2) that there is an indirect causal relationship between the two, with one disorder affecting a third variable in a way that increases the likelihood of the second disorder; and (3) that there are common factors that increase the risk of both disorders. These are discussed in more detail below.

4.6.1 DIRECT CAUSAL RELATIONSHIP

There is a range of causal relationships that have been used to explain specific types of comorbidity between substance use problems and other mental health problems. Mental disorders have been argued to cause substance use disorders; and vice versa.

4.6.1.1 MENTAL HEALTH PROBLEMS CAUSE SUBSTANCE USE PROBLEMS

A plausible hypothesis of the relationship between substance use disorders and other mental health problems is that persons with mental health problems begin to use substances in an attempt to alleviate the symptoms of their illness, but develop problematic use as a result of their over-use (Khantzian, 1985; Khantzian, 1997; Pope, 1979). The assumption of this “self-medication” hypothesis is that the substances used by such persons will be selected for their specific effects upon mood and cognition. For example, it has been suggested that persons who are heroin dependent use heroin to ameliorate aggression and rage, while persons who are cocaine dependent use it to alleviate symptoms of depression (Khantzian, 1985).
A variation of the self-medication hypothesis has also been used to explain the relationship between schizophrenia and substance use. One such hypothesis is that persons with schizophrenia use tobacco to reduce positive symptoms such as hallucinations and delusions (Gilbert & Gilbert, 1995) and also to reduce negative symptoms such as blunted affect, apathy and anhedonia (Gilbert & Gilbert, 1995; McEvoy & Brown, 1999).

However, the evidence that specific drugs are used to “treat” specific symptoms is less than compelling (Mueser et al., 1998). For example, self-report studies of persons with schizophrenia and substance use disorder have found very little evidence that different substances are used to alleviate specific mood states or symptoms (Dixon, Haas, Weiden, Sweeney, & Franes, 1991b; Noordsy et al., 1991). Furthermore, patterns of substance use among persons with psychotic disorders tend to reflect substance availability and hence show the same patterns of substance use as are found in the general population (Hall, 1998a).

The common co-occurrence of alcohol use and anxiety disorders has suggested the so-called “tension reduction” hypothesis (Cappell & Greeley, 1987). This hypothesis proposes that persons with anxiety disorders use alcohol to relieve anxiety or distress, and that problematic use becomes more likely (being reinforced) because alcohol becomes the means to control these negative mood states (Cappell & Greeley, 1987). This hypothesis is consistent with the acute anxiolytic effects of alcohol (Allan, 1995). However, it is less consistent with what is known about the longer term effects of alcohol consumption. The effects of chronic alcohol use in high doses include increased anxiety (Stockwell & Bolderston, 1987; Stockwell, Hodgson, & Rankin, 1982). Studies of phobic disorders have also found that phobic anxiety is not alleviated by alcohol use (Marshall et al., 1997).

A more general form of the self-medication hypothesis proposes that substances are used in an attempt to relieve a variety of dysphoric moods, such as depression and anxiety, general malaise and boredom (Mueser et al., 1998). Research on self-reported reasons for substance use has provided some support for this notion (e.g. Warner et al., 1994); but it can be argued that alleviating dysphoria is simply one among many risk factors – such as poor social skills, poor social functioning and peer group influences – that increase the likelihood of both substance use and mental disorders (Mueser et al., 1998).
4.6.1.2 Substance Use Problems Cause Mental Health Problems

A different type of direct causal hypothesis is that substance use problems precipitate mental health problems. For example, there is evidence that some persons may develop depression that is secondary to alcohol dependence (Schuckit et al., 1997a; Schuckit et al., 1997b) in the sense that it develops after alcohol dependence and is likely to remit with abstinence from alcohol (Brown & Schuckit, 1988).

There has also been considerable debate over whether cannabis use is causally related to schizophrenia (Blanchard, Brown, Horan, & Sherwood, 2000; Hall, 1998a; Hall & Degenhardt, 2000; McKay & Tennant, 2000; Mueser et al., 1998; Thornicroft, 1990; Thornicroft, 1992). Some have argued that cannabis use can trigger a “cannabis psychosis” (Solomons, Neppe, & Kuyl, 1990), while others have argued that its use might precipitate schizophrenia in vulnerable individuals (Andreasson, Allebeck, & Rydberg, 1987).

Comorbidity between different substance use problems has also been explained in causal terms. For instance, it has been hypothesised that the use of cannabis leads to the later use of other illicit drugs (O’Donnell & Clayton, 1982). There has been a great deal of debate about this “gateway hypothesis”. A strong relationship exists between the use of cannabis and the later use of other illicit substances (Fergusson & Horwood, 1997; Fergusson & Horwood, 2000; Kandel & Faust, 1975; Kandel, Yamaguchi, & Chen, 1992), and it persists after statistical control for a wide range of personal, family background and environmental factors (Fergusson & Horwood, 2000). Nevertheless, it could be that other variables account for the association, which have not been considered in research to date. Alternatively, common genetic factors may play some role in increasing the likelihood of both cannabis use and other substance use, a possibility that has been given some support by twin studies (Tsuang et al., 1998). These possibilities are considered in Section 4.6.3 below.
4.6.2 INDIRECT CAUSAL RELATIONSHIP

An indirect causal relationship would exist between two comorbid disorders if one disorder had an effect upon another factor that, in turn, increased the likelihood of developing the second disorder. For example, research has shown that the presence of early-onset substance use disorders reduces the likelihood of completing high school, entering tertiary education, and completing tertiary education (Kessler et al., 1995a). Difficulties encountered because of poor educational achievement might subsequently increase the likelihood of other problems, such as depression and continued substance use problems.

Similarly, persons who are alcohol dependent may be more likely to lose their job because of poor work performance or absenteeism. Indeed, one of the criteria for DSM-IV substance use disorders is disruption to or failure to complete roles such as occupational requirements (American Psychiatric Association, 1994). Unemployment could then lead to depression because of the lack of a regular income and perceived damage to their career.

4.6.3 COMMON FACTORS

Common risk factors may well explain an association between two disorders (Caron & Rutter, 1991; Kessler, 1995; Mueser et al., 1998). These common factors might be biological, personality, social and environmental, or a combination of these factors.

4.6.3.1 BIOLOGICAL FACTORS

Neurotransmitter function

There is suggestive evidence that common physiological factors may explain the co-occurrence of different substance use disorders (homotypic comorbidity). This is plausible given that different substances act upon similar brain loci and upon the same neurotransmitter systems (Koob & LeMoal, 1997; Krishnan-Sarin et al., 1999; Nutt, 1997). Furthermore, some of the underlying neural substrates of mental disorders and substance use disorders are similar. As described in Chapters Two and Three, there is considerable
evidence that both substance use disorders and mental disorders are characterised by disturbances in monoamine neurotransmitter function (Doris et al., 1999; Iqbal & Van Praag, 1995; Koob & LeMoal, 2001; Koob & LeMoal, 1997). Some have argued that one reason for comorbidity between alcohol use disorders and anxiety disorders may be reduced serotonin function (Tollefson, 1991).

**Genetic factors**

The possibility of a common genetic vulnerability to problematic use of different substances was examined in a sample of male twins (True et al., 1999a; Tsuang et al., 1998). One of these studies examined the genetic and environmental contributions to illicit substance abuse of, and dependence on, cannabis, stimulants, sedatives, opiates and psychedelics (Tsuang et al., 1998). It found that while the vulnerability to dependence upon different substance types had some unique (drug-specific) genetic effects (0% for psychedelics, 5% sedatives, 9% stimulants, 11% cannabis, 38% heroin) there was a significant common genetic component. This comprised 6% of the variance for heroin use disorders, 22% for cannabis, stimulants, sedatives, and 26% for psychedelic use disorders. Analysis revealed that a “common vulnerability” model provided the simplest explanation of the data, with around one third of the variance of this common vulnerability caused by genetic effects.

A similar analysis of alcohol and nicotine dependence (True et al., 1999a) found that there was a significant common genetic vulnerability ($r = 0.68$) to both nicotine and alcohol dependence among male twins, with 26% of the variance in the risk for alcohol dependence shared with the genetic risk of nicotine dependence. This research needs to be replicated among female twins.

Twin studies have also provided some evidence that there are common genetic influences upon substance use disorders and mental disorders (i.e. for heterotypic comorbidity). For example, research has suggested that common genetic factors increase the risk of alcohol dependence, anxiety symptoms, and affective symptoms (Tambs, Harris, & Magnus, 1997).
A twin study of women also found that there were significant common genetic factors implicated in the comorbidity between major depression and tobacco smoking (Kendler et al., 1993b). This study found that the heritability of liability to tobacco smoking and major depression was 55% and 48%, respectively. Analyses were conducted to examine whether there was a causal relationship between tobacco smoking in major depression, or whether common factors accounted for the association that was observed between the two. The best explanation of the co-occurrence of tobacco smoking and major depression in this sample was a common genetic factor. There was no evidence of common environmental factors. The correlation between smoking and major depression due to these genetic factors was estimated at + 0.56 (Kendler et al., 1993b).

4.6.3.2 INDIVIDUAL FACTORS

Temperament is commonly associated with substance use and mental health, particularly the trait of neuroticism. Persons scoring high on neuroticism have been characterised as more anxious, worrying, depressed and moody (Eysenck & Eysenck, 1991). As reviewed in Chapter Two, persons who are heavy substance users score higher on neuroticism than those who are not. Chapter Three showed that persons who suffer from mood and anxiety disturbances also have higher levels of trait neuroticism, and a considerable part of the liability to both mood and anxiety disorders is explained by higher levels of trait neuroticism.

4.6.3.3 SOCIAL AND ENVIRONMENTAL FACTORS

Common genetic influences or individual factors play an incomplete part in explaining comorbidity. Twin studies have also shown that shared environmental factors increase the likelihood of both alcohol dependence and major depression among women (Tambs et al., 1997; True et al., 1999a; Tsuang et al., 1998). Tsuang and colleagues found that two thirds of the common vulnerability to different types of illicit drug use disorders was explained by shared environmental factors (Tsuang et al., 1998).
This is not surprising, given that there is a wealth of evidence that a number of factors are common to both mental disorders and substance use disorders. For example, social disadvantage is more common among persons who: are problematic substance users (Institute of Medicine, 1996); who meet criteria for mood disorders and anxiety disorders (Blazer, 1995; Kessler et al., 1994; Weissman et al., 1991); and who meet criteria for psychotic disorders, and there is evidence to suggest that this is not merely because of social drift after developing the disorder (Mueser et al., 1998). For all these groups of disorders, studies have shown that there are higher rates of separation and divorce, and a lower likelihood that persons will be married or in a defacto relationship (Blazer, 1995; Jablensky et al., 1991; Kessler et al., 1994; Weissman et al., 1991).

There is also a number of other factors that have been similarly associated with substance use disorders and with mental disorders, such as parental psychiatric illness and family dysfunction (Fergusson, Horwood, & Lawton, 1990; Fergusson, Horwood, & Lynskey, 1994; Rutter, 1987; Velez, Johnson, & Cohen, 1989). It is possible that these social factors serve to increase the apparent “comorbidity” of mental disorders.

The study by Kendler and colleagues cited above also found that common genetic influences explained the co-occurrence of nicotine dependence and major depression (Kendler et al., 1993b). Another study examined this issue using data from a longitudinal study of adolescents from Christchurch, New Zealand (Fergusson, Lynskey, & Horwood, 1996). It examined the association between nicotine dependence and major depression while controlling for a large number of demographic variables, family background characteristics, personal characteristics. It found – in apparent contrast to the Kendler study – that the co-occurrence of the two could be almost completely explained by common environmental factors, and that the most parsimonious explanation of the relationships between the two did not include a causal relationship (Fergusson et al., 1996).

While this may appear to be a contradiction of the Kendler study, it must be borne in mind that genetic and environmental factors are not independent. As noted in Chapter Three, for example, there is evidence of a genetic influence both upon exposure to stressful life events, and in responses to them (Kendler et al., 1993a; Kendler, 1998; Kendler et al., 1995a). Hence, in controlling for a large number of environmental factors, Fergusson and
colleagues may well have been controlling for some of the genetic influences upon both nicotine dependence and major depression. What is clear from both of these studies, regardless of which sort of influence accounted for the comorbidity (environmental and/or genetic influences), both studies agreed in that there was no evidence that major depression caused nicotine dependence or vice versa.

A similar conclusion was reached by Lynskey and colleagues in an examination of liability to alcohol, tobacco and cannabis use using the same New Zealand cohort (Lynskey et al., 1998). This study found that the simplest explanation of the relationship between alcohol, tobacco and cannabis use was a “common vulnerability” model of increased liability to the use of the three substances, which could be completely explained by a large number of environmental factors included in the analyses (Lynskey et al., 1998).

4.6.3.4 Summary

Given the broad convergence of risk factors for both problematic substance use and mental disorders, a plausible hypothesis for the comorbidity between these disorders is that substance use and mental disorders (mood disorders, anxiety disorders and psychotic disorders) share common risk factors and life pathways. A number of longitudinal cohort and twin studies have explicitly examined this hypothesis and have concluded that common factors explain the comorbidity between: alcohol, tobacco and cannabis use (Lynskey et al., 1998); dependence on different illicit drugs (Tsuang et al., 1998); alcohol and nicotine dependence (True et al., 1999a); and nicotine dependence and major depression (Fergusson et al., 1996; Kendler et al., 1993b). Hence, it is possible that any comorbidity observed in the Australian population might also be explained by common factors.
4.7 CONCLUSIONS

An examination of patterns of comorbidity between substance use and mental health is important for a number of reasons. First, it can provide important information about the aetiology of these different disorders. If disorders are likely to co-occur, then it could be the case that there is some causal or other relationship between the two disorders that explains this co-occurrence. Second, it can give important indicators about likely treatment needs of persons with substance use problems. This is important both on a general, service provision level, as well as on an individual, clinical level.

One of the most important requirements for any study of comorbidity is the need to avoid significant biases that exist in the patterns of comorbidity that are observed in clinical samples. It is important to use general population samples to ensure that the significant biases existing in clinical samples are avoided. Only then can questions of aetiology and treatment begin to be answered.

There are several reasons why comorbidity might be observed. These include direct and indirect causal relationships. They also include the possibility that comorbidity arises because some of the factors that are associated with one disorder are also associated with the other. In this way, “common factors” could explain the co-occurrence of two disorders.

This thesis uses data from a national sample of Australian adults to address some of these issues. It explores the general population patterns of association between alcohol, tobacco and cannabis use, and other substance use and mental health problems. The results will give an indication of how the use of these three substances is associated with other mental health problems in the Australian adult population. If they are associated, the patterns may have implications for service provision and treatment. Furthermore, a number of participant characteristics will be included in multiple regression analyses to see if these characteristics explain the observed associations between alcohol, tobacco or cannabis use, and other mental health problems. These results may have implications for theory.
5 THE EPIDEMIOLOGY OF SUBSTANCE USE AND MENTAL DISORDERS IN AUSTRALIA: THE NATIONAL SURVEY OF MENTAL HEALTH AND WELL-BEING

The National Survey of Mental Health and Well-Being is the first Australian survey of the mental health of a nationally representative sample of adults. This Chapter uses NSMHWB data to provide an overview of the prevalence of the major substance use and mental disorders in the Australian adult population.

In 1992, senior Australian researchers began considering the planning of a national survey of the prevalence of mental disorders in the Australian population (Henderson, Andrews, & Hall, 2000). This work was begun for three reasons.

First, while some research had been carried out with clinical populations in Australia, the findings of these studies only applied to persons who had come into contact with treatment services. Such persons would be only a proportion of all persons who have mental health problems (Kessler et al., 1994; Narrow, Regier, Rae, Manderscheid, & Locke, 1993).

Second, while studies of the major mental disorders had been conducted overseas, it was not necessarily appropriate to apply the estimates from these studies to the Australian population. In particular, there were doubts about the applicability of data on service use, given very different health care systems in Australia and the United States.

Third, some prevalence studies that had been carried out in Australia (Henderson et al., 2000) had been limited to cities or small communities, and they did not use structured interviews to assess standardised diagnostic criteria for disorders (Andrews et al., 1977; Henderson et al., 1979; Krupinski & Stoller, 1971; Krupinski et al., 1967). Only by conducting a national study with a representative sample of Australian adults, using a structured diagnostic interview, could accurate information be obtained on the prevalence of mental disorders among Australians.
The NSMHWB was therefore conducted in order to provide representative information on the mental health of Australian adults aged 18 years and over. There were three major aims of the survey (Henderson et al., 2000): (a) to estimate the prevalence of mental disorders in the general population; (b) to estimate the amount of disability associated with such disorders; and (c) to estimate the use of health and other treatment services by persons with such disorders.
5.1 Chapter Aims

The present Chapter aims to do the following:

1. Describe the design and conduct of the NSMHWB;
2. Outline the prevalence of DSM-IV substance use disorders, mood disorders, anxiety disorders and psychosis “cases” as found in the NSMHWB; and
3. Summarise the major demographic correlates of these disorders.

The primary aim of this Chapter is to provide an overview of the findings. For details of all prevalence estimates and analyses of associations, see Appendix D.
5.2 Method

5.2.1 Sample

The NSMHWB sample was representative of residents in private dwellings across all States and Territories in Australia. The sample excluded special dwellings (hospitals, nursing homes, hostels etc.), and dwellings in remote and sparsely populated areas of Australia.

Dwellings were selected using random stratified multistage area sampling (Thompson, 1970). This was done as follows (Tony Cheshire, personal communication): the area-based selection was carried out so that all sections of the population living in private dwellings within the geographical scope of the survey were represented in the sample. Each State and Territory in Australia was stratified geographically and independent samples were taken from these strata. These strata each contained a number of Collection Districts (CDs) as defined in the 1991 Australian Population and Housing Census. A sample of CDs was taken from each stratum and divided into a number of blocks. A sample of these blocks was then selected for inclusion in the survey so that each dwelling within a stratum had a known and equal chance of participation. Within each block a random list of dwellings was selected for inclusion. In each household, the person aged at least 18 years with the next birthday was asked to participate.

Approximately 13,600 private dwellings were approached, with a final sample size of 10,641 persons, giving a response rate of 78%.

5.2.2 Survey Conduct

The survey was conducted by the Australian Bureau of Statistics (ABS) in 1997. All interviewers were experienced lay interviewers with the ABS. Supervisors of interviewers in each Australian State and Territory were trained at the World Health Organization Training
and Reference Centre for the Composite International Diagnostic Interview in Sydney. All completed a further course on how to train field staff.

Trained survey interviewers met with each designated respondent to administer the interview. The interviewer read the questions and recorded participants’ responses on a laptop computer. This use of a computer to record answers in real-time differed from the ECA and NCS, which used pencil and paper. Studies have since shown excellent agreement between responses recorded via pencil and paper and those recorded via laptop computer (Peters, Clarke, & Carroll, 1999). The interviewers were given 24-hour access to a psychiatrist to deal with any concerns that arose in the course of the interview.

### 5.2.3 Survey Design and Content

Mental disorders were assessed by a modified version of the Composite International Diagnostic Interview (CIDI), the CIDI version 2.1 (Andrews & Peters, 1998; World Health Organization, 1997), which yielded diagnoses of both ICD-10 and DSM-IV disorders. Appendix A shows DSM-IV criteria for all the disorders discussed below. The CIDI is the most widely used interview in large epidemiological studies (Bland et al., 1988; Kessler et al., 1994; Robins & Regier, 1991). Questioning was restricted to symptoms in the last 12 months to minimise the uncertainty about recall of symptoms over longer periods.

#### 5.2.3.1 Reliability of the CIDI

**Inter-rater reliability**

Perhaps not surprisingly for a highly structured interview, CIDI assessments of mental disorders have been shown to have excellent inter-rater reliability (Andrews & Peters, 1998; Cottler et al., 1991; Wittchen et al., 1991). In an assessment of the CIDI (pre version 1.0) conducted as part of a large international field trial of the World Health Organization (WHO), Wittchen and colleagues found that the median value of Kappa for all items assessed was 0.9; only three of the 20 DSM-III diagnoses (somatisation, schizophreniform disorder, and anorexia) had a Kappa value of less than 0.9 (Wittchen et al., 1991). A similarly large field study of the inter-rater reliability of DSM-III-R and ICD-10 substance...
use disorders involving 18 centres around the world found that all substance use symptoms had a Kappa value of at least 0.94 (Cottler et al., 1991). An examination of DSM-III anxiety and mood disorders assessed by the CIDI found that all diagnoses had Kappa values of 1.00 for both current and lifetime diagnoses (Andrews, Peters, Guzman, & Bird, 1995).

**Test-retest reliability**

There have also been a number of studies examining the test-retest reliability of the CIDI. In reviews of such studies, both Wittchen (1994) and Andrews and Peters (1998) concluded that the CIDI had good to excellent reliability for most disorders assessed.

The World Health Organization conducted a comprehensive assessment of the test-retest reliability of CIDI assessments of lifetime substance use disorders in seven sites around the world (Ustun et al., 1997). The tests were administered with a median period of 1 week between assessment, with different interviewers. The choice of lifetime diagnoses is likely to have produced conservative estimates of reliability, compared to 12-month diagnoses (Andrews & Peters, 1998; Cottler et al., 1991; Ustun et al., 1997; Wittchen et al., 1991). Even so, the CIDI was found to have very good test-retest reliability for ICD-10 dependence diagnoses, with most substance dependence diagnoses having Kappa values of between 0.7 – 0.8 (Ustun et al., 1997). There was lower reliability for ICD-10 substance harmful use diagnoses, with values generally between 0.6 and 0.7. These findings are consistent with earlier examinations of the reliability of the CIDI, which found good levels of reliability of the CIDI (Andrews & Peters, 1998; Cottler et al., 1991; Ustun et al., 1997; Wittchen et al., 1991). Studies of the test-retest reliability of the anxiety and mood disorders assessed in the CIDI have also found good to excellent reliability (Andrews & Peters, 1998; Peters, in preparation; Semler et al., 1987).

**5.2.3.2 VALIDITY OF THE CIDI**

There are fewer studies of the validity of CIDI-derived diagnoses (Andrews & Peters, 1998; Brugha, Bebbington, & Jenkins, 1999). One issue that faces epidemiological surveys of the nature of the NSMHWB is that such surveys are highly structured interviews that are explicitly designed to be administered by lay interviewers who do not necessarily have
clinical experience (Brugha et al., 1999). This means that there is no way in which clinical judgement or flexible cross-questioning can be involved in the interview (Brugha et al., 1999), elements of what some call the “art” of the psychiatric interview (Lewis, Pelosi, Araya, & Dunn, 1992). However, by making interviews highly structured, the interview is also more standardised, and hence, more reliable (Brugha et al., 1999; Lewis et al., 1992).

Reviews of those studies of the CIDI’s validity that do exist have concluded that the validity of the CIDI is acceptable (Andrews & Peters, 1998; Wittchen, 1994). In an early study comparing the agreement between the Present State Examination (PSE) and CIDI interviews, the agreement for syndromes was adequate (overall Kappa = 0.55) (Farmer, Katz, McGuffin, & Bebbington, 1987). Similarly, Janca et al. (1992) found good levels of agreement between CIDI and clinicians’ assessments (overall Kappa = 0.77). Peters and Andrews compared the CIDI mood and anxiety disorder modules and clinical LEAD (Longitudinal, Expert, All Data) diagnoses and found that the CIDI detected 88% of the LEAD diagnoses, but that the CIDI produced more diagnoses than the LEAD diagnoses (Peters & Andrews, 1995). The validity of the CIDI has also been supported by broad agreement between the findings of the ECA and the NCS (Bland et al., 1988; Robins & Regier, 1991).

Thus, while community epidemiological surveys such as the NSMHWB may not provide perfect estimates of the prevalence of mental disorders in the community, it is likely that the estimates are very reliable and present a reasonably valid portrait of the pattern of disorders in the community.

5.2.3.3 ASSESSMENT OF ALCOHOL, TOBACCO, CANNABIS AND OTHER SUBSTANCE USE DISORDERS

Alcohol

Respondents were asked if they had consumed at least 12 standard drinks (10g alcohol) within the past 12 months. All those who reported such use, and who had consumed more than 3 standard drinks on one occasion, were assessed for symptoms of DSM-IV alcohol abuse and dependence. While this differs slightly from DSM-IV criteria (which do not require a level or pattern of drinking), pilot testing of the NSMHWB survey revealed that
when assessed for symptoms of abuse and dependence, persons who had not consumed at least this level of alcohol in the past year did not report symptoms of abuse or dependence.

**Tobacco**

All persons were asked whether they currently used tobacco; if so, they were asked if their use was regular (at least daily). Symptoms of DSM-IV nicotine abuse and dependence were not assessed in the NSMHWB. However, it is highly likely that many persons who reported current tobacco use would have been classified under DSM-IV as nicotine dependent. Previous research has suggested that between 55% - 87% of current smokers are nicotine dependent (Breslau, Kilbey, & Andreski, 1991; Giovino et al., 1995; Woody et al., 1993).

**Cannabis**

Persons were asked if they had used cannabis (marijuana and hashish) more than five times in the past 12 months. If participants reported such use, they were assessed for symptoms of cannabis abuse and dependence. The requirement of more than 5 occasions was based on the assumption that even as few as six occasions might be sufficient for development of a substance use disorder, and that substance use disorders would be extremely rare among persons who had used the drug less than five times in the past 12 months.

**Other drugs**

The drug groups below were selected to reflect the most widely used extramedical drugs among Australian adults, as indicated in the Australian National Drug Strategy Household surveys (Makkai & McAllister, 1998). As for cannabis, persons were asked if they had used any of the following drug types more than five times in the past 12 months:

- **Stimulants**: amphetamines, ecstasy, cocaine, speed and other stimulants which can be obtained by medical prescription including, dexedrine, preludin and ritalin;
- **Sedatives**: barbiturates and tranquillisers and other sedatives which can be obtained by medical prescription including, ativan, librium, megloton, normison, rohypnol, serepax, valium, xanax;
- Opioids such as heroin and opium as well as other opioids and analgesics which can be obtained on medical prescription including, codeine, doloxene, methadone, morphine, percodan and pethidine.

If participants reported such use of any of the drug classes, they were assessed for symptoms of abuse of and dependence on that drug class. Respondents were asked separate questions about these drug types. The questions asked about the use of drugs such as cannabis and the “extramedical use” of prescribed drugs such as benzodiazepines. The questions asked whether drugs and medicines had been used “in larger amounts than was prescribed or for a longer period than was prescribed” or used “more than five times when they were not prescribed for you, to get high, to relax, or to make you feel better, more active, or alert”.

5.2.3.4 ASSESSMENT OF MOOD DISORDERS

All persons were asked if they had experienced a period of at least 2 weeks in the past 12 months when they had felt sad or depressed, or had lost interest in most things. Those who had were assessed for DSM-IV major depression.

All persons were asked if they had had a period of at least 2 years where they felt sad or depressed most days, without having an interruption of such feelings for 2 months. Those who reported this, and for whom the period had extended into the past year, were assessed for DSM-IV dysthymia.

Persons were assessed for DSM-IV bipolar I and II disorders if they reported a period of at least 4 days where they were so happy or excited that they got into trouble or friends/family were concerned.

Those who met criteria for any of the above mood disorders were classified as meeting criteria for a mood disorder.
5.2.3.5 ASSESSMENT OF ANXIETY DISORDERS

If respondents reported that they had an unusually strong fear or avoidance of a range of social situations in the past 12 months, they were assessed for DSM-IV social phobia.

All persons were asked if they had had an unusually strong fear or avoidance of situations, such as being outside home alone or being alone on a bus. If so, they were assessed for symptoms of DSM-IV agoraphobia.

All persons were asked if they had experienced attacks of fear in which they felt anxious, frightened or very uneasy, which did not occur in a life-threatening situation and which was unexpected. If so, they were assessed for symptoms of DSM-IV panic disorder.

All persons were asked if they had had a period of at least one month in the past year when they felt generally anxious or worried, and if so, they were asked about symptoms of DSM-IV generalised anxiety disorder.

Persons who reported they had been bothered by recurrent unpleasant and persistent thoughts in the past 12 months were assessed for DSM-IV obsessive-compulsive disorder.

Finally, all persons were asked if they had ever experienced a range of extremely stressful or upsetting events (such as being in combat, being sexually assaulted); those who had were assessed for DSM-IV posttraumatic stress disorder.

Those who met criteria for any of the above anxiety disorders were classified as meeting criteria for an anxiety disorder.

5.2.3.6 ASSESSMENT OF PSYCHOSIS

The Psychosis Screener (PS) was developed for use in the NSMHWB by Jablensky and colleagues. The PS used elements of the CIDI to assess the presence of characteristic psychotic symptoms. It comprised seven items (see Table 5.1), three of which (1a, 2a, 3a)
were asked only if the respondent endorsed a previous question (1, 2, 3 respectively). The first six items covered the following features of psychotic disorders: delusions of control, thought interference and passivity (Question 1 and 1a); delusions of reference or persecution (Question 2 and 2a); and grandiose delusions (Question 3 and 3a). The final item (Question 4) assessed whether a respondent had ever received a diagnosis of schizophrenia. Total scores ranged from zero to six (if a person endorsed question 3a, this was scored “-1”, while if they did not endorse it, it was scored “0”).

Table 5.1: Questions included in the psychosis screener

<table>
<thead>
<tr>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. In the past 12 months, have you felt that your thoughts were being</td>
</tr>
<tr>
<td>directly interfered with or controlled by another person?</td>
</tr>
<tr>
<td>1a. Did it come about in a way that many people would find hard to</td>
</tr>
<tr>
<td>believe, for instance, through telepathy?</td>
</tr>
<tr>
<td>2. In the past 12 months, have you had a feeling that people were too</td>
</tr>
<tr>
<td>interested in you?</td>
</tr>
<tr>
<td>2a. In the past 12 months, have you had a feeling that things were</td>
</tr>
<tr>
<td>arranged so as to have a special meaning for you, or even that harm</td>
</tr>
<tr>
<td>might come to you?</td>
</tr>
<tr>
<td>3. Do you have any special powers that most people lack?</td>
</tr>
<tr>
<td>3a. Do you belong to a group of people who also have these special</td>
</tr>
<tr>
<td>powers?</td>
</tr>
<tr>
<td>4. Has a doctor ever told you that you may have schizophrenia?</td>
</tr>
</tbody>
</table>

The effectiveness of this screener in detecting cases of schizophrenia or schizoaffective disorders was evaluated using a sample of persons from an inpatient psychiatric setting, and a sample of persons from a variety of mental health services (unpublished analyses by L. Degenhardt; for details see Appendix B). These analyses indicated that a score of three or more was the statistically optimum cut-off, and discriminated adequately between cases and non-cases of schizophrenia or schizoaffective disorder. Hence, all persons who scored three or more on the screener were classed as likely “cases” of psychosis.
5.2.3.7 DEMOGRAPHIC VARIABLES

A number of demographic variables are considered in this Chapter, and are included in multiple regression analyses in later Chapters. These are as follows:

- Gender (reference category: female);
- Age (reference category: 18-24 years, compared to 25-34, 35+);
- Education (reference category: completed less than secondary education, compared to completed secondary education, completed post-secondary education);
- Relationship status (reference category: currently married or defacto; compared to separated/divorced/widowed/never married);
- Employment status (reference category: employed or not in the labour force; compared to unemployed).

More detailed breakdowns of these categories are presented in Appendix D for some outcomes (for example, alcohol and tobacco use). However, the above categorisations are those used in all analyses of associations and multiple regressions reported in the body of this thesis.

5.2.3.8 NEUROTICISM

Scores on the Neuroticism scale of the EPQ were estimated (Eysenck & Eysenck, 1991). A 12-item scale was used, with resulting scores ranging from 0 to 12. The questions from this scale are presented in Appendix C. The reliability of the scale was assessed using coefficient Alpha (\( \alpha = 0.79 \)).

5.2.4 DATA ANALYSIS

Conceptually, two types of analyses are reported in this thesis: (a) those that estimate the prevalence of disorders in the Australian population; and (b) those that examine the
strength of associations between variables, such as between demographics variables and mental disorders. The former analyses are weighted, and the latter are not, for reasons that are examined below.

5.2.4.1 PREVALENCE ESTIMATES

Previous research has indicated that survey sample design needs to be taken into account when using survey data to make estimates that are representative of the general population from which the sample came (Little, Lewitzky, Heeringa, Lepkowski, & Kessler, 1997). Little and colleagues examined the effect of weighting data on estimates in the NCS. They found that while the size of the estimates tended to change very little, but the width of the error band around the estimates increased significantly when weighting was taken into account (Little et al., 1997). This is because clustered samples underestimate the variance in the population. In the population (as in many natural populations), those living near each other tend to be similar, so the variance within clusters is smaller than it is in the population as a whole (Thompson, 1970).

For this reason, all prevalence estimates derived from the NSMHWB data in this thesis were weighted. The data were weighted for two types of errors, variation in probability of being selected for interview within and between households, and variation of the sample from the characteristics of the national population. Estimates were weighted to conform to independent population estimates by state, part of state, age and sex. Balanced repeated replicate weights were used to account for the complex survey sampling design. Prevalence estimates and their standard errors were calculated using SUDAAN Version 7.5.3 (Research Triangle Institute, 1997).

5.2.4.2 ANALYSES OF ASSOCIATIONS BETWEEN VARIABLES

There has been considerable debate about whether to use weights in analyses of associations such as regressions (DuMouchel & Duncan, 1983; Kish & Frankel, 1974; Little, 1991; Little et al., 1997; Pfefferman, 1993). Little and colleagues argued that weighting in regressions might have little use since any biases in unweighted data would
tend to cancel each other out in these analyses. They concluded that there would “not be much payoff in the setting of the NCS” to conduct regressions using weighted data (p.448).

This thesis follows their practice in using unweighted data in analysing associations. In order to take account of the overestimation of the precision of estimates, a more stringent significance level (namely p <0.01) has been used to assess associations between variables.

95% confidence intervals of odds ratios are reported throughout this thesis, because this is standard practice in psychiatric epidemiology. Note is made if the 0.01 level of significance is not reached (this only occurred in intermediate analyses; noted in Appendices).

The associations between demographic variables and the mental health variables (DSM-IV mood and anxiety disorders, and psychosis “case” status) in this Chapter were examined using logistic regression, with the mental health variables as the outcome variables. All ordinal logistic regression (OLR) analyses and logistic regression analyses were carried out using STATA (STATA Corporation, 1997; STATA Corporation, 2001).

The strength of relationships between variables (such as demographic variables) and the level of substance involvement were calculated using OLR, with the substance use variable as the outcome variable. OLR takes into account the ordering of an ordered categorical outcome variable (Bender & Grouven, 1997). While more common analytic methods such as logistic regression produce estimates of the size of the odds ratio for a dichotomous outcome variable, simply classifying an ordered scale into one dichotomous variable would mean losing information about the intervals along the scale. The alternative would be to carry out a series of logistic regressions in which the dichotomous outcome variable was classified according to the different cut-points of the scale.

OLR produces an estimate of the average change in the odds for each additional point along the ordered scale (here, for each level of involvement with cannabis, alcohol or other substance use). This means that one average odds ratio can be used, as opposed to several odds ratios for each demographic variable examined and for each level of involvement with substance use. OLR thus provides a more parsimonious method of analysing these relationships. The odds ratio produced can be thought of as an estimate of the average direction and strength of the relationship between the predictor variable and the ordered categorical outcome variable.
5.3 Results

This section gives an overview of the prevalence of mental disorders and substance use, and summarises the major demographic correlates of these mental health variables. Each section summarises the relationships between the outcome (such as substance use disorders) and demographic characteristics such as marital status, educational attainment, age and gender. The details of statistical analyses upon which the summaries are based are provided in Appendix D, where the results of regression analyses are presented for all substances, mood disorders, anxiety disorders and psychosis cases.

5.3.1 Prevalence of Mental Disorders

Figure 5.1 shows the prevalence of mental disorders in the past year according to gender (for details of prevalence estimates, see Table D1 in Appendix D). Overall, the most common mental disorders were DSM-IV substance use disorders (abuse of, or dependence upon, alcohol, cannabis, sedatives, stimulants or opiates), with 7.9% of the population aged 18 years and older meeting such criteria in the past year. Approximately 6.7% of persons met criteria for a DSM-IV mood disorder within the past year, and 5.6% met criteria for a DSM-IV anxiety disorder. Using the “case” cut-off point for the psychosis screener, 0.99% of persons screened as likely cases of psychosis.

Among males, by far the most common disorders were DSM-IV substance use disorders, with almost one in eight males (11.5%) meeting criteria for a substance use disorder in the past year. Among females, the most common mental disorders were DSM-IV mood disorders, with one in eleven (9%) meeting such criteria in the past year.
5.3.2 Substance Use

Figure 5.2 shows the prevalence of substance use according to gender. The most commonly used substance reported by both males and females was alcohol, with around 84% of males and 64% of females reporting drinking at least 12 standard drinks of alcohol within the past 12 months. Tobacco was the next most commonly used substance, with around one in four males and females reporting current tobacco use (23% of females, 27% of males).

Cannabis was the next most frequently reported substance used, with 10.1% of males and 4.2% of females reporting use more than 5 times within the past year. The use of other drugs – sedatives, stimulants or opiates – was reported by smaller proportions: 3.4% of females and 3.8% of males.
5.3.3 Substance use disorders

Figure 5.3 shows the prevalence of the different substance use disorders according to gender. The prevalence of substance use disorders was distributed similarly to the prevalence of substance use. Among both males and females, by far the most common substance use disorder in the Australian adult population was DSM-IV alcohol dependence, with 6.1% of males and 2.3% of females meeting such criteria. The prevalence of alcohol abuse and cannabis dependence was similar. Among males, the prevalence was 2.9% for alcohol abuse and 2.3% for cannabis dependence; for females, it was 0.9% and 0.7% respectively. Cannabis use disorders were the most prevalent substance use disorders after alcohol use disorders.

Smaller proportions (less than 1% for both males and females) met criteria for abuse of or dependence upon the other substances assessed in the survey (sedatives, stimulants and opiates). While the estimates for these substance use disorders were small (and therefore a relatively large band of error may surround the prevalence estimates), there did not appear to be a significantly higher rate of these disorders among males than females, as was seen for cannabis and alcohol use disorders.
5.3.3.1 **ALCOHOL**

A number of demographic characteristics were significantly related to alcohol use (details of all prevalence estimates and significance tests can be found in Appendix D). Males were much more likely than females to report the use of alcohol (74% vs. 61%), and to meet criteria for alcohol abuse or dependence (9% vs. 3.2%).

There was also a pronounced age-related pattern of involvement with alcohol. Those aged 18-24 years were most likely to meet criteria for alcohol abuse or dependence (5.2% and 9.3% respectively), with the prevalence decreasing among older groups, such that only 0.8% of those aged 75 years and over met criteria for either alcohol abuse or dependence.

Education level was related to alcohol involvement. Persons who had completed secondary education or higher were more likely than those with less education to meet criteria for DSM-IV alcohol dependence within the past 12 months (5.3% and 4.2%, compared to 3.6%). Those with less than secondary education were more likely to report not having used alcohol within the past 12 months (34.9%, vs. 26.7% and 20.8% of those with...
secondary and postsecondary education, respectively).

The unemployed were much more likely to meet criteria for alcohol dependence (10.2%) or abuse (4.6%) within the past year than those who were employed or not in the labour force.

Marital status was strongly associated with the extent of involvement with alcohol use. Those who had never married were most likely to meet criteria for alcohol abuse (4.3%) or dependence (9.3%). Those who were widowed were most likely to report no alcohol use within the past 12 months (55%); while those who were currently married or in a de facto relationship were more likely to report alcohol use without meeting criteria for a use disorder. Those who were separated or divorced were more likely than those who were currently married or in a de facto relationship to have met criteria for alcohol dependence (5.8% vs. 2.5%).

Neuroticism showed a “J-curve”, with non-drinkers reporting higher levels than those who used alcohol without meeting criteria for a use disorder (M = 2.7 vs. 2.4, respectively). Those meeting criteria for alcohol abuse or dependence reported the highest levels of neuroticism (M = 3.3 and 4.7, respectively).

5.3.3.2 TOBACCO

Higher proportions of males than females reported being current (27% vs. 23%) or former (32% vs. 22%) smokers. Current tobacco use was more common among younger persons (34% of those aged 18-24 years vs. 8% of those aged 75 years and over), while older persons were most likely to have given up (37% of those aged 75 years and over, compared to 10% of those aged 18-24 years).

Current tobacco smoking was more common among those who had completed fewer years of education. Those who were unemployed were more likely to be current smokers than those who were employed or not in the labour force (48% vs. 24%), while employed persons were more likely to have given up smoking (27% vs. 19%).
Current tobacco users had higher average neuroticism scores than those who had never smoked (M = 3.1 vs. 2.4 respectively), with former smokers reporting levels that were more similar to never smokers (M = 2.6).

5.3.3.3 CANNABIS

Males were more likely than females to be more heavily involved with cannabis use: 3.6% of males met criteria for cannabis abuse or dependence, and another 6.5% reported cannabis use, compared to 0.9% and 3.3% of females. Age was negatively related to cannabis involvement, with younger persons much more likely to use cannabis (11.8% of 18-24 year olds) and to meet criteria for cannabis abuse or dependence (8% of 18-24 year olds) than older persons (2.3% and 0.5% of those over 35 years).

Cannabis use was more likely among the unemployed: 8.8% of unemployed persons met criteria for cannabis dependence, compared to 1.5% of those who were employed and 0.5% of those not in the labour force. Heavier involvement with cannabis use was also associated with a lower likelihood of being married or in a defacto relationship: 3.0% of those who were not married/defacto met criteria for cannabis dependence, compared to 0.7% who were married/defacto.

Education was marginally related to cannabis use (those with secondary education were slightly more likely than those with less education to be more heavily involved with cannabis use – average OR = 1.28, 95%CI 1.02, 1.60; see Appendix D).

Neuroticism was higher among those reporting heavier involvement with cannabis use. Those who did not report using cannabis reported the lowest levels (M = 2.5), with higher mean scores with increased cannabis involvement, such that cannabis dependent persons reported the highest levels (M = 4.1).
5.3.3.4 SEDATIVES, STIMULANTS AND OPIATES

As noted above, males were no more likely than females to report the use of sedatives, stimulants or opiates, nor to meet criteria for abuse of or dependence upon any of these drug types. The age-related patterns of involvement with these drugs were similar to those for alcohol, tobacco and cannabis. Younger persons were more likely to use these substances and to meet criteria for problematic use of them. Among those aged 18-24 years, 1.9% met criteria for abuse/dependence of sedatives, stimulants or opiates, compared to 1.5% of those who were 25-34 years, and 0.5% of those aged 35 years and above.

Educational attainment was not significantly related to involvement with these substances. However, those who were married or in a defacto relationship were significantly less likely to be involved in any way with the use of these substances: 1.7% of those who were not currently married/defacto met criteria for a use disorder, compared to 0.4% of those who were currently married/defacto. Unemployment was also related to involvement with these substances, with unemployed persons more likely to meet criteria for a use disorder than those who were employed or not in the labour force (1.9% vs. 0.9%, respectively). Neuroticism scores were significantly higher among persons reporting the use of sedatives, stimulants or opiates. Non-users reported the lowest levels of neuroticism (M = 2.5), with mean levels of users ranging from 4.1 (those who reported use without meeting criteria for a use disorder) to 6.1 (those meeting criteria for abuse).

5.3.4 MOOD DISORDERS

The prevalence of the DSM-IV mood disorders assessed in the NSMHWB according to gender is shown in Figure 5.4. By far the most prevalent mood disorder was major depression, with 6.3% of the population meeting such criteria within the past 12 months (4.3% of males and 8.2% of females). Around 1.1% met criteria for dysthymia, and 0.1% met criteria for bipolar disorder.
In contrast to substance use disorders, females were more likely than males to meet criteria for a mood disorder (8.5% vs. 4.9%). The association between age and mood disorders also differed slightly from that observed for the substance use disorders. There was a less marked decline in prevalence with age. The prevalence of mood disorders was similar among those aged 18 to 54 years – between 7.6% (25 to 34 years) and 8% (35 to 44 years) – with the prevalence declining rapidly thereafter. Only 1% of those aged over 75 years had met criteria for a mood disorder within the past year.

The level of education completed was unrelated to the prevalence of mood disorders. Marital status, however, was significantly related to mood disorders, with those who were not currently married or in a de facto relationship having higher rates of mood disorders (9.1% vs. 5.4% of those who were married/de facto). Unemployed persons (12%) were also more likely than those who were working or not in the labour force (6.5%) to have met criteria for a mood disorder.

Levels of neuroticism were higher among those meeting criteria for a mood disorder: the mean of those without a mood disorder was 2.4, compared to a mean score of 5.9 for those who did have a mood disorder.
5.3.5 Anxiety Disorders

Figure 5.5 shows the prevalence of the DSM-IV anxiety disorders assessed in the NSMHWB according to gender. The most prevalent anxiety disorder was generalised anxiety disorder (GAD), with 2.6% of persons meeting such criteria within the past year (approximately 2.2% of males and 2.9% of females). Approximately 1.6% of persons met criteria for panic/agoraphobia, while 1.3% of persons met criteria for post-traumatic stress disorder (PTSD) or social phobia. The least prevalent anxiety disorder was obsessive-compulsive disorder, with 0.7% of persons meeting criteria for this disorder within the past year.

The patterns in the Australian population observed for mood disorders were generally the same for anxiety disorders. Anxiety disorders were significantly more common among females than males (6.8% vs. 4.4%). This was particularly the case for panic/agoraphobia. Anxiety disorders were also more common among older persons, although again the decline with age was less marked than was observed for substance use disorders. Among 18 to 24 year olds, the prevalence rate was 5.9%, compared to rates of around 7% for those aged 25 to 34 years, 35 to 44 years, and 45 to 55 years (see Appendix D). The rates of anxiety disorders declined among older groups: 3.9% of 55 to 64 years olds met criteria for an anxiety disorder, 2% of those aged 65 to 74 years, and 1.2% of those aged over 75 years.

Figure 5.5: Weighted prevalence of DSM-IV anxiety disorders according to gender

Note: PTSD = post-traumatic stress disorder; GAD = generalised anxiety disorder; OCD = obsessive-compulsive disorder.
Marital status and employment were both significantly related to the prevalence of anxiety disorders. Those who were not married or in a defacto relationship were more likely than those who were in such a relationship to meet criteria for an anxiety disorder (7.4% vs. 4.7%, respectively). Unemployed persons were also much more likely to have met criteria for an anxiety disorder, with 13% meeting such criteria, compared to 5.3% of those who were working or not in the labour force.

Education level was not significantly related to the likelihood of meeting criteria for an anxiety disorder. Around 6% of those with less than secondary education, 5.2% of those who had completed secondary education, and 5.5% of those who had postsecondary education met criteria for an anxiety disorder within the past year.

Neuroticism was strongly related to the presence of an anxiety disorder. Among those who met such criteria, the mean neuroticism score was 6.6, compared to a mean score of 2.4 among those who did not meet such criteria.

**5.3.6 Psychosis**

Similar proportions of males and females screened positively for psychosis (0.9% and 1% respectively). The prevalence of likely cases of psychosis declined rapidly after the age of 44 years. Among those aged between 18 years and 45 years, the prevalence was around 1.4%. Among those aged 45 to 54 years, this proportion dropped to 0.8%, with 0.3% or less of those aged 55 years and over screening positively for psychosis.

Marital status and employment status were both significantly related to psychosis: those who were neither married nor in a defacto relationship were more likely to have screened positively for psychosis than those who were married/defacto (1.6% vs. 0.6%). Those who were unemployed (3.3%) were more likely than those who were working or not in the labour force (0.8%) to screen positively for psychosis. Neuroticism was significantly related to screening positively for psychosis. Those who screened positively had a mean score of 6.0, compared to a mean score of 2.6 among those who did not screen positively for psychosis.
5.4 DISCUSSION

The NSMHWB provides the first estimates of the prevalence of mental disorders in the Australian general population. It represents a significant advance in the knowledge of the epidemiology of mental disorders among Australian adults.

DSM-IV mental disorders were relatively common among Australian adults. The most prevalent mental disorders among Australian adults were DSM-IV substance use disorders, with 8% meeting such criteria in the past year. The most prevalent substance use disorders among Australian adults were alcohol abuse and dependence, and cannabis dependence. Around 7% of adults met criteria for a DSM-IV mood disorder within the past year (the most common of which was depression), and around 6% met criteria for an anxiety disorder. The estimated prevalence of psychosis was 0.9%.

The pattern of mental disorders that was produced from the NSMHWB was similar to those produced by the major US epidemiological surveys, the ECA and the NCS (Kessler et al., 1994; Robins & Regier, 1991). However, the prevalence estimates for the three major classes of disorder produced in the NSMHWB appeared to be slightly lower. For example, in the NCS, 17% of adults aged 15 to 54 years were estimated to have met criteria for an anxiety disorder within the past year (around 12% of males and 23% of females) (Kessler et al., 1994). This may have been due to several differences between the surveys. First, there were differences in the diagnostic systems upon which the different surveys were based (the ECA used DSM-III, the NCS used DSM-III-R, while the NSMHWB used DSM-IV). Second, it may be in part due to differences in age of the samples, particularly with respect to the NCS, which only included persons aged 15 to 54 years, compared to 18 to 85 years in the NSMHWB; given the strong decline in prevalence of substance use disorders and other mental disorders with age, the higher prevalence estimates of the NCS may not be surprising. Third, there were differences in the disorders included for assessment in the different surveys. For example, specific phobias were not assessed in the NSMHWB; the NCS estimated that around 4% of males and 13% of females aged 15 to 54 years had met criteria for a simple phobia within the past 12 months (Kessler et al., 1994).
It is likely that, had such disorders been assessed in the NSMHWB, the overall prevalence of anxiety disorders (and therefore of all mental disorders) would have been higher. Finally, given discussion of the validity of instruments used in field assessments of mental disorders (Andrews & Peters, 1998; Brugha et al., 1999; Regier et al., 1998; Wittchen, 1994), it may be that differences in estimates of the prevalence of mental disorders resulted from developments in the survey instruments used in each survey, and with problems with each instrument. However, the pattern of disorders was consistent across all surveys (Kessler et al., 1994; Robins & Regier, 1991). The correlates of disorders were also similar across the surveys. All mental disorders declined in prevalence with age; males were more likely to have met criteria for substance use disorders, and females were more likely to have met criteria for mood and anxiety disorders.

5.4.1 Strengths

The NSMHWB was the first study of mental health involving a representative sample of Australian adults. It used a structured diagnostic interview developed using an international collaborative process, and which has been shown to be highly reliable and to have good validity when compared with other methods of assessing mental disorders. It produced reliable estimates of the most common mental disorders, specifically, substance use disorders, mood disorders and anxiety disorders. The estimates were weighted in order to ensure they were representative of persons across the country. The NSMHWB is therefore a major advance in the knowledge of the mental health of the Australian general population.

The NSMHWB was shown to be highly acceptable to participants. Very few who began the interview did not complete it, and the response rate was similar to those of previous general population surveys. The pattern of estimates was consistent with previous general population studies, particularly the NCS and the ECA.
5.4.2 LIMITATIONS

There were some limitations of the NSMHWB. First, estimates of the less common mental disorders may not be highly reliable, simply because the sample size of 10,641 could not provide highly reliable estimates of less common disorders.

Second, it is difficult to make reliable estimates of the prevalence of disorders in some sections of the Australian community. These include Aboriginal and Torres Strait Islander populations and specific ethnic groups of non-English speaking backgrounds. Although they were represented in proportion to their numbers in the population, there were too few participants in these groups identified in the NSMHWB to provide useful estimates. Third, the prevalence estimates of mental disorders among older persons may not be highly reliable, because mental disorders are less common among this group (Robins & Regier, 1991).

Fourth, the non-response rate (22%) may have been a source of error in the estimates. The NCS involved extensive efforts to re-contact and interview those who initially refused to participate in the survey (Kessler, 1994a), and the results suggested that the rate of disorders among this group was higher than among those who initially agreed to be interviewed. This may mean that the rates of disorders produced by the NSMHWB are underestimates.

Finally, the NSMHWB was explicitly designed as a general population interview of persons in private dwellings; it did not include those in hostels, prison, hospitals, college, armed services, prisons, or those with no fixed address. However, the NSMHWB included a Low Prevalence Study (LPS) study of persons with psychotic disorders who were in contact with health services in a number of cities (Jablensky et al., 2000), which assessed persons using a structured diagnostic interview, and provides a means of assessing the validity of the findings from the NSMHWB with respect to likely cases of psychosis. Other populations may be better assessed using methods such as censuses in prisons (Butler, 1997) or targeted sampling of groups such as homeless persons (Buhrich, Hodder, & Teesson, 2000a; Buhrich, Hodder, & Teesson, 2000b; Teesson, Hodder, & Buhrich, 2000).
5.4.3 CORRELATES

In this Chapter, relationships were examined between demographic and personality variables and substance use and the mental disorders examined here (see Appendix D for details of the analyses). This was done in order to identify any variables having common relationships with both substance involvement and with mood and anxiety disorders, and possible cases of psychosis. These analyses found that there were similar relationships between substance use, anxiety and mood disorders, and psychosis “caseness” and most of the variables considered in this Chapter. Table 5.2 shows the pattern of relationships that was found across the substance use and mental disorders examined.

Table 5.2: Associations between demographic and personality variables, and substance use and mental disorders

<table>
<thead>
<tr>
<th></th>
<th>Gender¹</th>
<th>Age</th>
<th>Education</th>
<th>Employment</th>
<th>Relationship</th>
<th>Neuroticism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>+</td>
<td>-</td>
<td>+²</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Other drug use</td>
<td>0</td>
<td>-</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Mood disorders</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Psychosis</td>
<td>0</td>
<td>-</td>
<td>0</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

Note: 1. reference category female.
2. those with secondary education were more likely to be more heavily involved with cannabis than those with less than secondary education; there was no association between postsecondary education and cannabis involvement.

+    = a significant positive association between the level of the correlate and the substance use or mental health variables.
-    = a significant negative association.
0    = no significant association.
Age was negatively related to all outcomes, with younger persons more likely to use substances, more likely to meet criteria for a mood or an anxiety disorder, and more likely to screen positively for psychosis.

Unemployed persons were more likely to report greater levels of involvement with all substances examined here, to meet criteria for mood disorders, anxiety disorders and to screen positively for psychosis. Heavier involvement with substance use, and meeting criteria for other mental health problems were all associated with a lower likelihood of being married or in a defacto relationship.

Neuroticism was significantly higher among all groups of persons reporting mental health problems and greater involvement with substance use. This is consistent with previous literature that has identified neuroticism as a risk factor for anxiety and mood disorders, and clinical research that has found neuroticism to be higher among persons in treatment for problematic substance use.

Education was not significantly related to anxiety or mood disorders, or to the likelihood of screening positively for psychosis. It was related to involvement with alcohol, with more educated persons more likely to be more involved with alcohol use. By contrast, tobacco users were less well educated. The relationship between cannabis use and education was marginally significant, while there was no significant relationship between educational attainment and other substance use.

Gender was related in different ways to substance use and to other indicators of mental health. Males were more likely than females to meet criteria for substance use disorders, whereas females were more likely to meet criteria for mood and anxiety disorders. There was no significant relationship between gender and psychosis “caseness”.

The relationships between these variables and the substance use/mental health variables observed here are consistent with previous research on the epidemiology and correlates of substance use and mental health (for detail, see Chapters Two and Three). Because most of the variables examined showed similar relationships between alcohol, tobacco and cannabis involvement, other substance involvement, and mental health, it is possible that these
common relationships might account for any bivariate associations observed between alcohol, tobacco and cannabis involvement, and these other variables. This possibility is explored in later Chapters.
5.5 CONCLUSIONS

The NSMHWB provided the first estimates of the prevalence of mental disorders in the general Australian population. It represents a significant advance in the knowledge available about the mental health of Australian adults. The NSMHWB was consistent with the findings of epidemiological studies conducted in other countries in finding that mental disorders are prevalent in the general population. Given that mental disorders are commonly experienced, it is important to have a good knowledge of their distribution and related characteristics, which will have implications for so many adults.

There were notable similarities in the sociodemographic correlates of the disorders examined here (substance use disorders, mood disorders, anxiety disorders and screening positively for psychosis). Disorders were all more common among: younger persons; persons who were not married or in a de facto relationship; unemployed persons; and those who had higher levels of neuroticism.

These results suggest two possibilities: that comorbidity might be expected since similar groups are likely to have these disorders; and that these factors might partly explain why these disorders co-occur in the general population.

As noted in Chapter Four, it is only by examining general population patterns of association between different mental disorders that we can accurately examine the degree of comorbidity between mental disorders, and start to explore why such comorbidity might exist. In the following four Chapters, data from the NSMHWB will be used to begin this process. Specifically, Chapter Six examines patterns of comorbidity of alcohol use, Chapter Seven examines patterns of comorbidity of tobacco use, Chapter Eight examines patterns of comorbidity of cannabis use, and Chapter Nine compares the comorbidity patterns across these three drug types.
6 **Patterns of Comorbidity Associated with Alcohol Use**

As Chapter Two outlined, and as was shown in Chapter Five, alcohol is the most commonly used psychoactive substance in the general population. The finding that alcohol use disorders are among the most common mental disorders in the Australian adult population (Chapter Five) also confirms that it is important to examine patterns of comorbidity with mental health according to level of involvement with alcohol use.

Chapter Four outlined some of the reasons why comorbidity might occur, and the fact that it is important to use general population samples to examine patterns of comorbidity, since clinical samples are affected by significant sources of bias that will affect the patterns observed. The present Chapter outlines epidemiological research on the relationship between alcohol use and mental health. A number of key research issues are identified and are addressed using data from the NSMHWB.

### 6.1.1 Alcohol Use and Other Substance Use

Clinical research (reviewed in Chapter Four) has revealed high rates of comorbidity between problematic alcohol use and other substance use and substance use disorders. As noted in Chapter Four, however, clinical research cannot be relied upon to provide an indication of the relationships in the general community.

Epidemiological research, predominantly in the US, has found that persons who meet criteria for alcohol use disorders are likely to also meet criteria for other substance use disorders. The ECA found that those with alcohol abuse or dependence were significantly more likely to have used other drugs, and to meet criteria for another drug use disorder.

---

1 Study reported in L. Degenhardt & W. Hall (submitted), Patterns of comorbidity between alcohol use and other substance use and disorders in the Australian population, *Drug and Alcohol Review*.

See also Appendix L for peer reviewed papers and conference presentations arising from this thesis.
(Helzer et al., 1991). Slightly more than one in five persons (22%) who met lifetime criteria for alcohol abuse or dependence also met criteria for another substance use disorder, with the majority of such persons meeting criteria for a cannabis use disorder (Helzer et al., 1991).

Similar results were found in the NCS. Those who met criteria for alcohol abuse or dependence at some time in their lives were significantly more likely to meet criteria for other drug abuse or dependence. Drug use disorders were reported among approximately one third of persons with lifetime alcohol abuse (30% of men, and 33% of women) and in just under half of persons who met lifetime criteria for alcohol dependence (41% of men and 47% of women) (Kessler et al., 1997b).

These patterns of comorbidity between alcohol use disorders and other substance use disorders were also found in the NLAES (Grant, 1997). Finally, a study that used data from US, Canadian, French, Mexican and Dutch epidemiological surveys found an association between alcohol use problems and other substance use problems in all study sites (Merikangas et al., 1998a).

### 6.1.2 Alcohol Use and Mood Disorders

The patterns found in clinical research examining relationships between mood disorders and problematic alcohol use (Chapter Four) have been corroborated by the findings of the major US epidemiological studies. The ECA found that persons who met lifetime criteria for DSM-III alcohol abuse/dependence were more likely to meet criteria for a mood disorder such as mania (5.4 times more likely), major depression (1.6 times) and dysthymia (1.7 times) (Helzer et al., 1991). Similar patterns were found in the NCS (Kessler, 1995; Kessler et al., 1997b).

The UK National Psychiatric Morbidity Survey assessed “neurotic and depressive” disorders using the Clinical Interview Schedule Revised (CIS-R) (Farrell et al., 1998). Persons who were classified as “neurotic” were more likely to be regular drinkers and more likely to be alcohol dependent than those who were not so classified (Farrell et al., 1998).
The study using data from US, Canadian, French, Mexican and Dutch epidemiological surveys also found an association between lifetime alcohol use problems and other substance use problems in all study sites (Merikangas et al., 1998a). A study has also been carried out in which four epidemiological studies (the ECA, the NCS, the Epidemiologic Study of Puerto Rico and the Zurich Cohort Study of Young Adults) were compared for the relationship between alcohol use disorders and mood disorders (Swendsen et al., 1998). In all samples, the presence of a lifetime alcohol use disorder predicted higher odds of meeting criteria for a mood disorder (odds ratios of between 2.3 and 3.8), after accounting for age, gender and education.

6.1.3 Alcohol Use and Anxiety Disorders

Epidemiological research has also found that the association between alcohol use disorders and anxiety disorders observed in clinical settings also exists in general population samples. In the ECA, there were elevated rates of all DSM-III anxiety disorders assessed (panic disorder, obsessive-compulsive disorder, and phobic disorder) among persons meeting lifetime criteria for DSM-III alcohol abuse or dependence (Helzer et al., 1991). The prevalence of lifetime DSM-III panic disorder was 2.6 times higher among persons meeting lifetime criteria for DSM-III alcohol abuse or dependence (Helzer et al., 1991). Phobic disorders were 1.4 times more prevalent among persons meeting lifetime criteria for alcohol abuse or dependence, while obsessive-compulsive disorder was two times more prevalent (Helzer et al., 1991).

These associations were also observed among the anxiety disorders assessed in the NCS (Kessler, 1995; Kessler et al., 1997b). The UK’s National Psychiatric Morbidity Survey, as mentioned above, found that persons with high rates of neurotic symptoms were more likely to be problematic alcohol users (Farrell et al., 1998).

The comparative study cited above (Merikangas et al., 1998a) found an association between lifetime alcohol use disorders and anxiety disorders in epidemiological samples in the US, Canada, France, Mexico and the Netherlands (Merikangas et al., 1998a). The study by Swendsen and colleagues also cited above (Swendsen et al., 1998) found that in all four
samples, the presence of a lifetime alcohol use disorder predicted higher odds of meeting criteria for an anxiety disorder (odds ratios of between 2.1 and 2.5) after accounting for age, gender and education.

### 6.1.4 Alcohol Use and Psychosis

The ECA estimated that the rate of schizophrenia was 3.4 times higher among those with a lifetime DSM-III diagnosis of alcohol abuse or dependence (Helzer et al., 1991). There has also been an analysis using ECA data of the relationship between drug use and a “self-reported psychotic experience” in persons under 50 years (Tien & Anthony, 1990). In this study, a “case” was a person who reported experiencing at least one psychotic symptom (from 12 Diagnostic Interview Schedule (DIS) items) within a follow up year. A diagnosis of lifetime DSM-III alcohol abuse/dependence predicted an eight-fold increased risk of reporting at least one psychotic symptom in the follow-up period (RR = 7.9, 95%CI 2.0, 31.4) (Tien & Anthony, 1990). This was after adjusting for baseline psychopathology (mood, anxiety and personality disorders) and sociodemographic variables.

The UK National Psychiatric Morbidity Survey found that persons in institutions with schizophrenia, delusional disorders or affective psychoses did not appear to have higher rates of heavy or dependent alcohol use, but this may have been due to their institutionalisation. In contrast, homeless persons (who were likely to have had psychotic disorders) had higher rates than the general population of heavy and dependent alcohol use (Farrell et al., 1998).

### 6.1.5 Research Issues

#### 6.1.5.1 Australian Patterns of Comorbidity

There has been no previous examination of alcohol use disorders in the Australian general population using a standardised diagnostic interview. While other epidemiological research, the majority of which has been carried out in the US, provides an indication of
the patterns one might expect in the Australian population, it may be inappropriate to assume that the relationships are the same (Henderson et al., 2000).

6.1.5.2 MEASUREMENT OF ALCOHOL USE

As noted above, previous epidemiological surveys have suggested that problematic alcohol use (as defined by diagnostic criteria for alcohol abuse/dependence) is associated with higher rates of other mental health problems. However, there has been less examination of the mental health characteristics of persons who drink alcohol without meeting criteria for an alcohol use disorder. This is important because there is recent evidence that there may not be a linear relationship between alcohol involvement and physical illness (Ashley et al., 1997; Chyou et al., 1997; Hanna, Chou, & Grant, 1997; Keil, Chambless, Doring, Filipiak, & Stieber, 1997; Renaud, Gueguen, Schenker, & d'Houtaud, 1998; Thun, Peto, Lopez, & al., 1997).

Some researchers have reported a “J-shaped” relationship between alcohol use and physical health. Light drinkers have been reported to have fewer medical problems, particularly cardiovascular disease (including mortality from this disease), than both non-drinkers and heavy drinkers (Chyou et al., 1997; Thun et al., 1997). This finding has led to suggestions that moderate alcohol use may have a protective effect upon the cardiovascular system. This finding has been disputed, however, with others asserting that this apparent curve may be due to the confounding effects of the different characteristics of these groups, such as socio-economic status (SES), employment, education, age and gender (Fillmore et al., 1998a; Fillmore et al., 1998b; Hanna et al., 1997; Leino et al., 1998).

Research has provided suggestive evidence that a similar “J-curve” might exist for alcohol use and mental health (Baum-Baicker, 1985; Chick, 1999b). One study of a sample of young British adults reported that heavy alcohol use and no alcohol use were bivariately associated with greater psychological distress than moderate alcohol use (Power, Rodgers, & Hope, 1998). A review of studies (most of which were conducted in the US and usually community-based) found that 11 of 13 studies in which the subjective well-being of light drinkers was compared with that of abstainers found that light drinkers reported better
subjective health, as assessed by the GHQ, treatment seeking, and other indicators (Chick, 1999b). Some of these studies controlled for the effects of demographic variables (Leifman, Kuhlhorn, Allebeck, Andreasson, & Romelsjo, 1995; Liptin, 1994; Lyons, Lo, Monghan, & Littlepage, 1995; Poikolainen & Vartiainen, 1999), and some adjusted for family psychiatric history (Leifman et al., 1995) and physical disability (Lyons et al., 1995). More recently, a study of adults in Canberra, Australia, reported that non-drinkers had greater levels of psychological distress than moderate drinkers, who had the highest levels of psychological well-being of all the alcohol user groups (Rodgers et al., 2000).

It is of some interest to examine whether this J-curve association exists for mental disorders based on diagnostic criteria, such as mood disorders and anxiety disorders. Notably, while previous epidemiological research has looked at the likelihood of comorbidity among persons who report alcohol use (e.g. Merikangas et al., 1998a), such examinations have included those meeting criteria for abuse and dependence in this group, so it is difficult to know what the prevalence of these disorders is in those who use alcohol but who do not have an alcohol use disorder. It is also of interest to see if any association remains after controlling for major demographic characteristics, which some have argued explains the association observed for physical health (Fillmore et al., 1998a; Fillmore et al., 1998b; Hanna et al., 1997; Leino et al., 1998). The present study examines these issues.

6.1.5.3 What is the cause of any association?

As noted in Chapter Four, there are a number of reasons why disorders may co-occur (Angold et al., 1999; Caron & Rutter, 1991; Kessler, 1995). First, there may be a causal relationship between them, with the presence of one disorder making another more likely to develop. Second, an indirect causal relationship may exist, where one disorder affects a third variable, which increases the risk of the second disorder. Third, it may be that there is no causal relationship between two variables, but rather, that common or associated risk factors are shared (Caron & Rutter, 1991; Kessler, 1995).

The present study will accordingly examine some common factors that could explain the co-occurrence of alcohol use, other substance use, and mental disorders. These factors
were examined in Chapter Five where it was found that a number of different characteristics were similarly related to alcohol use, other substance use, mood disorders, anxiety disorders, and psychosis. These potential common factors include demographic characteristics of users, the personality trait of neuroticism, and patterns of other drug use.
6.2 AIMS

The present study examines patterns of 12-month comorbidity between alcohol use, abuse and dependence, and both substance use and mental disorders using data from the Australian National Survey of Mental Health and Well-Being (NSMHWB).

The following questions are addressed:

1. What are the patterns of comorbidity between the level of involvement with alcohol use (no use, use without meeting criteria for a use disorder, abuse and dependence) and the following:
   a. Tobacco, cannabis and other substance use;
   b. DSM-IV cannabis and other substance use disorders;
   c. DSM-IV mood disorders;
   d. DSM-IV anxiety disorders;
   e. Psychosis?

2. Are these associations (if any) explained by differences between the groups in demographic characteristics, neuroticism or other substance use?

3. Does the presence of a comorbid disorder affect the likelihood of treatment seeking among alcohol users?
6.3 Method

For details of the design and conduct of the NSMHWB, see Chapter Five.

6.3.1 Alcohol involvement

A four-level variable was created: no alcohol use in the past 12 months, alcohol use without meeting criteria for a DSM-IV disorder, meeting criteria for DSM-IV alcohol abuse, and meeting criteria for DSM-IV alcohol dependence.

6.3.2 Outcome variables

1. Other substance use
   • Tobacco: Persons who reported current daily tobacco use were coded as regular tobacco users.
   • Cannabis: Persons were coded as using cannabis if they reported using cannabis more than five times within the past year.
   • Other drugs: Persons were coded as using other drugs if they reported using sedatives, stimulants or opiates more than five times within the past year.

2. Other substance abuse/dependence
   • Cannabis: Persons were coded as meeting criteria for a cannabis use disorder if they met criteria for DSM-IV cannabis abuse or dependence.
   • Other drugs: Persons were coded as meeting criteria for an "other drug use disorder" if they met criteria for DSM-IV sedative, stimulant or opiate abuse or dependence.

3. Anxiety and mood disorders
   • Anxiety disorders: Persons were coded as meeting criteria for a DSM-IV anxiety disorder if they met criteria for one or more of the following: panic disorder, agoraphobia, social
phobia, generalised anxiety disorder, obsessive-compulsive disorder, or post-traumatic stress disorder.

- Mood disorders: Persons were coded as meeting criteria for a DSM-IV mood disorder if they met criteria for major depressive disorder, dysthymia, bipolar I disorder, or bipolar II disorder.

### 4. Psychosis
Persons were considered to be a psychosis “case” if they scored three or more on the psychosis screener (see Chapter Five for details).

### 6.3.3 Covariates

Several variables were considered which may have been related to both tobacco use and to other substance use and mental health. More details on these variables, and their relationships with alcohol use and mental health, are provided in Chapter Five.

#### 1. Social and demographic characteristics
- Gender;
- Age;
- Education;
- Relationship status;
- Employment status.

#### 2. Other substance use
These variables were only included in multiple regressions in which anxiety disorders, mood disorders and psychosis case status were the outcome variables.
- Regular tobacco use: daily tobacco use;
- Cannabis use: the use of cannabis more than five times within the past 12 months;
- Other drug use: the use of sedatives, stimulants or opiates more than five times within the past 12 months.
3. Personality
Scores on the neuroticism scale of the EPQ were included in the present analyses. Persons scoring highly on measures of neuroticism have been characterised as moody, anxious and irritable (Eysenck & Eysenck, 1991). Chapter Five and Appendix C give more details on this scale.

6.3.4 Treatment Seeking
A person was coded as having sought help for a mental health problem if they reported using any of the following for a mental health problem: admission to a hospital, psychiatric ward, drug and alcohol unit, or other hospital for a mental health problem; or having seen a general practitioner, psychologist, psychiatrist, social worker, mental health team, counsellor, nurse, ambulance officer, surgeon, physician, pathologist, radiologist, chemist, or other health professional.

6.3.5 Data Analysis
Weighted estimates of the 12-month prevalence and comorbidity of DSM-IV alcohol use disorders are presented in this Chapter. More detail of weighting and regression approaches is provided in Chapter Five. Prevalence estimates and their standard errors were calculated using SUDAAN Version 7.5.3 (Research Triangle Institute, 1997).

Bivariate associations between alcohol use and outcome variables were examined using logistic regression. In all regressions, alcohol involvement was dummy coded, with each level of alcohol involvement (drinking without disorder, DSM-IV abuse, DSM-IV dependence) compared against non-drinkers as the reference category. Generation of odds ratios (OR) and 95% confidence intervals (95%CI) for bivariate associations, and multiple regression analyses, were carried out using STATA (STATA Corporation, 1997; STATA Corporation, 2001).
Stepwise multiple regressions were performed during which the following variables were added at each step:

1. Social and demographic characteristics;
2. Other substance use (when the outcome variables were mood or anxiety disorders, and psychosis “caseness”);
3. Neuroticism.

This Chapter only presents results from the first and final models. The detailed results of intermediate regression analyses are provided in Appendix E.
6.4 RESULTS

Approximately one quarter of persons (27%) had not consumed 12 or more standard drinks of alcohol in the past year. Two thirds (68%) had used alcohol without meeting criteria for a DSM-IV use disorder, while 1.9% met criteria for alcohol abuse and 4.1% met criteria for dependence (for more details of prevalence estimates see Chapter Five and Appendix D).

6.4.1 OTHER SUBSTANCE USE AND SUBSTANCE USE DISORDERS

Those who did not drink alcohol were least likely to report the use of other drug types in the past year. This applied to regular tobacco use, cannabis use, and illicit drug use (Table 6.1). Among those who drank alcohol without meeting criteria for a use disorder, one quarter (24%) were regular tobacco users, 7% reported cannabis use, and 3% reported using other drugs. These proportions increased with increasing involvement with alcohol. Among those who were alcohol dependent, half (51%) were regular tobacco users, one third (31%) were cannabis users, and 15% reported using other drugs more than five times in the past year (Table 6.1). Those who reported alcohol use without meeting criteria for a use disorder, and those who met criteria for alcohol abuse, had rates of other substance use that were between these extremes.

Multiple regression analyses did not change these bivariate patterns substantially (see Appendix E for details of analyses at intermediate steps). After adjusting for all other variables considered in multiple regressions, regular tobacco use remained significantly more common among drinkers than non-drinkers, with those who used alcohol remaining between 1.8 - 4.2 times more likely than non-drinkers to be current regular smokers (Table 6.1). Those who met criteria for DSM-IV alcohol abuse or dependence were also more likely than non-problematic drinkers to report regular tobacco use, as shown by the fact that the 95% confidence intervals for the adjusted odds ratios do not overlap (Table 6.1).
Cannabis use in the past 12 months also remained significantly more common in drinkers than non-drinkers (Table 6.1). The adjusted odds ratios increased among those with more problematic alcohol use (adjusted OR = 3.0 for non-problematic use; OR = 7.5 for abuse; OR = 9.0 for dependence), with those meeting criteria for alcohol abuse or dependence most likely to report cannabis use. Use of sedatives, stimulants or opiates within the past year also remained more likely among all alcohol users than non-users, with those who met criteria for DSM-IV alcohol abuse or dependence remaining most likely to use these other drugs (adjusted OR = 3.6 and 4.5, respectively).

Table 6.1: Weighted prevalence of substance use, unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95%CI) according to alcohol involvement

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>Regular tobacco use</th>
<th>Cannabis use</th>
<th>Other drug use</th>
</tr>
</thead>
<tbody>
<tr>
<td>% (SE)</td>
<td>Unadjusted OR</td>
<td>Unadjusted 95%CI</td>
<td>Adjusted OR1</td>
</tr>
<tr>
<td>No alcohol use</td>
<td>15.3 (0.9)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>23.9 (0.6)</td>
<td>1.72</td>
<td>1.54, 1.92</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>48.7 (8.6)</td>
<td>5.31</td>
<td>3.95, 7.24</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>51.0 (4.0)</td>
<td>5.75</td>
<td>4.66, 7.10</td>
</tr>
<tr>
<td>No alcohol use</td>
<td>1.9 (0.5)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>7.1 (0.4)</td>
<td>3.61</td>
<td>2.73, 4.76</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>27.3 (7.7)</td>
<td>17.57</td>
<td>11.53, 26.76</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>31.5 (2.9)</td>
<td>22.20</td>
<td>15.96, 30.88</td>
</tr>
<tr>
<td>No alcohol use</td>
<td>2.8 (0.4)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>3.0 (0.4)</td>
<td>1.23</td>
<td>0.94, 1.60</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>10.9 (2.8)</td>
<td>4.13</td>
<td>2.41, 7.10</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>15.3 (3.2)</td>
<td>7.26</td>
<td>5.15, 10.26</td>
</tr>
</tbody>
</table>

1. Adjusted for age, gender, educational attainment, relationship status, employment status and neuroticism
The associations observed for other substance use were also observed for DSM-IV cannabis and other substance use disorders (Table 6.2). Around one in 100 non-drinkers met criteria for a cannabis use disorder, with less than one percent meeting criteria for another drug use disorder. These proportions increased as involvement with alcohol increased, such that one in seven (15%) alcohol dependent persons met criteria for a cannabis use disorder (unadjusted OR = 19.3 compared to non-drinkers), and one in 14 (7%) met criteria for a sedative, stimulant or opiate use disorder (OR = 10.0; Table 6.2). Notably, alcohol use was not associated with other drug use disorders.

Table 6.2: Weighted prevalence, unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95%CI) of DSM-IV substance use disorders according to alcohol involvement

<table>
<thead>
<tr>
<th></th>
<th>Prevalence</th>
<th>OR</th>
<th>95%CI</th>
<th>Adjusted OR</th>
<th>95%CI</th>
<th>Adjusted 95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (SE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cannabis use disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol use</td>
<td>0.9 (0.2)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>1.8 (0.2)</td>
<td>1.87</td>
<td>1.22, 2.86</td>
<td>1.45</td>
<td>0.92, 2.27</td>
<td></td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>20.6 (3.6)</td>
<td>11.22</td>
<td>5.97, 21.11</td>
<td>3.52</td>
<td>1.79, 6.92</td>
<td></td>
</tr>
<tr>
<td></td>
<td>15.3 (2.7)</td>
<td>19.28</td>
<td>12.06, 30.88</td>
<td>5.81</td>
<td>3.50, 9.65</td>
<td></td>
</tr>
<tr>
<td><strong>Other drug use disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>0.7 (0.3)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
<td></td>
</tr>
<tr>
<td>Alcohol use</td>
<td>0.6 (0.1)</td>
<td>0.74</td>
<td>0.44, 1.24</td>
<td>0.90</td>
<td>0.52, 1.56</td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>2.2 (1.3)</td>
<td>2.90</td>
<td>0.99, 8.51</td>
<td>2.05</td>
<td>0.67, 6.27</td>
<td></td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>7.3 (2.3)</td>
<td>9.97</td>
<td>5.72, 17.39</td>
<td>4.76</td>
<td>2.57, 8.83</td>
<td></td>
</tr>
</tbody>
</table>

1. Adjusted for age, gender, educational attainment, relationship status, employment status and neuroticism
2. Caution should be taken in interpreting this estimate due to the large amount of error surrounding the estimate.

Table 6.2 also shows the odds ratios and their 95% confidence intervals produced after the final multiple logistic regression. These adjusted odds ratios control for the effects of demographic variables (age, gender, education, marital status, and employment status), and neuroticism. Appendix E shows additional statistics from these analyses.
Clearly, those who were problematic alcohol users were more likely than those who were not to also report using other substances problematically, even after adjusting for demographics and neuroticism. Those who met criteria for alcohol abuse or dependence remained significantly more likely than non-drinkers to also meet criteria for a cannabis use disorder (adjusted OR = 3.5 and 5.8, respectively). Those who met criteria for alcohol dependence remained more likely than non-drinkers to meet criteria for another drug use disorder. Thus, the association between alcohol use disorders and substance use disorders could not be explained by the common effects of demographic variables and neuroticism on each of these outcomes.

6.4.2 DSM-IV MOOD AND ANXIETY DISORDERS

Findings on comorbidity with mood and anxiety disorders are presented together since the pattern of relationships was found to be the same for both groups of disorders. Table 6.3 shows the prevalence of mood and anxiety disorders by level of involvement with alcohol. The prevalence of anxiety disorders was significantly lower for those who drank without having a use disorder (4.5%) than it was among those who did not drink alcohol (6.5%; OR = 0.8). Similarly, 7.3% of non-drinkers met criteria for a mood disorder, compared to 5.5% of those who drank without having a use disorder (OR = 0.8). Those who met criteria for DSM-IV alcohol abuse did not differ significantly from non-drinkers in the prevalence of either anxiety or mood disorders (Table 6.3).

The pattern was distinctly different for persons who met criteria for DSM-IV alcohol dependence: around one in five (20%) also met criteria for an anxiety disorder, and one in four (24%) also had a mood disorder. Persons meeting criteria for DSM-IV alcohol dependence were 4.5 times more likely than non-drinkers (95%CI: 3.5, 5.7) to have an anxiety disorder, and 4.4 times more likely than non-drinkers to have a mood disorder (95%CI: 3.4, 5.8).
Table 6.3: Weighted prevalence, unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95% CI) of DSM-IV mood and anxiety disorders according to alcohol involvement

<table>
<thead>
<tr>
<th></th>
<th>Prevalence</th>
<th>OR</th>
<th>95% CI</th>
<th>Adjusted OR</th>
<th>Adjusted 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (SE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Anxiety disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol use</td>
<td>6.5 (0.5)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>4.5 (0.4)</td>
<td>0.78</td>
<td>0.65, 0.93</td>
<td>1.01</td>
<td>0.81, 1.25</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>4.9 (1.9)</td>
<td>0.73</td>
<td>0.37, 1.45</td>
<td>0.49</td>
<td>0.23, 1.05</td>
</tr>
<tr>
<td></td>
<td>19.5 (2.7)</td>
<td>4.42</td>
<td>3.39, 5.76</td>
<td>1.83</td>
<td>1.30, 2.59</td>
</tr>
<tr>
<td><strong>Mood disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>7.3 (0.4)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>5.5 (0.3)</td>
<td>0.82</td>
<td>0.70, 0.97</td>
<td>0.99</td>
<td>0.82, 1.20</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>6.1 (2.0)</td>
<td>0.90</td>
<td>0.50, 1.60</td>
<td>0.64</td>
<td>0.34, 1.22</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>24.0 (4.0)</td>
<td>4.47</td>
<td>3.48, 5.74</td>
<td>1.99</td>
<td>1.46, 2.73</td>
</tr>
</tbody>
</table>

1. Adjusted for age, gender, educational attainment, relationship status, employment status, other substance use and neuroticism

These patterns in the prevalence of anxiety and mood disorders hence form a J-shaped curve in which those at the “extremities” of involvement in alcohol use, the “no use” and “dependent use” groups, had higher rates of anxiety and mood disorders than those with “intermediate” levels of involvement.

The adjusted odds ratios produced after controlling for demographics, neuroticism and other drug use are also displayed in Table 6.3. After adjusting for these other factors, there were no differences between non-drinkers and drinkers, or between non-drinkers and those who met criteria for DSM-IV alcohol abuse, in the likelihood of meeting criteria for a DSM-IV mood or anxiety disorder. The differences between non-problematic drinkers and non-drinkers did not remain after controlling for neuroticism (see Appendix E for results of the other multiple regression analyses).
In contrast, persons who met criteria for DSM-IV alcohol dependence were still significantly more likely than non-drinkers to meet criteria for a mood disorder (OR = 2.0) or an anxiety disorder (OR = 1.8) after adjusting for the other factors considered here. They were also more likely than drinkers and those who met criteria for alcohol abuse, to have such disorders (as indicated by the non-overlap between the 95% confidence intervals of respective the odds ratios).

6.4.3 PSYCHOSIS

The proportion of persons who screened positively for psychosis according to involvement with alcohol use is shown in Table 6.4. Slightly less than one percent of non-drinkers and drinkers screened positively for psychosis, and 1.8% of those meeting criteria for DSM-IV alcohol abuse screened positively. There were no significant differences between these groups (Table 6.4). Persons who met criteria for DSM-IV alcohol dependence were 6.4 times more likely than non-drinkers to screen positively for psychosis (4.3% vs. 0.7%, respectively).

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>OR</th>
<th>95% CI</th>
<th>Adjusted OR</th>
<th>Adjusted 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>No alcohol use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol use</td>
<td>0.7 (0.16)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>0.8 (0.14)</td>
<td>1.06</td>
<td>0.67, 1.68</td>
<td>1.21</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>1.8 (1.3)^2</td>
<td>2.55</td>
<td>0.88, 7.39</td>
<td>1.46</td>
</tr>
<tr>
<td></td>
<td>4.3 (1.3)</td>
<td>6.37</td>
<td>3.59, 11.34</td>
<td>1.76</td>
</tr>
</tbody>
</table>

1. Adjusted for age, gender, educational attainment, relationship status, employment status, other substance use, and neuroticism
2. Caution should be taken in interpreting this estimate due to the large amount of error surrounding the estimate.
This significant bivariate relationship did not remain after controlling for demographics, neuroticism and other drug use (Table 6.4). The relationship was significantly reduced after accounting for other substance use (OR 2.6; 95%CI 1.3, 5.0 – Appendix E); and the addition of neuroticism in the regression (adjusted odds ratios, Table 6.4) removed the association.

6.4.4 Treatment seeking

Table 6.5 shows the prevalence of treatment seeking for a mental health problem among those with alcohol abuse and dependence according to the presence of other mental health and substance use problems. It must be noted that a large amount of error surrounds some of the estimates, so caution must be taken in their interpretation. However, given this caveat, it appears that those who met criteria for alcohol dependence had only a small chance of having sought treatment for a mental health problem, unless they had a comorbid substance use disorder (sedatives, stimulants or opiates) or another mental disorder. The same pattern appeared to exist for persons with alcohol abuse, although the amount of error surrounding these estimates was proportionally much larger.

This suggests that persons with alcohol dependence who come to the attention of mental health services are more likely than alcohol dependent persons in the general population to have other mental disorders. This was shown to be the case: among those with alcohol dependence who had sought treatment for a mental health problem, 52.5% (SE 5.9%) met criteria for a mood disorder, 46.7% (SE 9.2%) met criteria for an anxiety disorder, 11.8% (SE 3.0%) met criteria for an other drug use\(^2\) disorder, and 8.7% screened positively for psychosis (SE 3.2%).

\(^2\) Sedative, stimulant or opiate use disorder
Table 6.5: Weighted prevalence of treatment seeking for a mental health problem by persons with alcohol use disorders, according to the presence of other disorders

<table>
<thead>
<tr>
<th></th>
<th>No mood disorder</th>
<th>Mood disorder</th>
<th>No anxiety disorder</th>
<th>Anxiety disorder</th>
<th>No psychosis case</th>
<th>Psychosis “case”</th>
<th>No cannabis use disorder</th>
<th>Cannabis use disorder</th>
<th>No other drug use disorder</th>
<th>Other drug use disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol abuse</td>
<td>9.1 (3.3)</td>
<td>51.8 (17.3)*</td>
<td>10.2 (3.5)</td>
<td>41.5 (16.6)</td>
<td>11.0 (3.2)</td>
<td>51.3 (54.3)*</td>
<td>12.7 (3.8)</td>
<td>3.5 (4.0)*</td>
<td>11.3 (3.2)</td>
<td>31.1 (34.6)*</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>18.5 (23)</td>
<td>64.6 (7.8)</td>
<td>19.6 (37)</td>
<td>70.8 (8.4)</td>
<td>28.2 (24)</td>
<td>60.3 (20.7)*</td>
<td>29.7 (3.3)</td>
<td>29.0 (14.3)*</td>
<td>28.1 (2.4)</td>
<td>48.1 (10.3)</td>
</tr>
</tbody>
</table>

* These estimates must be considered with caution given the large amount of error surrounding the estimates.
6.5 Discussion

Alcohol use is the most common form of substance use, and alcohol use disorders are among the most common disorders in the Australian adult population. Bivariate analyses revealed that there were two distinct patterns of comorbidity between alcohol use and other mental disorders. First, other substance use problems (homotypic comorbidity) followed a linear pattern. They were more likely among persons who were alcohol users, and these problems were more likely in persons who met criteria for alcohol abuse or dependence.

In contrast, other mental health problems (heterotypic comorbidity) did not follow a linear pattern: non-drinkers had higher rates of DSM-IV mood and anxiety disorders than non-problematic drinkers, whereas dependent drinkers reported the highest rates overall. Only alcohol dependence was associated with a higher rate (compared to non-drinkers) of psychosis as measured by the screening questionnaire.

6.5.1 Alcohol Use and Other Substance Use and Substance Use Disorders

Persons meeting criteria for DSM-IV alcohol dependence were most likely to have a range of other substance use problems, including regular tobacco use (51%), DSM-IV cannabis use disorders (15%), and other drug use disorders (7%). Non-drinkers, in contrast, were least likely to: be regular tobacco users (15%); meet criteria for a cannabis use disorder (1%); and use other drug types (3%). These findings are consistent with previous epidemiological research showing that those persons with alcohol abuse or dependence were significantly more likely to have used other drugs, and to have met criteria for another drug use disorder (Grant, 1997; Helzer et al., 1991; Kessler et al., 1997b). Alcohol users who did not meet criteria for alcohol use disorders were also more likely to report the use of cannabis and tobacco, and to meet criteria for a cannabis use disorder, than were non-drinkers.
Multiple regression analyses revealed that while all levels of alcohol use remained associated with other substance use after controlling for demographics and trait neuroticism, it was only alcohol abuse and dependence that remained associated with substance use disorders. In particular, the association between alcohol abuse and dependence, and cannabis and other substance use disorders, was not accounted for by the other variables considered here.

On the basis of these cross-sectional data, it is difficult to explore a number of explanations proposed to explain such comorbidity: that the co-occurrence is explained by common genetic factors (True et al., 1999a; True et al., 1999b; Xian et al., 2000) or common environmental factors (True et al., 1999b; Xian et al., 2000); that there is a causal relationship between alcohol dependence and other substance dependence, with alcohol acting as a “gateway” to other drug use (Kandel & Faust, 1975; Kandel, Davies, Karus, & Yamaguchi, 1986; Kandel et al., 1992); or that alcohol and other substance dependence are part of a general vulnerability to problem behaviour (Jessor & Jessor, 1977).

### 6.5.2 Alcohol Use and Anxiety and Mood Disorders

Persons meeting criteria for DSM-IV alcohol dependence were more likely than non-drinkers to meet criteria for DSM-IV anxiety and mood disorders. These differences did not appear to be completely mediated by the effects of demographics, trait neuroticism, or other drug use. Persons who met criteria for alcohol abuse did not appear to differ from non-drinkers in the rates of mood and anxiety disorders.

The patterns for alcohol dependence are consistent with US epidemiological data (Helzer et al., 1991; Kessler, 1995; Kessler et al., 1997b). The finding of a “J-curve”, in which alcohol users reported lower levels of mood disorders than non-users, is also consistent with previous community research which has suggested that light alcohol consumption is associated with better subjective health than abstention (Baum-Baicker, 1985; Chick, 1999b; Leifman et al., 1995; Liptin, 1994; Lyons et al., 1995; Poikolainen & Vartiainen, 1999; Power et al., 1998; Rodgers et al., 2000).
Interestingly, this J-curve relationship appeared to be due to higher levels of neuroticism among non-drinkers. Previous research suggests that when a particular type of substance use is prevalent in a population (as is alcohol), those who report no use may show poorer social adjustment and mental health than those who report occasional use (Shedler & Block, 1990). In particular, these researchers found that young persons reporting no cannabis use were more withdrawn, socially isolated and anxious than those reporting experimental cannabis use. The present finding might be interpreted in a similar manner—that given the high prevalence of alcohol use in the Australian population, abstention from alcohol use is an indicator of poorer social adjustment. In this case, it appeared that those who reported that they did not drink alcohol in the past year also reported that they were anxious, moody and irritable as a personality trait. This possibility cannot be further explored using the current data, and future research might evaluate the reasons for this association.

Alcohol dependence remained associated with higher rates of mood and anxiety disorders, whereas alcohol abuse was never associated with increased rates of these disorders. This suggests that while alcohol abuse is associated with other substance use problems, it is not a marker for these mental disorders. In contrast, alcohol dependence appears to be a marker for all these problems.

It is difficult, on the basis of the present cross-sectional data, however, to further examine the possible reasons for this association. Some of the other possibilities are that a causal relationship exists between alcohol dependence and mood and anxiety disorders (Schuckit et al., 1997a), that other common factors explain the relationship, or that some indirect relationship exists between them. Common factors might include common genetic or environmental factors. An analysis of the genetic contributions to six mental disorders among a sample of female twins found that the genetic contribution to lifetime alcohol dependence was largely (but by no means completely) separate from the genetic contribution to lifetime depression, panic disorder, generalised anxiety disorder, and phobia (Kendler et al., 1995b). Other research that focused upon alcohol dependence and major depression found that there were genetic and environmental factors common to both disorders (Kendler, Heath, Neale, Kessler, & Eaves, 1993c). Consistent with this is the finding that childhood adversity increases the liability to both major depression (Kessler & Magee, 1993) and to alcohol dependence (Kendler et al., 1996b).
Future research might examine this possibility with other mood and anxiety disorders. This needs to be done in samples of both males and females, since there is evidence that genetic factors may differ between males and females in explaining comorbidity between alcohol dependence and major depression (Prescott, Aggen, & Kendler, 2000a). Further longitudinal research is also needed to examine the possible direct and indirect effects of these disorders upon each other.

6.5.3 Alcohol Use and Psychosis

Alcohol dependence was strongly associated on a bivariate level with an increased likelihood of screening positively for psychosis. This relationship did not remain after conducting multiple regression analyses, but given the width of the confidence interval (0.9-3.4) a relationship cannot be excluded. Given the strong bivariate association, however, it is of interest to examine the prevalence of alcohol use disorders among those meeting criteria for psychosis in a national sample, given a relative lack of population level research on this issue. Such an exercise will be conducted in Chapter Ten, where the patterns of substance use among those who screened positively for psychosis in the NSMHWB will be explored in more detail.

6.5.4 Treatment Implications

Among alcohol dependent persons, the presence of another substance use disorder (sedatives, stimulants or opiates), or of a mood, anxiety or likely psychotic disorder, were all associated with higher chances of having sought assistance for a mental health problem. The presence of a comorbid cannabis use disorder did not appear to be strongly related to an increased likelihood of treatment seeking for a mental health problem among persons with alcohol use disorders.

The present analyses suggested that alcohol dependent persons who come to the attention of mental health professionals are more likely to have other substance use and mental disorders compared to alcohol dependent persons in the general community. This is consistent with previous research examining the effect of comorbid disorders upon the
likelihood of treatment seeking (Galbaud Du Fort et al., 1993; Kessler, 1995). Given that comorbid problems are even more likely among alcohol dependent persons who have sought treatment than they are in the general population, attention needs to be given to these possibilities in both assessment and treatment.

Persons with alcohol use disorders need to be assessed for other substance use and mental health problems. There are short and easily administered screening instruments such as the Severity of Dependence Scale (SDS) (Gossop, Griffiths, Powis, & Strang, 1992) and the Addiction Severity Index (ASI) (McLellan, Luborsky, Woody, & O’Brien, 1980) which have been shown to be reliable and valid screening instruments for the problematic use of cannabis, amphetamines, opiates and cocaine in a range of populations (Alterman et al., 1998; Appleby, Dyson, Altman, & Luchins, 1997; Gossop et al., 1995; Joyner, Wright, & Devine, 1996; McCusker, Bigelow, Servignon, & Zorn, 1994; Swift, Copeland, & Hall, 1998; Topp & Mattick, 1997). There is also a need to assess anxiety and mood disorders among alcohol dependent persons (Mattick, Oliphant, Bell, & Hall, 1996), among whom these disorders are prevalent, with around half of alcohol dependent persons who had sought treatment meeting criteria for these disorders. Screening for the presence of psychotic symptoms is also indicated, given the finding that one in 12 alcohol dependent persons who had sought treatment also screened positively for psychosis.

Those with alcohol use disorders might need assistance for the treatment of these comorbid substance use and mental disorders. It seems likely that a significant proportion of alcohol dependent persons in treatment will meet criteria for substance use disorders, mood disorders, and anxiety disorders. Research on the most appropriate interventions for persons with alcohol use problems and comorbid problems is incomplete. The research in this area will be discussed in Chapter Twelve.
6.6 Conclusions

Patterns of comorbidity of alcohol use varied according to the type of comorbidity under examination. Homotypic comorbidity (comorbidity with other substance use and use disorders) followed a linear pattern, with those who were more involved with alcohol use reporting higher rates of substance use and substance use disorders. In contrast, heterotypic comorbidity (comorbidity with mood disorders and anxiety disorders) followed a curvilinear pattern, with non-drinkers and those meeting criteria for alcohol dependence having the highest rates of these disorders. Comorbidity with psychosis was observed only among alcohol dependent persons.

Multiple regression analyses suggested that alcohol dependence was the only level of involvement with alcohol that was associated with any form of heterotypic comorbidity. Future research is needed to examine the possible reasons for the association between alcohol dependence and other mental health problems.

Comorbidity was also associated with having sought treatment for a mental health problem. There is a need for research to examine the most appropriate interventions for persons with comorbid substance use and comorbid mental disorders. This issue is discussed in Chapter Twelve.

The pattern of different relationships across different types of comorbidity found here suggests that when considering alcohol use and alcohol use disorders, different patterns of comorbidity may be differentially important. Such a possibility may also exist for patterns of comorbidity between tobacco use and mental health. This will be explored in the next Chapter.
7 PATTERNS OF COMORBIDITY ASSOCIATED WITH TOBACCO USE

Chapter Six examined the relationship between alcohol use and a range of mental health problems, and revealed interesting differences between different forms of comorbidity. The present Chapter examines patterns of comorbidity between tobacco use and mental health.

As noted in Chapter Two, tobacco is one of the most widely used licit substances in the general population (Anthony et al., 1994; Australian Institute of Health and Welfare, 1999; Farrell et al., 1998; Warner et al., 1995). Chapter Five showed that one in four adults reported current tobacco use. Given the high prevalence of its use, an examination of comorbidity patterns holds significant implications for public health.

7.1.1 TOBACCO USE AND OTHER SUBSTANCE USE

Community surveys have found that those who use tobacco are likely to use other substances (Henningfield et al., 1990). Using data from the 1985 US National Household Survey on Drug Abuse (NHSDA), Henningfield and colleagues found that there was a strong relationship between current tobacco use and alcohol, cannabis and cocaine use. For example, among 18 to 25 year olds 83% of smokers reported current (past month) alcohol use, 35% reported current cannabis use, and 14% reported current cocaine use (Henningfield et al., 1990). In comparison, among 18-25 year olds who did not smoke, 65% reported current alcohol use, 14% reported current cannabis use, and 4% reported current cocaine use.

1 Study published in L. Degenhardt & W. Hall (2001). The relationship between tobacco use, substance use disorders and mental health: Results from the National Survey of Mental Health and Well-Being. Nicotine and Tobacco Research, 3(3), 225-234. See also Appendix L for peer reviewed papers and conference presentations arising from this thesis.
Tobacco use has also been associated with substance use disorders. A US study of young adults (21 to 30 years) sampled from a Health Maintenance Organization (HMO) also found a relationship between tobacco smoking dependence upon alcohol, cannabis and other drugs (Breslau, 1995). Among nicotine dependent smokers, 27% were alcohol dependent, 18% were cannabis dependent, and 9% were cocaine dependent, with increased odds ratios of between 3 to 12 relative to non-smokers. Those who were smokers but were not nicotine dependent also had higher odds of substance dependence relative to non-smokers (odds ratios in the range 2 to 7), with 23% alcohol dependent, 11% cannabis dependent, and 5% cocaine dependent. In previous analyses of this data, Breslau and colleagues also found a relationship between the level of nicotine dependence and the prevalence of substance use disorders, with smokers who were more dependent having a higher prevalence of all substance use disorders than less dependent smokers (Breslau et al., 1991).

The ECA did not assess tobacco use. The NCS did assess tobacco use, but at the time of this study there were no reports on the association between tobacco use and substance use disorders in the NCS.

7.1.2 Tobacco use and mood disorders

Research on smoking has been conducted in the US among adults in the community (Anda et al., 1990), and studies have examined tobacco use and depression among samples of young adults in the US (Breslau et al., 1991; Breslau, Kilbey, & Andreski, 1994) and Australia (Patton et al., 1998). These studies have found that major depression is more common among persons who are nicotine dependent.

In the study by Breslau (1995) of young American adults in a HMO, 27% of lifetime DSM-III-R nicotine dependent smokers met criteria for DSM-III-R major depression at some point in their lives, compared to 12% of non-dependent smokers and 9% of those who had never smoked. Similarly, in a cohort of New Zealand adolescents, 23% of persons with major depression in the past year were nicotine dependent, compared to 5% of those who were not depressed (Fergusson et al., 1996).
Another analysis of the HMO sample by Breslau and colleagues found that the prevalence of DSM-III-R mania and hypomania was also elevated, with those with moderate dependence upon nicotine having a lifetime prevalence of 8%, compared to 2% of mildly dependent smokers and 4% of those who had never met criteria for nicotine dependence (including non-dependent smokers and persons who had never smoked) (Breslau et al., 1991).

The UK National Psychiatric Morbidity Survey assessed “neurotic and depressive” disorders using the Clinical Interview Schedule Revised (CIS-R) (Farrell et al., 1998). This survey found that in the UK general population, having a high CIS-R score (and being classified as “neurotic”) was associated with higher rates of tobacco use.

7.1.3 Tobacco Use and Anxiety Disorders

Epidemiological research has also found comorbidity between tobacco use and anxiety disorders. The study by Breslau found that 47% of those with lifetime nicotine dependence met criteria for a lifetime anxiety disorder, compared to 34% of nondependent smokers and 24% of persons who had never smoked (Breslau, 1995).

These elevated rates are consistent with research in cohorts of adolescents and young adults (Kandel et al., 1986; Patton et al., 1998). Furthermore, a recent analysis of data from the NCS found that tobacco smoking was significantly associated with panic attacks, particularly when there was a history of smoking and major depression (Breslau & Klein, 1999).

7.1.4 Tobacco Use and Psychosis

There has been much less examination of the relationship between tobacco use and psychosis in the general population. One recent epidemiological study in the UK showed that persons with psychotic illnesses sampled from treatment services in the UK general population had an extremely high prevalence of tobacco use (Farrell et al., 1998).
7.1.5 RESEARCH ISSUES

While the NCS did assess nicotine abuse and dependence (Anthony et al., 1994), no examination of the NCS data of the patterns of comorbidity between tobacco use and mental health problems other than panic (Breslau & Klein, 1999) existed at the time that the analyses reported in this Chapter were planned and conducted.

There is other epidemiological evidence from the US and UK indicating that tobacco use and mental health problems are associated in the general population. In particular, there is evidence that tobacco use and other substance use are strongly associated, and evidence that tobacco use and depression are associated (Breslau, 1995; Breslau et al., 1991; Breslau, Kilbey, & Andreski, 1993; Farrell et al., 1998).

7.1.5.1 AUSTRALIAN ESTIMATES

There has been no comprehensive analysis of the patterns of relationship between tobacco use and mental disorders in the Australian population. The present study will examine the relationships between tobacco use and both other substance use and mental disorders among Australian adults.

7.1.5.2 CURRENT VERSUS FORMER SMOKERS

Given the findings suggesting that smokers with other mental health problems may find it more difficult to cease smoking (Anda et al., 1990), it is of interest to examine whether former smokers have rates of mental disorders that differ from lifetime non-smokers, or current smokers. This may be examined using data from the NSMHWB, since all persons were asked if they had ever been smokers.
7.1.5.3 WHAT IS THE CAUSE OF ANY ASSOCIATION?

The present study will examine some common factors that could explain the co-occurrence of tobacco use with other substance use and mental disorders. These factors were those identified in Chapter Five as being similarly related to tobacco use, other substance use, mood disorders, anxiety disorders, and psychosis, namely, demographic characteristics, the personality trait of neuroticism, and patterns of other substance use.
7.2 Aims

The current study examines the following questions:

1. Is there an association between tobacco use (never and former), and:
   
   a. Alcohol, cannabis and other substance use;
   b. DSM-IV alcohol, cannabis and other substance use disorders;
   c. DSM-IV mood disorders;
   d. DSM-IV anxiety disorders;
   e. Psychosis?

2. Are these associations (if any) explained by differences between the groups in demographics, neuroticism or other drug use?

3. Does the presence of a comorbid disorder affect the likelihood of treatment seeking among tobacco users?
7.3 Method

For detail of the design and conduct of the NSMHWB, see Chapter Five.

7.3.1 Tobacco involvement

Persons were categorised as current tobacco smokers, former smokers, or persons who had never smoked. All analyses were carried out using two dummy coded variables for tobacco use, to compare the “never smoker” group as the reference category with “former smokers” and “current smokers”. Current smokers were not divided into “daily” and “non-daily” because the “non-daily” category did not sufficiently distinguish between persons who smoked very rarely and those who smoked much more frequently. Separate analyses comparing rates of mood or anxiety disorders among non-daily/daily smokers indicated that there were no significant differences between them.

7.3.2 Outcome variables

1. Other substance use
   - Alcohol: Persons were coded as using alcohol if they reported drinking 12 standard drinks of alcohol within the past year.
   - Cannabis: Persons were coded as having used cannabis if they reported using cannabis more than 5 times within the past year.
   - Other drugs: Persons were coded as using other drugs if they reported using sedatives, stimulants or opiates more than 5 times within the past year.

2. Other substance abuse and dependence
   - Alcohol: Persons were coded as meeting criteria for an alcohol use disorder if they met criteria for DSM-IV alcohol abuse or dependence.
   - Cannabis: Persons were coded as meeting criteria for a cannabis use disorder if they met criteria for DSM-IV cannabis abuse or dependence.
• Other drugs: Persons were coded as meeting criteria for an “other drug use disorder” if they met criteria for DSM-IV abuse of or dependence on sedatives, stimulants or opiates.

3. Anxiety and mood disorders
• Anxiety disorders: Persons were coded as meeting criteria for a DSM-IV anxiety disorder if they met criteria for one or more of the following: panic disorder, agoraphobia, social phobia, generalised anxiety disorder, obsessive-compulsive disorder, or post-traumatic stress disorder.
• Mood disorders: Persons were coded as meeting criteria for a DSM-IV mood disorder if they met criteria for major depressive disorder, dysthymia, bipolar I disorder, or bipolar II disorder.

4. Psychosis
Persons were classified a psychosis “case” if they scored three or more on the psychosis screener (see Table 5.1 for details).

7.3.3 Covariates

A number of variables were considered which may have been related to both tobacco use and to other substance use and mental health. More details on these variables, and their relationships with tobacco use and mental health, are provided in Chapter Five.

1. Social and demographic characteristics
• Gender;
• Age;
• Education;
• Relationship status;
• Employment status.
2. Other substance use
These variables were only included in multiple regressions in which anxiety disorders, mood disorders and psychosis case status were the outcome variables.

- DSM-IV alcohol abuse/dependence;
- Cannabis use: the use of cannabis more than five times in the past 12 months;
- Other drug use: the use of sedatives, stimulants or opiates more than five times within the past 12 months.

3. Personality
Scores on the neuroticism scale of the EPQ were included in the present analyses. Persons scoring highly on measures of neuroticism have been characterised as moody, anxious and irritable (Eysenck & Eysenck, 1991). Chapter Five and Appendix C give more details on this scale.

7.3.4 Treatment seeking
A person was coded as having sought help for a mental health problem if they reported using any of the following for a mental health problem: admission to a hospital, psychiatric ward, drug and alcohol unit, or other hospital for a mental health problem; or having seen a general practitioner, psychologist, psychiatrist, social worker, mental health team, counsellor, nurse, ambulance officer, surgeon, physician, pathologist, radiologist, chemist, or other health professional.

7.3.5 Data analysis
As described in Chapters Five and Six, weighted estimates of the prevalence of tobacco use and comorbidity are presented in this Chapter. Prevalence estimates and their standard errors were calculated using SUDAAN Version 7.5.3 (Research Triangle Institute, 1997). Bivariate associations between tobacco use and outcome variables were examined using logistic regression. For all odds ratios the “never smoker” group was used as the reference. Odds ratios (OR) and 95% confidence intervals (95%CI) for bivariate associations, and
multiple regression analyses, were carried out using STATA (STATA Corporation, 1997; STATA Corporation, 2001).

Multiple stepwise regressions were performed during which a series of steps in which the following variables were added at each step:

1. Social and demographic characteristics;
2. Other drug use (when the outcome variables were mood or anxiety disorders, and psychosis “caseness”);
3. Neuroticism.

This Chapter only presents results from the first and final models. The details of intermediate regression analyses are provided in Appendix F.
7.4 Results

One in four persons (25%) reported that they were current tobacco users, and 27% reported that they had smoked at some time in their lives (for more details of prevalence estimates see Chapter Five and Appendix C).

7.4.1 Other Substance Use and Use Disorders

Table 7.1 shows the prevalence of other substance use according to tobacco use status. Clearly, those who reported current tobacco use were more likely to have reported the use of other substances than former smokers and people who had never smoked. This is demonstrated by the fact that current smokers were significantly more likely than never smokers to report all forms of substance use, and the unadjusted 95% confidence intervals of current smokers did not overlap with former smokers. More than four in five current smokers (83%) reported alcohol use within the past 12 months, compared to 80% of former smokers and 65% of never smokers. Furthermore, 6% of smokers reported other drug use, compared to 3% and 2% of former smokers and those who had never smoked, respectively.

The strongest relationship was between current tobacco smoking and cannabis use. Around 18% of current smokers also reported the use of cannabis within the past 12 months, compared to 5% of former smokers and 4% of never smokers. Compared to never smokers, current smokers were 7.6 times more likely to report cannabis use (Table 7.1). Former smokers also had significantly higher rates of all forms of substance use than did never smokers.

After controlling for demographic variables and neuroticism in multiple regression analyses, these relationships essentially remained the same (adjusted OR, Table 7.1). Current smokers were still twice as likely to report other drug use, 2.5 times as likely to report alcohol use, and 6 times as likely to report cannabis use, compared to never
smokers. Former smokers remained intermediate between never smokers and current smokers, but still had significantly higher odds of using all substances compared to never smokers.

### Table 7.1: Weighted prevalence, unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95%CI) of substance use according to tobacco use

<table>
<thead>
<tr>
<th></th>
<th>Prevalence</th>
<th>Unadjusted</th>
<th>Unadjusted</th>
<th>Adjusted</th>
<th>Adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (SE)</td>
<td>OR</td>
<td>95%CI</td>
<td>OR1</td>
<td>95%CI1</td>
</tr>
<tr>
<td>Alcohol use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>65.4 (0.8)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>79.5 (0.7)</td>
<td>1.94</td>
<td>1.75, 2.16</td>
<td>1.97</td>
<td>1.75, 2.20</td>
</tr>
<tr>
<td>Current smoker</td>
<td>82.8 (0.9)</td>
<td>2.50</td>
<td>2.23, 2.80</td>
<td>2.54</td>
<td>2.25, 2.87</td>
</tr>
<tr>
<td>Cannabis use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>3.0 (0.4)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>4.9 (0.4)</td>
<td>1.87</td>
<td>1.46, 2.39</td>
<td>2.67</td>
<td>2.05, 3.47</td>
</tr>
<tr>
<td>Current smoker</td>
<td>17.5 (1.2)</td>
<td>7.61</td>
<td>6.22, 9.32</td>
<td>6.30</td>
<td>5.08, 7.81</td>
</tr>
<tr>
<td>Other drug use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>2.5 (0.3)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>3.3 (0.4)</td>
<td>1.43</td>
<td>1.09, 1.87</td>
<td>1.40</td>
<td>1.05, 1.85</td>
</tr>
<tr>
<td>Current smoker</td>
<td>6.1 (0.5)</td>
<td>2.62</td>
<td>2.06, 3.33</td>
<td>2.04</td>
<td>1.59, 2.62</td>
</tr>
</tbody>
</table>

1. Adjusted for age, gender, educational attainment, relationship status, employment status and neuroticism

Current tobacco smokers were five times more likely than never smokers to meet criteria for an alcohol use disorder (13% vs. 3%, respectively; Table 7.2). They were also around 5.5 times more likely to meet criteria for a sedative, stimulant, or opiate use disorder (2.4% vs. 0.4%). The association with cannabis use disorders was stronger, with current smokers around nine times more likely than never smokers to meet criteria for a cannabis use disorder (Table 7.2). Former smokers had significantly higher rates of alcohol use
disorders than never smokers (5% vs. 3%; OR 1.7, 95%CI 1.4, 2.2), but no other significant univariate differences existed between these two groups.

The strength of the association between tobacco use and all substance use disorders was reduced after controlling for demographic variables and neuroticism (Table 7.2) but all relationships remained significant (see Appendix E for details of other regression analyses). Current tobacco users remained: more likely to have a sedative, stimulant, or opiate use disorder (OR 4.7); more likely to meet criteria for an alcohol use disorder (OR 3.7); and more likely to meet criteria for a cannabis use disorder (OR 5.9; Table 7.2). Former smokers also remained significantly more likely to meet criteria for an alcohol use disorder (OR 1.9), a cannabis use disorder (OR 2.2), or another drug use disorder (OR 1.8) after adjusting for the factors examined here.

Table 7.2: Weighted prevalence, unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95%CI) of DSM-IV substance use disorders by tobacco use

<table>
<thead>
<tr>
<th></th>
<th>Prevalence % (SE)</th>
<th>Unadjusted OR</th>
<th>Unadjusted 95%CI</th>
<th>Adjusted OR1</th>
<th>Adjusted 95%CI1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alcohol use disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Former smoker</td>
<td>3.1 (0.3)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Current smoker</td>
<td>4.8 (0.9)</td>
<td>1.74</td>
<td>1.37, 2.21</td>
<td>1.91</td>
<td>1.48, 2.47</td>
</tr>
<tr>
<td></td>
<td>13.1 (0.8)</td>
<td>5.00</td>
<td>4.09, 6.11</td>
<td>3.65</td>
<td>2.94, 4.52</td>
</tr>
<tr>
<td><strong>Cannabis use disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>0.8 (0.2)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>1.0 (0.3)</td>
<td>1.52</td>
<td>0.93, 2.49</td>
<td>2.23</td>
<td>1.33, 3.73</td>
</tr>
<tr>
<td>Current smoker</td>
<td>6.4 (0.7)</td>
<td>9.10</td>
<td>6.27, 13.20</td>
<td>5.91</td>
<td>4.00, 8.73</td>
</tr>
<tr>
<td><strong>Other drug use disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>0.4 (0.1)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>0.5 (0.2)</td>
<td>1.46</td>
<td>0.77, 2.80</td>
<td>1.78</td>
<td>1.17, 2.72</td>
</tr>
<tr>
<td>Current smoker</td>
<td>2.4 (0.4)</td>
<td>5.47</td>
<td>3.29, 9.12</td>
<td>4.68</td>
<td>3.39, 6.46</td>
</tr>
</tbody>
</table>

1. Adjusted for age, gender, educational attainment, relationship status, employment status and neuroticism
7.4.2 DSM-IV Mood and Anxiety Disorders

Mood and anxiety disorders are presented together since the patterns of association with tobacco use were found to be similar. Current smokers were more likely than never smokers to have met criteria for a mood disorder within the past year (11% vs. 5%; OR 2.3), and to have met criteria for an anxiety disorder (9% vs. 4%, OR 2.5; Table 7.3). This difference was reduced, but remained significant after adjusting for covariates. The odds of having a mood disorder were still 1.4 times higher, and the odds of an anxiety disorder 1.5 times higher among current smokers compared to those who had never smoked (Table 7.3). There were no significant differences between those who had formerly smoked and those who had never smoked in the rates of mood and anxiety disorders (Table 7.3).

Table 7.3: Weighted prevalence, unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95%CI) of DSM-IV mood and anxiety disorders according to tobacco use

<table>
<thead>
<tr>
<th></th>
<th>Prevalence % (SE)</th>
<th>Unadjusted OR</th>
<th>Unadjusted 95%CI</th>
<th>Adjusted OR¹</th>
<th>Adjusted 95%CI¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anxiety disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>4.2 (0.3)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>4.9 (0.4)</td>
<td>1.13</td>
<td>0.92, 1.40</td>
<td>1.01</td>
<td>0.79, 1.28</td>
</tr>
<tr>
<td>Current smoker</td>
<td>9.3 (0.8)</td>
<td>2.54</td>
<td>2.13, 3.03</td>
<td>1.50</td>
<td>1.21, 1.87</td>
</tr>
<tr>
<td><strong>Mood disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>5.1 (0.4)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>5.8 (0.5)</td>
<td>1.15</td>
<td>0.95, 1.39</td>
<td>1.06</td>
<td>0.86, 1.31</td>
</tr>
<tr>
<td>Current smoker</td>
<td>10.9 (0.8)</td>
<td>2.32</td>
<td>1.97, 2.72</td>
<td>1.37</td>
<td>1.13, 1.67</td>
</tr>
</tbody>
</table>

¹ Adjusted for age, gender, educational attainment, relationship status, employment status, other substance use and neuroticism
7.4.3 **Psychosis**

Around one in 250 of those who had never smoked (0.5%) screened positively for psychosis, compared to one in 43 current smokers (2.3%; Table 7.4). There were no differences between those who had formerly smoked and those who had never smoked in the likelihood of screening positively for psychosis. Current smokers remained 2.9 times more likely to screen positively for psychosis than those who had never smoked after adjusting for covariates in multiple regression analyses (95%CI 1.8, 4.8; Table 7.4).

Table 7.4: Weighted prevalence, unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95%CI) of screening positively for psychosis according to tobacco use

<table>
<thead>
<tr>
<th></th>
<th>Prevalence</th>
<th>Unadjusted</th>
<th>Unadjusted 95%CI</th>
<th>Adjusted OR</th>
<th>Adjusted 95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (SE)</td>
<td>OR</td>
<td></td>
<td>OR1</td>
<td>95%CI1</td>
</tr>
<tr>
<td>Psychosis “case”</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>0.4 (0.1)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>0.7 (0.2)</td>
<td>1.51</td>
<td>0.84, 2.71</td>
<td>1.39</td>
<td>0.76, 2.54</td>
</tr>
<tr>
<td>Current smoker</td>
<td>2.3 (0.4)</td>
<td>5.51</td>
<td>3.46, 8.76</td>
<td>2.89</td>
<td>1.75, 4.77</td>
</tr>
</tbody>
</table>

1. Adjusted for age, gender, educational attainment, relationship status, employment status, other substance use and neuroticism

7.4.4 **Treatment Seeking**

Table 7.5 shows the prevalence of having sought treatment for a mental health problem among current tobacco users, according to the presence of mental disorders or substance use disorders. As is clearly shown, the best predictor of treatment seeking among was the presence of other mental health problems. In particular, those who met criteria for a mood or an anxiety disorder were highly likely to have seen someone for assistance with a mental health problem. Current tobacco use did not appear to be associated with having sought
treatment: around 60% of those meeting criteria for a mood or anxiety disorder had sought help for a mental health problem, with little variation according to tobacco use status.

A similar pattern was found when examining persons according to whether they had screened positively for psychosis. Around 50% of persons who screened positively for psychosis had sought help for a mental health problem, regardless of tobacco use status. In contrast, roughly 10% of those who had not screened positively sought treatment; although the 14% estimate – among current smokers - was higher than for the other two groups (9% and 10% - as indicated by non-overlapping standard errors of the estimates), the clinical significance of the difference is questionable. Similarly, the presence of a substance use disorder (cannabis, alcohol, sedatives, stimulants, or opiates) was associated with a higher likelihood of having sought treatment for a mental health problem.

These findings suggest that the prevalence of other substance use and mental disorders is likely to be higher among tobacco users who come to the attention of treatment services. Indeed, among current tobacco users who had sought treatment for a mental health problem: 44.7% (SE 5.6%) met criteria for a mood disorder, 40.9% (SE 3.1%) met criteria for an anxiety disorder, 22.9% (SE 4.0%) met criteria for an alcohol use disorder, 8.4% (SE 1.4%) met criteria for an other drug use disorder, 7.8% (SE 2.8%) met criteria for cannabis dependence, and 6.6% (SE 1.0%) screened positively for psychosis.
Table 7.5: Weighted prevalence of treatment seeking for a mental health problem by current tobacco users, according to the presence of other disorders

<table>
<thead>
<tr>
<th>Among current tobacco users with...</th>
<th>Prevalence of service use for a mental health problem % (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No mood disorder</td>
<td>9.2 (1.5)</td>
</tr>
<tr>
<td>Mood disorder</td>
<td>60.9 (3.1)</td>
</tr>
<tr>
<td>No anxiety disorder</td>
<td>9.7 (1.1)</td>
</tr>
<tr>
<td>Anxiety disorder</td>
<td>65.2 (3.5)</td>
</tr>
<tr>
<td>No psychosis</td>
<td>14.2 (1.1)</td>
</tr>
<tr>
<td>Psychosis “case”</td>
<td>43.6 (6.2)</td>
</tr>
<tr>
<td>No substance use disorder</td>
<td>14.7 (1.2)</td>
</tr>
<tr>
<td>Substance use disorder¹</td>
<td>27.4 (4.7)</td>
</tr>
</tbody>
</table>

1. Substance use disorders included: cannabis, alcohol, sedatives, stimulants, and opiates.
7.5 DISCUSSION

This Chapter has examined the homotypic comorbidity between tobacco use and other substance use; and heterotypic comorbidity between tobacco use and mood disorders, anxiety disorders, and psychosis. Two patterns were observed. First, both current and former smoking was associated with homotypic comorbidity. Both smoking groups had a greater likelihood of other substance use and substance use disorders compared to those who had never smoked. Second, current smoking was associated with heterotypic comorbidity, as assessed by mood disorders, anxiety disorders, and a screener for psychosis, but former smoking was not.

7.5.1 TOBACCO USE AND OTHER SUBSTANCE USE

All forms of substance use, and DSM-IV alcohol, cannabis and other substance use disorders were significantly more common among current smokers than among those who had never smoked. This is consistent with findings of previous clinical and community research (Breslau et al., 1991; DiFranza & Guerrera, 1990; Hays et al., 1998; Henningfield et al., 1990; Madden et al., 1997; Miller et al., 1996). In a recently published analysis of NCS data, Lasser and colleagues (2000) also found that smoking rates were significantly higher among those who met lifetime or one-month criteria for alcohol or other substance abuse or dependence.

Interestingly, former smokers had higher rates of alcohol use disorders than those who had never smoked, and after adjusting for other factors they also had higher rates of cannabis use disorders.

For all substance use disorders examined here, the association with current smoking was not explained by the covariates examined here. It is also consistent with the results of a study examining the association between tobacco use and psychostimulant use in an analysis of US national household survey data (Wu & Anthony, 1999). This finding is
consistent with the NCS study by Lasser and colleagues (2000), which found that the associations observed between smoking and substance use disorders also remained significant after adjusting for gender, age and geographic region.

The issue of why the use of different drug types is correlated has been the subject of considerable debate. One view, the “gateway hypothesis”, characterises the “developmental sequence” of drug use (Kandel & Faust, 1975; Kandel et al., 1986; Kandel et al., 1992). This proposes that substance use progresses through stages, with progression to a higher stage made more likely by use of a drug at an earlier stage. In this sequence, the earliest stage tends to be the use of tobacco and alcohol. The use of cannabis and other so-called “harder” drugs occurs later on, and is more likely to occur after the use of tobacco or alcohol.

This may describe the pattern in which drug use occurs, but other factors may explain the pattern. Longitudinal research suggests that much of the association between the use of different drug types is due to common risk factors which may be thought to constitute a “pathway” in which all types of drug use are made more likely. For example, research has found that persons with more risk factors such as poor parental relationships and low self-esteem, were more likely to use all drug types (Lynskey et al., 1998; Newcomb et al., 1986). Other research has found that individuals with early drug use are also likely to subsequently associate with delinquent peers and move out of home, factors that increase the likelihood of poor outcomes later on (Fergusson & Horwood, 1997).

The present analyses have taken into account a number of factors that have been found to be characteristic of this “pathway”, including unemployment and lower educational achievement. While accounting for these factors reduced the size of the relationship, the association between smoking and other drug use disorders remained strong. Nevertheless, there are many possible covariates that have not been included in the present analyses, including genetic factors and other factors such as family characteristics (Lynskey et al., 1998; Newcomb et al., 1986). There has been an increasing amount of research in recent years that has examined the role of genetic factors in liability to problematic substance use. Since significant genetic factors have been found to play a part in the liability to nicotine dependence (Heath & Martin, 1993; Kendler et al., 1993b; Kendler et al., 1999), and
some of the liability to nicotine and alcohol dependence is shared (True et al., 1999a); it is possible that vulnerabilities may be similar across other drug types, given evidence that different drugs act upon the same neurotransmitters and neurotransmitter systems (Julien, 2001). Future research might simultaneously evaluate the role of common environmental and genetic influences on the comorbidity between tobacco use and the use of other substances.

7.5.2 TOBACCO USE AND MOOD AND ANXIETY DISORDERS

In Australia, current smokers were more likely to have a mood disorder and this relationship remained when controlling for demographic variables, neuroticism, and other drug use. Current smokers also had higher rates of anxiety disorders. Former smokers did not have elevated rates of either mood or anxiety disorders.

These findings are consistent with previous research in other populations showing an association between tobacco use and anxiety and mood disorders (Anda et al., 1990; Breslau et al., 1991; Glassman, Helzer, & Covey, 1990; Glassman et al., 1988; Hughes et al., 1986; Johnson et al., 2000; Kandel & Davies, 1986; Kandel et al., 1986; Kendler et al., 1993b; Lasser et al., 2000; Patton et al., 1998; Pohl et al., 1992; Pomerleau, 1997). Recent research has also found a positive dose-response relationship between tobacco smoking and the risk of suicide among older professional males in the US, a relationship that persisted after controlling for factors such as age, marital status, alcohol use and a number of physical health indices (Miller, Hemenway, & Rimm, 2000).

While the association between mood and anxiety disorders and current tobacco use in the Australian population was not explained by the variables considered here, it is difficult on the basis of the present data to examine some of the other possible reasons for the association. The reasons for the connections between tobacco use and these disorders have been the focus of considerable debate (Gilbert & Gilbert, 1995; Glass, 1990; Glassman, 1993; Pomerleau, 1997).
Hypotheses that have been proposed include the possibilities that shared genetic factors (Kendler et al., 1993b) or a range of shared environmental and family environment factors explain the relationship (Fergusson et al., 1996). Both hypotheses have received support in previous twin studies (Kendler et al., 1993b) and cohort studies (Fergusson et al., 1996). These findings are consistent with research that has shown that tobacco use and depression at one point in time are both predictive of each other at a later point in time. Depressive symptoms predict smoking at a later age (Breslau et al., 1993; Kandel & Davies, 1986; Kendler et al., 1999), and a history of nicotine dependence predicts major depression during a follow-up period (Breslau et al., 1993).

Alternatively, since depressed mood and anxiety are symptoms of nicotine withdrawal (Madden et al., 1997), it could be that the association between current anxiety/mood disorders and current tobacco use reflects the fact that persons with anxiety or mood disorders may find it more difficult to give up smoking once they have started (Gilbert & Gilbert, 1995). Consistent with this possibility is research that found that nicotine dependent persons who also had major depression or anxiety disorders reported more severe nicotine withdrawal symptoms (Breslau, Kilbey, & Andreski, 1992). The findings from the NSMHWB are consistent with this possibility: former smokers did not have higher rates of mood or anxiety disorders than those who had never smoked. Future research needs to examine these possibilities.

7.5.3 Tobacco use and psychosis

Current smokers were significantly more likely to screen positively for psychosis. This finding is in accord with recent epidemiological research showing that persons with psychotic illnesses in the UK general population have a high prevalence of tobacco use (Farrell et al., 1998). This association remained significant after controlling for demographics, other substance use and neuroticism. This association is explored further in Chapter Ten, where the substance use patterns of likely cases of psychosis in the NSMHWB are further examined.
7.5.4 Treatment Implications

Examination of treatment seeking revealed that the proportion of persons reporting that they had sought help for mental health problems was higher among current smokers who also met criteria for a substance use disorder, and among those current smokers who met criteria for other mental disorders. This is consistent with previous research that has examined the effect of comorbidity on the likelihood of treatment seeking, which has also shown that higher rates of comorbidity will be observed among clinical samples (Berkson, 1946; Caron & Rutter, 1991; Galbaud Du Fort et al., 1993; Kessler, 1995).

This suggests that smokers who come to the attention of treatment services are even more likely than smokers in the general population to have other substance use and mental health problems. These results come as increasing attention is being given to smoking cessation treatment in persons with problematic substance use (McIlvain & Bobo, 1999). It may be appropriate to also target smoking among persons who are attempting to modify their problematic substance use (Bobo, McIlvain, Lando, Walker, & Leed-Kelly, 1998; Hurt et al., 1994; McIlvain & Bobo, 1999; Sobell & Sobell, 1996).

Research is increasingly investigating the effectiveness of interventions for smokers who also have mood disorders (Hall et al., 1998; Hughes, Goldstein, Hurt, & Shiffman, 1999a; Hurt et al., 1997; Jorenby et al., 1999; Tsoh et al., 2000) and anxiety disorders (Cinciripini et al., 1995; West & Shiffman, 2001). However, the research on this topic is far from comprehensive, and future work needs to identify the most appropriate interventions for such groups. This issue is discussed further in Chapter Twelve.

Around half of those who were current smokers and who screened positively for psychosis had seen a professional for a mental health problem. It is likely that persons coming to the attention of treatment services for help with psychosis-related symptoms will also be smokers. The clinical implications of this will be discussed in Chapter Ten, when the substance use patterns of psychosis cases are further explored.
7.6 Conclusions

This Chapter has shown that in the general adult population of Australia, there is significant comorbidity between tobacco use and a range of other mental health problems. Current tobacco smoking was significantly related to the use and problematic use of alcohol, cannabis and other drug types, and to poorer mental health. Although controlling for potential confounding factors reduced the strength of the association, a significant relationship remained between tobacco use and all types of comorbidity examined.

Given that anxiety and mood disorders are among the most common disorders in the general population, the relationships found between tobacco use and anxiety and mood disorders highlight a continued need for effective treatments for these groups. Future research needs to examine effective interventions for persons who are considering cessation of tobacco use, who also have other substance use and mental disorders. This is discussed further in Chapter Twelve.

The strong relationship between current smoking and psychotic symptoms suggests that more work is needed to establish effective cessation methods for smokers with psychotic illnesses. Given that there was such a relationship, the issue of tobacco use among cases of psychosis is explored in Chapter Ten.

Tobacco use has consistently been found to be a marker of poorer mental health. Given that research has suggested that these other mental health problems reduce the likelihood of successful quitting, public health initiatives could promote the message that those who seek help to give up smoking may have other substance use or mental health problems. The next Chapter examines patterns of comorbidity for cannabis, the most commonly used illicit drug in the Australian population.
8 PATTERN S OF COMORBIDITY ASSOCIATED WITH CANNABIS USE

As noted in Chapter Two, cannabis is the most widely used illicit substance in many countries including Australia. Chapter Five also showed that cannabis use disorders are the most commonly occurring substance use disorders in the Australian population after alcohol use disorders. The goal of the present Chapter is to examine population patterns of homotypic and heterotypic comorbidity associated with increasing levels of involvement with cannabis use.

8.1.1 CANNABIS USE AND OTHER SUBSTANCE USE

In the ECA, it was found that approximately one in 23 persons (4.4%) had met criteria for DSM-III cannabis abuse or dependence in their lifetime, 38% of whom experienced problems in the past year (Anthony & Helzer, 1991). Among lifetime cannabis users, 36% met lifetime criteria for an alcohol use disorder (Helzer et al., 1991). Information on comorbidity between cannabis use disorders and other drug use disorders was not specifically reported. Cannabis disorders were combined with other illicit drugs to define a category of “drug use” disorders (of which cannabis use disorders were the most common). The rate of lifetime alcohol abuse/dependence among persons with any drug abuse/dependence was 4.1 times greater than among those without drug abuse/dependence (Anthony & Helzer, 1991).

Similarly, the NCS found that DSM-III-R drug abuse/dependence was likely to co-occur with alcohol abuse/dependence (Kessler et al., 1997b). Using a proxy measure of cannabis use...
dependence in an analysis of national US survey data, Kandel and colleagues found that cannabis dependent persons were more likely to report getting drunk more often, to smoke tobacco more heavily and to have used more illicit drug types in the past year, than non-dependent cannabis users (Kandel et al., 1997).

The Ontario Health Survey, a representative household survey of adults aged 15 to 64 years in Ontario, found that 18% of those who met lifetime criteria for DSM-III-R alcohol abuse or dependence met lifetime criteria for DSM-III-R cannabis abuse/dependence, compared to 1.3% of those who had never met criteria for an alcohol use disorder (Ross, 1995).

Information on 12-month population patterns of comorbidity between cannabis use and other substance use was provided in an analysis of data from the National Longitudinal Alcohol Epidemiologic Study (NLAES) (Grant & Pickering, 1998). Among those who met criteria for DSM-IV cannabis abuse and dependence in the past year, 14% and 23%, respectively, met criteria for another illicit drug use disorder in the past year; while 20% and 28%, respectively, reported other illicit drug use (at least 12 times lifetime, and once in the past year) (Grant & Pickering, 1998). These rates were significantly higher than among cannabis users who did not meet criteria for cannabis abuse or dependence.

Similar patterns were found for comorbidity with alcohol use disorders: of those who met criteria for cannabis dependence, 63% also met criteria for alcohol dependence, and 9%, alcohol abuse. Among those who met criteria for cannabis abuse, the figures were 24% and 41% (Grant & Pickering, 1998). These patterns suggest that cannabis dependent persons are more likely to have an alcohol use disorder, as well as other illicit drug use and use disorders. Alcohol abuse and dependence remained significant predictors of cannabis abuse in multivariate analyses, and alcohol dependence and other drug use disorders remained significant predictors of cannabis dependence (Grant & Pickering, 1998).

**8.1.2 Cannabis use and mood disorders**

It is not clear what the relationship was between cannabis use and mood disorders in the ECA and the NCS because they have reported on “drug use disorders” (which includes
cannabis and other substance use disorders) when examining patterns of comorbidity with anxiety and mood disorders. We do know, however, that cannabis use disorders are among the most prevalent drug use disorders in both the ECA and the NCS (Anthony & Helzer, 1991; Anthony et al., 1994). The ECA found that those meeting lifetime criteria for DSM-III drug use disorders had rates of lifetime DSM-III mood disorders that were between 3.5 and 10.7 times higher than those without drug use disorders (Anthony & Helzer, 1991). The nationally representative NCS found that among those persons meeting criteria for lifetime DSM-III-R drug abuse and dependence, 28% and 39%, respectively, met criteria for a DSM-III-R mood disorder (Kessler et al., 1996).

The NCS also found that 12-month comorbidity rates between drug use disorders and mood disorders were also elevated (Kessler et al., 1996). Among those meeting 12-month criteria for DSM-III-R drug abuse, 15% met criteria for a mood disorder, compared to 32% of persons meeting criteria for drug dependence (Kessler et al., 1996). The NLAES found that persons meeting criteria for DSM-IV major depression within the past year had 6.4 times the odds of meeting criteria for DSM-IV cannabis abuse/dependence than those without major depression (6% vs. 1% respectively)(Grant, 1995). Among those meeting criteria for cannabis abuse and dependence, 14% and 29%, respectively, met criteria for major depression in the past year (Grant & Pickering, 1998).

One study used a sample of cannabis users attending college, with two groups: 45 “heavy users” (used cannabis daily for at least 2 years) and 44 “occasional users” (users who had never used cannabis more than 10 times per month) (Kouri, Pope, Yurgelun-Todd, & Gruber, 1995). These two groups were compared for rates of DSM-III-R psychiatric disorders. The rates of mental disorders were low, with 6% of heavy users and 10% of occasional users meeting criteria for a DSM-III-R mood, anxiety or eating disorder. There were no significant differences between the groups for any psychiatric diagnoses. However, these samples were small, the sample was young, and it was selected from a college population. Thus, the ability to generalise these findings to the general population is limited.

A study of cannabis use and depressive symptoms found that frequency of cannabis use was not associated with depression among a sample of young adult males (Green & Ritter,
A weak association observed between early initiation of cannabis use and depression was not significant after controlling for educational attainment, marital status, alcohol and tobacco use (Green & Ritter, 2000).

A study of male army draftees using cannabis but no other illicit drugs found that more problematic cannabis users had a higher rate of DSM-III-R axis I and axis II psychiatric disorders (Troisi, Pasini, Saracco, & Spalletta, 1998). There was a univariate relationship between increasing involvement with cannabis use (use, abuse and dependence) and increasing scores on the Beck Depression Inventory (BDI) (Troisi et al., 1998). However, the study did not compare these patterns to the rates of disorder among draftees who did not use cannabis, nor to those draftees who used cannabis and other illicit drugs, who would presumably form a large proportion of cannabis users (Kandel et al., 1997). Further, the DSM-III-R disorders for which the draftees met criteria were not specified.

Some research has examined the association between “general life satisfaction” and cannabis use, as opposed to depression in particular. Research with a cohort of young adults found that greater involvement with cannabis was associated with a lower degree of life satisfaction, and a higher chance of having consulted a mental health professional or having been hospitalised for a psychiatric disorder (Kandel, 1984).

Some research has found that cannabis use may be related to general social functioning (Shedler & Block, 1990). Among a cohort of adolescents followed longitudinally, those who had experimented with cannabis reported better social adjustment than those who had never used cannabis or those who were heavy users. This U-shaped curve was thought to indicate that cannabis use needed to be considered within social and personal contexts, and that patterns of use were symptomatic of underlying psychological states, rather than being causes of them. Problematic cannabis use was argued to be a symptom of emotional distress and maladjustment, while experimentation was an indicator of being well adjusted. Never having tried cannabis use, it was argued, was symptomatic of poor social adjustment, anxiety, and emotional constriction (Shedler & Block, 1990). However, these relationships could have been affected by the high prevalence of cannabis use in this birth cohort.
More recently, a study examining similar groups of adolescents according to cannabis use (abstainers, experimenters and frequent users) found differences between abstainers, and experimenters, and frequent users of cannabis, all of whom had higher levels of depression according to the Brief Symptom Inventory (BSI) (Milich et al., 2000). “Heavy” users were defined as those using cannabis at least 40 times and at least one other illicit drug, while experimenters had used cannabis less than 10 times and had not used more than one other illicit drug; while abstainers had not used cannabis or any other illicit other drugs. Hence the drug use patterns of these groups differ in more ways than their frequency of cannabis use.

8.1.3 Cannabis use and anxiety disorders

Unfortunately, there has been a paucity of research conducted to examine how cannabis use is related to lasting anxiety levels, or anxiety disorders. The study of US adolescents discussed above (Milich et al., 2000) found that frequent cannabis users had higher levels of anxiety according to the BSI than those who did not use cannabis, or who had only experimented with it (Milich et al., 2000). However, it must be remembered that “heavy” users were using at least one other illicit drug type, while “experimenters” had not used more than one other drug type, and “abstainers” had used no other drug types.

In the study of male army draftees discussed above, scores on the Spielberger State Anxiety Index were higher among those more heavily involved with cannabis use (dependent or abuse) (Troisi et al., 1998). Cannabis involvement was not associated with scores on Spielberger’s Trait Anxiety Index (Troisi et al., 1998).

Zablocki and colleagues (1991) interviewed 460 members of a commune who had used cannabis in a study of cannabis use and psychological distress. Overall, neither the amount or the recency of cannabis use were associated with increased psychological distress as measured by the Symptom Checklist-90’s Global Severity Index, the depression index, or the anxiety index (Zablocki et al., 1991). However, in individuals characterised as “highly introspective” - on a scale that included such items as “How much do you think about yourself?” and “How much do you try to figure yourself out?” - the recency of cannabis
was associated with higher levels of anxiety and psychological distress (Zablocki et al., 1991).

Rates of lifetime DSM-III anxiety disorders in the ECA were between 1.9 and 3.3 times higher among those meeting lifetime criteria for DSM-III drug abuse/dependence than among those without such a disorder (Anthony & Helzer, 1991). The NCS found that among those who met criteria for DSM-III-R lifetime drug abuse, 35% met criteria for a DSM-III-R anxiety disorder, with over half of those who were drug dependent (54%) meeting such criteria (Kessler et al., 1996). 12-month rates were also elevated: 24% of those meeting criteria for drug abuse and 46% of those who were drug dependent also met criteria for an anxiety disorder (Kessler et al., 1996).

8.14 Cannabis Use and Psychosis

The ECA found that schizophrenia was 5.9 times more common among persons meeting lifetime criteria for DSM-III drug abuse or dependence (Anthony & Helzer, 1991). There has also been an analysis of the relationship between drug use and a “self-reported psychotic experience” using ECA data (Tien & Anthony, 1990). After adjusting for baseline psychopathology (mood, anxiety and personality disorders) and sociodemographic variables, daily cannabis use (RR = 2.0, 95%CI 1.25, 3.12) was a significant predictor of reporting one or more psychotic symptom during the follow-up year (Tien & Anthony, 1990).

8.15 Summary

Despite the limitations in the quality and quantity of research in this area, at present the weight of evidence favours the view that individuals who meet criteria for a cannabis use disorder may have heightened risks of a range of mental health problems including problematic substance use, and higher levels of depression, anxiety and psychosis. In the next section, we discuss some of the possible explanations for this apparent association, and the limitations of existing research.
8.1.6 RESEARCH ISSUES

8.1.6.1 SAMPLING ISSUES

It is difficult to know how generalisable the findings of some of the above studies may be. First, some of the samples were extremely small (Kouri et al., 1995), making the findings less reliable since a large amount of error may be involved. Second, it is unclear how representative these samples were of the groups they came from. Third, many of the groups sampled were specific populations such as college students (Kouri et al., 1995), young adult males (Green & Ritter, 2000), army draftees (Troisi et al., 1998) or commune members (Zablocki et al., 1991). Fourth, some studies grouped participants so that they differed in drug use patterns other than cannabis use (Milich et al., 2000; Shedler & Block, 1990), while other studies did not compare cannabis users with non-users (Kouri et al., 1995; Troisi et al., 1998; Zablocki et al., 1991), or to those who used other drug types (Troisi et al., 1998).

As noted in Chapter Four, unless representative samples of the general community are used in examining patterns of comorbidity, biases may affect the makeup of samples (Berkson, 1946; Caron & Rutter, 1991; Galbaud Du Fort et al., 1993). If representative samples of the general population are used, these biases can be avoided, and the estimates of comorbidity may be taken to indicate general patterns of co-occurrence. Furthermore, in using such population samples it is possible to examine rates of treatment seeking among persons with or without a comorbid mental health problem.

8.1.6.2 MEASUREMENT OF CANNABIS USE

Numerous issues exist regarding the measurement of cannabis use in previous research. First, some of the major previous epidemiological studies have grouped cannabis with other drugs (Anthony & Helzer, 1991; Kessler et al., 1996), so it is not clear whether the patterns found for “drug abuse/dependence” are the same as would be found for cannabis alone. Second, some studies have grouped abuse and dependence into “use disorders” (Anthony & Helzer, 1991). One epidemiological study has examined cannabis abuse and dependence separately for comorbidity with major depression (Grant, 1995). It would be
desirable to do this with other disorders. Third, other studies have considered cannabis use without distinguishing level of involvement (Abel, 1971; Gale & Guenther, 1971; Gruber, Pope, & Oliva, 1997; Milich et al., 2000; Shedler & Block, 1990; Zablocki et al., 1991). It is important to explore how cannabis use, abuse and dependence are separately related to other substance use and mental health.

8.1.6.3 What is the cause of any association?

Chapters Four and Six reviewed the fact that there are several reasons why disorders may co-occur (Angold et al., 1999; Caron & Rutter, 1991; Kessler, 1995). The present Chapter examines some common factors that could explain the co-occurrence of cannabis use, other substance use and mental disorders. These potential common factors include demographic characteristics of users, the personality trait of neuroticism, and patterns of other drug use: alcohol, tobacco and other illicit drugs.
8.2 AIMS

The present study examines patterns of 12-month comorbidity between cannabis use, abuse and dependence, and a range of measures of substance use and mental health using data from the Australian National Survey of Mental Health and Well-Being (NSMHWB).

The following questions are addressed:

1. Is there an association between cannabis use, DSM-IV abuse and dependence, and:
   a. Tobacco, alcohol and other substance use;
   b. DSM-IV alcohol and other substance use disorders;
   c. DSM-IV mood disorders;
   d. DSM-IV anxiety disorders;
   e. Psychosis?

2. Are these associations (if any) explained by differences between the groups in demographics, neuroticism or other drug use?

3. Does the presence of a comorbid disorder affect the likelihood of treatment seeking among cannabis users?
8.3 Method

For details of the NSMHWB sample design and conduct, see Chapter Five.

8.3.1 Cannabis involvement

In the present study, involvement with cannabis use was categorised into four categories: five or fewer occasions of use in the past 12 months (termed “no use”), use more than five times in the past 12 months without meeting criteria for DSM-IV abuse or dependence (“cannabis use”), DSM-IV cannabis abuse, and DSM-IV cannabis dependence.

8.3.2 Outcome variables

1. Other substance use

- Alcohol: Persons were coded as using alcohol if they reported drinking 12 standard drinks of alcohol within the past year.
- Tobacco: Persons who reported using tobacco were coded as tobacco users.
- Other drugs: Persons were coded as using other drugs if they reported using sedatives, stimulants or opiates more than five times within the past year.

2. Other substance abuse and dependence

- Alcohol abuse and dependence: Persons were coded as meeting criteria for DSM-IV alcohol abuse or dependence.
- Other drug abuse and dependence: Persons were coded as meeting criteria for “other drug abuse” or “other drug dependence” if they met DSM-IV criteria for abuse of or dependence on sedatives, stimulants or opiates.
3. Anxiety and mood disorders

- Anxiety disorders: Persons were coded as meeting criteria for a DSM-IV anxiety disorder if they met criteria for panic disorder, agoraphobia, social phobia, generalised anxiety disorder, obsessive-compulsive disorder, or post-traumatic stress disorder.
- Mood disorders: Persons were coded as meeting criteria for a DSM-IV mood disorder if they met criteria for major depressive disorder, dysthymia, bipolar I disorder, or bipolar II disorder.

4. Psychosis

Persons were considered to be a psychosis “case” if they scored three or more on the psychosis screener.

8.3.3 Covariates

A number of variables were considered which may have been related to both tobacco use and to other substance use and mental health. More details on these variables, and their relationships with cannabis use and mental health, are provided in Chapter Five.

1. Social and demographic characteristics

- Gender;
- Age;
- Education;
- Relationship status;
- Employment status.
2. Other substance use

These variables were only included in multiple regressions in which anxiety disorders, mood disorders, and psychosis case status were the outcome variables.

- Other drug use: the use of stimulants, sedatives or opiates more than five times in the past 12 months;
- DSM-IV alcohol abuse/dependence;
- Regular tobacco use: daily tobacco use.

3. Personality

Scores on the neuroticism scale of the EPQ were included in the present analyses. Persons scoring highly on measures of neuroticism have been characterised as moody, anxious and irritable (Eysenck & Eysenck, 1991). Chapter Five and Appendix C give more details on this scale.

8.3.4 Treatment seeking

A person was coded as having sought help for a mental health problem if they reported the use of any of the following for help with a mental health problem: admission to a hospital, psychiatric ward, drug and alcohol unit, or other hospital for a mental health problem; or having seen a general practitioner, psychologist, psychiatrist, social worker, mental health team, counsellor, nurse, ambulance officer, surgeon, physician, pathologist, radiologist, chemist, or other health professional.

8.3.5 Data analysis

Weighted estimates of the 12-month prevalence of DSM-IV cannabis use disorders, affective and anxiety disorders, and patterns of comorbidity, are presented in this report. More detail of weighting and regression approaches is provided in Chapter Five. All
prevalence estimates and their standard errors were calculated using SUDAAN Version 7.5.3 (Research Triangle Institute, 1997).

Bivariate associations between cannabis use and outcome variables were examined using logistic regression. In all regressions, cannabis involvement was dummy coded, with each level of involvement (cannabis use without disorder, DSM-IV cannabis abuse, DSM-IV cannabis dependence) compared to non-users as the reference category. Odds ratios (OR) and 95% confidence intervals (95%CI) for bivariate associations, and multiple regression analyses, were performed using STATA (STATA Corporation, 1997; STATA Corporation, 2001).

Multiple regressions were carried out in a series of steps in which the following variables were added at each step:

1. Social and demographic characteristics;
2. Other drug use (when the outcome variables were mood or anxiety disorders, and psychosis “caseness”);
3. Neuroticism.

This Chapter only presents results from the first and final models. For details of other regressions, see Appendix G.
8.4 Results

Around 1 in 20 persons (4.8%) reported using cannabis more than five times in the past year without meeting criteria for a DSM-IV cannabis use disorder. A further 0.8% met criteria for cannabis abuse, while 1.5% met criteria for cannabis dependence (for more details of prevalence estimates see Chapter Five and Appendix C).

8.4.1 Other Substance Use and Use Disorders

The prevalence of other substance use according to level of cannabis use is shown in Table 8.1. Among those with heavier involvement with cannabis, regular tobacco use was found to be much more likely. One fifth (20%) of those who reported no cannabis use in the past year reported being regular smokers, compared to half of those who reported cannabis use (51%), and 70% of cannabis dependent persons. Compared to non-users of cannabis, regular tobacco use was between 4.3 and 8.9 times more likely among cannabis users (Table 8.1).

Similar relationships existed between the level of cannabis involvement and alcohol use. Cannabis users (regardless of level of involvement) were more likely than non-users to report alcohol use in the past year (Table 8.1). Cannabis dependent persons appeared to have slightly lower increased odds compared to other cannabis user groups (2.5 vs. 6.0, 5.8).

The use of sedatives, stimulants or opiates (“other drug use”) was also more likely among cannabis users (Table 8.1). Cannabis users were all much more likely to report using at least one of these other drug types (cannabis use 14%, abuse 12%, dependence 27%) compared to non-users (3%). Notably, the prevalence of other drug use among cannabis dependent persons was substantially higher than all other groups, although given the band of error around this estimate, the 95% confidence interval overlapped with the cannabis use and abuse groups.
<table>
<thead>
<tr>
<th>Substance Use Category</th>
<th>Prevalence (% (SE))</th>
<th>OR 95%CI</th>
<th>Adjusted OR 1</th>
<th>Adjusted 95%CI 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular tobacco use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cannabis use</td>
<td>20.7 (0.5)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>51.1 (2.6)</td>
<td>4.34</td>
<td>3.61, 5.22</td>
<td>3.34</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>60.1 (7.2)</td>
<td>5.62</td>
<td>3.55, 8.92</td>
<td>3.32</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>70.4 (8.6)</td>
<td>8.94</td>
<td>6.25, 12.77</td>
<td>5.16</td>
</tr>
<tr>
<td>Alcohol use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cannabis use</td>
<td>72.1 (0.6)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>94.3 (1.8)</td>
<td>6.00</td>
<td>4.16, 8.65</td>
<td>4.64</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>94.9 (2.9)</td>
<td>5.77</td>
<td>2.33, 14.30</td>
<td>3.59</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>87.4 (2.9)</td>
<td>2.46</td>
<td>1.55, 3.91</td>
<td>1.87</td>
</tr>
<tr>
<td>Other drug use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cannabis use</td>
<td>2.6 (0.2)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>14.4 (2.2)</td>
<td>5.81</td>
<td>4.38, 7.70</td>
<td>5.34</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>12.4 (4.1)</td>
<td>5.35</td>
<td>2.73, 10.52</td>
<td>4.45</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>26.8 (9.0)</td>
<td>11.33</td>
<td>7.64, 16.80</td>
<td>8.76</td>
</tr>
</tbody>
</table>

1. Adjusted for age, gender, educational attainment, relationship status, employment status and neuroticism

Table 8.1 also shows the adjusted odds ratios produced after adjusting for demographics and neuroticism. As can be seen, all levels of cannabis use remained associated with similarly increased odds, relative to non-users of cannabis, of reporting regular tobacco use (OR 3.3 – 5.2) and other drug use (OR 4.5 – 8.8), after adjusting for all factors considered here (adjusted OR column, Table 8.1). All groups of cannabis users had higher odds of using alcohol, although the relationship between cannabis dependence and alcohol use was less strong than for other user groups.
The prevalence of alcohol and other drug abuse and dependence according to level of involvement with cannabis use is shown in Table 8.2. Cannabis users (regardless of level of use) all had similarly increased odds of meeting criteria for alcohol abuse relative to non-users (OR 4.8-6.1): between 7-10% of cannabis user groups met criteria for alcohol abuse, compared to 1.5% of non-users (Table 8.2). Cannabis users (without abuse/dependence) were over 5 times more likely than non-users to meet criteria for alcohol dependence (14% vs. 3% of non-users). Those who met criteria for cannabis abuse (27%) or dependence (29%) were even more likely to meet criteria for alcohol dependence - increased odds of 13.6 and 12.4 respectively. As indicated by the fact that the 95% confidence intervals did not overlap, those who met criteria for cannabis abuse or dependence were more likely than cannabis users to meet criteria for alcohol dependence.

Table 8.2 also shows the prevalence of other drug abuse and dependence according to level of cannabis use. Cannabis users were more likely than non-users to meet criteria for sedative abuse (OR 6.2) and dependence (OR 5.8). Those who met criteria for cannabis abuse or dependence were much more likely than non-users to meet criteria for drug abuse, with increased odds of 30.9 and 42.9, respectively. The relationship with other drug dependence varied slightly: cannabis dependence was by far the most strongly related to an increased risk of meeting criteria for drug dependence, with almost one in five (18%) meeting such criteria - they were almost 45 times more likely to meet such criteria than non-users of cannabis. Cannabis users also had increased odds of drug dependence (OR 5.8), but the relationship with cannabis abuse was not significant.
Table 8.2: Weighted prevalence, unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95%CI) of DSM-IV substance abuse and dependence according to cannabis involvement

<table>
<thead>
<tr>
<th></th>
<th>Prevalence</th>
<th>OR</th>
<th>95%CI</th>
<th>Adjusted OR</th>
<th>Adjusted 95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (SE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Alcohol abuse</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cannabis use</td>
<td>1.5 (0.2)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>6.6 (1.6)</td>
<td>4.81</td>
<td>3.22, 7.18</td>
<td>2.55</td>
<td>1.67, 3.90</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>9.8 (4.6)</td>
<td>6.08</td>
<td>2.60, 14.23</td>
<td>2.19</td>
<td>0.91, 5.28</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>8.6 (3.0)</td>
<td>5.69</td>
<td>3.01, 10.76</td>
<td>1.81</td>
<td>0.90, 3.60</td>
</tr>
<tr>
<td><strong>Alcohol dependence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cannabis use</td>
<td>3.1 (0.3)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>13.9 (2.7)</td>
<td>5.24</td>
<td>3.97, 6.92</td>
<td>2.91</td>
<td>2.15, 3.93</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>27.3 (8.1)</td>
<td>13.56</td>
<td>8.22, 22.39</td>
<td>5.50</td>
<td>3.19, 9.48</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>28.6 (5.1)</td>
<td>12.38</td>
<td>8.52, 18.00</td>
<td>4.64</td>
<td>3.04, 7.08</td>
</tr>
<tr>
<td><strong>Other drug abuse</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cannabis use</td>
<td>0.1 (0.04)*</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>0.7 (0.4)*</td>
<td>6.21</td>
<td>2.02, 19.11</td>
<td>4.18</td>
<td>1.70, 18.78</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>4.1 (3.2)*</td>
<td>30.89</td>
<td>8.62, 110.67</td>
<td>20.49</td>
<td>7.50, 131.11</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>6.2 (3.0)*</td>
<td>42.93</td>
<td>17.52, 105.18</td>
<td>20.91</td>
<td>11.22, 99.80</td>
</tr>
<tr>
<td><strong>Other drug dependence</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cannabis use</td>
<td>0.4 (0.1)*</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>2.5 (1.3)*</td>
<td>5.84</td>
<td>3.06, 11.17</td>
<td>4.31</td>
<td>2.14, 8.69</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>1.6 (1.6)*</td>
<td>3.09</td>
<td>0.42, 22.77</td>
<td>1.78</td>
<td>0.23, 13.94</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>17.6 (6.7)*</td>
<td>44.79</td>
<td>26.33, 76.21</td>
<td>28.02</td>
<td>14.40, 54.53</td>
</tr>
</tbody>
</table>

1. Adjusted for age, gender, educational attainment, relationship status, employment status and neuroticism

* Caution should be taken when interpreting this estimate due to the large amount of error surrounding the estimate.
Table 8.2 also shows the adjusted odds ratios of other substance abuse and dependence according to level of cannabis use. Alcohol abuse did not remain associated with cannabis abuse or dependence after adjusting for demographics and neuroticism. In contrast, cannabis users remained 2.5 times more likely than non-users to meet criteria for alcohol abuse after adjusting for all other factors considered here (adjusted OR column, Table 8.2).

The relationship was different for alcohol dependence. Although the strength of the association was approximately halved after controlling for demographic factors (see Appendix G for details), and further reduced after accounting for neuroticism, all groups of cannabis users remained significantly more likely than non-users to meet criteria for alcohol dependence. There were no significant differences between different cannabis user groups in the odds of alcohol dependence relative to non-users, with ORs of between 2.9 and 5.5 after adjusting for demographics and neuroticism (Table 8.2).

Table 8.2 also shows that all cannabis users (regardless of the level) had higher odds of meeting DSM-IV criteria for abuse of sedatives, stimulants or opiates after adjusting for demographics and neuroticism. Cannabis users remained around four times more likely than non-users to meet such criteria, with those meeting criteria for cannabis abuse and dependence, and 20 to 21 times more likely, respectively, to meet criteria for other drug abuse (adjusted OR column, Table 8.2). While there was a large amount of error associated with these estimates (as indicated by the size of the confidence intervals), the lower limits of the odds ratios for cannabis abuse and dependence were 7.5 and 11.2, which were marked increases in odds relative to non-users of cannabis.

The pattern was different for other drug dependence. Cannabis dependence remained by far the most strongly associated with sedative/stimulant/opiate dependence. After adjusting for demographics and neuroticism, those who met criteria for cannabis dependence remained 28 times more likely than non-users to meet criteria for dependence on at least one of these drug types within the past year. In contrast, cannabis abuse was not significantly associated with other drug dependence, and cannabis users remained significantly more likely to meet such criteria than non-users (adjusted OR 4.3).
8.4.2 MOOD AND ANXIETY DISORDERS

Findings on comorbidity between cannabis involvement, and mood and anxiety disorders, are presented together since the pattern of relationships was the same. There were significant bivariate relationships between involvement with cannabis and the prevalence of mood and anxiety disorders (Table 8.3). The prevalence of mood disorders increased from around 6% among non-users to 14% among those meeting criteria for cannabis dependence. Cannabis users were between 2-3 times more likely to meet criteria for a mood disorder compared to non-users (Table 8.3).

Similarly, whereas only 5% of non-users of cannabis met criteria for a DSM-IV anxiety disorder, this proportion increased to one in six among those who met criteria for cannabis dependence (17%). Cannabis users (OR 1.8) and those meeting criteria for cannabis dependence (OR 4.3) were significantly more likely than non-users to meet criteria for an anxiety disorder (Table 8.3).

Demographic variables did not account for the bivariate patterns of comorbidity between cannabis use and mood and anxiety disorders. All significant relationships observed on a bivariate level remained after including demographic variables (Table G3, Appendix G). These relationships changed significantly after controlling for demographics and other drug use (Table G3, Appendix G). Once regular tobacco use, DSM-IV alcohol use disorders, and other drug use were included in the multiple regressions, no significant relationships remained between any level of cannabis involvement and either mood or anxiety disorders (Table G3, Appendix G). This appeared to be due to a reduction in the size of the effects rather than to loss of precision (i.e. the ORs were markedly reduced, with a much smaller increase in the size of the confidence intervals). The inclusion of neuroticism scores in the final model (adjusted OR in Table 8.3) did not change any of these patterns. Table 8.3 shows the final results of multiple regression analyses (see Appendix G for details of other regressions).
### Table 8.3: Weighted prevalence, unadjusted and adjusted odds ratios (OR) and 95% confidence intervals (95%CI) of DSM-IV anxiety and mood disorders according to cannabis involvement

<table>
<thead>
<tr>
<th></th>
<th>Prevalence % (SE)</th>
<th>OR</th>
<th>95% CI</th>
<th>Adjusted OR¹</th>
<th>Adjusted 95% CI¹</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anxiety disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cannabis use</td>
<td>5.4 (0.3)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>8.0 (1.2)</td>
<td>1.78</td>
<td>1.31, 2.41</td>
<td>0.88</td>
<td>0.60, 1.29</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>6.4 (2.8)</td>
<td>1.10</td>
<td>0.44, 2.73</td>
<td>0.37</td>
<td>0.13, 1.05</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>16.5 (3.6)</td>
<td>4.30</td>
<td>2.88, 6.40</td>
<td>1.41</td>
<td>0.83, 2.37</td>
</tr>
<tr>
<td><strong>Mood disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cannabis use</td>
<td>6.2 (0.3)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>12.1 (2.7)</td>
<td>2.24</td>
<td>1.73, 2.91</td>
<td>1.30</td>
<td>0.94, 1.79</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>18.6 (5.3)</td>
<td>2.88</td>
<td>1.61, 5.17</td>
<td>1.50</td>
<td>0.75, 2.99</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>13.6 (2.6)</td>
<td>2.85</td>
<td>1.86, 4.35</td>
<td>0.91</td>
<td>0.54, 1.53</td>
</tr>
</tbody>
</table>

1. Adjusted for age, gender, educational attainment, relationship status, employment status, other substance use and neuroticism

### 8.4.3 Psychosis

A significant association existed between cannabis involvement and the proportion of persons screening positively for psychosis (Table 8.4). While 0.7% of non-users screened positive, around 2% of users, 4% of those with cannabis abuse, and 7% of those with cannabis dependence screened positively. These prevalence estimates translated into odds of screening positively for psychosis that were between 4-11 times greater among cannabis users compared to non-users (bivariate odds ratios 3.6 – 10.8; Table 8.4).

After conducting multiple regression analyses that controlled for other drug use, demographic variables, and neuroticism, those meeting criteria for cannabis dependence
were still around three times more likely to screen positively for psychosis than non-users of cannabis (OR = 2.9, 95%CI: 1.4, 6.0; Table 8.4). However, cannabis use and DSM-IV cannabis abuse were not significantly associated with screening positively for psychosis after controlling for the other factors examined here.

Table 8.4: Weighted prevalence, unadjusted and adjusted odds ratios (OR) and confidence intervals (95%CI) of screening positively for psychosis, according to cannabis involvement

<table>
<thead>
<tr>
<th></th>
<th>Prevalence</th>
<th>OR</th>
<th>95%CI</th>
<th>Adjusted OR</th>
<th>Adjusted 95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (SE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Psychosis “case”</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cannabis use</td>
<td>0.7 (0.1)</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>2.4 (0.7)</td>
<td>3.56</td>
<td>2.05, 6.23</td>
<td>1.50</td>
<td>0.81, 2.80</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>3.9 (2.8)</td>
<td>4.64</td>
<td>1.43, 14.98</td>
<td>1.78</td>
<td>0.51, 6.23</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>6.8 (3.2)</td>
<td>10.80</td>
<td>5.91, 19.89</td>
<td>2.89</td>
<td>1.39, 5.99</td>
</tr>
</tbody>
</table>

1. Adjusted for age, gender, educational attainment, relationship status, employment status, other substance use and neuroticism

**8.4.4 TREATMENT SEEKING**

Table 8.5 shows the proportion of persons who had met criteria for cannabis abuse and dependence who had sought help for a mental health problem according the presence of other substance use and mental disorders. Persons who also met criteria for a mood or anxiety disorder in addition to meeting criteria for cannabis abuse or dependence were more likely to have sought help for a mental health problem. Two thirds of those who had also met criteria for a mood disorder had sought treatment; even higher proportions of those who also met criteria for an anxiety disorder had sought treatment. Approximately 80% of cannabis dependent persons who also screened positively for psychosis had sought mental health treatment. While alcohol use disorders did not appear to be associated with a different likelihood of having sought treatment, the simultaneous presence of another drug
use disorder was associated with a higher likelihood of having sought treatment. Hence, comorbid problems predicted a higher likelihood of treatment seeking among persons with cannabis use disorders.

Persons meeting criteria for cannabis dependence who had sought mental health treatment were more likely than those in the general population to also meet criteria for a wide range of comorbid problems. Among cannabis dependent persons who had sought treatment for a mental health problem: 48.7% (SE 9.2%) met criteria for an anxiety disorder, 32.4% (SE 7.8%) met criteria for a mood disorder, 34.1% (SE 17.3%) met criteria for alcohol dependence, 31.5% (SE 13.3%) met criteria for dependence on other drugs, and 22.4% (SE 10.4%) screened positively for psychosis. Comparison with the overall rates presented in previous tables (Tables 8.2-8.4) reveals that these rates are substantially higher than the rates occurring among cannabis dependent persons in the general population.
<table>
<thead>
<tr>
<th></th>
<th>Prevalence of service use for a mental health problem</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (SE)</td>
</tr>
<tr>
<td>No mood disorder</td>
<td></td>
</tr>
<tr>
<td>Mood disorder</td>
<td></td>
</tr>
<tr>
<td>No anxiety disorder</td>
<td></td>
</tr>
<tr>
<td>Anxiety disorder</td>
<td></td>
</tr>
<tr>
<td>Non-case of psychosis</td>
<td></td>
</tr>
<tr>
<td>Psychosis &quot;case&quot;</td>
<td></td>
</tr>
<tr>
<td>No alcohol use disorder</td>
<td></td>
</tr>
<tr>
<td>Alcohol use disorder</td>
<td></td>
</tr>
<tr>
<td>No other drug use disorder</td>
<td></td>
</tr>
<tr>
<td>Other drug use disorder</td>
<td></td>
</tr>
</tbody>
</table>

| Cannabis abuse | 7.8 (3.6)* | 65.4 (17.0) | 21.9 (4.8) | 100 (0.0) | 184 (5.4) | 27.8 (37.2)* | 19.4 (7.6)* | 17.0 (7.6)* | 16.5 (5.4) | 64.0 (43.7)* |
| Cannabis dependence   | 20.9 (4.3) | 63.7 (14.2) | 16.4 (4.3) | 79.2 (9.2) | 22.3 (3.6) | 87.9 (16.4) | 27.3 (7.3) | 25.8 (16.7)* | 22.2 (5.7) | 47.9 (10.6) |

* This estimate must be considered with caution given the large amount of error surrounding the estimate.
8.5 Discussion

Three patterns of comorbidity were observed in this Chapter. First, all levels of cannabis use were related to substance use and substance use disorders, and multiple regression analyses did not affect these associations. Second, heavier involvement with cannabis use was correlated with a higher prevalence of mood and anxiety disorders, but this relationship did not persist after taking account of other substance use. Third, cannabis dependence remained associated with a higher likelihood of screening positively for psychosis after adjusting for all other factors considered in multiple regression analyses.

8.5.1 Cannabis Use and Other Substance Use

Cannabis users, and those meeting criteria for cannabis abuse and dependence, were highly likely to use a range of the other substances and to be problematic users of these substances. Regular tobacco use was reported by 20% of non-users of cannabis, compared to 50-70% of persons with some involvement with cannabis use. Cannabis users (regardless of the level of use) had similarly increased odds of alcohol and other drug use.

The pattern was somewhat different for abuse and dependence upon other substances. Those who met criteria for cannabis dependence were most likely to also meet criteria for dependence upon sedatives, stimulants or opiates. Those who met criteria for either abuse or dependence upon cannabis were most likely to also meet criteria for abuse of other drugs, and dependence upon alcohol. All cannabis use groups had similarly increased risks of meeting criteria for alcohol abuse relative to non-users of cannabis. Cannabis users (who did not meet criteria for abuse/dependence) also had increased odds of these disorders relative to non-users.

There are numerous possible reasons for the fact that all these associations remain significant after statistical adjustment. The first is that the associations are explained by factors common to the use of different substances that were not considered in these
analyses. In this way, cannabis use and other substance use are two outcomes, unrelated to each other, that co-occur because many of the risk factors for each are similar or the same (MacCoun, 1998). For example, research has found that persons with higher numbers of social or environmental risk factors such as poor parental relationships and social disadvantage have been found to be more likely to use all substance types (Lynskey et al., 1998; Newcomb et al., 1986).

It may also be that common familial factors increase the likelihood of substance misuse in general (Merikangas et al., 1998b). In particular, genetic vulnerabilities appear to increase the likelihood of dependence on a range of substance types (Kendler et al., 1999; Kendler et al., 1994; Kendler & Prescott, 1998a; Kendler & Prescott, 1998b; Kendler et al., 1997b). These vulnerabilities could be common across drug types, a hypothesis that was supported in a recent examination of nicotine and alcohol dependence among twins (True et al., 1999a).

A second possibility is that there is a causal relationship between cannabis use and other substance use. Sometimes called the “gateway hypothesis”, this view proposes that substance use progresses through stages, with progression to a higher stage made more likely by use of a drug at an earlier stage (Kandel & Faust, 1975; Kandel et al., 1986; Kandel et al., 1992; Yamaguchi & Kandel, 1984a; Yamaguchi & Kandel, 1984b).

There are a number of ways in which cannabis use might be causally related to other drug use problems (Fergusson & Horwood, 2000). First, cannabis could encourage experimentation with other drugs because its use was pleasurable (Fergusson & Horwood, 2000; MacCoun, 1998). Second, cannabis use could lead to a greater likelihood of a social context in which illicit drug use of other kinds is more likely, for example, through peer affiliations and proximity to sources of illicit drugs (Fergusson & Horwood, 1997; MacCoun, 1998). Third, it could be that cannabis use is one part of a developmental pathway in which cannabis use is one indicator of a more “deviant” developmental path (Fergusson & Horwood, 2000; Sroufe, 1997). A recent longitudinal study examined these possibilities and found that cannabis use preceded other illicit drug use in almost all cases; that cannabis and other illicit drug use were characterised by similar risk factors; and that even after adjusting for a large number of individual, social, familial and lifestyle factors,
those who had used cannabis at least 50 times in a year were still 60 times more likely than non-users to have used illicit drugs (Fergusson & Horwood, 2000). This finding does not rule out the possibility that common genetic factors may have explained the relationship.

8.5.2 Cannabis Use and Mood and Anxiety Disorders

There was a significant bivariate association between involvement with cannabis use and the prevalence of DSM-IV mood and anxiety disorders. Among those meeting criteria for cannabis dependence in the past year, just over one in seven met criteria for a mood disorder (14%), while one in six met criteria for an anxiety disorder (17%). In comparison, 6% of non-users met criteria for a mood disorder, and 5% met criteria for an anxiety disorder. These associations are consistent with the results of the NLAES (Grant, 1995), and with the ECA and NCS (Anthony & Helzer, 1991; Kessler et al., 1996).

The bivariate relationships between cannabis use and mood and anxiety disorders did not remain in multiple regression analyses. In particular, it was after controlling for other drug use that these relationships disappeared. In other words, once account was taken of the higher rates of other drug use among both cannabis users and those with a mood/anxiety disorder, there was no significant association between cannabis use and either mood or anxiety disorders. The association between cannabis use, anxiety and mood disorders seemed to arise because cannabis users were more likely to: meet criteria for an alcohol use disorder; to smoke tobacco regularly; to use other drug types; and have higher neuroticism scores.

These results do not rule out an indirect relationship between cannabis use and anxiety or depression. For example, cannabis users might be more likely to develop other drug use problems, and this drug use might in turn increase the risk of depression. The present data do not allow a test of this hypothesis - longitudinal studies are needed to do so. Prospective studies might also examine the effect of reducing cannabis and other drug use on anxiety and depression among cannabis users who are anxious and/or depressed.
Some other indirect relationship could exist. For example, it may be that cannabis use at an early age increases the likelihood of lower educational attainment (Lynskey & Hall, 2000). Poorer educational qualifications could limit a person’s employment prospects and unemployment may subsequently lead to depression. This is an instance where the mental health consequences of cannabis use might arise through other factors.

8.5.3 Cannabis Use and Psychosis

In the Australian adult population, persons who used cannabis were more likely to screen positively for psychosis. Around one in 143 persons who were non-users screened positively, with the prevalence increasing as involvement with cannabis increased, such that one in 15 persons who met criteria for cannabis dependence also screened positively for psychosis.

After controlling for demographics, neuroticism and other substance use, the relationship between cannabis dependence and psychosis was still significant. There are several possible reasons for this association (Hall, 1998a; McKay & Tennant, 2000), which have been the subject of considerable debate. Given the findings of this Chapter, and the relative lack of epidemiological research on persons with psychosis, Chapter Ten examines patterns of substance use, including cannabis use, among the persons who screened positively for psychosis in the NSMHWB. This Chapter goes into greater detail of the clinical and theoretical implications of the findings. Chapter Eleven further explores the hypothetical relationships between cannabis use and psychosis through mathematical modelling of the relationships.

8.5.4 Treatment Implications

The current findings have significant implications for treatment provision. There was an extremely high prevalence of other drug use problems among persons with problematic cannabis use in the general population. The presence of another substance use disorder also appeared to be associated with a greater likelihood of having sought help for a mental health problem. Around one in three persons with cannabis dependence who had sought
treatment also met criteria for alcohol dependence and for other drug dependence. Around one in three had met criteria for a mood disorder (32%), and almost half (49%) met criteria for an anxiety disorder, and 22% screened positively for psychosis. These elevated rates are consistent with other research examining this issue (Berkson, 1946; Caron & Rutter, 1991; Galbaud Du Fort et al., 1993).

Because research into treatment for cannabis dependence is a relatively recent phenomenon (Stephens, Roffman, & Simpson, 1994), there is a lack of evidence on the effect of co-occurring substance use problems on treatment outcomes for cannabis dependence. However, given some evidence that persons with tobacco use or alcohol use disorders may have a poorer treatment outcome when there are comorbid problems (Borrelli et al., 1996; Hasin et al., 1996; Kessing, 1999; Tsoh et al., 2000), until research evidence is available, it may be wise to cautiously assume that comorbid substance use and mental disorders problems may worsen treatment outcome for cannabis dependence.

There is a need for further research into the effect of comorbid problems upon treatment outcome for cannabis dependence.

The present study shows that cannabis dependent persons who come to the attention of treatment services for mental health problems also have other substance use and mental disorders. This possibility needs to be kept in mind by clinicians. The use of simple screening instruments for other substance use and for mental health problems needs to be considered. Among those who do have comorbid problems, interventions for such problems may need to be integrated with treatment for cannabis dependence. There is also a great need for future research into treatment for cannabis dependence to also examine treatments for comorbid substance use and mental health problems.
8.6 Conclusions

There was a strong relationship between the level of cannabis involvement, and both other substance use and other substance use disorders in the general Australian population. There was an extremely high prevalence of other drug use problems among persons with problematic cannabis use in the general population. These associations were not accounted for by demographic factors or neuroticism. From the present data, it is not possible to identify the nature of the relationship between cannabis use and other drug use. Other substance use needs to be considered when people request treatment for problematic cannabis use.

There was also a significant bivariate relationship between the level of cannabis involvement, and mood and anxiety disorders. However, this relationship did not remain after considering other drug use and trait neuroticism – raising doubts about a direct causal relationship between cannabis use and these disorders. This finding does not exclude the possibility that an indirect causal relationship exists, for example, if cannabis use increased the likelihood of other substance use, which then increased the risks of depression and anxiety.

The comorbidity of anxiety and mood disorders with cannabis dependence still needs to be considered in treatment of both cannabis dependence and depression/anxiety. Future work might examine the effect of other mental health problems on treatment for cannabis dependence, and investigate more comprehensive therapies for cannabis dependent persons. This is particularly important since cannabis dependent persons coming to the attention of treatment services will be much more likely to have multiple mental health problems that need to be addressed in treatment.

Given that the patterns of comorbidity observed for alcohol, tobacco and cannabis use appeared to differ, the next Chapter directly compares the patterns of comorbidity between these three substances and other substance use and mental disorders in the NSMHWB.
9  A COMPARISON OF THE COMORBIDITY PATTERNS OF ALCOHOL, TOBACCO AND CANNABIS USE\(^1\)

The previous three Chapters have separately examined the patterns of heterotypic and homotypic comorbidity of alcohol, tobacco and cannabis use. These analyses found that the use of each of these three drug types was indeed associated with other substance use, other substance use disorders and with other mental disorders.

However, there was no direct comparison of patterns of comorbidity across the three drug types. Previous epidemiological research has compared: the risks of substance dependence among users of a substance (the conditional prevalence of dependence); and the physical health effects of substance use. The findings of these efforts will be outlined below.

9.1.1 COMPARATIVE ANALYSES

A comparative approach has previously been adopted to compare the prevalence of dependence among users of different drugs (Anthony et al., 1994). Anthony and colleagues examined the prevalence of the use of a range of different drug types, and the prevalence of dependence among users of these substances. They found that this conditional prevalence of dependence varied across different drug types. Around 15% of persons who reported ever using alcohol had met criteria for alcohol dependence at some point in their lives, compared to 32% of those who ever reported using tobacco met criteria for nicotine dependence, and 9% of those who reported ever using cannabis met criteria for cannabis dependence (Anthony et al., 1994). The prevalence of heroin dependence among those who had ever used heroin was around 25%; among those who had ever used cocaine or

See also Appendix L for peer reviewed papers and conference presentations arising from this thesis.
psychoactive stimulants, the proportions who had met criteria for dependence were 17% and 11% respectively. 

These findings could reflect differences in the dependence potential of these different drug types. Substance use problems may be more likely to develop among persons with certain characteristics (see Chapter Five; Kandel et al., 1997; Robins & Regier, 1991), but the strength of these relationships may differ between substances (see Appendix D; Anthony et al., 1994). While psychoactive drugs act on similar pathways in the brain (DiChiara & North, 1992; Koob & LeMoal, 1997; Nutt, 1997), they may also have individual effects upon neurotransmitters (Nutt, 1997).

Epidemiologists have also compared the morbidity and mortality attributable to alcohol, tobacco and illicit drugs (English et al., 1995; Murray & Lopez, 1996). These analyses have provided two types of information: (a) a comparison of the relative total burden of disease attributed to these three classes of substance; and (b) a comparison of the types of health burden attributable to the use of these substances.

In 1990, alcohol, tobacco and illicit drug use were estimated to have accounted for 10%, 12% and 2%, respectively, of the burden of premature mortality and disability in established market economies (Murray & Lopez, 1997). English and colleagues provided information on the specific health conditions caused by alcohol, tobacco and illicit substance use (English et al., 1995). Their analyses suggested that, for example, alcohol use was more strongly associated with road accidents, trauma, suicide and cancer; tobacco was related to cancer and heart disease; and illicit drugs were associated most strongly with overdose and suicide.

A qualitative comparison has also been made of the physical and psychological risks of alcohol, cannabis, nicotine and opiates (Hall, Degenhardt, & Lynskey, 2001; Hall, Room & Bondy, 1999b). This review suggested that, for example, both tobacco and cannabis use shared the risks associated with smoking as a route of administration; while alcohol carried a greater risk than cannabis, if used during pregnancy, of causing damage to the foetus. Heavy alcohol use produced significant cognitive impairments that did not appear to occur among heavy long term cannabis users (Hall et al., 2001; Hall et al., 1999b).
9.1.2 Research Issues

Comparisons of the mental health correlates and consequences of alcohol, tobacco and cannabis use are in their infancy. The NSMHWB provides an opportunity to directly compare relationships between alcohol, tobacco and cannabis and mental health problems. Such a comparison may disclose whether involvement with any drug is associated with comorbidity in general, or if the three drugs have different patterns of association with other mental health problems. If the latter were the case, it may have implications for: theories of the aetiology of comorbidity; for treatment of drug use disorders; and for public health approaches to reducing the harm caused by these drugs.

There do not appear to be any published comparisons of how these three drugs are related to other mental disorders in the general population. For example, analyses of the NCS have focused on explaining associations between a single drug type and other mental disorders (e.g. Kessler et al., 1997b; Lasser et al., 2000; Warner et al., 1995). While such analyses provide important information about persons who use a specific drug, they raise several issues. First, if other substance use is not considered in the analyses, the other mental health problems associated with the specific drug may reflect the use of other drugs or the effects of polydrug use. Second, there is no direct comparison of the strength of the association between the use of different drug types and other mental disorders. The present study aims to compare the patterns of comorbidity of alcohol, cannabis and tobacco in the same population sample while controlling for the use of other substances and sociodemographic characteristics of the users.
The NSMHWB provided nationally representative data on the mental health of Australian persons aged 18 years and over. This means that we can be confident that the results found are representative of the adult population in general. It also involved the assessment of participants with standardised diagnostic criteria that have been shown to be reliable and valid. The aims of the present study are as follows:

1. To compare the relationships between the level of involvement with use of alcohol, tobacco and cannabis, and the following indices of mental well-being:
   a. Other substance use (stimulants, sedatives or opiates);
   b. DSM-IV substance use disorders;
   c. DSM-IV mood disorders;
   d. DSM-IV anxiety disorders;
   e. Psychosis.

2. To examine whether other factors (such as demographic variables, other substance use and neuroticism) might explain observed associations.
9.3 Method

For details of the design and conduct of the NSMHWB, see Chapter Five.

9.3.1 Measures

9.3.1.1 Alcohol use

A four-level variable was created: no alcohol use in the past 12 months, alcohol use without meeting criteria for a DSM-IV disorder, meeting criteria for DSM-IV alcohol abuse, and meeting criteria for DSM-IV alcohol dependence.

9.3.1.2 Tobacco use

Persons who reported using tobacco were coded as tobacco users. It is likely that the majority of persons who reported current tobacco use would have been nicotine dependent, since previous research has estimated that 55-87% of current tobacco users are nicotine dependent (Breslau et al., 1991; Woody et al., 1993).

9.3.1.3 Cannabis use

Involvement with cannabis use was categorised as a four level variable: fewer than six occasions of use in the past 12 months (termed “no use”), more frequent use without meeting criteria for DSM-IV abuse or dependence (“cannabis use”), DSM-IV cannabis abuse, and DSM-IV cannabis dependence.
9.3.1.4 Outcome variables

1. Other substance use

Persons were coded as using “other substances” if they reported using sedatives, stimulants or opiates more than five times within the past year.

2. Other substance abuse/dependence

Persons were coded as meeting criteria for an “other substance use disorder” if they met criteria for DSM-IV sedative, stimulant or opiate abuse or dependence.

3. Anxiety disorders

Persons were coded as meeting criteria for a DSM-IV anxiety disorder if they met criteria for panic disorder, agoraphobia, social phobia, generalised anxiety disorder, obsessive-compulsive disorder, or post-traumatic stress disorder.

4. Mood disorders

Persons were coded as meeting criteria for a DSM-IV mood disorder if they met criteria for major depressive disorder, dysthymia, bipolar I disorder, or bipolar II disorder.

5. Psychosis

Persons were considered to be a psychosis “case” if they scored three or more on the psychosis screener (see Chapter Five).

9.3.1.5 Covariates

1. Social and demographic characteristics
   - Gender;
   - Age;
   - Education;
   - Relationship status;
   - Employment status.
2. Other substance use

Note that this variable was only included in analyses examining comorbidity with anxiety and mood disorders, and psychosis case status. All persons were asked about the use of illicit stimulants, sedatives or opiates more than five times in the past 12 months; as well as the extramedical use of prescribed stimulants, sedatives or opiates more than five times in the past 12 months. If persons reported such use, for the current study they were considered to have “used other drugs” within the past year.

3. Personality

Scores on the neuroticism scale of the EPQ were included in the present analyses. Persons scoring highly on measures of neuroticism have been characterised as moody, anxious and irritable (Eysenck & Eysenck, 1991).

9.3.2 Data analysis

Weighted estimates of the 12-month prevalence and comorbidity are presented in this Chapter. More detail of weighting and regression approaches is provided in Chapter Five. Prevalence estimates and their standard errors were calculated using SUDAAN Version 7.5.3 (Research Triangle Institute, 1997).

Multiple logistic regression analyses were carried out for each outcome. A series of logistic regression analyses was carried out using STATA 5.0 for Windows (STATA Corporation, 1997). The first regression was a bivariate logistic regression in which only the cannabis, alcohol or tobacco involvement variable was included to predict the outcome variable. Cannabis and alcohol involvement were dummy coded, with each level of involvement (cannabis/alcohol use without disorder, DSM-IV abuse, DSM-IV dependence) compared to non-users as the reference category. For tobacco, the reference category was persons reporting no tobacco use.
Stepwise multiple regression analyses were carried out in which the following variables were added at each step:

1. Cannabis, alcohol and tobacco use included together in the multiple regression;
2. Social and demographic characteristics;
3. Other drug use (when the outcome variables were mood or anxiety disorders, and psychosis “caseness”);

This Chapter only presents results from the first (bivariate) and final (full) models. The details of intermediate regression analyses are provided in Appendix H.
9.4 Results

Alcohol was the most widely used drug class, with two thirds of Australian adults (68%) reporting they had used alcohol in the past year without meeting criteria for a use disorder, and a further 6% meeting criteria for alcohol abuse or dependence. One quarter (25%) of Australian adults reported current tobacco use. One in twenty persons (5%) reported cannabis use without meeting criteria for a use disorder, while around 2% met criteria for a cannabis use disorder in the past year.

9.4.1 Other Substance Use

Figure 9.1 shows the prevalence of the use of sedatives, stimulants or opiates within the past 12 months, according to the level of involvement with cannabis, alcohol and tobacco (see also Table 9.1 for details). In all figures presented, tobacco use has been placed in the “use” category, as nicotine dependence was not assessed. It is likely, however, that many if not most of those who reported using tobacco would have met criteria for nicotine dependence (Breslau et al., 1991; Giovino et al., 1995; Woody et al., 1993).

Figure 9.1: Weighted prevalence of sedative/stimulant/opiate use according to level of involvement with alcohol, cannabis and tobacco
Cannabis users were much more likely to report using at least one of these other drug types (cannabis use 14%, cannabis abuse 12%, cannabis dependence 27%) compared to non-users (3%), with odds ratios ranging from 5.4 – 11.3 (Figure 9.1, Table 9.1).

The association with alcohol use was weaker (Figure 9.1, Table 9.1). Alcohol use (without disorder) was not associated with an increased likelihood of using sedatives, stimulants or opiates. Those meeting criteria for alcohol abuse or dependence were more likely than users/non-users to report use of these other drug types (ORs 4.1, 7.3 respectively). Tobacco use was associated with a doubling of the likelihood of having used these other drug types (6% vs. 3%, OR 2.3).

A similar pattern of associations existed with other substance use disorders. Cannabis use (regardless of the level of involvement) was strongly associated with problematic drug use (Figure 9.2, Table 9.1). By far the strongest marker of other drug use disorders was cannabis dependence, which was associated with a 34.5 times greater likelihood of meeting criteria for another drug use disorder (compared to non-users of cannabis). Those who were alcohol dependent were ten times more likely to meet criteria for another drug use disorder than non-drinkers (Table 9.1). The other alcohol use groups (use and abuse) did not differ significantly from non-users of alcohol in the likelihood of meeting criteria for another drug use disorder. Tobacco use, in contrast, was a significant marker of increased risk of meeting criteria for another drug use disorder, with increased odds relative to non-users of 4.7 (95%CI 3.1, 7.1).

Figure 9.2: Weighted prevalence of other drug use disorders according to level of involvement with alcohol, cannabis and tobacco
Table 9.1: Weighted prevalence, unadjusted odds ratios (OR) and 95% confidence intervals (95%CI) for other substance use according to alcohol, cannabis and tobacco use

<table>
<thead>
<tr>
<th></th>
<th>Prevalence</th>
<th>OR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (SE)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other substance use</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>2.8 (0.4)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>3.0 (0.4)</td>
<td>1.23</td>
<td>0.94, 1.60</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>10.9 (2.8)</td>
<td>4.13</td>
<td>2.41, 7.10</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>15.3 (3.2)</td>
<td>7.26</td>
<td>5.15, 10.26</td>
</tr>
<tr>
<td>No cannabis use</td>
<td>2.6 (0.2)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>14.4 (2.2)</td>
<td>5.81</td>
<td>4.37, 7.69</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>12.4 (4.1)</td>
<td>5.35</td>
<td>2.72, 10.49</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>26.8 (9.0)</td>
<td>11.32</td>
<td>7.61, 16.79</td>
</tr>
<tr>
<td>No tobacco use</td>
<td>2.8 (0.2)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>6.1 (0.5)</td>
<td>2.27</td>
<td>1.84, 2.78</td>
</tr>
<tr>
<td><strong>Other substance use disorder</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>0.7 (0.3)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>0.6 (0.1)</td>
<td>0.74</td>
<td>0.44, 1.24</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>2.2 (1.3)</td>
<td>2.90</td>
<td>1.00, 8.50</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>7.3 (2.3)</td>
<td>9.96</td>
<td>5.70, 17.37</td>
</tr>
<tr>
<td>No cannabis use</td>
<td>0.5 (0.1)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>3.1 (1.1)</td>
<td>5.58</td>
<td>3.14, 9.98</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>4.1 (3.2)</td>
<td>7.27</td>
<td>2.22, 23.76</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>17.6 (6.7)</td>
<td>34.52</td>
<td>20.49, 56.83</td>
</tr>
<tr>
<td>No tobacco use</td>
<td>0.4 (0.1)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>2.4 (0.4)</td>
<td>4.69</td>
<td>3.10, 7.09</td>
</tr>
</tbody>
</table>
Table 9.2 shows the odds ratios produced after accounting for other factors that may have explained the higher rates of other substance use among cannabis, alcohol and tobacco users (namely, social and demographic factors, and neuroticism). After adjusting for these other factors, tobacco use was no longer associated with an increased likelihood of using sedatives, stimulants or opiates (OR 1.2, 95%CI 0.95, 1.53). In contrast, all levels of cannabis involvement remained associated with an increased likelihood of using these other drug types after multiple regressions were carried out, with adjusted odds ratios of between 3.2 and 6.8 (Table 9.2). Alcohol abuse and alcohol dependence also remained associated with other drug use: those meeting criteria for alcohol abuse or dependence were still around three times more likely than non-users to report using at least one of these other drug types.

While the strength of the relationships between alcohol, tobacco and cannabis use, and other substance use disorders, was significantly reduced in all cases, the relative patterns changed very little after controlling for demographics and neuroticism (Table 9.2). Those who were cannabis dependent still had the highest increased odds, relative to non-users, of meeting criteria for other drug use disorders (OR 14.0). Those meeting criteria for alcohol dependence (OR 2.7) and tobacco users (OR 1.9) still had increased odds. Cannabis use (OR 3.1) was still associated with meeting criteria for another drug use disorder. Although the odds ratio for cannabis abuse was no longer significant, this may have been due to the small sample size and corresponding lack of precision of the estimates (OR 3.1, 95%CI 0.8, 10.9).
Table 9.2: Adjusted odds ratios (OR) and 95% confidence intervals (95%CI) for other substance use and substance use disorders according to alcohol, cannabis and tobacco use

<table>
<thead>
<tr>
<th></th>
<th>Adjusted OR$^1$</th>
<th>Adjusted 95%CI$^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Other substance use</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1.29</td>
<td>0.97, 1.71</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>2.55</td>
<td>1.41, 4.59</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>3.08</td>
<td>2.07, 4.57</td>
</tr>
<tr>
<td>No cannabis use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>4.38</td>
<td>3.18, 6.04</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>3.24</td>
<td>1.55, 6.78</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>6.75</td>
<td>4.25, 10.70</td>
</tr>
<tr>
<td>No tobacco use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>1.21</td>
<td>0.95, 1.53</td>
</tr>
<tr>
<td><strong>Other substance use disorder</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>0.77</td>
<td>0.44, 1.35</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>1.20</td>
<td>0.37, 3.86</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>2.73</td>
<td>1.42, 5.27</td>
</tr>
<tr>
<td>No cannabis use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>3.10</td>
<td>1.63, 5.90</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>3.02</td>
<td>0.84, 10.95</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>14.06</td>
<td>7.38, 26.76</td>
</tr>
<tr>
<td>No tobacco use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>1.99</td>
<td>1.24, 3.19</td>
</tr>
</tbody>
</table>

$^1$ Adjusted for demographics and neuroticism and considering the three drugs simultaneously in regressions.
9.4.2 Mood and Anxiety Disorders

Figure 9.3 shows the prevalence of DSM-IV mood disorders according to alcohol use, cannabis use and tobacco use; bivariate odds ratios of these disorders among users compared to non-users are also shown in Table 9.3.

The prevalence of mood disorders was higher among those who met criteria for alcohol dependence than non-drinkers. Alcohol dependent persons were 4.5 times more likely to meet criteria for a mood disorder than were non-drinkers (24% vs. 7%, respectively). In contrast, those who reported drinking without meeting criteria for an alcohol use disorder had a significantly lower rate of mood disorders compared to non-drinkers (5.5% vs. 7.3%). Those meeting criteria for alcohol abuse (6%) did not differ from non-drinkers in the proportion who met criteria for a mood disorder (Figure 9.3, Table 9.3).

Figure 9.3: Weighted prevalence of mood disorders according to level of involvement with alcohol, cannabis and tobacco

All levels of cannabis use were associated with higher rates of mood disorders, with odds ratios of between 2.2 and 2.9 compared to non-users (Table 9.3). Tobacco use was also associated with a doubling of the likelihood of meeting criteria for a mood disorder (OR 2.2).
Table 9.3: Weighted prevalence, unadjusted odds ratios (OR) and 95% confidence intervals (95%CI) of DSM-IV mood and anxiety disorders according to alcohol, tobacco and cannabis use

<table>
<thead>
<tr>
<th></th>
<th>% (SE)</th>
<th>OR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mood disorder</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>7.3 (0.4)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>5.5 (0.3)</td>
<td>0.82</td>
<td>0.70, 0.97</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>6.1 (2.0)</td>
<td>0.90</td>
<td>0.50, 1.60</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>24.0 (4.0)</td>
<td>4.47</td>
<td>3.48, 5.74</td>
</tr>
<tr>
<td>No cannabis use</td>
<td>6.2 (0.3)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>12.1 (2.7)</td>
<td>2.24</td>
<td>1.73, 2.91</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>18.6 (5.3)</td>
<td>2.88</td>
<td>1.61, 5.17</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>13.6 (2.6)</td>
<td>2.85</td>
<td>1.86, 4.35</td>
</tr>
<tr>
<td>No tobacco use</td>
<td>5.4 (0.4)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>10.9 (0.8)</td>
<td>2.20</td>
<td>1.90, 2.54</td>
</tr>
<tr>
<td><strong>Anxiety disorder</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>6.5 (0.5)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>4.5 (0.4)</td>
<td>0.78</td>
<td>0.65, 0.93</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>4.9 (1.9)</td>
<td>0.73</td>
<td>0.37, 1.44</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>19.5 (2.7)</td>
<td>4.42</td>
<td>3.39, 5.75</td>
</tr>
<tr>
<td>No cannabis use</td>
<td>5.4 (0.3)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>8.0 (1.2)</td>
<td>1.78</td>
<td>1.31, 2.41</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>6.4 (2.8)</td>
<td>1.10</td>
<td>0.44, 2.73</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>16.5 (2.6)</td>
<td>4.30</td>
<td>2.88, 6.40</td>
</tr>
<tr>
<td>No tobacco use</td>
<td>4.5 (0.3)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>9.3 (0.8)</td>
<td>2.42</td>
<td>2.07, 2.83</td>
</tr>
</tbody>
</table>
A similar pattern was observed for anxiety disorders (Figure 9.4, Table 9.3). Alcohol dependence and cannabis dependence were associated with increased risks of anxiety disorder (OR 4.4 and 4.3, respectively), while tobacco use was associated with a 2.4 times greater chance of meeting criteria for an anxiety disorder (Table 9.3). Alcohol users who did not meet criteria for an alcohol use disorder were less likely to have an anxiety disorder than non-drinkers (4.5% vs. 6.5% respectively), while those meeting criteria for alcohol abuse did not differ from non-drinkers in their risk of meeting criteria for an anxiety disorder (Figure 9.4).

Figure 9.4: Weighted prevalence of anxiety disorders according to level of involvement with alcohol, cannabis and tobacco

These patterns changed markedly after multiple regression analyses (Table 9.4). No level of cannabis use was associated with an increased risk of meeting criteria for a mood disorder after the effects of demographics, other drug use and neuroticism were considered. The significant bivariate association disappeared after considering tobacco, alcohol and cannabis and other drug use simultaneously (see Appendix H for details of intermediate steps in the regression analyses). In contrast, alcohol dependence and tobacco use remained associated with a higher likelihood of meeting criteria for a mood disorder. Alcohol dependent
persons were still twice as likely to meet criteria for a mood disorder (OR 2.0), while tobacco users were still 1.5 times more likely.

As can be seen in Table 9.4, cannabis use was no longer associated with anxiety disorders after adjustment for other variables in multiple regressions. This relationship disappeared after including alcohol, tobacco and other drug use in the analysis (see Appendix H). Alcohol use and abuse were also not significantly associated with anxiety disorders. In contrast, alcohol dependence and tobacco use remained significant markers of anxiety disorders (OR 1.9 and 1.7, respectively).
Table 9.4: Adjusted odds ratios (OR) and 95% confidence intervals (95% CI) of DSM-IV mood and anxiety disorders according to alcohol, tobacco and cannabis use

<table>
<thead>
<tr>
<th></th>
<th>Adjusted OR&lt;sup&gt;1&lt;/sup&gt;</th>
<th>Adjusted 95% CI&lt;sup&gt;1&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mood disorder</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>0.98</td>
<td>0.81, 1.19</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>0.64</td>
<td>0.34, 1.21</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>1.98</td>
<td>1.45, 2.72</td>
</tr>
<tr>
<td>No cannabis use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>1.30</td>
<td>0.94, 1.79</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>1.46</td>
<td>0.73, 2.91</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>0.91</td>
<td>0.54, 1.54</td>
</tr>
<tr>
<td>No tobacco use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>1.48</td>
<td>1.24, 1.76</td>
</tr>
</tbody>
</table>

| **Anxiety disorder**   |                         |                              |
| No alcohol use         | 1.00                    | --                           |
| Alcohol use            | 1.01                    | 0.81, 1.25                   |
| Alcohol abuse          | 0.49                    | 0.23, 1.05                   |
| Alcohol dependence     | 1.85                    | 1.31, 2.62                   |
| No cannabis use        | 1.00                    | --                           |
| Cannabis use           | 0.87                    | 0.59, 1.27                   |
| Cannabis abuse         | 0.37                    | 0.13, 1.04                   |
| Cannabis dependence    | 1.42                    | 0.84, 2.39                   |
| No tobacco use         | 1.00                    | --                           |
| Tobacco use            | 1.66                    | 1.36, 2.01                   |

1. Adjusted for demographics, other drug use and neuroticism, and considering the three drugs simultaneously in regressions.
9.4.3 Psychosis

Figure 9.5 shows the association between screening positively on the psychosis screener and the use of alcohol, cannabis and tobacco (see also Table 9.5). As can be seen in the bivariate odds ratios, all levels of cannabis use, alcohol dependence, and tobacco use were associated with significantly increased risks of screening positively for psychosis (Table 9.5). Those meeting criteria for alcohol dependence were 6.4 times more likely than non-drinkers to screen positively, while tobacco users were 4.7 times more likely. Cannabis dependence was associated with an eleven-fold risk of screening positively for psychosis relative to non-users (OR 10.8). Alcohol use and abuse were not associated with increased risks of screening positively for psychosis compared to non-drinkers.

Figure 9.5: Weighted prevalence of persons screening positively for psychosis according to level of involvement with alcohol, cannabis and tobacco
Table 9.5: Weighted prevalence and unadjusted odds ratios (OR) and confidence intervals (95%CI) of screening positively for psychosis according to alcohol, tobacco and cannabis use

<table>
<thead>
<tr>
<th></th>
<th>% (SE)</th>
<th>OR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>No alcohol use</td>
<td>0.7 (0.2)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>0.8 (0.1)</td>
<td>1.06</td>
<td>0.67, 1.68</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>1.8 (1.3)</td>
<td>2.55</td>
<td>0.88, 7.39</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>4.3 (1.3)</td>
<td>6.37</td>
<td>3.59, 11.34</td>
</tr>
<tr>
<td>No cannabis use</td>
<td>0.7 (0.1)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>2.4 (0.7)</td>
<td>3.56</td>
<td>2.05, 6.23</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>3.9 (2.8)</td>
<td>4.64</td>
<td>1.43, 14.98</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>6.8 (3.2)</td>
<td>10.80</td>
<td>5.91, 19.89</td>
</tr>
<tr>
<td>No tobacco use</td>
<td>0.5 (0.1)</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>2.3 (0.4)</td>
<td>4.65</td>
<td>3.19, 6.75</td>
</tr>
</tbody>
</table>

After conducting multiple regressions in which these three drug types, the use of sedatives, stimulants or opiates, demographics and neuroticism were considered simultaneously, only cannabis dependence and tobacco use remained significantly associated with increased odds of screening positively for psychosis (OR 2.8 and 2.5, respectively; Table 9.6). The relationship between alcohol dependence and psychosis did not remain significant.
Table 9.6: Adjusted odds ratios (OR) and confidence intervals (95% CI) of screening positively for psychosis according to alcohol, tobacco and cannabis use

<table>
<thead>
<tr>
<th></th>
<th>Adjusted OR¹</th>
<th>Adjusted 95% CI¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>No alcohol use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1.22</td>
<td>0.74, 2.01</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>1.46</td>
<td>0.47, 4.51</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>1.70</td>
<td>0.87, 3.30</td>
</tr>
<tr>
<td>No cannabis use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>1.45</td>
<td>0.77, 2.70</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>1.76</td>
<td>0.50, 6.18</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>2.84</td>
<td>1.37, 5.90</td>
</tr>
<tr>
<td>No tobacco use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>2.47</td>
<td>1.63, 3.75</td>
</tr>
</tbody>
</table>

¹. Adjusted for demographics, other drug use and neuroticism, and considering the three drugs simultaneously in regressions
9.5 Discussion

This Chapter has compared the patterns of comorbidity of alcohol, cannabis and tobacco with other substance use, anxiety and mood disorders, and screening positively for psychosis. These analyses revealed differences between the three substances in: (a) the types of comorbidity observed; (b) the strength of the relationships; and (c) the extent to which the associations could be explained by common factors. Table 9.7 summarises the patterns of heterotypic and homotypic comorbidity observed between alcohol, tobacco and cannabis, after adjustment for the factors considered in multiple regressions.

9.5.1 Other Substance Use and Use Disorders

When each drug was considered separately, the use of alcohol, cannabis or tobacco use was associated with an increased likelihood of using all substance types considered here. They were also all associated with the problematic use of other substance types. Alcohol and cannabis abuse/dependence were the strongest markers for other substance use and use disorders.

In many cases, this association was not explained by the common factors examined (Table 9.7). The increased rates of other substance use and use disorders among alcohol users and those meeting criteria for alcohol abuse, compared to rates of substance use and use disorders found in non-users of alcohol appeared to be accounted for by the common factors considered here.

In contrast, alcohol dependence, tobacco use and cannabis involvement remained associated with higher rates of substance use and substance use disorders. Hence, it did not appear to be the case that the higher rates of substance use problems simply reflected demographic differences between groups, levels of neuroticism, nor that it reflected the use of multiple drug types. More comprehensive discussions of the implications of these findings for each individual drug type are provided in Chapters Six, Seven and Eight.
Table 9.7: Patterns of association between alcohol, tobacco and cannabis use, and other mental health problems after adjusting for other factors

<table>
<thead>
<tr>
<th></th>
<th>Alcohol</th>
<th>Tobacco Use</th>
<th>Cannabis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>U</td>
<td>A</td>
<td>D</td>
</tr>
<tr>
<td>Other substance use</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Other substance use disorders</td>
<td>X</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Mood disorders</td>
<td>X</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>X</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Screening positively for psychosis</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

Note:  
X = no significant association remained;  
✓ = a significant association remained;  
U = use without meeting criteria for DSM-IV abuse or dependence;  
A = DSM-IV abuse; and  
D = DSM-IV dependence.

It is difficult to distinguish between a number of possible explanations for these observed patterns of association in cross-sectional data. The first possibility is that there is no causal relationship between the use of alcohol, tobacco, cannabis and other types of substance use, but that other common factors that were not considered here were responsible for the association. These might be environmental factors or genetic factors. A second possibility is that there is a causal connection between the use of one substance, and increased likelihood of using another. Regardless of the reasons for the findings of the present report, however, it is clear that tobacco, alcohol and cannabis use are all associated with higher risks of other substance use. This finding has implications for the physical and mental health of users. It also has implications for treatment, since it is likely that persons seeking treatment for an alcohol, tobacco or cannabis use disorder is likely to be
problematic users of other drugs. The theoretical and treatment implications of these findings are discussed in Chapter 12.

9.5.2 Mood and Anxiety Disorders

On a bivariate level, all levels of cannabis use were associated with increased rates of anxiety and mood disorders. In contrast, alcohol use (without disorder) was associated with lower rates of anxiety and mood disorders. Alcohol abuse was not associated with a higher risk of anxiety and mood disorders than non-drinkers. Alcohol dependence was strongly associated with an increased likelihood of both disorders. Tobacco use was also associated with a higher risk of both anxiety and mood disorders.

These patterns changed significantly after considering demographics, the use of multiple drug types, and neuroticism (Table 9.7). Cannabis use, abuse and dependence were no longer associated with mood or anxiety disorders after these analyses. After including alcohol, and tobacco in the analysis, cannabis use was no longer significantly associated with anxiety or mood disorders (see Table H2, Appendix H). By contrast, alcohol dependence and tobacco use remained significant markers for an increased likelihood of anxiety and mood disorders after multiple regression analyses that controlled for cannabis use and all other variables considered here (Table 9.7).

There has been concern over the possibility that cannabis use, particularly among young persons, is in some way causally related to depression. The present report found that this relationship does not appear to hold in the Australian adult population. Instead, the association arose because cannabis users were more likely to also meet criteria for an alcohol use disorder, smoke tobacco, and use other drug types, all of which were associated with higher rates of mental health problems. The present findings suggest that it may be more appropriate to direct attention to the use of these other drug types when considering mood disorders in young adults. Chapter Twelve discusses the theoretical and treatment implications of these findings further.
9.5.3 Psycheosis

Alcohol dependence, tobacco use and cannabis involvement were all associated on a bivariate level with higher chances of screening positively for psychosis, as assessed by a short screening questionnaire for psychotic symptoms. Cannabis dependence was most strongly associated with screening positively for psychosis.

After controlling for other factors via multiple regression analyses, however, only cannabis dependence and tobacco use were correlated with screening positively for psychosis (Table 9.7). The strength of the association was similar for both tobacco use and cannabis dependence (odds ratios of 2.5 and 2.8, respectively).

The association between cannabis and tobacco use and mental health needs to be disseminated to persons at risk of psychotic illness, to persons who have already been diagnosed with a psychotic illness, and to persons who are heavy substance users. The risks of exacerbation of, or relapse to mental health problems, also need to be highlighted.
9.6 Conclusions

In this general population sample, the strongest predictors of homotypic comorbidity (sedative, stimulant or opiate use and use disorders) were alcohol dependence and involvement with cannabis use, with cannabis dependence being the strongest predictor overall.

By contrast, the strongest predictor of two types of heterotypic comorbidity - anxiety and mood disorders - was alcohol dependence. These findings did not appear to be explained by the other factors considered here. Screening positively for psychosis was most strongly associated with cannabis use (with cannabis dependence again the strongest predictor overall).

Tobacco smoking was a consistent marker of poorer mental health in general, and remained associated with mood and anxiety disorders, substance use disorders, and screening positively for psychosis after common factors were examined.

These findings suggest that different drug types are differentially associated with a range of other mental health problems. This may be because different factors are responsible for the comorbidity between the use of different substances and separate mental health problems. These differential risks may need to be taken into account in treatment if borne out in further research.

Cannabis dependence and tobacco use remained significantly associated with psychosis. There has been limited epidemiological investigation of the substance use patterns of persons with psychosis. Given this lack, and given the burden that psychosis places both upon the individual sufferer, their family and the community at large, the next Chapter provides a more detailed examination of the substance use patterns of persons who screened positively for psychosis in the NSMHWB sample.
10 COMORBIDITY BETWEEN PSYCHOSIS AND SUBSTANCE USE

Previous Chapters have examined comorbidity with psychosis “caseness” among the users of alcohol, tobacco and cannabis. These analyses revealed that persons who were more heavily involved with all of these substances were more likely to screen positively for psychosis. This pattern of comorbidity may have considerable significance, given the chronicity of psychotic disorders such as schizophrenia (Eaton et al., 1992a; Eaton et al., 1992b; Hall et al., 1985; Mason et al., 1996b), the disability sufferers often experience (Keith et al., 1991), and the burden such disorders also place upon the community at large (Hall et al., 1985; Knapp, 1997). Despite this, there is a relative dearth of population-level examinations of comorbidity between psychosis and substance use in general population samples.

The present Chapter focuses on substance use among persons who are likely to meet criteria for psychosis (i.e. from the opposite perspective to previous Chapters). It explores in detail the prevalence of substance use among cases of psychosis; and looks at the association between psychotic symptoms and problematic substance use. Most of the evidence on the association between psychosis and substance use comes from studies of persons with schizophrenia or schizoaffective disorder, the disorders which make up the majority of psychotic disorders (Keith et al., 1991).

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See also Appendix L for peer reviewed papers and conference presentations arising from this thesis.
There has been some examination of the population-level association between psychosis and substance use problems in the general population. Cuffel and colleagues reported on patterns of substance use among 231 cases of schizophrenia identified in the ECA study (Cuffel, Heithoff, & Lawson, 1993). The most commonly used substances were alcohol (37%) and cannabis (23%), followed by stimulants and hallucinogens (13%), narcotics (10%) and sedatives (8%).

There has also been an analysis using ECA data of the relationship between substance use and a “self-reported psychotic experience” (Tien & Anthony, 1990). In this paper, a “case” was a person who (under the age of 50 years) reported experiencing at least one psychotic symptom (from 12 Diagnostic Interview Schedule (DIS) items) within a follow up year. Age-matched cases (n=477) and controls (n=1,818) were compared in a series of logistic regressions controlling for baseline mental health problems and demographic factors. Daily cannabis use (RR = 2.0, 95%CI 1.25, 3.12) and lifetime DSM-III alcohol abuse/dependence (RR = 7.9, 95%CI 1.99, 31.41) were significant predictors of reporting one or more psychotic symptoms after controlling for baseline psychopathology and sociodemographic factors (Tien & Anthony, 1990).

Kendler and colleagues used NCS data to examine the prevalence of alcohol and other drug abuse/dependence among persons who met criteria for DSM-III-R nonaffective psychosis (schizophrenia, schizoaffective disorder, schizophreniaiform disorder, delusional disorder, and psychosis not otherwise specified) (Kendler et al., 1996a). They found that among persons who met such criteria, 43% met DSM-III-R criteria for alcohol dependence, 38% met criteria for drug dependence, 57% met criteria for alcohol abuse/dependence, and 45% met criteria for drug abuse/dependence (Kendler et al., 1996a). The odds of having these disorders were between 4 (alcohol use disorders) and 7 times (drug dependence) greater in persons who met criteria for nonaffective psychosis, compared to those who did not.
10.1.2 SUMMARY

There is evidence that problematic substance use is likely to co-occur with schizophrenia. Problematic substance use is a health concern regardless of a person’s mental health because of the physiological and psychological harms that may result (English et al., 1995). However, problematic substance use has also been found to correlate with a number of adverse outcomes among schizophrenic persons.

In research involving samples of persons in contact with treatment services, problematic substance use has been associated with symptom worsening or relapse (Carey et al., 1991; Salyers & Mueser, 2001), a higher rate of rehospitalisation (Haywood et al., 1995), homelessness or housing instability (Caton et al., 1994; Drake et al., 1991), poor compliance with medication (Pristach & Smith, 1990), poor response to antipsychotic medication (Bowers et al., 1990; Lutz, 1976; Salyers & Mueser, 2001), poorer social functioning (Salyers & Mueser, 2001), increased burden upon the sufferer’s family (Clark, 1994), and increased treatment costs (Bartels et al., 1993). These associations suggest that the co-occurrence of substance use problems with psychotic disorders may have a significant, negative impact upon outcome.

10.1.3 RESEARCH ISSUES

10.1.3.1 LIMITATIONS OF CLINICAL RESEARCH

While clinical evidence suggests cause for concern, there are several reasons why such research may not reveal an accurate picture of the association between substance use and psychotic illness in the general population. First, clinical samples may be subject to a number of selection biases as reviewed in Chapter Four (Berkson, 1946; Caron & Rutter, 1991; Galbaud Du Fort et al., 1993).

Second, there are a number of factors that could explain an association between problematic substance use and psychosis. For example, persons with substance use disorders are more likely to be younger (Anthony et al., 1994; Robins & Regier, 1991), as are persons with psychotic disorders (Jablensky et al., 1991). Furthermore, at younger ages
(with which this report is concerned) the incidence of psychosis is higher among males (Jablensky et al., 1991), who have a higher prevalence of substance use and substance use disorders (Anthony & Helzer, 1991; Anthony et al., 1994; Helzer et al., 1991).

A number of demographic correlates, such as employment and marital status, are similarly related to substance use problems and to psychosis (Anthony & Helzer, 1991; Anthony et al., 1994; Helzer et al., 1991; Jablensky et al., 1991; Warner et al., 1995). Finally, other mental disorders, which tend to co-occur among schizophrenic persons (Bartels et al., 1992; Bartels & Drake, 1989; Kendler et al., 1996a; Poyurovsky, Fuchs, & Weizman, 1999; Siris et al., 2001), are also likely to co-occur among persons with substance use problems (Kessler et al., 1997b; Robins & Regier, 1991). It is possible that some of these common factors may explain observed associations between substance use and psychotic disorders.

10.1.3.2 AUSTRALIAN ESTIMATES

Research using the ECA and NCS data provided important US population-level data on substance-associated risks of experiencing at least one psychotic symptom or meeting criteria for psychosis, one question that remains unanswered, however, is: do the associations observed in the North American general population exist in other countries?

10.1.3.3 LIABILITY TO DEVELOPING PROBLEMATIC SUBSTANCE USE

A second research question raised by the ECA and NCS is whether persons with psychotic disorders are more liable than persons without psychosis to develop substance use problems when they use such substances. Some researchers have suggested that persons with psychosis have a “psychobiological vulnerability” to problematic substance use (Mueser et al., 1998) that may increase their sensitivity to the effects of psychoactive substances. One consequence may be that persons with psychosis develop substance-related problems at lower levels of use. Alternatively, it may be that persons with psychotic disorders are more likely to become heavier users of substances when they use them (i.e. that there is a lower threshold for substance-related problems, and/ or that they are more likely to make the transition to heavier use).
The hypothesis of psychobiological vulnerability may be evaluated by examining the conditional prevalence of substance use disorders among users, i.e. the proportion of persons who use a substance and also report problematic use. This approach has previously been to examine the dependence liability of different substances (Anthony et al., 1994). In the present context, if persons with a psychotic disorder are more liable to problematic substance use, then the conditional prevalence estimate for this group should be higher than it is for those without psychotic disorders.

10.1.3.4 NUMBER OF PSYCHOTIC SYMPTOMS

A third issue worth examining is whether there is a relationship between problematic drug use and the number of psychotic symptoms that a person reports. Any such relationship needs to be examined while controlling for the effects of demographic characteristics, personality, and other mental health problems.

One way to examine the association between substance use and the number of psychotic symptoms is to use ordinal logistic regression (OLR). OLR takes into account the ordering of an ordered categorical outcome variable (in this case, the number of reported psychotic symptoms) (Bender & Grouven, 1997). While more common analytic methods such as logistic regression produce estimates of the size of the odds ratio for a dichotomous outcome variable, classifying an ordered categorical scale into a dichotomous variable loses information about the intervals along the scale. OLR produces an estimate of the average change in the odds for each additional point on the ordered scale (here, for each additional psychotic symptom reported). This allows one average odds ratio to be used to summarise the association between predictors and the ordered categorical outcome variable.
10.2 AIMS

The aims of the present study are therefore to:

1. Estimate the prevalence of psychosis in the Australian population among those under 50 years;

2. Provide estimates in the Australian population of the association between psychosis and drug use. The following substance use patterns are examined:
   a. Use of alcohol, cannabis, sedatives, stimulants and opiates;
   b. Regular use of tobacco, alcohol and cannabis; and
   c. DSM-IV abuse of or dependence upon alcohol, cannabis, sedatives, stimulants and opiates;

3. Examine the conditional prevalence of substance use disorders among users who did and did not screen positively for psychosis; Examine whether there was an association between problematic drug use and increasing numbers of psychotic symptoms using OLR, while taking account of demographic characteristics, measures of mental health and of personality.
10.3 Method

For details of the NSMHWB design and content, see Chapter Five. In the present analyses, only persons under the age of 50 years were included in the analysis, leaving a total of 6,722 persons in the sample. This was done because both psychotic disorders and substance use are more common among younger persons (Robins & Regier, 1991), while organic mental disorders, some of which have psychotic symptoms, are more common among older persons (Henderson, 1998; Jorm, 1998; Kukull & Ganguli, 2000). Limiting the sample to adults under 50 years also made the current analysis consistent with previous US population research (Tien & Anthony, 1990).

10.3.1 Psychosis Screener

This screener was developed for use with general population samples. The psychosis screener (PS) was developed for use in the NSMHWB, using elements of the CIDI to assess the presence of characteristic psychotic symptoms. It comprised 7 items, three of which (1a, 2a, 3a) were asked only if the respondent endorsed a previous question (1, 2, 3 respectively). The first 6 items covered the following features of psychotic disorders: delusions of control, thought interference and passivity (Question 1 and 1a); delusions of reference or persecution (Question 2 and 2a); and grandiose delusions (Question 3 and 3a). The final item (Question 4) assessed whether a respondent had ever received a diagnosis of schizophrenia. Scores ranged from zero to six (if a person endorsed question 3a, this was scored “-1”, while if they did not endorse it, it was scored “0”). Detail on the validation and the specific questions included in this screener is provided in Chapter Five.

In the present study, there were two indicators of psychotic symptoms used. The first was an indicator of likely psychosis “case” status. Persons who obtained a score of three or more on the screener were coded as psychosis “cases”. This indicator was used to estimate the prevalence of substance use and substance use disorders among likely cases of psychosis in the general Australian population.
The second measure was the score on the screener, with scores ranging from zero to a maximum of six. This was used in ordinal logistic regression analyses to examine associations between substance use and the number of psychotic symptoms reported.

10.3.2 **Outcome Variables**

10.3.2.1 **Other Substance Use**

- **Alcohol**: Persons were coded as using alcohol if they reported drinking 12 standard drinks of alcohol within the past year. All drinkers were assessed for their frequency of drinking, and those reporting daily drinking during the past 12 months were categorised as daily drinkers.
- **Tobacco**: Persons who reported using tobacco daily were coded as regular tobacco users.
- **Cannabis**: Persons were coded as using cannabis if they reporting using cannabis more than five times within the past year. Those reporting at least weekly use were coded as weekly users.
- **Sedatives**: Persons were coded as using sedatives if they reported using sedatives more than 5 times within the past year.
- **Stimulants**: Persons were coded as using stimulants if they reported using stimulants more than five times within the past year.
- **Opiates**: Persons were coded as using opiates if they reported using opiates more than five times within the past year.

10.3.2.2 **Other Substance Use Disorders**

- **Alcohol**: abuse or dependence.
- **Cannabis**: abuse or dependence.
- **Sedatives**: abuse or dependence.
- **Stimulants**: abuse or dependence.
- **Opiates**: abuse or dependence.
**10.3.3 Data analysis**

Bivariate associations between “case” status and drug use variables were examined. The first group of these was substance use. The second group of variables was frequent use: daily use was examined in the case of alcohol and tobacco, and at least weekly use in the case of cannabis. The third group of variables was the presence or absence of DSM-IV use disorders.

The conditional prevalence—prevalence among users—was estimated for DSM-IV alcohol and cannabis abuse and dependence, as well as for other drug use disorders (abuse/dependence). Sedative, stimulant and opiate use disorders were combined due to the low rates of use and the likelihood that there would be significant error in estimates of conditional prevalence for the separate substance use disorders.

Prevalence estimates were weighted to conform to independent population estimates by State, part of State, age and sex, and balanced repeated replicate weights used to account for the complex survey sampling design. Prevalence estimates and their standard errors were calculated using SUDAAN Version 7.5.3 (Research Triangle Institute, 1997).

A series of ordinal logistic regressions (OLR) were carried out using STATA (STATA Corporation, 1997; STATA Corporation, 2001). OLR takes into account the natural ordering of the levels of an ordinal outcome variable. It produces an average odds ratio that represents that average change in odds for each additional point along the scale. The first OLR included the following demographic variables as predictors:

- sex (reference ‘female’);
- age (reference ‘18-24’; comparison groups ‘25-34’, ‘35+’);
- employment (reference ‘employed’; comparison ‘not in the labour force/ unemployed’);
- educational attainment (reference ‘less than secondary’; comparison groups ‘secondary’, ‘post-secondary’);
- marital status (reference ‘married/ defacto’; comparison group ‘divorced/ separated/ widowed/ never married’).
The second OLR added the following mental health variables as predictors:

- neuroticism;
- DSM-IV anxiety disorder (reference ‘no’);
- DSM-IV mood disorder (reference ‘no’).

The third OLR added the following measures of drug use:

- regular tobacco use (reference ‘no’);
- DSM-IV abuse: alcohol, cannabis, sedatives, stimulants, and opiates (reference ‘no’);
- DSM-IV dependence: alcohol, cannabis, sedatives, stimulants, and opiates (reference ‘no’).

All demographic variables were retained. Significant mental health and drug use variables were retained in the final model. Successive models were checked for changes in significance using the likelihood ratio test. The proportional odds assumption (POA) was tested for each significant predictor variable (this is the assumption made in ordinal logistic regression that the size of the logit is similar between each cut point on the ordinal scale). The POA was tested by carrying out a series of logistic regressions examining different cut-points on the ordinal scale; that is, scores of 1, 2, 3, 4, and 5. The size of the logits were compared, and the POA was considered to have been met if the 95%CI of the logits overlapped for all cut-points. For all the significant predictors, the POA was met, indicating the average odds ratio from the OLR was an appropriate statistic (Bender & Grouven, 1997).
10.4 Results

A total of 99 persons under the age of 50 years screened positively for psychosis (a weighted prevalence rate of 1.2% in this age group). Table 10.1 shows the prevalence of substance use and DSM-IV substance use disorders according to case status. The odds of regular tobacco use were around four times greater among those screening positively for psychosis (60%), compared to non-cases (27%).

Similar proportions of cases and non-cases reported that they had used alcohol within the past 12 months (78%). However, a greater proportion of cases reported daily alcohol use: around one in four cases compared to just under one in seven non-cases. There was an even stronger relationship between case status and the risk of meeting criteria for a DSM-IV alcohol use disorder: around one in four cases met criteria for abuse or dependence, compared to one in 12 non-cases – a fourfold increase in odds.

Persons who screened positively for psychosis were significantly more likely than those who did not to report cannabis use within the past 12 months (30% vs. 10% respectively). Furthermore, weekly cannabis use was around four times more common among cases (23% vs. 7%, respectively), and cases were six times more likely than non-cases to meet criteria for DSM-IV cannabis abuse or dependence (16% vs. 3%, respectively).

Similar patterns were observed for sedative, stimulant and opiate use within the past 12 months. Less than 2% of non-cases reported the use of each of these drugs, compared to between 5% and 11% of cases. Cases were also significantly more likely to meet criteria for sedative, stimulant and opiate use disorders. Given the small numbers of users, caution must be taken in these estimates, as significant error may be involved (reflected in the size of the 95% confidence intervals around the odds ratios).
Table 10.1: Weighted prevalence of substance use and DSM-IV substance use disorders, according to psychosis “case” status

<table>
<thead>
<tr>
<th></th>
<th>Non-cases</th>
<th>Psychosis “cases”</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Regular tobacco use</td>
<td>27.3</td>
<td>59.9</td>
<td>3.97</td>
<td>2.64, 5.97</td>
</tr>
<tr>
<td>% Alcohol use</td>
<td>77.7</td>
<td>78.4</td>
<td>1.01</td>
<td>0.63, 1.64</td>
</tr>
<tr>
<td>% Daily alcohol use</td>
<td>15.2</td>
<td>23.5</td>
<td>1.71</td>
<td>1.07, 2.74</td>
</tr>
<tr>
<td>% Alcohol use disorder</td>
<td>8.2</td>
<td>23.7</td>
<td>3.93</td>
<td>2.48, 6.24</td>
</tr>
<tr>
<td>% Cannabis use</td>
<td>10.5</td>
<td>30.4</td>
<td>3.98</td>
<td>2.59, 6.14</td>
</tr>
<tr>
<td>% Weekly cannabis use</td>
<td>6.9</td>
<td>22.6</td>
<td>4.15</td>
<td>2.58, 6.68</td>
</tr>
<tr>
<td>% Cannabis use disorder</td>
<td>3.3</td>
<td>16.2</td>
<td>5.86</td>
<td>3.37, 10.18</td>
</tr>
<tr>
<td>% Sedative use</td>
<td>1.9</td>
<td>11.4</td>
<td>7.32</td>
<td>3.99, 13.44</td>
</tr>
<tr>
<td>% Sedative use disorder</td>
<td>0.6</td>
<td>4.6</td>
<td>10.11</td>
<td>4.20, 24.36</td>
</tr>
<tr>
<td>% Stimulant use</td>
<td>1.3</td>
<td>10.1</td>
<td>10.22</td>
<td>5.26, 20.87</td>
</tr>
<tr>
<td>% Simulant use disorder</td>
<td>0.5</td>
<td>3.2</td>
<td>9.57</td>
<td>3.30, 27.77</td>
</tr>
<tr>
<td>% Opiate use</td>
<td>1.3</td>
<td>5.1</td>
<td>4.74</td>
<td>2.02, 11.10</td>
</tr>
<tr>
<td>% Opiate use disorder</td>
<td>0.4</td>
<td>1.9</td>
<td>7.93</td>
<td>2.36, 26.64</td>
</tr>
</tbody>
</table>

While the prevalence estimates in Table 10.1 indicate how common use disorders were among the entire sample of persons included for analysis, the figures in Table 10.2 indicate how common use disorders were among those who used the substances. These conditional prevalence estimates of drug use disorders are one way of estimating the liability of users to problematic substance use. A higher conditional prevalence estimate indicates that a greater proportion of people who report any use of a substance will also report problematic use of that substance.
As Table 10.2 shows, among alcohol and cannabis users, there was no relationship between psychosis case status and the likelihood of meeting criteria for DSM-IV abuse. Similarly, users of other drug types (sedatives, stimulants or opiates) who screened positively for psychosis were no more likely than non-cases who were users to meet criteria for other DSM-IV drug use disorders (sedatives, stimulants or opiates). This means that among those who reported using sedatives, stimulants or opiates, for example, those who had screened positively for psychosis were no more likely to have problematic use of these drugs than those who had not screened positively.

Table 10.2: Proportion of users meeting criteria for a DSM-IV use disorder according to psychosis case status

<table>
<thead>
<tr>
<th></th>
<th>Non-cases</th>
<th>Psychosis “cases”</th>
<th>OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% of users</td>
<td>% of users</td>
<td></td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>3.5</td>
<td>5.5</td>
<td>1.62 (0.59, 4.48)</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>7.0</td>
<td>24.7</td>
<td>5.03 (3.01, 8.41)</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>10.8</td>
<td>11.9</td>
<td>0.88 (0.26, 2.96)</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>20.5</td>
<td>41.3</td>
<td>2.86 (1.37, 5.99)</td>
</tr>
<tr>
<td>Other drug use disorder</td>
<td>31.0</td>
<td>33.5</td>
<td>1.51 (0.59, 3.83)</td>
</tr>
</tbody>
</table>

There was a significant relationship for both alcohol and cannabis dependence (Table 10.2). Cases who reported cannabis use in the past year were almost three times more likely to be dependent upon cannabis than non-cases who had used cannabis (95%CI 1.4, 6.0). This translated into an estimated 41% of cases who used cannabis meeting criteria for dependence, compared to 21% of non-cases who had used cannabis. Similarly, cases who had used alcohol were five times more likely to be alcohol dependent than non-cases who...
had used alcohol – one in four cases who were drinkers (25%) compared to one in 14 non-cases who were drinkers (7%).

Table 10.3 presents the mental health and substance use variables that remained significant in the final OLR model; for simplicity, demographic variables are not presented here (details of these can be found in Appendix I). Higher scores on the Neuroticism scale of the EPQ were associated with higher psychoticism scores. Both DSM-IV mood and anxiety disorders were significantly associated with higher PS scores (average OR 1.8 and 1.7, respectively). This meant, for example, that persons who reported one psychotic symptom (a score of one) were around 73% more likely than those who did not report any symptoms to meet criteria for an anxiety disorder. Those who reported three symptoms (a score of three) were around 2.2 times more likely than those who did not report any psychotic symptoms to meet criteria for an anxiety disorder.

Taking into account the effects of these mental health and demographic factors, several problematic substance use variables remained significant predictors of psychotic symptoms (Table 10.3). With each additional symptom reported, there was a doubling of the odds of cannabis dependence (OR=2.0). There was a somewhat smaller increase in the odds of alcohol dependence and regular tobacco use per additional psychotic symptom (around 1.45). Opiate abuse was 6.1 times more likely per additional symptom, although the 95% confidence interval around this estimate was very wide because of the low prevalence of use (1.3, 29.1).
Table 10.3: Significant predictors of psychosis scores - results of ordinal logistic regression

<table>
<thead>
<tr>
<th>Predictor</th>
<th>z</th>
<th>Coefficient</th>
<th>SE</th>
<th>OR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPQ Neuroticism score</td>
<td>10.02</td>
<td>0.140</td>
<td>0.014</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DSM-IV mood disorder</td>
<td>5.59</td>
<td>0.611</td>
<td>0.109</td>
<td>1.84</td>
<td>1.49, 2.28</td>
</tr>
<tr>
<td>Regular tobacco use</td>
<td>4.66</td>
<td>0.362</td>
<td>0.078</td>
<td>1.44</td>
<td>1.23, 1.67</td>
</tr>
<tr>
<td>DSM-IV anxiety disorder</td>
<td>4.57</td>
<td>0.549</td>
<td>0.120</td>
<td>1.73</td>
<td>1.37, 2.19</td>
</tr>
<tr>
<td>DSM-IV cannabis dependence</td>
<td>3.77</td>
<td>0.681</td>
<td>0.181</td>
<td>2.00</td>
<td>1.39, 2.80</td>
</tr>
<tr>
<td>DSM-IV alcohol dependence</td>
<td>3.06</td>
<td>0.387</td>
<td>0.127</td>
<td>1.47</td>
<td>1.15, 1.89</td>
</tr>
<tr>
<td>DSM-IV opiate harmful use</td>
<td>2.27</td>
<td>1.810</td>
<td>0.796</td>
<td>6.10</td>
<td>1.28, 29.05</td>
</tr>
</tbody>
</table>

\( \chi^2_{16} df = 647.32, p < .0001, \text{pseudo } R^2 = 0.09 \) Demographic variables included in this model, but for simplicity, are not presented here; details for these can be found in Appendix I.

* p < .05. ** p < .005. *** p < .001
10.5 Discussion

In the Australian population, people who screened positively on a psychosis screener were likely to have significant substance use problems. The majority of these persons were daily tobacco smokers, around one in four reported daily alcohol use, and a similar proportion reported at least weekly cannabis use. A significant minority met criteria for alcohol and cannabis abuse/dependence. Furthermore, one in five reported the use of sedatives, stimulants or opiates more than five times within the past year, and one third of these users met criteria for a use disorder. The rates of illicit drug use, and of regular and problematic use of all substances, were all significantly higher than those among non-cases.

These findings are consistent with clinical research involving persons with psychotic disorders, which has found high rates of tobacco use (Glassman, 1993; Goff et al., 1992; Masterson & O’Shea, 1984), cannabis use and use disorders (Cantor-Graae, Nordstrom, & McNeil, 2001; Fowler et al., 1998; Wheatley, 1998), alcohol use disorders (Cantor-Graae et al., 2001; Drake et al., 1989; Drake & Wallach, 1989; Fowler et al., 1998), and other illicit drug use disorders (Cantor-Graae et al., 2001; Drake & Wallach, 1989).

They are also consistent with the findings of the ECA, which found elevated rates of schizophrenia among persons with drug and alcohol use disorders (Anthony & Helzer, 1991; Cuffel et al., 1993; Helzer et al., 1991); a recent analysis of NCS data also found high rates of tobacco smoking among persons with psychosis (Lasser et al., 2000).

10.5.1 Increased Liability to Problematic Substance Use Among Likely Cases of Psychosis?

Of particular concern was the finding that persons who screened positively for psychosis who used alcohol and cannabis were more likely to be dependent upon alcohol and cannabis than users who did not screen positively. This was examined by calculating the prevalence of cannabis and alcohol dependence among users of these substances. Cases
who reported cannabis use were almost three times more likely to be dependent users than non-cases who had used cannabis. Cases who had used alcohol were five times more likely to be alcohol dependent than non-cases who had used alcohol.

It may be that such persons are at higher risk of developing problematic use when they use these drugs. This could be for a number of reasons. For example, it could be that persons with psychotic disorders have a lower threshold for developing substance-related problems, suggesting that substance use impairs role functioning more easily. This possibility was supported by research comparing schizophrenic persons who were problematic alcohol users with persons who had a “primary” alcohol use problem: while both groups had significant substance use problems, schizophrenic persons were using significantly lower amounts (Drake et al., 1990). This lower threshold for problems related to substance use may not be surprising given that persons with psychotic disorders are likely to have a range of problems that already impair their social, occupational and other functioning (Mueser et al., 1992). Supportive evidence of this is the finding that persons with psychosis who are alcohol dependent have lower levels of physical dependence on alcohol than “primary” alcohol abusing populations (Mueser et al., 1998).

Second, an increased vulnerability to problematic substance use has been discussed in more biological terms by Mueser and colleagues (1998). They discussed the possibility that persons with psychosis might be more sensitive to the effects of psychoactive substances. This has been supported in pharmacological “challenge” tests, which have shown that persons with schizophrenia are more sensitive than controls to the effects of psychostimulant drugs (Janowsky & Davis, 1976; Lieberman, Kane, & Alvir, 1987).

Regardless of the mechanisms for any increased liability to problematic alcohol and cannabis dependence, the finding of the present study is worrying because the use of cannabis has been associated with increases worsening of psychotic symptoms (Jablensky et al., 1991; Linszen, Dingemans, & Lenior, 1994; Martinez-Arevalo, Calcedo-Ordonez, & Varo-Prieto, 1994). Further studies are needed to replicate and explicate this finding. Dependent cannabis use would presumably increase any such risks of exacerbation. Given that dependent cannabis use was more common among persons screening positively for psychosis, this is also deserving of further research.
10.5.2 LIMITATIONS

One limitation of this study was that the psychosis screener was (by definition) not an instrument designed to produce diagnoses of DSM-IV psychotic illnesses. This means that some persons who were classed as “cases” may not have met diagnostic criteria for psychotic illnesses, and some persons who may have met such criteria may not have been correctly identified as “cases”. Some researchers have expressed concern about the validity of field assessments of psychotic disorders, particularly among substance using members of the population (Blanchard et al., 2000). Although structured interviews produce reliable assessments (Blanchard et al., 2000), these researchers have argued that accurate assessment of psychotic disorders requires the collation of multiple sources of information (Blanchard et al., 2000). This is difficult in surveys done in the general population.

Nevertheless, the prevalence estimate of psychosis produced in the NSMHWB (1.2%; 95%CI 1-1.4%) is similar to that produced in the ECA using diagnoses of DSM-III psychotic disorders (0.8-1.2%) (Keith et al., 1991). Furthermore, unless there was a relationship between the reported substance use and the construct that the psychosis screener was attempting to measure, which is unlikely, such measurement error is likely to reduce the strength of the association observed here between substance use and “caseness”.

Another factor to consider was that the NSMHWB was a household survey – it did not assess persons in dwellings such as hospitals, inpatient psychiatric institutions, and correctional facilities. This meant that persons with psychotic disorders who were in such facilities were not included in the survey; such persons would have been likely to have more severe psychiatric problems, and perhaps more likely to have substance use problems. However, this is not likely to have affected the strength of the observed association between substance use and psychotic symptoms - rather, it would most likely have meant that persons who had more severe symptoms of psychosis, with more severe substance use problems, were undersampled (meaning that those from the “extremes” of the distribution were not included).

The impact of these measurement and sampling limitations can be assessed by comparing the findings of the NSMHWB with those of the Low Prevalence Study (LPS) carried out in
Perth, Melbourne, Brisbane and Canberra at the same time by Jablensky and colleagues (2000). The LPS was designed to sample persons who met diagnostic criteria for psychotic illnesses, who were sampled from treatment services in each city. The study sample comprised persons who were assessed by experienced clinicians according to ICD-10 criteria for psychotic disorders. Furthermore, unlike the NSMHWB, which only assessed persons in residential dwellings, significant proportions of this sample resided in: institutions (20%); hostels (14%); and lived in rooming houses, hotels, shelters or were homeless (9%) during the past month (Jablensky et al., 2000).

Table 10.4 shows the prevalence of substance use and substance use disorders in the NSMHWB sample, and in the LPS sample. Even though all diagnoses in the LPS sample were lifetime diagnoses, it is reassuring that drug use patterns were markedly similar in the LPS and the NSMHWB samples (Table 10.4). Just over one in three persons with psychosis from both the LPS sample (37%) and the NSMHWB (37%) reported drinking alcohol at least several times per week in the last year. At least weekly cannabis use was also reported by almost identical proportions of both samples (24% of the LPS sample, 23% of the NSMHWB sample). Three in ten (30%) of the LPS sample met lifetime criteria for alcohol abuse or dependence, with 25% meeting lifetime criteria for cannabis abuse/dependence and 13% met lifetime criteria for abuse/dependence on other drugs (Jablensky et al., 2000). Current tobacco smoking (any use) was reported by 73% of males and 56% of females (vs. 64% and 65% of the NSMHWB sample). The slightly higher estimates of the LPS are expected given that these estimates are of lifetime prevalence, whereas those of the NSMHWB are past year only.
Table 10.4: Prevalence of substance use and substance use disorders among cases from the NSMHWB sample, and from the Low Prevalence Study sample

<table>
<thead>
<tr>
<th></th>
<th>NSMHWB “cases”¹</th>
<th>Low Prevalence study²</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Tobacco use</td>
<td>64 (males); 65 (females)</td>
<td>73 (males); 56 (females)</td>
</tr>
<tr>
<td>% Near daily alcohol use</td>
<td>37</td>
<td>37</td>
</tr>
<tr>
<td>% Alcohol use disorder</td>
<td>24</td>
<td>30</td>
</tr>
<tr>
<td>% At least weekly cannabis use</td>
<td>23</td>
<td>24</td>
</tr>
<tr>
<td>% Cannabis use disorder</td>
<td>16</td>
<td>25</td>
</tr>
<tr>
<td>% Other drug use disorder</td>
<td>7</td>
<td>13</td>
</tr>
</tbody>
</table>

¹. All diagnoses 12-month DSM-IV
². All diagnoses lifetime ICD-10

10.5.3 IMPLICATIONS FOR THEORY

This study found that some patterns of problematic substance use predicted of higher scores on the psychosis screener, even after accounting for demographics, neuroticism, and DSM-IV anxiety and mood disorders. The confounding variables considered here did not explain the bivariate associations between screening positively for psychosis and problematic substance use. Hence, this study indicated that the association between psychotic symptoms and a number of indicators of problematic substance use (particularly cannabis and alcohol dependence, and regular tobacco use) in the Australian population is not due to the effects of demographic characteristics, personality, or to the presence of other mental health problems.
Given the cross-sectional nature of the data from the NSMHWB, however, it is difficult to distinguish between other competing explanations for the associations observed here. These include the following hypotheses: that there are common causes of psychosis and substance use, which were not considered here, such as shared genetic vulnerabilities; that substance use is a form of self-medication for persons with psychosis; that psychosis is caused by substance use; and that substance use exacerbates or precipitates psychotic symptoms among individuals vulnerable to psychotic illness (e.g. Blanchard et al., 2000; Hall, 1998a; Hall & Degenhardt, 2000; McKay & Tennant, 2000). Much of this debate has centred on hypothesised relationships between cannabis use and psychosis.

A cohort study of Swedish conscripts found that cannabis use was related to an increased risk of receiving a diagnosis of schizophrenia within the following 15 years (Andreasson et al., 1987). Prospective studies of persons with psychosis have found that cannabis use predicted relapse to psychotic symptoms among persons with psychotic disorders (Jablensky et al., 1991; Linszen et al., 1994; Martinez-Arevalo et al., 1994). In the study by Jablensky and colleagues (1991), “street drug” use was associated with: a poorer course over a 2-year follow-up period; a greater percentage of time during follow-up spent in psychotic episodes; a smaller percentage of times spent in full remission of symptoms; and a smaller percentage of time spent with unimpaired social functioning. This relationship existed after adjusting for age, gender, marital status, premorbid adjustment, and a number of indicators of social adjustment and social support (Jablensky et al., 1991). However, there was no adjustment for other mental health problems, or the use of substances such as alcohol.

The latter statistical adjustments were made in a prospective study of 93 persons with first-episode psychosis followed up over one year (Linszen et al., 1994). An association was found between cannabis use and relapse to psychotic symptoms after adjusting for age at admission, gender, and alcohol use.

There is a difficulty in separating the contributions that cannabis, alcohol and other substances may make to the exacerbation of schizophrenic symptoms. The concurrent use of alcohol is common among schizophrenic persons (Soyka, 2000), and the heavier their cannabis use, the more likely they are to use psychostimulants and hallucinogens (Mueser et
al., 1992). Replication of the prospective studies discussed above is needed. Furthermore, controlled outcome studies of substance abuse treatment for persons with psychosis are also needed to see whether cessation of drug use predicts improvement in psychotic symptoms (Hall, 1998a).

10.5.4 IMPLICATIONS FOR TREATMENT

Regardless of the reasons for the associations observed between psychosis and problematic substance use, it is still the case that Australian persons who reported increasing number of psychotic symptoms were much more likely to have a wide range of substance use problems. This suggests that the higher rates of substance use problems found among clinical samples of schizophrenic persons are also found among persons with psychosis in the general population.

The need for treatment to target both substance use and mental health problems among persons with psychosis (Bellack & Gearon, 1998; Bennett, Bellack, & Gearon, 2001; Drake, Bartels, Teague, Noordsby, & Clark, 1993; Drake, Mercer-McFadden, Mueser, McHugo, & Bond, 1998) was supported by evidence in this study that this association holds in the general population. There are a number of treatment implications of the current findings.

First, such persons are at risk of the possible mental health risks of such substances. These need to be disseminated to persons at risk of psychotic illness (for example, those with a family history of such disorders), to persons who have already been diagnosed with a psychotic illness, and to persons who are heavy substance users. While there needs to be further clarification of the risks, at present it would seem warranted to advise such persons that any substance use may exacerbate their illnesses.

Second, more attention needs to be given to the physical health risks of heavy or problematic substance use. The higher rate of tobacco smoking among persons who screened positively for psychosis means they are at greater risk of tobacco-related diseases such as lung cancer (US Surgeon General, 1982). This risk may be particularly high since there is some evidence that persons with psychosis smoke more heavily and use higher tar
cigarettes (Masterson & O'Shea, 1984), both of which would increase smoking-related harms. Cannabis smokers may also face physical health risks, particularly if it smoked regularly over a long period of time (Donald, 1991; Hall & Solowij, 1998; Hall, Solowij, & Lemon, 1994; Tashkin, 1999; Taylor, 1988; Van Hoozen & Cross, 1997). These risks include problems with respiratory function and chronic bronchitis (Hall, 1998b; Taylor, Poulton, Moffitt, Ramankutty, & Sears, 2000; Van Hoozen & Cross, 1997), and perhaps an increased risk of developing mouth and throat cancers (Zhang et al., 1999). Significant risks of heavy alcohol use have been well documented, and include cognitive impairment, liver damage, and cardiovascular disease (English et al., 1995). The problematic use of substances such as opiates, sedatives and stimulants is also associated with adverse health outcomes such as fatal overdose, liver and kidney problems (English et al., 1995).

Chapter Twelve outlines some of the issues surrounding treatment of persons with comorbid substance use disorders and psychosis.
10.6 Conclusions

In the Australian population, persons who screened positively for psychosis were more likely to use tobacco, cannabis and alcohol regularly, and to meet criteria for substance use disorders in the past year. They also appeared to be more likely to be dependent upon cannabis and alcohol if they reported using these drugs, suggesting greater vulnerability to develop dependence than persons who did not screen positively.

The present study suggests that in the Australian population, problematic substance use is much more likely among persons reporting an increasing number of psychotic symptoms. Future work might evaluate interventions to reduce problematic substance use among persons with psychotic symptoms.

The association between problematic substance use and psychotic symptoms was not explained by demographic characteristics, or by the presence of anxiety or mood disorders. The odds of cannabis and alcohol dependence, and regular tobacco use, were significantly greater with each additional psychotic symptom reported. This finding is of particular concern given the high prevalence of these three substance use problems in this population.

There has been considerable interest in particular in the comorbidity between cannabis use and psychosis. While the analyses presented in this Chapter show a moderate degree of comorbidity between cannabis use and psychosis, the study is limited in its ability to explore some of the possible mechanisms that might explain the association: suggested relationships have included the possibility that cannabis use causes psychosis, that cannabis use precipitates psychosis among vulnerable individuals, and that cannabis use worsens the prognosis of persons who have already developed psychosis. Chapter Eleven uses mathematical modelling to explore the implications for the prevalence of cannabis use and psychosis in the general population if these putative relationships were true.
11 MODELLING SOME PUTATIVE RELATIONSHIPS BETWEEN CANNABIS USE AND PSYCHOsis

Chapter Ten documented an association between cannabis use and psychotic symptomatology, which remained after adjustment for possible confounding variables. However, given that the study was cross-sectional, only past year cannabis dependence was assessed, and only a limited number of possible confounding variables were examined, it is difficult to test the hypotheses that have been proposed to explain comorbidity between cannabis use and psychosis.

A number of such hypotheses have been put forward and widely debated in the field (e.g. Batel, 2000; Blanchard et al., 2000; Gruber & Pope, 1994; Hall, 1998a; Hall & Degenhardt, 2000; McKay & Tennant, 2000; Mueser et al., 1998; Rosenthal, 1998; Thornicroft, 1990). Four of these hypotheses will be examined below. Briefly, they are:

1. That cannabis use causes psychosis. In this case, cannabis use precipitates schizophrenia in persons who would not otherwise have developed the illness;
2. That cannabis use precipitates schizophrenia only among persons who were vulnerable to developing schizophrenia (e.g. through family history of the illness);
3. That cannabis use by persons with schizophrenia worsens symptoms or prolongs the illness, so that remission of psychotic symptoms is less likely;
4. That those with schizophrenia are more liable to develop heavy or problematic use of cannabis if they begin using it.

There is also a lack of consensus on which of these explanations of the comorbidity is the most accurate; notably, these hypotheses are not mutually exclusive. The background and evidence regarding these hypotheses is discussed in Appendix J.
11.1.1 THEORETICAL AND STATISTICAL BACKGROUND

In this Chapter a series of predictions are tested that these hypotheses make about trends in psychosis that would occur in the general population if they were true, given increases in the prevalence of cannabis use. Mathematical modelling is used to consider the plausibility of four of the more commonly discussed explanations of the association between cannabis use and psychosis. This method combines empirically derived information with the relationships predicted between different parameters by the hypotheses. It can begin to map out the expected trends in the general population that would be observed given specific relationships between cannabis use and psychosis. The predicted trends in psychosis and cannabis use are then compared with evidence on observed patterns. As noted previously, psychotic disorders are a group of disorders that includes schizophrenia and schizoaffective disorders, which are the most common psychotic disorders (Keith et al., 1991); most of the published evidence on psychosis discussed in this Chapter concerns schizophrenia.

There has been a dramatic increase in the prevalence of cannabis use within the Australian general population over the past few decades, which has been extensively documented (Degenhardt et al., 2000; Donnelly & Hall, 1994; Makkai & McAllister, 1998; McCoy, 1980). Given this increase, it is possible to derive from these hypotheses very specific predictions concerning the prevalence and incidence of psychosis in the general population, and the prevalence of cannabis use among persons with psychosis. The predictions generated from each of these four hypotheses are summarised in Table 11.1 and are discussed below.
Table 11.1: Predicted trends in schizophrenia, and in cannabis use among persons with schizophrenia, given an increase in the prevalence of regular cannabis use in the general population

<table>
<thead>
<tr>
<th>Trends in schizophrenia</th>
<th>Trends in cannabis use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence</td>
</tr>
<tr>
<td>(1) Causal</td>
<td>✦</td>
</tr>
<tr>
<td>(2) Precipitation</td>
<td>✧</td>
</tr>
<tr>
<td>(3) Worse prognosis</td>
<td>✧</td>
</tr>
<tr>
<td>(4) Increased risk of</td>
<td>✧</td>
</tr>
<tr>
<td>dependence</td>
<td></td>
</tr>
</tbody>
</table>

Note: ✧ = no change; ✦ = increase; ✧ = decrease

11.1.1.1 Hypothesis 1: Cannabis use causes psychosis

This hypothesis assumes that cannabis use induces psychotic illness that would not otherwise have occurred. This hypothesis has arisen from a number of studies documenting psychosis that were argued to have been induced by cannabis use (often called “cannabis psychoses”) (Basu, Malhotra, Bhagat, & Varma, 1999; Bernardson & Gunne, 1972; Carney, Bacelle, & Robinson, 1984; Chopra & Smith, 1974; Eva, 1992; Solomons et al., 1990; Tennant & Groesbeck, 1972; Wylie, Scott, & Burnett, 1995). It has also arisen from studies documenting an increased likelihood of psychosis among cannabis users (e.g. Andreasson et al., 1987).

If the relationship is causal, then an increase in the number of people using cannabis regularly should produce an increase in the number of incident cases of psychosis in the population. If we assume that these cases have the same likelihood of persistence as others, this would also increase the prevalence of schizophrenia in the population. As there has been a dramatic rise in the prevalence of cannabis use in successive birth cohorts in Australia (Degenhardt et al., 2000), this hypothesis would therefore predict that there should be a greater number of cases of psychosis among more recent birth cohorts. The
age of onset may also decrease if the prevalence of regular cannabis use increases among younger persons, thus effectively increasing the number of early onset cases of psychosis. This causal hypothesis also predicts a rise in the prevalence of cannabis use among persons with schizophrenia, since an increasing number of cases would have been caused among persons who were cannabis users.

11.1.1.2 Hypothesis 2: Cannabis Use Precipitates Psychosis among Vulnerable Individuals

A second hypothesis is that regular cannabis use precipitates schizophrenia only among vulnerable individuals, that is, among persons who would have developed the disorder regardless of whether they used cannabis or not (Hall, 1998a). This is derived from some evidence that (a) persons with first-episode schizophrenia who used cannabis were younger than those who did not use cannabis (Linszen et al., 1994; Mathers, Ghodse, Caan, & Scott, 1991; Rolfe et al., 1993); (b) cannabis use tended to precede the development of psychotic symptoms (Allebeck, Adamsson, Engstrom, & Rydberg, 1993; Hambrecht & Haefner, 2000; Linszen et al., 1994); and (c) among first-episode cases of psychosis, those who used cannabis were more likely to have a family history of psychosis (McGuire et al., 1995).

According to this hypothesis, an increase in the prevalence of regular cannabis use in the general population would not affect the overall number of persons who developed psychosis (i.e. the overall incidence rates would not be altered). This model does predict, however, that some persons would develop the illness at an earlier age than they might otherwise have done. Hence, the incidence rates of persons using cannabis might be thought of as shifting “downwards” in the life span without an overall increase in incidence. This might have some implications for the chronicity of psychotic disorders, since earlier onset cases are more likely to have a chronic course. This could marginally increase prevalence. Since some cases would be precipitated by the use of cannabis, the hypothesis predicts that the prevalence of cannabis use among persons with psychosis would increase as the prevalence increased in the general population. It might also predict an increased rate of cannabis use among persons with chronic cases of psychosis.
11.1.1.3 Hypothesis 3: Cannabis use worsens the prognosis of persons with schizophrenia

On this hypothesis, cannabis use worsens the prognosis of schizophrenic persons - in that it increases the relapse rates of schizophrenia. There is some evidence to suggest that those who use cannabis are more likely to suffer a relapse (Jablensky et al., 1991; Linszen et al., 1994). Therefore, in this model, there is no increase in the incidence of schizophrenia among regular cannabis users, but those persons who have psychosis who are regular cannabis users are more likely to have a relapse after their initial episode. Hence, it may be the case that the number of persons in the population with chronic psychosis increases. Since cannabis use plays no part in the development of psychosis, there would be no change in the age of onset of psychosis. The prevalence of cannabis use among persons with schizophrenia would increase, since a greater number of chronic cases of psychosis would be cannabis users.

11.1.1.4 Hypothesis 4: Regular cannabis use is more likely among persons with psychosis

This hypothesis proposes that persons with schizophrenia are more likely to become regular, or problematic users of cannabis, if they use it at all (Mueser et al., 1998). There is no causal relationship between cannabis use and psychosis, so there is no effect upon the number of incident cases of schizophrenia nor upon the prevalence of schizophrenia. There would also be no change in the age of onset of psychosis. It would predict that an increase in the prevalence of cannabis use in the general population would lead to an increase in the prevalence of regular cannabis use among persons with psychosis.
11.2 AIMS

The present Chapter models predictions about trends in the incidence and prevalence of schizophrenia derived from four hypotheses of the relationship. It uses estimates of key parameters derived from research on the incidence, prevalence, chronicity and outcome of schizophrenia, and research on patterns of cannabis use, to derive these predictions. These predictions are compared with what is known about trends in cannabis use and psychosis in Australia and other developed countries.

Specifically, this Chapter aims to:

1. Model the prevalence of schizophrenia over the life course, given estimates of the incidence and chronicity of schizophrenia from published data, and given what is known about mortality of persons with schizophrenia;


3. Examine the trends in the number of cases of schizophrenia that would be observed in these cohorts, given four different hypotheses about the relationship between cannabis use and schizophrenia, namely, (a) that it is causal, (b) that it precipitates the disorder among vulnerable persons, (c) that it exacerbates the disorder, and (d) that persons with schizophrenia are more liable to develop regular cannabis use;

4. Compare these predictions with the published literature on the incidence and prevalence of schizophrenia. This will form the basis of an evaluation of the relative value of each of the hypotheses.
11.3 Method

11.3.1 Parameters for Schizophrenia

The sources of estimates for key parameters were taken from published literature on the incidence, chronicity and mortality of persons with schizophrenia.

11.3.1.1 Incidence of Schizophrenia

It was assumed that schizophrenia does not develop before the age of 15 years, and that new cases do not occur after the age of 54 years (Goldstein, Hall, & Andrews, 1984). Gender-specific incidence rates were used since males and females have consistently been shown to have differing incidence rates of schizophrenia, with males having an earlier average age of onset of schizophrenia than females (Jablensky et al., 1991; Jones & Cannon, 1998). Estimates of the average incidence rate of schizophrenia per 100,000 population per year by age and gender were obtained from previous research using a case register from New South Wales, Australia (see Table K1 in Appendix K) (Goldstein et al., 1984). Notably, these incidence rates were derived from data that applied to a period (1974-1977) in Australia before cannabis use became widespread among young adults (Donnelly & Hall, 1994).

11.3.1.2 Chronicity of Schizophrenia

Previous work estimating the economic costs of schizophrenia incorporated a review of what was known about the long-term outcomes of schizophrenia, and included a panel of psychiatrists who were experts in the treatment of schizophrenia (Hall et al., 1985). This panel reached a consensus about the following distribution of long-term outcomes of persons with schizophrenia: 25% of persons with schizophrenia would have a “good” outcome (a single episode with 60 days in hospital, six visits to a doctor, medication and no work for 6 months, no residual disability). More recent evidence has been consistent with
this estimate that around 25% of patients will not relapse after long follow-up periods (Eaton et al., 1992a; Eaton et al., 1992b; Mason et al., 1996b). Hall and colleagues also estimated that 40% would have a “median” outcome (an average of 0.08 admissions to hospital per year, six doctor visits per year, continuous medication for life, and 36 weeks out of work per year); and 35% would have a “poor” outcome (0.16 visits to hospital per year, 12 doctor visits per year, continuous medication, never work again) (Hall et al., 1985).

A number of studies of the outcome of schizophrenia have found that relapse tends to be in the first few years after the initial episode, with rates of relapse levelling off afterwards (Carone, Harrow, & Westermeyer, 1991; Eaton et al., 1992a; Eaton et al., 1992b; Mason et al., 1996b). For the purposes of the present study, it will be assumed that over a period of 4 years, 75% of incident cases of schizophrenia will relapse. Hence, it is conversely assumed that 25% of cases have a “good” outcome (Eaton et al., 1992a; Eaton et al., 1992b; Hall et al., 1985; Mason et al., 1996b).

Relapse is more likely in cases with an earlier age of onset of schizophrenia (Eaton et al., 1992a; Eaton et al., 1992b). Research using a case register in Victoria, Australia, found that persons with the earliest age of onset (15-19 age group) were most likely to relapse, with the following relative risks (compared to the 15-19 age group) for older age groups: 0.84 (20-29), 0.73 (30-39), 0.68 (40-49), 0.59 (50-59) (Eaton et al., 1992a; Eaton et al., 1992b). Using data provided on the age distribution of cases in this register, estimates were made of the probability of relapse (assuming an overall relapse rate of 75%; Figure 11.1; see also Table K2 in Appendix K).
11.3.1.3 Mortality of People with Schizophrenia

Based on a meta-analysis carried out by Brown (1997), the aggregate crude mortality rate of schizophrenia was estimated to be 189 deaths per 10,000 population per year. The general population mortality rate was estimated from Australian Bureau of Statistics data on rates of death per 10,000 population per year. In this study, the rate in the general population was assumed to equal the rate among non-schizophrenic persons. For males the average rate of death was assumed to be 9 per 10,000 population per year; for females, an average of 5 per 10,000 population per year.

11.3.2 Parameters for Cannabis Use

Data on lifetime patterns of cannabis use were obtained from two sources: a longitudinal study that examined the natural history of cannabis use (Chen & Kandel, 1995); and data from the Australian National Drug Strategy Household Survey (NDHSV), which has been used previously to estimate birth cohort trends in drug use (Degenhardt et al., 2000).
11.3.2.1 Natural History of Cannabis Use

Estimates of lifetime patterns of cannabis use were made using longitudinal data on the natural history of cannabis use (Chen & Kandel, 1995). Almost no users initiated cannabis use after 28 years. The prevalence of lifetime cannabis use in this cohort by age 34-35 years was approximately 73.7%: 78.9% among males and 69.2% among females. Figure 11.2 shows the pattern of cannabis use over the ages of 15 to 35, estimated from Chen and Kandel (1995).

Figure 11.2: Prevalence of monthly cannabis use by age and gender (Chen and Kandel, 1995)

Using this pattern of data, estimates of the actual prevalence of monthly cannabis use among Australian birth cohorts were obtained from data from the 1998 NDSHS, which provided estimates of the lifetime prevalence of cannabis use in the general Australian population.

The proportion using cannabis at least monthly for each birth cohort was estimated by multiplying the above rates by the ratio of the proportion of persons in the birth cohort who had used cannabis to the proportion in Chen and Kandel’s cohort (for details of prevalence estimates according to age and gender, see Table K3 in Appendix K). The prevalence of lifetime cannabis use according to birth cohort in the Australian population is presented in Table K4 in Appendix K. Note that for comparative purposes, Chen and Kandel’s study included persons who were born between 1955-1959: the prevalence of
lifetime cannabis use among males in the Australian birth cohort 1955-1959 is 59.6%, compared to a significantly higher rate of 78.9% in the US cohort. From these estimates, and using the estimated patterns from Chen and Kandel, the prevalence of monthly cannabis use according to age among males and females was modelled (Figure K3 in Appendix K).

The modelling also had to take account of the fact that the age of first cannabis use has decreased substantially in Australia among successive birth cohorts (Degenhardt et al., 2000). Figure 11.3 shows the lifetime prevalence of cannabis use by age among Australians according to birth cohort (taken from (Degenhardt et al., 2000)). Clearly, not only has the lifetime prevalence increased substantially with each successive birth cohort (as indicated by a higher final prevalence), it has also begun at a younger age (as indicated by the steeper slope).

**Figure 11.3: Prevalence of lifetime cannabis use according to age and birth cohort, 1998 NDSHS (Degenhardt et al., 2000)**

Any modelling of the natural history of cannabis use among Australians thus needs to take into account not only the lifetime prevalence, but also the earlier onset of use. The mean age of first reported use of cannabis has decreased by an average of approximately 2 years with each successive birth cohort (for details of the average age of first cannabis use according to the 1998 NDSHS, see Appendix K).
From these data, the following assumptions were made:

- That a curve of similar shape existed for each birth cohort as was observed by Chen and Kandel (1995);
- That the relative position of these curves moved to the left by 2 years for each successive birth cohort;
- That the absolute position of these curves could be estimated by anchoring the birth cohort that included the years in which the cohort in Chen and Kandel’s study was included (i.e. the 1955 to 1959 birth cohort). Thus, the relative proportions using cannabis at least monthly in the 1960-1964 birth cohort occurred 2 years earlier in the life span than it did for the 1955-1959 birth cohort, and in the 1950-1954 birth cohort, they occurred 2 years later. A lower limit was placed upon the younger cohorts (given what was known about the proportions reporting first use of cannabis at these younger ages from the 1998 NDSHS). Hence, for example, the peak periods of cannabis use for the birth cohorts born between 1965-1969, 1970-1974, 1975-1979, were estimated to be between the ages of 15 and 20, compared to 17-22 years for the 1960-1964 birth cohort, 19-24 years for the 1955-1959 birth cohort and so on;
- That there were no differences between birth cohorts in the duration of monthly cannabis use. It is possible, given some evidence of increasing cannabis use and cannabis-related problems among young persons (Conroy & Copeland, 1998; Substance Abuse and Mental Health Services Administration, 2000), that this not be the case among more recent birth cohorts. However, there were no good data on birth cohort trends in the peak period of use of cannabis, so for the purposes of the current study, this simpler assumption was made. In this way, the estimates made here are likely to reduce estimated differences between birth cohorts, making the findings here conservative in terms of differences between birth cohort;
- Since lifetime prevalence estimates were used to estimate the natural history of cannabis use, the slightly lower estimates for the youngest cohort (1975-1979) mean that lower estimates are produced for this cohort than the 1970-1974 cohort; this may mean that slight underestimates are produced for this cohort, since they had not yet passed the peak period of initiation to cannabis use (Chen & Kandel, 1995);
- Note that in producing the estimates of at least weekly cannabis use, it was assumed that half of those reporting at least monthly use would be using weekly.
11.3.2.2 Mortality of Cannabis Users

It was assumed that cannabis use does not increase mortality in persons with or without schizophrenia. This is based on previous research that has failed to find an increased risk of mortality among cannabis using males aged 34-36 years after adjusting for alcohol and other drug use (Andreasson & Allebeck, 1990), nor among cannabis using males and females aged 15 to 49 years (Sidney, Beck, Tekawa, Quesenberry, & Friedman, 1997).

11.3.3 Application to Australian Population Numbers

Estimates of the size of each birth cohort were made from data published by the Australian Bureau of Statistics on June 30th of each year, which estimated the numbers of persons in the population according to age and gender. Estimates of cohort size were made using data on the numbers of each year of birth when aged 15 years. Hence, for example, the 1940-1944 birth cohort population numbers were estimated from those aged 15 in the years 1955 to 1959.

11.3.4 Equations

\[ C = \text{prevalence of regular cannabis use} \]
\[ I = \text{age-specific incidence rate of schizophrenia} \]
\[ R = \text{age-specific relapse rate of schizophrenia} \]

Note that based on previous research (see above), it was assumed that relapses occurred in the first four years after development of the disorder (i.e. that 25% of all relapsing cases relapsed each year over the first four years).

\[ N(\text{alive year } 2) = N(\text{alive at year } 1) - N(\text{deaths among schizophrenic persons in year } 1) - N(\text{deaths among non-schizophrenic persons in year } 1) \]

\[ \text{Prevalence of schizophrenia at year } 2 = \frac{[N(\text{incident cases}) + N(\text{existing cases}) - N(\text{deaths among schizophrenic persons in yr } 1)]}{N(\text{alive year } 2)} \]
11.3.4.1 HYPOTHESIS 1: CAUSAL RELATIONSHIP

It was hypothesised that weekly cannabis use doubled the risk of developing schizophrenia - in other words, that regular cannabis users had an incidence rate of schizophrenia that was double that among persons who did not use cannabis. This risk ratio is based on previous work by Tien and Anthony (1990), Andreassen and colleagues (1987), and the NSMHWB (Chapter Ten).

\[ N(\text{incident cases at year n}) = (I_n^cC_n^w*2 + I_n^c(1 - C_n^w)) * N(\text{without schizophrenia at year n}) \]

\[ N(\text{chronic cases at year 2}) = N(\text{incident cases year 1}) * R * 0.25 \]
\[ N(\text{chronic cases at year 3}) = N(\text{incident cases year 2}) * R * 0.25 + N(\text{incident cases year 1}) * R * 0.5 \]
\[ N(\text{chronic cases at year 4}) = N(\text{incident cases year 3}) * R * 0.25 + N(\text{incident cases year 2}) * R * 0.5 + N(\text{incident cases year 1}) * R * 0.75 \]
\[ N(\text{chronic cases at year 5}) = N(\text{incident cases year 4}) * R * 0.25 + N(\text{incident cases year 3}) * R * 0.5 + N(\text{incident cases year 2}) * R * 0.75 + N(\text{incident cases year 1}) * R \]

11.3.4.2 HYPOTHESIS 2: CANNABIS USE PRECIPITATES PSYCHOSIS AMONG VULNERABLE INDIVIDUALS

This hypothesis assumes that there is no effect of regular cannabis use upon overall incidence or chronicity of psychosis, but that among persons who use cannabis there is a reduced age of onset of psychosis.

It was assumed that persons using cannabis develop the illness one year earlier than those who do not use cannabis regularly. This estimate was taken from the study of Linszen and others in which those who used cannabis were on average 1 year younger than those who did not use cannabis (Linszen et al., 1994).
N(incident cases at year n) = I_n * N(without schizophrenia at year n)

N(chronic cases at year 2) = N(incident cases year 1) * R * 0.25
N(chronic cases at year 3) = N(incident cases year 2) * R * 0.25 + N(incident cases year 1)* R * 0.5
N(chronic cases at year 4) = N(incident cases year 3) * R * 0.25 + N(incident cases year 2) * R * 0.5 + N(incident cases year 1) * R * 0.75
N(chronic cases at year 5) = N(incident cases year 4) * R * 0.25 + N(incident cases year 3) * R* 0.5 + N(incident cases year 2) * R * 0.75 + N(incident cases year 1) * R

### 11.3.4.3 Hypothesis 3: Cannabis use worsens prognosis

It was assumed that the chance of relapse (i.e. the occurrence of further psychotic episodes) was increased by 2.5 times among weekly cannabis users. This was based upon the findings of the Linszen and colleagues study, which found that those using cannabis at least weekly were 2.5 times more likely to relapse to psychotic symptoms (Linszen et al., 1994).

The model also assumed that a) there is no association between cannabis use and precipitation of psychosis; and b) that the percentage of persons using cannabis is initially the same among schizophrenic and non-schizophrenic persons.

N(incident cases at year n) = I_n * N(without schizophrenia)

N(chronic cases at year 2) = N(incident cases year 1) * (2*R*C + R*(1-C))/4
N(chronic cases at year 3) = N(incident cases year 2) * (2*R*C + R*(1-C))/4 + N(incident cases year 1) * (2*R*C + R*(1-C))/2
N(chronic cases at year 4) = N(incident cases year 3) * (2*R*C + R*(1-C))/4 + N(incident cases year 2) * (2*R*C + R*(1-C))/2 + N(incident cases year 1) * (2*R*C + R*(1-C))*0.75
N(chronic cases at year 5) = N(incident cases year 2) * (2*R*C + R*(1-C))/4 + N(incident cases year 2) * (2*R*C + R*(1-C))/2 + I_2 * (2*R*C + R*(1-C))*0.75 + N(incident cases year 2) * (2*R*C + R*(1-C))
11.3.4.4 Hypothesis 4: Regular cannabis use is more likely among persons with psychosis

This hypothesis assumes that there is no effect of cannabis use upon either incidence or outcome (chronicity) of psychosis. The prevalence of regular (weekly) cannabis use among persons with psychosis was assumed to be double that in the general population. This is taken from research suggesting that regular or dependent cannabis use is twice as likely among persons who meet criteria for psychosis (Chapter Ten; Andreasson et al., 1987; Tien & Anthony, 1990).
11.4 RESULTS

11.4.1 MODELLING THE PREVALENCE OF SCHIZOPHRENIA

Figure 11.4 shows a model of the prevalence of schizophrenia among Australian males and females according to age. It is possible to see that by age 54 (the upper limit at which it was assumed new cases of schizophrenia could occur), the prevalence of schizophrenia was 1.17% for males, and 1.08% for females. This estimate is at the upper limits of estimates of the prevalence of schizophrenia (Jablensky et al., 1991; Robins & Regier, 1991). However, note that if the point prevalence of schizophrenia is estimated in 1998 for the whole population examined here (birth cohorts 1940 – 1979; for details see Appendix K), the population estimate is 0.7%, which is very similar to previous studies that have attempted to estimated the population prevalence of schizophrenia (Jablensky et al., 2000; Jablensky et al., 1991; Robins & Regier, 1991).

Figure 11.4: Modelled prevalence of schizophrenia over the lifespan according to gender
11.4.2 Modelling the natural history of cannabis use

Figure 11.5 shows the models of the natural history of cannabis use for the different birth cohorts. As can be seen, the onset of the peak prevalence of regular cannabis use becomes earlier for more recent birth cohorts, and the peaks are higher for these earlier birth cohorts.

Figure 11.5: Model of the natural history of cannabis use among Australian males and females by birth cohort
11.4.3 Data on Trends in the Incidence of Schizophrenia

The data on trends in the incidence of schizophrenia are much less clear compared to data on trends in cannabis use. Numerous studies conducted in many countries including Australia (Parker, O’Donnell, & Walter, 1985), have reported declines in the incidence of schizophrenia over the past thirty years (Eagles & Whalley, 1985; Geddes, Black, Whalley, & Eagles, 1993; Joyce, 1987; Kendell, Malcolm, & Adams, 1993; Munk-Jorgensen, 1995; Munk-Jorgensen & Mortensen, 1992; Suvisaari, Haukka, Tanskanen, & Lonnqvist, 1999). However, these findings have not been universal: others have reported stable or increased rates (Bamrah, Freeman, & Goldberg, 1992; Castle, Wesseley, Der, & Murray, 1991; Haefner & an der Heiden, 1986; Harrison, Cooper, & Gancarczyk, 1991). One critical review concluded that incidence rates of psychosis in Australia had not changed in the period 1848 to 1978 (Haefner, 1987).

Factors underlying possible changes in the incidence of schizophrenia have been the subject of considerable debate over many years (Der, Gupta, & Murray, 1990; Eagles, 1991; Harrison & Mason, 1993; Jablensky, 1995; Kendell et al., 1993; Munk-Jorgensen, 1995; Stromgren, 1987; Torrey, 1989). Some have speculated that schizophrenia may be a “disappearing” disorder (Der et al., 1990; Eagles, 1991; Eagles & Whalley, 1985), or that a “metamorphosis” of schizophrenia may be occurring (Brewin et al., 1997; Zbin, Magaziner, & Steinhauser, 1983). Others have pointed to the fact that there have been: (a) a considerable shift in conceptualisations of psychotic disorders; (b) changes in diagnostic criteria; (c) earlier intervention with the disorder (leading to better outcome); (d) improvements in treatment; and (e) changes in the structure of service provision (Harrison & Mason, 1993; Jablensky, 1995; Kendell et al., 1993; Munk-Jorgensen, 1995). Yet again, others have pointed to reductions in some of the environmental risk factors for schizophrenia, such as poor maternal nutrition, infectious disease, and poor antenatal and perinatal care (Eagles, 1991; Takei, Lewis, Sham, & Murray, 1996). All of these factors make it difficult to be sure that observed declines in treated incidence reflect true declines in incidence.
One relatively recent study examined some of these issues when it compared two cohorts of first-onset cases admitted to psychiatric services in an area of the UK in 1978-1980 and 1992-1994 (Brewin et al., 1997). Retrospective methods were used to re-diagnose the first cohort, to ensure that both cohorts were diagnosed according to the same criteria, and diagnoses were made according to broad definitions of psychosis (with eight ICD-10 categories). Compared to the older cohort, the rate of schizophrenia was lower in the younger cohort while rates of other psychotic disorders increased. Overall, rates of psychotic disorders were the same in the two cohorts (Brewin et al., 1997). This finding is consistent with a more recent study, which found that incidence rates of schizophrenia decreased in Stockholm County, Sweden, during the period 1978-1994, while the combined incidence of schizophrenia and paranoid psychosis stayed the same (Osby et al., 2001).

In summary, it appears that there has been no increase in the incidence of schizophrenia. While there have been a number of studies suggesting a decrease in incidence, there are a number of factors that make it difficult to be certain that apparent reduced rates reflect true rates of incidence. As a result, it would seem that the most appropriate conclusion is that the incidence rates of schizophrenia have remained stable over past decades (and hence across different birth cohorts).

### 11.4.4 Data on Age of Onset of Schizophrenia

Both the “causal” and the “precipitation” hypotheses (hypotheses 1 and 2) lead to the prediction that the average age of onset of schizophrenia would have decreased as cannabis use increased (Table 11.1). A recent study of a register of first episode cases of psychosis has found a lower average age of onset of psychosis among more recent birth cohorts of persons with psychosis (DiMaggio, Martinez, Menard, Petit, & Thibaut, 2001). This study found that among more recent birth cohorts, the onset of psychosis was significantly younger.

However, the evidence concerning the average age of onset among first-episode cases of schizophrenia according to cannabis use status is less supportive. Some studies have found that first-episode cases who were cannabis users were significantly younger than non-users.
of cannabis (Linszen et al., 1994; Mathers et al., 1991; Rolfe et al., 1993). This evidence has been counterbalanced by a number of studies that have not found that persons who were using cannabis before the onset of their disorder were any younger than persons who were not using cannabis (Gut-Fayand et al., 2001; McGuire et al., 1994).

11.4.5 Data on Trends in the Prevalence of Regular Cannabis Use Among Persons with Schizophrenia

There are several difficulties in assessing the evidence on changes in the prevalence of regular cannabis use among schizophrenic persons over the past three decades. One problem is that many studies only report lifetime rates of use disorders. This makes it difficult to estimate how many persons would have met criteria for a disorder in a given year. Second, due to significant biases that are likely to exist in clinical samples (see Chapter Four), it is difficult to know whether variations in the prevalence of cannabis use across different samples reflects changes in prevalence or the effects of referral and admission policies. Finally, little data exist on the prevalence of cannabis use among persons with schizophrenia in the Australian general population.

One study was conducted in 1998 with a clinical sample of persons with schizophrenia living in the Hunter region of New South Wales, Australia (Fowler et al., 1998). The average age of the sample was 36 years, and around three quarters (72%) were male. Thirty percent had used cannabis use in the past 6 months, with 13% meeting criteria for cannabis abuse or dependence (Fowler et al., 1998). Just under three in ten (28%) of the sample had met criteria for cannabis dependence at some point in their lives, with 8% meeting criteria for cannabis abuse and another 30% reporting use without meeting criteria for a cannabis use disorder. These rates are considerably higher than those in the general population: the NSMHWB produced estimates of 12-month cannabis use and dependence of 7% and 2%, respectively (see Chapter Five).

An overview of findings from the 1997 Australian Low Prevalence Study (LPS) was recently published (Jablensky et al., 2000). This study only published lifetime rates of DSM-IV cannabis abuse or dependence: these rates were 33% among males and 13% among
females. As reported in Chapter Ten, the NSMHWB found that in the past year, 30% of persons who screened positively for psychosis reported using cannabis within the past year; 23% reported at least weekly use; and 16% met DSM-IV criteria for cannabis abuse or dependence.

Given that these studies are all quite recent, few conclusions can be drawn about trends in the prevalence of cannabis use among persons with psychosis in Australia. While there are data on the prevalence of cannabis use among clinical samples in US studies spanning over longer periods, the range of biases that affect clinical samples (as detailed in Chapter Four) makes it difficult to know whether any differences reflect changes in the prevalence of the population of persons with psychotic disorders such as schizophrenia, or simply reflect biases in the sampling.

Hence, it is difficult to make any conclusions about changes in the prevalence of cannabis use among this population over the past thirty years. It is probable that, just as the prevalence of cannabis use has increased in the general population of Australia over this time (Degenhardt et al., 2000), so too has the prevalence of cannabis use in persons with psychotic disorders. Whether the size of this increase has been larger among persons with psychotic disorders cannot be determined.
11.4.6 MODELLING THE HYPOTHEISED RELATIONSHIPS

11.4.6.1 HYPOTHESIS 1: CAUSAL RELATIONSHIP

Figure 11.6 shows the estimates of the prevalence of schizophrenia among males produced if cannabis use doubles the risk of psychosis among persons who use cannabis (Andreasson et al., 1987; Tien & Anthony, 1990).

Figure 11.6: Hypothesis 1 - Prevalence of schizophrenia among males by birth cohort, assuming that weekly cannabis use doubles the risk of developing schizophrenia

Taking the oldest and youngest birth cohorts, the prevalence of schizophrenia by age 25 years is estimated to be 0.38% among those in the 1940-1944 birth cohort, compared to 0.43% in the 1975-1979 birth cohort, a difference of 0.05%, which is a 14% increase in the prevalence. At age 20 years, the difference between the oldest and youngest birth cohorts in the number of cases of schizophrenia - caused by cannabis use - is 125 cases. The total would increase from 736 males aged 20 years in the 1940-1944 birth cohort, to 861 in the 1975-1979 birth cohort. This is an increase of 17% (between the calendar years 1960-1964 and 1995-2000) in the number of cases aged 20 years with schizophrenia coming to the attention of treatment services.
Table 11.2 shows these results in terms of the number of additional incident cases that would have occurred by age 35 years. Among the more recent birth cohorts – those born from the 1960s and later – if cannabis use caused psychosis, then by the time the cohorts reached the age of 35 years, there would be an additional 1225 – 1438 cases of schizophrenia per cohort. This would constitute an increase in size of the number of incident cases of schizophrenia of around 10% for each birth cohort, compared to a situation in which cannabis did not cause psychosis. The numbers for these later cohorts are many times larger than the numbers seen for the oldest birth cohort (180 additional cases).

Table 11.2: Hypothesis 1 - Modeled number of incident cases of psychosis by 35 years caused by cannabis use by the age of 35 years, by gender and birth cohort

<table>
<thead>
<tr>
<th>Birth Cohort</th>
<th>Total incident cases by 35 years assuming no link</th>
<th>Total incident cases by 35 years if cannabis use caused psychosis</th>
<th>Number of incident cases by 35 years caused by cannabis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
<td>Males</td>
</tr>
<tr>
<td>1940-44</td>
<td>3891</td>
<td>2898</td>
<td>3990</td>
</tr>
<tr>
<td>1945-49</td>
<td>5444</td>
<td>3903</td>
<td>5759</td>
</tr>
<tr>
<td>1950-54</td>
<td>5870</td>
<td>4380</td>
<td>6482</td>
</tr>
<tr>
<td>1955-59</td>
<td>6572</td>
<td>4896</td>
<td>7373</td>
</tr>
<tr>
<td>1960-64</td>
<td>7181</td>
<td>5301</td>
<td>7984</td>
</tr>
<tr>
<td>1965-69</td>
<td>6995</td>
<td>5197</td>
<td>7768</td>
</tr>
<tr>
<td>1970-74</td>
<td>7625</td>
<td>5664</td>
<td>8480</td>
</tr>
<tr>
<td>1975-79</td>
<td>6948</td>
<td>5128</td>
<td>7689</td>
</tr>
</tbody>
</table>

11.4.6.2 Hypothesis 2: Cannabis precipitates schizophrenia among vulnerable individuals

This second hypothesis assumes that regular cannabis use precipitates schizophrenia among persons who are vulnerable to developing the illness with the result that incident cases would occur at an earlier age among those who use cannabis regularly.
Table 11.3 shows the number of additional cases that would occur among 14 and 19 year olds, according to gender and birth cohort. The most marked effect occurs when the incidence rates among cannabis users are increased because they reflect the incidence rates among those a year older. The years in which this has the most noticeable effect are at age 14, when the only incident cases are among cannabis users (since it is assumed that the usual minimum age of onset of schizophrenia is 15 years), and at age 19 years, when persons using cannabis regularly have the same incidence rate as those who are 20 years old.

Hence, for example, in the 1940-1944 cohort, less than one case would have been precipitated at age 14 years. Among the younger male cohorts, however, the model estimated that around 50 cases of psychosis would be precipitated by cannabis use at age 14 years. Similar numbers were estimated at 19 years of age.

Table 11.3: Hypothesis 2 - Modelled number of additional cases that would be precipitated one year earlier by cannabis use by gender and birth cohort

<table>
<thead>
<tr>
<th></th>
<th>Cases precipitated at 14 years</th>
<th>Cases precipitated at 19 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
</tr>
<tr>
<td>1940-1944</td>
<td>0.2</td>
<td>0.01</td>
</tr>
<tr>
<td>1945-1949</td>
<td>0.4</td>
<td>0.05</td>
</tr>
<tr>
<td>1950-1954</td>
<td>1</td>
<td>0.07</td>
</tr>
<tr>
<td>1955-1959</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>1960-1964</td>
<td>31</td>
<td>16</td>
</tr>
<tr>
<td>1965-1969</td>
<td>49</td>
<td>16</td>
</tr>
<tr>
<td>1970-1974</td>
<td>54</td>
<td>18</td>
</tr>
<tr>
<td>1975-1979</td>
<td>48</td>
<td>17</td>
</tr>
</tbody>
</table>

11.4.6.3 Hypothesis 3: Cannabis worsens prognosis

The third hypothesis tested was the possibility that cannabis use increases the likelihood of relapse to psychotic symptoms. As noted in the methods section, based on a previous study which followed up a group of persons with recent onset psychoses (Linszen et al., 1994), it
was estimated that remission would be 2.5 times less likely among those using cannabis at least weekly. Since the prevalence of cannabis use is higher among more recent birth cohorts in Australia (Degenhardt et al., 2000), this hypothesis would predict a greater number of chronic cases among more recent birth cohorts.

According to the model, this hypothesis predicted that among the more recent birth cohorts, there would be an additional 106 – 130 chronic cases of schizophrenia attributable to cannabis use by the time the cohorts were aged 35 years (Table 11.4). These numbers would make up less than 1% of all chronic cases by this age in the Australian population (see Appendix K). These small numbers are explained by the fact that relapse rates among young adults with psychosis are extremely high. Consequently, an increase in the rate of relapse makes very little difference to the prevalence of chronic cases.

Table 11.4: Hypothesis 3 - Modelled number of additional chronic cases of psychosis due to cannabis use observed by the age of 35 years, by gender and birth cohort

<table>
<thead>
<tr>
<th>Birth Cohort</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>1940-44</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>1945-49</td>
<td>38</td>
<td>17</td>
</tr>
<tr>
<td>1950-54</td>
<td>68</td>
<td>25</td>
</tr>
<tr>
<td>1955-59</td>
<td>82</td>
<td>39</td>
</tr>
<tr>
<td>1960-64</td>
<td>77</td>
<td>49</td>
</tr>
<tr>
<td>1965-69</td>
<td>70</td>
<td>50</td>
</tr>
<tr>
<td>1970-74</td>
<td>76</td>
<td>54</td>
</tr>
<tr>
<td>1975-79</td>
<td>63</td>
<td>43</td>
</tr>
</tbody>
</table>

11.4.6.4 HYPOThESIS 4: REGULAR CANNABIS USE IS MORE LIKELY AMONG PERSONS WITH PSYCHOSIS

Figure 11.7 shows the prevalence of weekly cannabis use among persons with schizophrenia if it is assumed that persons with schizophrenia are twice as likely as their
peers in the general population to use cannabis weekly. This hypothesis assumes that cannabis use has no effect upon either the incidence or the prevalence of schizophrenia.

As can be seen, this hypothesis predicts that the prevalence of weekly cannabis use increases markedly among successive birth cohorts. For example, among males with schizophrenia aged 20 years, under 5% of those in the 1940-1944 birth cohort would have reported weekly cannabis use, compared to over 40% of those born after 1965. Similarly, among females with schizophrenia, at age 20 years around 2% of those born between 1940-1944 would be weekly cannabis users, compared to around 35% for those born after 1960.

**Figure 11.7: Hypothesis 4 - Modelled prevalence of weekly cannabis use among persons with schizophrenia by age and birth cohort**
11.4.7 Evaluation of the four hypotheses

11.4.7.1 Trends in the incidence of psychosis

Table 11.5 summarises the results of the examination of the predictions of the hypotheses, and their consistency with available data. As noted above, the evidence on the trends in incidence of schizophrenia suggests that, if anything, the incidence of all psychoses has remained stable, while the incidence of schizophrenia may have decreased. Hence, the available evidence did not support the prediction of hypothesis 1 that there would be an increase in the number of incident cases of psychosis among persons who would not otherwise have developed the disorder. The other three hypotheses all made predictions that were consistent with this evidence, that is, all predicted that an increase in the prevalence of cannabis use would not affect the incidence of psychosis.

Table 11.5: Consistency of predicted and actual trends in schizophrenia, and in cannabis use among persons with schizophrenia

<table>
<thead>
<tr>
<th></th>
<th>Trends in schizophrenia</th>
<th>Trends in cannabis use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Incidence</td>
<td>Prevalence</td>
</tr>
<tr>
<td>(1) Causal</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>(2) Precipitation</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>(3) Worse prognosis</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>(4) Increased risk of dependence</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Note: ✓ = evidence appeared to support the prediction of this hypothesis
X = evidence did not appear to support the prediction of this hypothesis
? = there was insufficient evidence to determine whether the prediction was supported or not

11.4.7.2 Trends in the prevalence of psychosis

The lack of any evidence of an increase in the prevalence of schizophrenia was not consistent with the predictions of hypothesis 1. One might expect an increase in the
number of persons with schizophrenia predicted by the hypothesis to have been noted by case registers. This does not appear to have occurred.

It is harder to be confident about the prediction of hypothesis 3, which predicted at most a 1% increase in the number of chronic cases of schizophrenia by age 35 years. Such a small increase in the number of chronic cases by age 35 years would be difficult to detect using existing empirical data. The data available therefore do not permit a rigorous test of this hypothesis. All that can be said is that the prediction is consistent with the available evidence. It is worth noting, however, that even if cannabis use predicted a greater likelihood of relapse, it makes a surprisingly small difference to the number of persons with schizophrenia who will relapse. Hypotheses 2 and 4 did not predict any change in the prevalence of psychosis so their predictions are also consistent with the available data.

11.4.7.3 TRENDS IN THE AGE OF ONSET OF SCHIZOPHRENIA

The evidence concerning the average age of onset of schizophrenia is limited so it is difficult to draw any firm conclusions on predictions about this indicator. Some evidence has suggested that the age of onset of schizophrenia has decreased in more recent birth cohorts, which is consistent with hypotheses 1 and 2. However, evidence from clinical samples of persons with first-episode psychosis has not consistently found that cannabis use was associated with an earlier onset of psychosis. Future work is needed to further examine this issue.

11.4.7.4 TRENDS IN THE PREVALENCE OF CANNABIS USE AMONG PERSONS WITH SCHIZOPHRENIA

The data on trends in the prevalence of cannabis use among persons with psychosis in Australia (and, indeed, anywhere) are so limited that it is extremely difficult to make any conclusions on this indicator. The high rates predicted by hypothesis 4 are consistent with the evidence provided from studies in recent years (Chapter Ten; Fowler et al., 1998; Jablensky et al., 2000); but it is difficult to know what these rates were in previous years. It is therefore difficult to draw any conclusions about the validity of this hypothesis.
11.5 DISCUSSION

This study used mathematical modelling to examine the implications of some of the plausible explanations of the association between cannabis use and schizophrenia. Four specific hypotheses were examined: (a) that cannabis use played a causal role in the onset of schizophrenia – in that it caused cases that would not otherwise have occurred; (b) that cannabis use precipitates the disorder among vulnerable individuals; (c) that cannabis use increases the likelihood that persons who have experienced an initial psychotic episode will relapse; and (d) that persons with schizophrenia who use cannabis are more likely to become regular users of it. As previously noted, these hypotheses are not necessarily mutually exclusive.

11.5.1 DOES CANNABIS USE CAUSE PSYCHOSIS?

The predictions of the hypothesis that cannabis causes psychosis were not supported by the available data on trends in the incidence of psychosis. There was no evidence that there has been an increase in the incidence or prevalence of psychosis over the past thirty years. This suggests that cannabis use does not cause cases of psychosis that would not otherwise have occurred.

One further point was clear. Even if regular cannabis use did double the risk of users developing schizophrenia (the “doubling” of risk being our best current estimate), it would be unlikely that there would be any noticeable change in the prevalence of schizophrenia. Even if every person in the general population used cannabis weekly, and cannabis use did double the risk of psychosis, the prevalence of schizophrenia would increase from 1% to 2%. This does put into context the maximum impact of cannabis on the population prevalence of schizophrenia. Even this change is not readily detected using existing epidemiological research methods (Kendell et al., 1993).
11.5.2 DOES CANNABIS USE PRECIPITATE PSYCHOSIS?

If cannabis use did precipitate psychosis among persons who were vulnerable to developing the disorder, there would have been an increase in the number of younger people who developed psychosis after using cannabis. In particular, an increase in the number of very young persons (14 years) would be predicted from the current models, when no such young persons would have developed the disorder at such a young age if no one used cannabis regularly. The numbers would have increased among successive birth cohorts, although the numbers were not large.

This hypothesis is consistent with: some evidence of a reduction in the age of onset of psychosis among persons born in more recent cohorts (DiMaggio et al., 2001); and with some evidence that cannabis users who had a first episode of psychosis were younger than non-users (Linszen et al., 1994; Mathers et al., 1991; Rolfe et al., 1993). It is also consistent with an increase in the number of psychoses in more recent times that have been diagnosed as “drug-induced” psychoses (Brewin et al., 1997).

11.5.3 DOES CANNABIS USE WORSEN PROGNOSIS?

The third possibility examined was that cannabis use increased the likelihood of relapse in schizophrenia. An increased relapse rate made little difference to the number of chronic cases that would be seen by age 35 years, only increasing the number of chronic cases by around 1%. This result is consistent with the elevated rates of cannabis use among persons with psychotic illnesses, and with the few prospective studies that have been carried out evaluating this issue, but it is difficult draw strong conclusions about the validity of this hypothesis.

One point that should be repeated is that it was assumed that initial rates of regular cannabis use among incident cases were the same as among non-cases. This would have made observed differences in the number of chronic cases smaller than if it was assumed that the rates were initially different. There is some evidence to suggest that even among
first-episode cases of psychosis, rates of cannabis use may be higher than in the general population.

One fact was clear, however: even if relapse was made more likely among regular cannabis users, because rates of relapse among younger persons are already so high, the effect that cannabis use had on overall numbers of chronic cases is relatively small.

**11.5.4 IS REGULAR CANNABIS USE MORE LIKELY AMONG PERSONS WITH SCHIZOPHRENIA?**

The models of this hypothesis are certainly consistent with the recently reported high prevalence estimates of cannabis use in Australian samples of persons with psychosis. However, given the absence of evidence on the prevalence of cannabis use over the past thirty years among persons with psychosis, it is difficult to evaluate this hypothesis further.
11.6 Conclusions

This study has examined a hotly debated issue from a different point of view – through the use of modelling, using epidemiological data to predict what changes we would expect to see in the incidence and prevalence of schizophrenia given a number of hypothesised relationships between cannabis use and psychosis. If cannabis caused schizophrenia among persons who would not otherwise have developed the disorder, significant increases would have occurred in the number of persons with the illness. Given that the incidence of schizophrenia is either unchanged or decreasing, such a causal relationship is unlikely.

All other hypotheses are consistent with the available data. However, it is difficult to judge which of these provides the best fit, or whether a combination of them may be most appropriate. If cannabis use acts as a precipitant of psychosis, we would have seen small increases in the number of early onset cases. If cannabis use increases the rate of relapse, we would have seen small increases in the number of chronic cases. Finally, if persons with psychosis were simply more likely to become regular cannabis users, we would expect to see no differences in the number incident or chronic cases, but a higher prevalence of regular use in this population. Future research needs to further examine these possibilities using prospective studies.

This approach has suggested that cannabis use is probably not causally related to psychosis in the strong sense of producing cases that would not otherwise have occurred. There is better support for a weaker causal hypothesis, that cannabis use may precipitate the disorder in persons who are vulnerable to developing psychosis. It may also worsen the course of the disorder among those who have already developed the disorder. This suggests that persons with psychosis or family history of the disorder may be well-advised to avoid using cannabis.

A similar approach to modelling may be useful in empirically assessing the plausibility of different relationships between risk factors and the incidence and prevalence of other mental disorders in the population.
This thesis has examined comorbidity between substance use and mental disorders among Australian adults. Research into comorbidity is a relatively recent phenomenon that was argued to be one of the most significant issues for research and treatment in the past decade (Kendall & Clarkin, 1992). However, as discussed in Chapter Four, much of the research on comorbidity has been conducted in clinical samples, which are prone to a range of biases that make it difficult to be confident that the patterns observed are representative of the general population (Caron & Rutter, 1991; Galbaud Du Fort et al., 1993). Although research into comorbidity has previously been conducted with general population samples, this thesis provides the first examination of comorbidity in the Australian population.

Two broad stages of enquiry were completed in the thesis. Chapter Two suggested, and Chapter Five confirmed, that substance use disorders were among the most common mental disorders in the Australian general population, with alcohol, tobacco and cannabis use disorders the most commonly reported. Patterns of comorbidity of these substances therefore affect the greatest number of persons in the Australian community.

The first stage of the empirical work involved an examination of the patterns of homotypic comorbidity (other substance use and use disorders) and heterotypic comorbidity (mental disorders) for alcohol, tobacco and cannabis. The following issues were addressed using data from the National Survey of Mental Health and Well-Being (NSMHWB), which involved the administration of a structured diagnostic interview to a representative sample of Australian adults:

a. What patterns of comorbidity exist between tobacco, alcohol and cannabis use, and other substance use and mental disorders?
b. Are these patterns of comorbidity explained by common factors?
c. Does the presence of comorbidity affect the likelihood that mental health treatment has been sought?
These analyses indicated potential differences across the three substances, so a comparative analysis was carried out in which the patterns of comorbidity of alcohol, tobacco and cannabis use and use disorders were directly compared.

The second stage involved a closer examination of the comorbidity between psychosis and substance use in the NSMHWB sample. Interest in this issue was motivated by two factors: (a) although psychotic disorders occur less commonly than other mental disorders, they are associated with a disproportionately large burden of disability, economic and social costs, and a high degree of chronicity (Eaton et al., 1992a; Eaton et al., 1992b; Hall et al., 1985; Keith et al., 1991; Knapp, 1997; Mason et al., 1996b); and (b) there is a relative dearth of population-level research on patterns of comorbidity among persons with psychosis. Given the debate surrounding problematic substance use in this population, the following work was conducted:

1. A detailed examination of substance use and substance use disorders among cases of psychosis in the NSMHWB sample;
2. Mathematical modelling of some of the hypothesised relationships that may explain observed patterns of comorbidity between cannabis use and psychosis.

The work of this thesis has implications for both theory and treatment. This Chapter summarises the findings of this thesis; discusses the implications of these findings and integrates them with other existing research; and highlights areas in which further research should be conducted.
12.1 Comorbidity in the Australian population

This thesis found that in a representative sample of the adult population of Australia, individuals with problematic substance use had elevated risks of a range of other substance use and mental health problems. Those meeting criteria for alcohol abuse or dependence in the past year were: five to six times more likely than non-drinkers to also use tobacco regularly; 11-19 times more likely to meet criteria for a cannabis use disorder; and those who were alcohol dependent were 10 times more likely to meet criteria for other drug use disorders (sedatives, stimulants or opiates), compared to non-drinkers. Rates of mood and anxiety disorders were around 4.5 times higher among alcohol dependent persons than among non-drinkers, while alcohol dependent persons were six times as likely to screen positively for psychosis.

Current tobacco users were five to nine times more likely than those who had never used tobacco to meet criteria for: an alcohol use disorder, another drug use disorder (sedatives, stimulants or opiates), or a cannabis use disorder. They were also more than twice as likely as those who had never smoked to meet criteria for a mood or anxiety disorder, and 5.5 times more likely to screen positively for psychosis.

Comorbidity was also observed among cannabis users. Regular tobacco use was between four and nine times more likely among cannabis users compared to non-users of cannabis. Cannabis users (regardless of level of use) were 5-6 times more likely than non-users to meet criteria for alcohol abuse, and those who met criteria for cannabis abuse or dependence were 12-14 times more likely than those who had not used cannabis to meet criteria for alcohol dependence. Cannabis dependent persons were also 45 times more likely than those who had not used cannabis in the past year to be dependent on sedatives, stimulants or opiates. The associations with mood and anxiety disorders were less strong, with cannabis users around 2-3 times more likely to meet criteria for a mood disorder, and cannabis dependent persons four times more likely to meet criteria for an anxiety disorder. Cannabis dependent persons were 11 times more likely to screen positively for psychosis.
12.2 EXPLANATIONS OF COMORBIDITY

There are two broad reasons why comorbidity might be observed: it may be artefactual or it may reflect true comorbidity between the disorders (Caron & Rutter, 1991). This thesis has examined aspects of both of these possibilities.

12.2.1 ARTEFACTUAL COMORBIDITY

Analyses of NSMHWB data in this thesis revealed that comorbidity was likely to be inflated in clinical samples in Australian treatment services, because of the higher rates of treatment seeking for mental health problems among persons with comorbid disorders. This was especially the case for persons with problematic alcohol, tobacco or cannabis use who also had mental disorders (mood disorders, anxiety disorders, or psychosis).

This meant that rates of mental disorders were particularly high among persons with problematic alcohol, cannabis or tobacco use who had sought treatment. Among alcohol dependent persons who had sought mental health treatment, around half met criteria for a mood (53%) or anxiety (47%) disorder; 12% met criteria for another drug use disorder (sedatives stimulants or opiates); and 9% screened positively for psychosis. Similarly, among cannabis dependent persons who had sought treatment, 49% met criteria for an anxiety disorder; one third met criteria for a mood disorder (32%), alcohol dependence (34%), or dependence on other drugs (32%); and 22% screened positively for psychosis. Tobacco users who had sought treatment also had high rates of other problems: 45% and 41% met criteria for a mood or anxiety disorder, respectively; 23% met criteria for an alcohol use disorder, while smaller proportions met criteria for cannabis dependence (8%), another drug use disorder (8%), or screened positively for psychosis (7%).

This finding parallels previous research that has found that comorbidity is elevated in treatment settings (Berkson, 1946; Caron & Rutter, 1991; Galbaud Du Fort et al., 1993; Roberts et al., 1978). This suggests that some of the comorbidity observed in clinical
samples is artefactual, and reflects sampling or referral biases, so it is critically important to use general population samples to examine comorbidity. This thesis has shown that although the rates of comorbid substance use and mental health problems are higher among treatment populations in Australia, nonetheless, comorbidity was observed in a general population sample (see Section 12.1), and is likely to reflect true comorbidity.

### 12.2.2 True Comorbidity

Comorbidity was observed in the general Australian population (Chapters Six to Eight). Both heterotypic and homotypic comorbidity were observed for alcohol, tobacco and cannabis use, but the patterns of comorbidity varied across the three substances (Chapter Nine). Table 12.1 summarises the patterns of comorbidity observed on a bivariate level (top rows). Given the representative sampling etc, we can conclude that this comorbidity represented true comorbidity and did not arise from sampling or other biases.

Patterns of homotypic comorbidity were similar across the three substances. Current tobacco use was a moderate predictor of homotypic comorbidity: current smokers were more likely than those who had never smoked to use other substances and to meet criteria for other substance use disorders (alcohol, cannabis and other drugs). Former tobacco users also had higher rates (relative to never users) of other substance use and alcohol use disorders.

Alcohol involvement was linearly related to homotypic comorbidity. Those who reported no alcohol use were least likely to report the use of other substances, and to meet criteria for substance use disorders. As involvement with alcohol increased, so too did the prevalence of other substance use and substance use disorders. Those who were alcohol dependent had the highest prevalence of other substance use and other substance use disorders.

Cannabis involvement was also linearly related to homotypic comorbidity. All levels of cannabis use were associated with increased risks of other substance use. Cannabis use disorders were associated with the highest rates of other substance use disorders, with cannabis dependence most strongly related to dependence upon sedatives, stimulants or
opiates. Comparative analyses revealed that of the three substances (alcohol, tobacco and cannabis), cannabis involvement was most strongly related to other substance use disorders. Thus, the nature of the patterns of homotypic comorbidity was similar across all three substances; but the strength of the relationship differed.

In contrast, patterns of heterotypic comorbidity differed across substances. Current tobacco users were more likely to meet criteria for mood and anxiety disorders, and to screen positively for psychosis, relative to those who had never used tobacco. Former smokers did not have higher rates of mental disorders (heterotypic comorbidity) than those who had never smoked.

Heterotypic comorbidity (with mood and anxiety disorders) was not linearly related to alcohol use. Instead, a “J-curve” was observed, in which those who met criteria for alcohol dependence, and non-drinkers, both had higher rates of mood and anxiety disorders than those who reported alcohol use without meeting criteria for a use disorder, and those who met criteria for alcohol abuse. Only alcohol dependence was associated with screening positively for psychosis.

The patterns of heterotypic comorbidity observed for cannabis use differed again. For mood disorders, there was an increased rate of a similar magnitude (odds of about 2-3 fold greater than non-users) that was the same irrespective of the level of involvement with cannabis use. The pattern for anxiety disorders was slightly different: anxiety disorders were slightly more common among cannabis users than non-users, and those who met criteria for cannabis dependence had the highest rates of anxiety disorders. Cannabis involvement was linearly related to psychosis “caseness”. Those who were more heavily involved with cannabis use were more likely to screen positively for psychosis.

12.2.2.1 Psychosis and Problematic Substance Use

Although psychotic disorders such as schizophrenia have been shown to be chronic disabling disorders that place a considerable burden upon the individual and the community, there is relatively little general population-based research on comorbidity with
substance use. Chapter Ten therefore focused on patterns of substance use and substance use disorders among likely cases of psychosis in the Australian population.

All forms of substance use and use disorders were more likely among persons who screened positively for psychosis. Persons who screened positively for psychosis were more likely than those who did not to have used alcohol, tobacco, cannabis, stimulants, sedatives and opiates. They were also more likely to have met criteria for all substance use disorders examined. A higher proportion of psychosis cases were cannabis and alcohol users, also met criteria for dependence, compared to non-cases who used these substances. This could indicate a lower threshold for developing problems related to alcohol and cannabis use, suggesting that substance use impairs role functioning more easily, a consequence that may not be surprising given that persons with psychotic disorders are likely to have a range of problems that already impair their social, occupational and other functioning (Mueser et al., 1992). Alternatively, it may indicate a greater sensitivity to the effects of psychoactive substances such as cannabis (Mueser et al., 1998).

12.2.2.2 SUMMARY

Types of comorbidity differed across alcohol, tobacco and cannabis. Homotypic comorbidity was similar: the use of all three was associated with increased odds of other substance use and other substance use disorders. This relationship was the strongest for cannabis use. Heterotypic comorbidity differed: tobacco use was a moderate marker of increased rates of all three groups of mental disorders (mood and anxiety disorders, and screening positively for psychosis); only alcohol dependence was related to increased rates of all groups of mental disorders; alcohol abuse was not associated with increased rates of any of the disorders, and alcohol use (without disorder) was associated with lower rates of anxiety and mood disorders. Cannabis use was related to a non-linear increase in rates of mood and anxiety disorders, while it was linearly related to psychosis.
12.2.3 EXPLANATIONS OF TRUE COMORBIDITY

Given that comorbidity was documented in the Australian general population, some consideration was given to the reasons for such comorbidity. There are a number of possible reasons why “true” comorbidity exists: common factors increase the likelihood of both disorders; one disorder causes the other; or there is an indirect relationship between the two disorders.

12.2.3.1 COMMON FACTORS

The possibility that common factors explained the observed patterns of comorbidity was examined to a limited extent using data from the NSMHWB. The reviews of literature on substance use disorders and mental disorders in Chapters Two and Three, respectively, suggested that persons with similar demographic characteristics, and persons with certain personality characteristics (namely higher levels of neuroticism), appeared to be more likely to meet criteria for all groups of disorders. These possibilities were confirmed in Chapter Five.

Multiple regression analyses were therefore carried out (Chapters Six to Nine) to test whether the comorbidity observed on a bivariate level was explained by demographics, other substance use and neuroticism. Table 12.1 shows the patterns of comorbidity observed after adjusting for the common factors considered in the analyses. Analyses revealed that for alcohol, tobacco and cannabis, homotypic comorbidity was generally not explained by the common factors examined here (adjusted associations, Table 12.1).

Some patterns of heterotypic comorbidity did change after multiple regression analyses were conducted, and these changes differed across the three substances (Table 12.1). Current tobacco use remained associated with all three groups of mental disorders after controlling for the common factors considered here. It did not appear that the demographics, other substance use or higher levels of neuroticism accounted for the association between tobacco use and these three groups of mental disorders.
Table 12.1: Patterns of comorbidity of alcohol, tobacco and cannabis use on an unadjusted (bivariate) level and after conducting multiple regression analyses (adjusted)

<table>
<thead>
<tr>
<th></th>
<th>Alcohol</th>
<th>Tobacco Use</th>
<th>Cannabis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>U</td>
<td>A</td>
<td>D</td>
</tr>
<tr>
<td><strong>Bivariate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol use disorders</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Regular tobacco use</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Cannabis use disorders</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Other substance use disorders</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Mood disorders</td>
<td>✓*</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>✓*</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td>Psychosis</td>
<td>X</td>
<td>X</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Adjusted</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol use disorders</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Regular tobacco use</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Cannabis use disorders</td>
<td>X</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>Other substance use disorders</td>
<td>X</td>
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<td>Mood disorders</td>
<td>X</td>
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<tr>
<td>Anxiety disorders</td>
<td>X</td>
<td>X</td>
<td>✓</td>
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<tr>
<td>Psychosis</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

Note: - = not applicable; X = no significant association; ✓ = a significant association; * alcohol users had lower rates than non-users; U = use without meeting criteria for DSM-IV abuse or dependence; A = DSM-IV abuse; and D = DSM-IV dependence.

In contrast, the “J-curve” observed between alcohol involvement and mood/anxiety disorders did not remain after adjusting for neuroticism. Specifically, it appeared that non-drinkers’ higher levels of neuroticism explained their higher rates of mood and anxiety disorders.
disorders compared to those who used alcohol without meeting criteria for a use disorder. Previous research suggests that when a particular type of substance use is highly prevalent in a population, those who report no use may show poorer social adjustment and mental health than those who do use it (Shedler & Block, 1990). The present finding suggests that given the high prevalence of alcohol use in the Australian population, not drinking is an indicator of poorer social adjustment – or of being more anxious, moody and irritable as a personality trait. Future research might evaluate the reasons for this association.

The association between alcohol dependence, and mood and anxiety disorders, did remain significant after controlling for the common factors using multiple regression analyses. In contrast, alcohol abuse was never associated with increased rates of mood or anxiety disorders, suggesting that although alcohol abuse is associated with other substance use problems, it is not associated with mental health problems.

The association between alcohol dependence and screening positively for psychosis also disappeared after taking account of other substance use and neuroticism, although the width of the 95% confidence interval of the adjusted odds ratio (0.91, 3.41) suggested that an association could not be ruled out. This contention was supported by the analyses in Chapter Ten, which suggested that alcohol dependence remained associated with increasing numbers of psychotic symptoms after controlling for other factors, including mood and anxiety disorders.

The association between cannabis use and mood/anxiety disorders did not remain after controlling for other substance use (the use of alcohol, tobacco, and other drugs). This suggests that the increased rates of mood and anxiety disorders among cannabis users may be explained by the fact that they also used a range of other substances, and it was this other substance use that was associated with mood and anxiety disorders. Future research is required to examine this finding further.

In contrast, cannabis dependence did remain associated with an increased likelihood of screening positively for psychosis, and increased numbers of psychotic symptoms, after controlling for the common factors examined here, which included neuroticism, mood and anxiety disorders, demographic variables and other substance use disorders (Chapter Ten).
Summary
This thesis has examined some common factors as possible reasons for homotypic and heterotypic comorbidity. Homotypic comorbidity did not appear to be explained by the factors examined here. Some heterotypic comorbidity was explained by common factors. This included comorbidity between: no alcohol use and mood and anxiety disorders; cannabis use and mood and anxiety disorders; and between cannabis use/abuse and psychosis. The patterns of heterotypic comorbidity of alcohol dependence and tobacco use did not appear to be explained by the common factors examined here; similarly, comorbidity between cannabis dependence and psychosis was not explained by the common factors examined in these analyses.

12.2.3.2 Explanations of the remaining associations
The analyses of the NSMHWB were limited in their ability to further explore reasons for the associations by the limited range of covariates examined and by the cross-sectional nature of the data. Different research designs will be needed to test these explanations.

Causal relationship
One possibility is that there is a causal relationship (either direct or indirect) between the use of different substances (hence explaining homotypic comorbidity) or between substance use disorders and mental disorders (explaining heterotypic comorbidity).

a) Homotypic comorbidity
There has been considerable debate about the correlation between the use of different drug types. The “gateway hypothesis”, characterises the “developmental sequence” of drug use (Kandel & Faust, 1975; Kandel et al., 1986; Kandel et al., 1992; Yamaguchi & Kandel, 1984a; Yamaguchi & Kandel, 1984b), in which progression to a higher stage is made more likely by use of a drug at an earlier stage. Evidence has consistently shown that tobacco and alcohol use generally precede illicit substance use, and cannabis use precedes the use of other illicit substances (Kandel & Faust, 1975; Kandel et al., 1986; Kandel et al., 1992; Wu & Anthony, 1999; Yamaguchi & Kandel, 1984a; Yamaguchi & Kandel, 1984b). The
The gateway hypothesis may describe the sequence in which substance use occurs, but it does not necessarily mean that the relationship is causal. The substance for which the most research has been conducted on this issue is cannabis: the evidence on this is outlined below.

There are a number of ways in which cannabis use might be causally related to other drug use problems (Fergusson & Horwood, 2000). First, cannabis could encourage experimentation with other drugs because its use was pleasurable (Fergusson & Horwood, 2000; MacCoun, 1998). Second, cannabis use could lead to a greater likelihood of a social context in which illicit drug use of other kinds is more likely, for example, through peer affiliations and access to other illicit drugs in the “black market” (Fergusson & Horwood, 1997; MacCoun, 1998). Third, it could be that cannabis use is one part of a “deviant” developmental path (Fergusson & Horwood, 2000; Sroufe, 1997). Cannabis use at an early age, for example, has been found to increase the likelihood that adolescents will subsequently associate with delinquent peers and move out of home; these factors subsequently increase the likelihood of poor psychosocial outcomes in early adult life (Fergusson & Horwood, 1997), including continued or escalated substance use (Newcomb & Bentler, 1988). This is an example of a possible indirect effect of cannabis use upon later illicit drug use.

In a recent longitudinal study, Fergusson and Horwood (2000) examined these possibilities. They found that cannabis use preceded other illicit drug use in almost all cases; that cannabis and other illicit drug use were characterised by similar risk factors; and that even after adjusting for a large number of factors, those who had used cannabis at least 50 times in a year were still 60 times more likely to have used other illicit drugs than non-users of cannabis (Fergusson & Horwood, 2000). The possibility that common genetic vulnerabilities may have explained this remaining association is considered below.

b) Heterotypic comorbidity

Possible causal explanations of heterotypic comorbidity have also been the subject of considerable debate. Some argue that substance use disorders develop as a result of attempts to “self-medicate” symptoms of psychological distress (Cappell & Greeley, 1987; Khantzian, 1997), but evaluations of such causal hypotheses have received mixed results. For example, alcohol can have sedating effects, but research examining the relationship
between alcohol use disorders and mood/anxiety disorders has not consistently found that alcohol use reduces stress among persons who are vulnerable to alcohol use disorders (Chick, 1999a). Patterns of substance use among persons with comorbid mental disorders have also been found to reflect availability of the drugs rather than reflecting the specific psychological effects of different substances (Dixon et al., 1991b; Hall, 1998a; Mueser et al., 1998; Noordsy et al., 1991).

A second causal hypothesis is that substance use problems precipitate mental health problems. Prospective studies have suggested that some persons develop depression and anxiety disorders following the development of alcohol dependence (Kushner, Sher, & Erickson, 1999; Schuckit et al., 1997a, 1997b), and some have found that major depression that develops after alcohol dependence remits with abstinence from alcohol (Brown & Schuckit, 1988).

In support of causal relationships, prospective studies of heterotypic comorbidity between alcohol and nicotine dependence, and mood and anxiety disorders (e.g. Kushner et al., 1999; Patton et al., 1998), have found, for example, that the presence of alcohol dependence at baseline predicts the development of an anxiety disorder during a follow-up period (Kushner et al., 1999). Although this temporal ordering is a necessary condition for a causal relationship, it is not sufficient to indicate that a causal relationship exists. Furthermore, the presence of an anxiety disorder predicts the development of alcohol use disorders during follow-up (Kushner et al., 1999). It may not be the case that there is a primary mechanism in which alcohol dependence causes anxiety disorders (or vice versa), and that either of these is the predominant reason for the comorbidity observed in general population samples. Rather, it may be that either (a) there are reciprocal causal mechanisms between the two (Chick, 1999a); or (b) common factors explain comorbidity between the two disorders, which simply happen to occur at different points in a person’s lifetime. This possibility will be considered below.

Causal explanations of comorbidity between cannabis use and psychosis have been extensively discussed in the literature (Batel, 2000; Blanchard et al., 2000; Gruber & Pope, 1994; Hall, 1998a; Hall & Degenhardt, 2000; McKay & Tennant, 2000; Mueser et al., 1998; Rosenthal, 1998; Thornicroft, 1990). This thesis used mathematical modelling (Chapter...
Eleven) to assess the fit between epidemiological data on trends in cannabis use and psychosis, and the hypothesis that cannabis use caused psychosis among persons who would not otherwise have developed the disorder. This hypothesis does not provide a good fit to the existing data: the predictions of a model in which cannabis use caused psychosis are not consistent with the observed stable (or decreasing) incidence and prevalence of psychosis over the past few decades during which there have been significant increases in the prevalence of cannabis use.

It was difficult to distinguish between the other three hypotheses that were examined (which are not necessarily mutually exclusive). If cannabis use precipitated psychosis among vulnerable persons (who would have developed the disorder anyway) we would expect to see a small increase in the number of early onset cases of psychosis, which is consistent with the limited data on this issue. If cannabis use increased the risk of relapse to schizophrenia, there would be a very modest increase in the number of chronic cases of psychosis (at the most, a 1% increase in the size of the population of persons with psychosis in more recent birth cohorts). If regular cannabis use was more likely to develop among persons with psychosis (without any causal relationships between the two), we would expect to see only a higher prevalence of regular cannabis use among persons with schizophrenia.

Given the very limited data, the plausibility of these three hypotheses cannot be further tested, and further research is required. This could include: prospective studies of persons with psychosis who use or do not use cannabis to examine the impact of cannabis use on relapse; assessment of trends in cannabis use among this population over time; and examinations of the effect of cessation of cannabis use on persons with psychotic symptoms who are cannabis users.

**Other common factors**

A wide number of factors that were not examined in this thesis might have been common to substance use and mental disorders, and could explain the relationships that were observed. These common factors may be shared genetic vulnerabilities, and/ or shared social and environmental factors. These possibilities are best explored using studies that
can examine the contributions of genetic factors to comorbidity (e.g. twin studies) and of environmental and social factors (e.g. longitudinal cohort studies).

It is likely that there are shared genetic factors that increase the likelihood of the patterns of homotypic comorbidity observed in the Australian population, because these psychoactive substances have similar effects upon key pathways in the brain (Koob, 2000; Koob & LeMoal, 1997; Nutt, 1997). Twin studies also suggest that genetic vulnerabilities increase the risk of dependence on individual substances (Heath, 1995; Heath et al., 1997; Kendler, Karkowski, Neale, & Prescott, 2000; Kendler et al., 1999; Kendler & Prescott, 1998a). Research with male twins has shown that common genetic vulnerabilities explain a significant part of the comorbidity between different types of drug dependence (True et al., 1999a; True et al., 1999b; Tsuang et al., 1998). Future research needs to examine the extent and nature of this common vulnerability, and to see if it also exists among females.

Shared genetic vulnerabilities may also explain some of the heterotypic comorbidity observed. For example, twin research suggests that common genetic vulnerabilities partly explain the comorbidity between major depression and nicotine and alcohol dependence (Kendler et al., 1993b; Kendler et al., 1993c). There may be gender differences in these effects (Prescott, Aggen, & Kendler, 2000b). Future research should examine possible common genetic vulnerabilities shared between alcohol, cannabis and tobacco use, and other mood and anxiety disorders.

It is also possible that a range of common social and environmental factors explain the associations that remained in the NSMHWB after multiple regression analyses were completed. Longitudinal research has found that multiple environmental factors increase the risk of substance use problems in general rather than the use of one substance in particular (Hawkins et al., 1992; Jessor & Jessor, 1977; Lynskey et al., 1998). The shared environmental factors that potentially explain homotypic comorbidity include: family functioning, parental relationships, and parental effectiveness (Fergusson et al., 1994; Fergusson & Horwood, 1997; Johnson, Cohen, Kasen, Smailes, & Brook, 2001; Kessler et al., 1996), self-esteem (Lynskey et al., 1998; Newcomb et al., 1986), peer affiliations (Fergusson & Horwood, 1997; Fergusson & Horwood, 2000; MacCoun, 1998), and social disadvantage (Fergusson & Horwood, 1997; Fergusson & Horwood, 2000; MacCoun,
Johnson and colleagues have recently reported that a constellation of factors such as: little time spent with the child, parental discord, poor supervision of the child, parental tobacco smoking and poor maintenance of the home, were predictive of children later developing a range of psychiatric disorders including substance use disorders (Johnson et al., 2001). Interestingly, this study also found that it was these “maladaptive parenting behaviours” rather than parental psychiatric disorders that predicted the development of psychiatric disorders in adolescence and early adulthood (Johnson et al., 2001).

Nonetheless, environmental factors are unlikely to wholly explain comorbidity. The best evidence against this comes from the study by Fergusson and Horwood (described above) that controlled for a very large number of background variables, family history variables, social and environmental variables, and individual variables. Control for these variables markedly reduced the strength of the relationship between the level of involvement with cannabis use and other illicit drug use, but it did not eliminate it (Fergusson & Horwood, 2000). As discussed above, it may be that Fergusson and Horwood’s finding can be explained by genetic vulnerabilities. Future work might examine this possibility.

12.2.3.3 CONCLUSIONS ON EXPLANATIONS OF COMORBIDITY

The current thesis has suggested that a limited range of common factors did not tend to explain the patterns of homotypic comorbidity observed in the Australian population. Nor did these common factors explain comorbidity between: mood and anxiety disorders, and alcohol dependence and tobacco use; psychosis, and alcohol and cannabis dependence, and tobacco use. These common factors did appear to explain comorbidity between cannabis use and mood and anxiety disorders. The cross-sectional epidemiological research reported in this thesis was able to carefully document the nature and extent of comorbidity between substance use and mental disorders, but it had a limited ability to test potential mechanisms underlying this association. It was able to exclude some common causal explanations, namely, age, gender and other demographic variables, other drug use and neuroticism.

Different types of research studies are needed to test other common factor explanations of these associations. Longitudinal studies are desirable to document the associations between
substance use and mental disorders among cohorts followed up over considerable periods of time, and for whom there are extensive data on social and environmental factors that may provide common explanations of comorbidity. Prospective studies are needed to observe the outcome of changes in substance use particularly among problematic users of alcohol, tobacco and cannabis who meet criteria for mental disorders. There is also a need to examine whether genetic factors explain these associations: future behavioural genetic research could examine in detail possible genetic influences upon heterotypic and homotypic comorbidity.
12.3 TREATMENT IMPLICATIONS

This thesis has also shown that among Australian adults with alcohol, tobacco or cannabis use problems, those who have other substance use or mental disorders are more likely to seek help for mental health problems. In particular, it was persons who had comorbid mood, anxiety or psychotic disorders that were most likely to have sought mental health treatment. This means that although in the community homotypic comorbidity among substance use disorders is of a similar or greater magnitude than heterotypic comorbidity, heterotypic comorbidity is more strongly associated with help seeking. As a result there will be particularly high rates of heterotypic comorbidity among Australian treatment populations. This finding is consistent with previous empirical research (Galbaud Du Fort et al., 1993; Kessler et al., 1996; Roberts et al., 1978; Wu, Kouzis, & Leaf, 1999)

It is therefore important for clinicians in both drug and alcohol treatment and mental health treatment services to assess whether there are any comorbid substance use and mental health problems. As noted in Chapters Six to Eight, there are suitable screening instruments available to assess the use of a wide range of substances among persons with mental disorders and screening tests for mood and anxiety disorders among persons with drug and alcohol use problems. Screening for possible psychotic symptoms is also indicated given the finding that one in twelve alcohol dependent persons (9%) and one in four cannabis dependent persons (23%) who had sought mental health treatment also screened positively for psychosis.

Given the extent of comorbidity observed among persons seeking treatment for mental health problems, the findings of thesis have important clinical implications. First, comorbid problems may have an effect upon the outcome of treatment. Second, different treatment approaches may be required for persons with comorbid problems. Evidence relevant to each possibility is briefly reviewed.
12.3.1 DO COMORBID PROBLEMS AFFECT TREATMENT OUTCOME?

The effects of comorbid mood and anxiety disorders upon treatment outcome for persons with alcohol, tobacco and cannabis dependence need to be more clearly elucidated. Some research has suggested that alcohol dependent persons with comorbid mood or anxiety disorders have a poorer clinical outcome than those without such disorders (Brunello et al., 2000; Chignon et al., 1998; Feinman & Dunner, 1996; Hasin et al., 1996; Kessing, 1999; Rouillon, 1996). In contrast, other research has not found such a relationship for alcohol dependent persons who meet criteria for major depression (Davidson & Blackburn, 1998; Lysney, 1998). This may be due in part to the fact that the clinical studies that found no effect upon clinical outcome comprised samples that were predominantly male, among whom the presence of a comorbid mood disorder may have less effect than upon females (Lysney, 1998). Future prospective research should examine the effects of comorbidity on clinical outcome for different subgroups, particularly such as gender.

There is also inconsistent evidence regarding outcome for comorbid alcohol and tobacco dependence. Longitudinal research has found that those with a lifetime history of alcohol use disorders are just as likely to successfully give up tobacco smoking as those without such a history (Breslau, Peterson, Schultz, Andreski, & Chilcoat, 1996); but treatment studies have suggested that persons with alcohol use disorders who smoke tobacco are more likely to return to drinking than those who stop smoking (Bobo et al., 1998; McIlvain & Bobo, 1999; Sobell & Sobell, 1996). This might be due to the timing of alcohol use disorders (current versus lifetime), suggesting that it is currently co-occurring substance use problems that affect treatment outcome. Future research needs to examine this possibility.

Epidemiological and clinical research has suggested that tobacco smokers with depression have lower rates of quitting (Anda et al., 1990; Glassman et al., 1990; Glassman et al., 1988). This implies that depressed smokers may have greater difficulty quitting use. Indeed, the findings of this thesis were consistent with this finding, as former smokers did not have higher rates of either mood or anxiety disorders than those who had never smoked. These findings are not consistent with longitudinal research, however, which found that a history of major depression did not affect the likelihood that tobacco smokers would
cease use (Breslau, Peterson, Schultz, Chilcoat, & Andreski, 1998). Again, the explanation may be that it is current depression, rather than lifetime depression, which decreases the likelihood of successful smoking cessation.

The findings from examinations of comorbidity between psychosis and substance use in this thesis supported clinical evidence of high rates of substance use and substance use disorders among persons with psychosis. It was of interest that cannabis dependence remained significantly positively associated with increases in the number of psychotic symptoms after adjustment for other factors. The modelling that was conducted in Chapter Eleven suggested that the hypothesis that cannabis use may worsen clinical outcomes among persons with psychosis was consistent with the limited empirical evidence. It is possible, given limited outcome studies examining this issue, that cannabis use may worsen the clinical outcome for persons with psychosis (Jablensky et al., 1991; Linszen et al., 1994). Future research is certainly required to further examine this issue, especially prospective studies that examine the effect of changes in cannabis use upon the outcome of psychosis. The effect of cannabis use treatment upon outcome for psychosis should also be evaluated.

12.3.1.1 CONCLUSIONS ON EFFECTS OF COMORBIDITY ON TREATMENT OUTCOME

Despite some suggestions that comorbid disorders may worsen treatment outcome among alcohol dependent persons, to date the research is limited and the results inconclusive. There is a need for future research to comprehensively document the effects of a range of comorbid substance use and mental disorders on treatment outcome for alcohol, nicotine and cannabis dependence; and the effects of comorbid alcohol, tobacco and cannabis use disorders on treatment outcome for other substance use and mental disorders.

12.3.2 TREATMENT APPROACHES

12.3.2.1 OTHER SUBSTANCE USE PROBLEMS

Persons with alcohol, cannabis or nicotine dependence, who are receiving treatment, might require assistance for their other substance use problems. It could be argued that targeting
the use of more than one substance simultaneously could place too many demands upon
the client. However, research examining the simultaneous treatment of alcohol and tobacco
use has revealed that such interventions are safe (Bobo & McIlvain, 1998; Hurt et al., 1994)
and that alcohol dependent clients who are attempting to stop drinking are often
considering simultaneous cessation of tobacco use (McIlvain & Bobo, 1999; Sees & Clarke,
1993).

Indeed, some encouraging research has suggested that the outcomes of alcohol treatment
are improved when cessation of tobacco use is also attempted (Bobo et al., 1998; McIlvain &
Bobo, 1999; Sobell & Sobell, 1996). This latter finding is important since many persons
with alcohol use problems will have more than one substance use problem, and targeting
these other problems might improve the effectiveness of treatment for alcohol
dependence.

Given the limited amount of research that has been carried out in this area, and since the
prevalence of multiple substance use disorders is likely to be very high in clinical
populations, more research is required to evaluate the effect (if any) upon outcome of the
simultaneous treatment of other substance use problems among persons with alcohol,
tobacco and cannabis use disorders. Research also needs to examine which are the most
effective types of interventions for persons with multiple substance use problems.

12.3.2.2 Comorbid Mood and Anxiety Disorders

The evidence on effective treatments for alcohol dependence in persons who also have
comorbid mood and anxiety disorders is far from adequate (Nunes, McGrath, & Quitkin,
1995). In fact, most research on the effectiveness of treatments for alcohol dependence has
excluded persons with comorbid disorders and vice versa (Nunes et al., 1995). There has
been more research conducted on appropriate interventions for tobacco smokers who also
suffer from depression. There appears to be no research on effective interventions for
cannabis dependent persons who also have mood or anxiety disorders. The limited
evidence on these issues is summarised below.
Cognitive behavioural interventions

There is evidence that cognitive and behavioural interventions (CBT) are effective treatments for alcohol, tobacco and cannabis dependence (Copeland, Swift, & Rees, 2001; Hall et al., 1998; Hester & Delaney, 1997; Lancaster & Stead, 2000; Lang, Engelder, & Brooke, 2000; Mattick & Baillie, 1992; Proudfoot & Teesson, 2000; Stead & Lancaster, 2000; Stephens, Curtin, & Roffman, 2000; Stephens et al., 1994; Teesson & Hall, 2000).

In one study, CBT for alcohol dependence delayed relapse to alcohol use among females with social phobia compared to twelve step programs such as Alcoholics Anonymous (AA) (Thevos, Roberts, Thomas, & Randall, 2000). CBT may therefore be a more appropriate intervention than AA for this group.

However, CBT without any other intervention may be less effective for alcohol dependent persons with comorbid disorders than among those with alcohol dependence only (Proudfoot & Teesson, 2000; Wilk, Jensen, & Havighurst, 1997). Accordingly, it may be appropriate to consider additional treatment components for persons with comorbid mood and anxiety disorders. Some CBT interventions for these comorbid mood and anxiety disorders have been evaluated.

Brown and colleagues found that providing CBT for comorbid major depression among alcohol dependent persons improved both depression and drinking outcomes in this group (Brown, Evans, Miller, Burgess, & Mueller, 1997). CBT that targets a range of cognitions and behaviours surrounding both tobacco use and depressed mood, in addition to nicotine replacement therapy (NRT), may also increase cessation rates among smokers with depression and/or mania (Hall et al., 1998; Hughes et al., 1999a). The effectiveness of CBT for tobacco smokers who also have anxiety disorders should be evaluated.

However, the very limited evidence for the effectiveness of a discrete CBT intervention for the comorbid anxiety disorder in addition to CBT for alcohol dependence is not as promising. One controlled trial evaluated CBT for both panic disorder and alcohol dependence compared to CBT for alcohol dependence alone (the usual treatment), and failed to find any differences in either drinking outcomes or panic symptoms at three, six or twelve months (Bowen, D'Arcy, Keegan, & Senthilselvan, 2000). A recent randomised
controlled trial in a sample of individuals with alcohol dependence and social phobia found that treatment of both social anxiety and alcohol use problems resulted in significantly worse drinking outcomes at three months than CBT for alcohol dependence alone (Randall, Thomas, & Thevos, 2001). Further research is required, but these findings suggest that it may not be sufficient to simply add further, discrete, CBT treatments, to improve treatment outcomes for persons with alcohol dependence and anxiety disorders.

**Pharmacological treatments**

There is evidence that antidepressant medication is of benefit for the treatment of persons with alcohol dependence and comorbid anxiety and mood disorders (Lynskey, 1998). Persons who were given fluoxetine, a serotonin-selective reuptake inhibitor (SSRI), in a 3-month trial had, fewer depressive symptoms and lower drinking levels at three months (Cornelius et al., 1997) and at 1 year (Cornelius et al., 2000) compared to persons given a placebo. This research has been supported by other studies of persons with both alcohol dependence and depression using tricyclic antidepressants such as imipramine (McGrath et al., 1996) and desipramine (Mason, Kocsis, Ritvo, & Cutler, 1996a).

For persons with alcohol dependence and comorbid bipolar disorder, some have recommended the aggressive stabilisation of manic symptoms and avoiding the use of antidepressants among this group, which may worsen outcome (Raimo & Schuckit, 1998). However, there is a lack of controlled evidence to support this treatment recommendation.

There is some evidence to suggest that pharmacological treatments may be effective among alcohol dependent persons with comorbid anxiety disorders. Benzodiazepines have historically been the first-line pharmacological treatment for anxiety disorders (Julien, 2001; Posternak & Mueller, 2001) but they do carry a risk of dependence (Julien, 2001; Sellers et al., 1993). There is also some evidence that alcohol dependent persons (or those at risk) may have an increased liability to developing problematic use of benzodiazepines (Ciraulo, Barnhill, Ciraulo, Greenblatt, & Shader, 1989; Ciraulo et al., 1988a; Ciraulo, Sands, & Shader, 1988b; Ciraulo et al., 1996). Alcoholics Anonymous (AA) has therefore argued that the use of benzodiazepines should be avoided among persons with alcohol dependence and anxiety disorders (Alcoholics Anonymous, 1984).
Others have disagreed with this view (Marshall et al., 1997; Posternak & Mueller, 2001). A recent review concluded that there was no evidence to suggest that there was any increased risk of dependence upon benzodiazepines among alcohol dependent persons compared to those without alcohol dependence (Posternak & Mueller, 2001). Moreover, benzodiazepine use did not appear to increase the risk of relapse to problematic alcohol use.

Alcohol dependent persons with comorbid anxiety disorders may also benefit from antidepressant medication, especially the SSRIs, which are increasingly advocated as first-line treatments for anxiety disorders (Julien, 2001). There also does not appear to be any risk of dependence upon antidepressants, and the newer antidepressants (SSRIs) are not dangerous if taken in overdose (Julien, 2001), thus avoiding the risks associated with benzodiazepines. An open label trial of sertraline, an SSRI, for the treatment of PTSD among alcohol dependent persons found that both alcohol consumption and PTSD symptoms were significantly reduced at three months (Brady, Sonne, & Roberts, 1995). Future placebo-controlled trials are needed to confirm and extend this finding, as well as investigate the effectiveness of sertraline among alcohol dependent persons with other comorbid anxiety disorders such as OCD, panic disorder, and social phobia.

Antidepressants have also been shown to be effective in assisting tobacco smokers to quit tobacco use. Bupropion – an atypical antidepressant with dopaminergic actions – has been found to double cessation rates compared to placebo (Hughes, Stead, & Lancaster, 1999b; Hurt et al., 1997; Jorenby et al., 1999). A study using nortriptyline, a tricyclic antidepressant, suggested that those with a history of major depression were just as likely as those without to successfully quit tobacco smoking (Hall et al., 1998). Nortriptyline may have increased the quitting rate among those with a history of depression so that it was the same as that in persons without depression. However, persons with a history of depression may be at higher risk of developing depression after quitting tobacco use, even after antidepressant treatment (Borrelli et al., 1996; Tsoh et al., 2000). This possibility needs to be considered.

The use of anxiolytics could be considered as another way to increase cessation rates among smokers with anxiety disorders. A recent review of the evidence concluded that the use of anxiolytics to aid smoking cessation in the general population of smokers concluded that their use was not supported by existing evidence (Hughes et al., 1999b). There may
nevertheless be a case for using anxiolytics with smokers with anxiety disorders who are attempting to give up. This is suggested by one study that found persons who had high anxiety levels were more likely to sustain abstinence from smoking while taking the anxiolytic buspirone, whereas those who had low anxiety were less likely to achieve abstinence using the drug (Cinciripini et al., 1995). Further research is needed in this area.

Given that many antidepressants are also effective in the treatment of anxiety disorders and are increasingly being used as first line treatments for these disorders (Julien, 2001), future research might examine whether antidepressant medication also improves the success of quit attempts of persons with anxiety disorders.

The use of NRT (including nicotine patches, nicotine gum, nasal sprays, and inhalers) has been shown to be effective in assisting tobacco smokers in general to quit (Silagy, Mant, Fowler, & Lodge, 1994). NRT may also aid attempts to quit among tobacco smokers with comorbid mood and anxiety disorders. Research has suggested that the combined use of nicotine patches and bupropion results in non-significant increases in smoking cessation rates compared to the use of bupropion alone (Jorenby et al., 1999). Furthermore, a recent review of the effectiveness of NRT found that such treatments were effective in reducing anxiety symptoms (West & Shiffman, 2001). This suggests that it may be important to offer such treatments to persons who are already suffering from anxiety problems, in an attempt to minimise the likelihood that nicotine withdrawal will exacerbate anxiety symptoms. Future investigations could examine the effectiveness of both NRT and antidepressant medication for tobacco smokers with other mood and anxiety disorders.

12.3.2.3 Comorbid psychotic disorders

There are few well-controlled evaluations of treatments for problematic substance use among persons with psychoses (Bellack & Gearon, 1998; Bennett et al., 2001; Drake et al., 1998; Kavanagh, 1995; Kavanagh, Young, Boyce, & Clair, 1998). Drake and colleagues reviewed 36 studies evaluating the effectiveness of integrated treatment for persons with psychotic disorders and substance use disorders. Only seven of these studies used an
experimental design (Drake et al., 1998). It did not appear that simply treating persons with psychosis in existing substance abuse treatment services was effective (Drake et al., 1998).

Two studies involved representative samples of schizophrenic outpatients in contact with treatment services (Hellerstein, Rosenthal, & Miner, 1995; Jerrell & Ridgely, 1995). In both studies there was encouraging evidence for the effectiveness of skills training and intensive case management (Bennett et al., 2001; Drake et al., 1998).

Bennett and colleagues reported on an intervention that taught behavioural skills, such as refusal skills training, problem solving and coping skills training (Bellack & Gearon, 1998; Bennett et al., 2001). A significant proportion of those who began treatment showed improvements in functioning and reductions in substance use, however a significant proportion of those who had enrolled did not initiate the treatment or dropped out, suggesting that retention in treatment is a significant issue among this group. Further controlled evaluations are needed, particularly given that CBT is effective in treating symptoms of psychosis among schizophrenic persons (Sensky et al., 2000).

Interventions to reduce tobacco use among persons with psychosis are needed given the high prevalence of use among this group. Despite concerns about the use of nicotine to self-medicate psychotic symptoms, one study found that smoking cessation did not exacerbate psychosis (Dalack, Becks, Hill, Pomerleau, & Meador-Woodruff, 1999).

Unfortunately, there is little research that has examined the adequacy of treatments (such as NRT) for this group, and some evidence that cessation rates are low among those who attempt to quit. One study found low rates of abstinence in a group of stabilised schizophrenic outpatients who were not problematic users of other substances. They were given NRT and six sessions of group therapy a week, but only 12% were abstinent at six months (Addington, el-Guebaly, Campbell, Hodgins, & Addington, 1998). Other recent research has found similarly low cessation rates (Ziedonis & George, 1997). A trial of the efficacy and tolerability of bupropion in combination with group therapy found that it was well tolerated (Weiner, Ball, Summerfelt, Gold, & Buchanan, 2001). Expired carbon monoxide levels also decreased significantly over the course of the study. Future controlled trials are needed to examine these treatment options further.
Of additional interest is the finding of a number of studies that atypical antipsychotic medication (clozapine) may be associated with lower rates of smoking, and with a reduction in the number of cigarettes smoked (Combs & Advokat, 2000; George, Sernyak, Ziedonis, & Woods, 1995; McEvoy et al., 1995b; McEvoy, Freudenreich, & Wilson, 1999). By contrast, traditional antipsychotics (such as haloperidol) have been associated with increased rates of smoking (Combs & Advokat, 2000; McEvoy, Freudenreich, Levin, & Rose, 1995a). These associations also deserve further investigation.

12.3.2.4 Conclusions on Treatments for Persons with Comorbid Substance Use and Mental Disorders

Despite the fact that there is increasing research examining the efficacy of interventions for persons with alcohol use disorders and mood and anxiety disorders, this evidence is by no means comprehensive over the spectrum of mood and anxiety disorders. Nor is there good evidence for various plausible combinations of treatment approaches. There is a need for rigorous research on the most effective treatment approaches for persons with both alcohol dependence and mood and anxiety disorders.

Increasing evidence suggests that antidepressant medication, in addition to CBT, may be an effective treatment approach for tobacco smokers with a history or current episode of depression. The effectiveness of these approaches for other mood and anxiety disorders should be the subject of future research. There is a need for research to examine interventions for persons with cannabis use disorders who also have comorbid substance use and mental health problems.

Controlled trials of interventions for comorbid substance use disorders among persons with psychosis are needed, given the limited evidence to date, the disappointing results of studies that have been published, and the high prevalence of substance use disorders among this population.

In general, it may be wise to consider a combination of integrated interventions for persons with comorbid mental and substance use disorders, as opposed to discrete components.
12.4 Conclusions

Patterns of comorbidity differ across different substances. In an examination of population patterns of comorbidity, which has avoided the biases that exist in clinical samples, this thesis has found that alcohol, cannabis and tobacco are differentially associated with different mental disorders. It may not be that the same factors underlie comorbidity for each of the three substances. This issue should be examined in future research.

While cross-sectional surveys such as the NSMHWB are important for their ability to document population-level associations between substance use and mental health, they have a limited ability to examine the reasons for the associations. Such work needs to be completed using other methods such as prospective studies of persons with the disorders in question; cohort studies; and treatment outcome studies. Based on the findings in this thesis, areas of particular interest include studies of comorbidity between: all forms of substance use; between alcohol dependence and mood and anxiety disorders; between tobacco use and all mental disorders; and between cannabis use and psychosis.

Regardless of the underlying reasons for the comorbidity observed in this thesis, the fact that it affects treatment seeking indicates that the findings have substantial treatment implications. There is a great need for future research to examine the implications of all forms of comorbidity for long-term outcome, and for the development and evaluation of effective treatment approaches for persons with comorbid substance use and mental disorders.
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APPENDIX A - DSM-IV DIAGNOSTIC CRITERIA USED TO DIAGNOSE THE MAJOR SUBSTANCE USE, MOOD, ANXIETY AND PSYCHOTIC DISORDERS

SUBSTANCE USE DISORDERS

DSM-IV SUBSTANCE ABUSE

A. A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring within a 12-month period:
   
   a. recurrent substance use resulting in failure to fulfil major role obligations at work, school, or home;
   
   b. recurrent substance use in situations in which it is physically hazardous (e.g. driving while intoxicated);
   
   c. recurrent substance-related legal problems;
   
   d. continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance;

B. The symptoms have not met criteria for substance dependence.
DSM-IV SUBSTANCE DEPENDENCE

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three or more of the following:

1. Tolerance, as defined by either:
   a. a need for markedly increased amounts of the substance to achieve intoxication or the desired effect;
   b. markedly diminished effect with continued use of the same amount of the substance;

2. Withdrawal, as manifested by either of the following:
   a. A characteristic withdrawal syndrome for the substance;
   b. The same or a closely related substance is used to relieve or avoid withdrawal symptoms;

3. the substance is taken in larger amounts of for a longer period than intended;

4. there is a persistent desire or unsuccessful efforts to cut down or control substance use;

5. a great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects;

6. important social, occupational or recreational activities are reduced or given up because of substance use;

7. substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
MOOD DISORDERS

DSM-IV MAJOR DEPRESSION

A. Presence of one or more major depressive episodes

**Depressive episode**

A. Five (or more of the following symptoms have been present during the same 2-week period and represent a change from previous functioning. At least one of the symptoms is depressed mood or loss of interest or pleasure:

1. Depressed mood most of the day nearly every day;
2. Markedly diminished interest or pleasure in all, or nearly all, activities most of the day, nearly every day;
3. Significant weight loss when not dieting or weight gain; or a significant increase or decrease in appetite;
4. Insomnia or hypersomnia nearly every day;
5. Psychomotor agitation or retardation nearly every day;
6. Fatigue or loss of energy nearly every day;
7. Feelings of worthlessness or excessive or inappropriate guilt nearly every day;
8. Diminished ability to think or concentrate, or indecisiveness, nearly every day;
9. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.

B. The symptoms do not meet criteria for a mixed (manic and depressive) episode.
C. The symptoms cause clinically significant distress or impairment in social, occupation or other important areas of functioning;
D. The symptoms are not due to the direct physiological effects of a substance or to a general medical condition;
E. The symptoms are not better accounted for by bereavement (i.e. loss of a loved one).

B. The major depressive episode is not better accounted for by schizoaffective disorder and is not superimposed in psychotic disorders.
C. There has not been a manic episode.
DSM-IV DYSTHYMIA

A. Depressed mood for most of the day, for more days than not, as indicated by either subjective account or observation by others, for at least 2 years.

B. While depressed, the presence of two or more of the following symptoms:

1. Poor appetite or overeating;
2. Insomnia or hypersomnia;
3. Low energy or fatigue;
4. Low self-esteem;
5. Poor concentration or difficulty making decisions;
6. Feelings of hopelessness.

C. During the 2-year period of the disturbance, the individual has never been without the symptoms from A and B for more than 2 months at a time.

D. No major depressive episode has been present during the first 2 years of the disturbance.

E. There has never been a manic episode.

F. The disturbance does not exclusively occur during the course of a psychotic disorder.

G. The symptoms are not due to the direct physiological effects of a substance or to a general medical condition.

H. The symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning.
**DSM-IV Bipolar I Disorder**

A. The presence of one or more manic or mixed episodes.

**Manic Episode**

A. A distinct period of abnormally and persisted elevated, irritated or expansive mood lasting at least 1 week (or any duration of hospitalisation is necessary).

B. During the period of the disturbance, three or more of the following symptoms have persisted (four if the mood is irritable):
   a. Grandiosity or inflated self-esteem;
   b. Decreased need for sleep;
   c. Pressure to talk;
   d. Flight of ideas;
   e. Distractibility;
   f. Increased goal directed activity;
   g. Excessive involvement in pleasurable activities.

C. The symptoms do not meet criteria for a mixed episode.

D. The mood disturbance is severe enough to cause marked impairment in occupational or social functioning, or necessitates hospitalisation to prevent harm to self or others.

E. The symptoms are not due to the direct effects of a substance or to a general medical condition.

**Mixed Episode**

A. The criteria are met for both a manic episode and a major depressive episode (except for duration) nearly every day during at least a 1-week period.

B. The mood disturbance is sufficiently severe to cause marked impairment in social, occupational or other important activities, or to necessitate hospitalisation to avoid harm to self or others.

C. The symptoms are not due to the direct effects of a substance or to a general medical condition.

B. The manic episode is not better accounted for by schizoaffective disorder and is not superimposed on psychotic disorders.
**DSM-IV Bipolar II Disorder**

A. Presence or history of one or more major depressive episodes (see above).

B. Presence or history of at least one hypomanic episode.

**Hypomanic Episode**

1. A distinct period of persistently elevated, expansive or irritable mood lasting for at least 4 days;

2. During the period of the mood disturbance, three or more of the following symptoms persisted (four if the mood is irritable) and were present to a significant degree:
   - Grandiosity or inflated self-esteem;
   - Decreased need for sleep;
   - Pressure to talk;
   - Flight of ideas;
   - Distractibility;
   - Increased goal directed activity;
   - Excessive involvement in pleasurable activities.

3. The episode is associated with an unequivocal change in functioning that isn’t characteristic of the person when not symptomatic;

4. The disturbance in mood and change in functioning are noticed by others;

5. The episode is not severe enough to cause marked impairment in social or occupational functioning or to necessitate hospitalisation;

6. The symptoms are not due to the direct physiological effects of a substance or a general medical condition.
ANXIETY DISORDERS

DSM-IV SOCIAL PHOBIA

A. A marked and persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. The individual fears that he or she will act in a way (or show anxiety symptoms) that will be humiliating or embarrassing;

B. Exposure to the feared situation almost invariably provokes anxiety, which may take the form of a situationally bound or situationally predisposed panic attack;

C. The person recognises that the fear is excessive or unreasonable;

D. The feared social or performance situations are avoided or else are endured with intense anxiety or distress;

E. The avoidance, anxious anticipation, or distress in the feared social or performance situation(s) interferes significantly with the person’s normal routine, occupational (academic) functioning, or social activities or relationships, or there is marked distress about having the phobia.
DSM-IV PANIC DISORDER (WITH OR WITHOUT AGORAPHOBIA)

A. Recurrent and unexpected panic attacks

<table>
<thead>
<tr>
<th>Panic attack</th>
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</thead>
<tbody>
<tr>
<td>1. Discrete period of intense fear or discomfort in which four or more of the following are present and reach a peak within 10 minutes</td>
</tr>
<tr>
<td>a. Heart pounding, palpitations</td>
</tr>
<tr>
<td>b. Sweating</td>
</tr>
<tr>
<td>c. Trembling or shaking</td>
</tr>
<tr>
<td>d. Shortness of breath</td>
</tr>
<tr>
<td>e. Choking</td>
</tr>
<tr>
<td>f. Chest pain</td>
</tr>
<tr>
<td>g. Nausea</td>
</tr>
<tr>
<td>h. Dizzy or lightheaded</td>
</tr>
<tr>
<td>i. Derealisation or depersonalisation</td>
</tr>
<tr>
<td>j. Fear of losing control or going crazy</td>
</tr>
<tr>
<td>k. Fear of dying</td>
</tr>
<tr>
<td>l. Numbness (paraesthesia)</td>
</tr>
<tr>
<td>m. Chills or hot flushes</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Agoraphobia</th>
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<tbody>
<tr>
<td>1. Anxiety about places or situations from which escape might be difficult or embarrassing or in which help might not be available (e.g. being outside home alone; being in a crowd; being on a bridge; travelling on a bus, train, automobile).</td>
</tr>
<tr>
<td>2. Situations are avoided or endured with marked distress or with anxiety about having a panic attack or panic-like symptoms, or require the presence of a partner.</td>
</tr>
<tr>
<td>3. The symptoms are not better accounted for by another disorder such as social phobia, specific phobia, OCD, posttraumatic stress disorder, or separation anxiety disorder.</td>
</tr>
</tbody>
</table>

C. At least one of the attacks has been followed by 1 month or more of one or more of the following:

1. Persistent concern about additional attacks
2. Worry about implications of the attack or its consequences
3. Significant change in behaviour as a result of the attacks.

D. The symptoms are not better accounted for by another disorder such as social phobia, specific phobia, OCD, posttraumatic stress disorder, or separation anxiety disorder.
DSM-IV POSTTRAUMATIC STRESS DISORDER

1. Person has been exposed to a traumatic event in which both of the following were present:
   1. Experienced, witnessed or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others;
   2. The person's response involved intense fear, helplessness or horror.

2. The traumatic event is persistently re-experienced in one or more of the following ways:
   1. Recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions;
   2. Recurrent distressing dreams of the event;
   3. Acting or feeling as if the traumatic event were recurring;
   4. Intense psychological distress at exposure to internal or external cues that symbolise or resemble an aspect of the traumatic event;
   5. Physiological reactivity on exposure to internal or external cues that symbolise or resemble an aspect of the traumatic event.

3. Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma) as indicated by three or more of the following:
   1. Efforts to avoid thoughts, feelings or conversations associated with the trauma;
   2. Efforts to avoid activities, places or people that arouse recollections of the trauma;
   3. Inability to recall an important aspect of the trauma;
   4. Markedly diminished interest or participation in significant activities;
   5. Feeling of detachment or estrangement from others;
   6. Restricted range of affect (e.g. loving feelings);
   7. Sense of foreshortened future.

4. Persistent symptoms of increased arousal (not present before the trauma) as indicated by two or more of the following:
   1. Difficulty falling or staying asleep;
   2. Irritability or outbursts of anger;
   3. Difficulty concentrating;
   4. Hypervigilance;
   5. Exaggerated startle response.

5. Duration of the disturbance is more than one month.

6. The disturbance causes clinically significant distress or impairment in social, occupational or other important areas of functioning.
DSM-IV GENERALISED ANXIETY DISORDER

A. Excessive anxiety and worry (apprehensive expectation) occurring more days than not
   for at least 6 months, about a number of events or activities.

B. The person finds it difficult to control the worry.

C. The anxiety and worry are associated with three or more of the following six symptoms
   (with at least some present for more days than not during the past 6 months)
   a. Restlessness or feeling keyed up or on edge
   b. Being easily fatigued
   c. Difficulty concentrating or mind going blank
   d. Irritability
   e. Muscle tension
   f. Sleep disturbance (falling sleep or restless unsatisfying sleep)

D. Focus of anxiety and worry is not confined to features of another axis I disorder (panic,
   social phobia, OCD, separation anxiety disorder, anorexia nervosa, somatisation
   disorder) and anxiety does not only occur during PTSD.

E. Anxiety, worry or symptoms cause clinically significant distress or impairment in social,
   occupational or other important areas of functioning.

F. Not due to direct physiological effects of a substance or to a general medical condition,
   and does not only occur during a mood disorder, a psychotic disorder.
PSYCHOTIC DISORDERS

DSM-IV SCHIZOPHRENIA

A. Characteristic symptoms: Two or more of the following characteristic symptoms present for a significant proportion of one month:
   a. Delusions;
   b. Hallucinations;
   c. Disorganised speech (such as incoherence);
   d. Grossly disorganised or catatonic behaviour;
   e. Negative symptoms: flattened affect, alogia (decreased speech productivity), avolition (inability to initiate/persist in goal-directed activity);

B. Social/occupational dysfunction: For a significant portion of the time since the onset of the disturbance, one or more of the major areas of functioning such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset (or if onset is during childhood or adolescence, failure to achieve expected levels of interpersonal, academic or occupational achievement);

C. Duration: Continuous signs of the disturbance persist for at least 6 months;

D. The disturbance is not due to substance use, a medical condition or a developmental disorder such as autism.
DSM-IV SCHIZOAFFECTIVE DISORDER

A. An uninterrupted period of illness during which, at some time, there is either a major depressive episode, a manic episode, or a mixed episode concurrent with symptoms that meet criterion A for Schizophrenia.

B. During the same period of illness, there have been delusions or hallucinations for at least 2 weeks in the absence of prominent mood symptoms;

C. Symptoms that meet criteria for a mood episode are present for a substantial portion of the total duration of the active and residual periods of the illness;

D. The disturbance is not due to the direct physiological effects of a substance or a general medical condition.
APPENDIX B - VALIDATION OF THE PSYCHOSIS SCREENER USED IN THE NATIONAL SURVEY OF MENTAL HEALTH AND WELL-BEING

[Unpublished analyses]

Psychotic disorders, such as schizophrenia, schizoaffective disorder and bipolar disorder, have a lower prevalence than other forms of mental illness such as depression and anxiety disorders, yet they impose a considerable public health burden because of their impact on sufferers and their families (Keith, Regier, & Rae, 1991). Persons with psychotic disorders also utilise a disproportionately high segment of health services.

Valid and reliable assessment of any disorder is a necessary precursor to effective treatment. Lengthy interview instruments exist for the assessment of psychotic disorders, but they often require accredited training to administer, and their length means they may not be appropriate for all situations. Validated screening instruments provide a useful alternative to the full assessment of a disorder. They have been developed for the assessment of mental disorders such as depression (the Beck Depression Inventory; (Beck, Ward, & Mendelson, 1961)) and anxiety (the State-Trait Anxiety Inventory; (Spielberger, 1983)). However, there has been a lack of effective, validated instruments for screening individuals for psychotic illness. Previously, research have designed the Psychosis Screening Questionnaire, designed to act as a brief screening instrument for the presence of psychotic disorders (Bebbington & Nayani, 1995). The Psychosis Screener (PS) was developed by researchers involved in the design of the National Survey of Mental Health and Well-Being for use in the Australian National Survey of Mental Health and Well-Being (NSMHWB) Survey of Adults in the general population. This represents one of few attempts to develop a screener for psychosis that was intended for use with general population samples.
Validation of the PS was conducted on two separate samples using Receiver Operating Characteristic (ROC) analyses to validate it against three diagnostic systems: the Diagnostic and Statistical Manual of Mental Disorders, 3rd edition-revised (DSM-III-R) (American Psychiatric Association, 1987); the International Classification of Diseases, 9th edition (ICD-9) (World Health Organization, 1977); and the International Classification of Diseases, 10th edition (ICD-10) (World Health Organization, 1993).

**Method**

**Sample**

Two samples were used in the analyses of the screener. The first (sample 1) contained 87 inpatients for whom screener items had been completed; the responses to the screener were compared with clinician-rated ICD-9 diagnoses obtained from hospital discharge records. The majority of persons in sample 1 (51.3%) met criteria for an ICD-9 diagnosis of affective psychoses (Table B1). A further 16% had been diagnosed as schizophrenic, with no persons diagnosed with schizoaffective disorder. Around a third of persons in sample 1 (31.3%) had received some other diagnosis.

The second sample (sample 2) was drawn from the Western Australian Study of Low Prevalence (Psychotic) Disorders. It contained 259 persons whose responses to the screener items were compared with ICD-10 and DSM-III-R diagnoses derived using the Diagnostic Interview for Psychosis (DIP). The DIP is a semi-structured, standardised interview using questions from the tenth edition of the Present State Examination (PSE-10), a component of the Schedules for Clinical Assessment in Neuropsychiatry (SCAN) set of instruments. The DIP elicits the 90 items of the Operational Criteria for Psychosis (OPCRIT) checklist (McGuffin, Farmer, & Harvey, 1991), enabling the computerised generation of diagnoses of psychosis according to several different operational criteria through the associated OPCRIT algorithm.
The distribution of diagnoses in sample 2 differed from that in sample 1, and there was a high level of concordance between the ICD-10 and DSM-III-R classification systems in sample 2 (Table B1). Just under half of the sample received a diagnosis of schizophrenia, while a further tenth received a diagnosis of schizoaffective disorder. Around one quarter met criteria for an affective psychosis, with the remaining fifth either receiving no diagnosis or meeting criteria for a non-psychotic mental disorder.

**Table B1: Patterns of mental disorders in the two samples**

<table>
<thead>
<tr>
<th></th>
<th>Sample 1</th>
<th>Sample 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICD-9 CM</td>
<td>DSM-III-R</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>16.0</td>
<td>47.1</td>
</tr>
<tr>
<td>Schizoaffective disorder</td>
<td>-</td>
<td>9.3</td>
</tr>
<tr>
<td>Affective psychosis</td>
<td>51.3</td>
<td>23.9</td>
</tr>
<tr>
<td>Other diagnosis</td>
<td>31.7(^1)</td>
<td>15.8(^2)</td>
</tr>
<tr>
<td>No diagnosis</td>
<td>-</td>
<td>3.9</td>
</tr>
</tbody>
</table>

\(^1\) Includes codes 290.21, 291.20, 294.90, 297.10, 300.0, 300.21, 300.30, 300.40, 301.40, 301.70, 301.90, 304.01, 307.10, 308.30, 309.00, 309.28, 310.90, 311.00, 313.00, 316.00, 780.30

\(^2\) Includes codes 296.21, 296.22, 296.23, 296.24, 297.1

\(^3\) Includes codes F32.0, F32.1, F32.11, F32.2, F32.3, F32.30.
PSYCHOSIS SCREENER

The Psychosis Screener (PS) uses elements of the Composite International Diagnostic Interview (CIDI) to assess the presence of characteristic psychotic symptoms. The Psychosis Screener comprises 7 items, three of which are asked only if the respondent endorses a previous question. The first 6 items cover the following features of psychotic disorders: delusions of control, thought interference and passivity (Question 1 and 1a); delusions of reference or persecution (Question 2 and 2a); and grandiose delusions (Question 3 and 3a). The final item records whether a respondent reports ever receiving a diagnosis of schizophrenia.

The screener was assessed for both narrow and broad definitions of psychosis. The narrow definition of psychosis was limited to diagnoses of either schizophrenia or a schizoaffective disorder. For sample 1, the relevant ICD-9 codes were 295 (all). For sample 2, the relevant ICD-10 codes were F20 (all) and F25 (all) and the relevant DSM-III-R diagnoses were 295 (all).

The broad definition of psychosis included diagnoses of affective psychoses in addition to schizophrenia and schizoaffective disorder. For sample 1, the relevant ICD-9 codes were 295 (all) and 296 (all). For sample 2, the relevant ICD-10 codes were F20 (all), F25 (all), F28 and F30 (all); the relevant DSM-III-R diagnoses were 295 (all), 296.4, 296.6 and 298.9.

DATA ANALYSIS

Receiver Operating Characteristic (ROC) analyses (Coombs, Dawes, & Tversky, 1970) were carried out using a macro program run within SYSTAT (B. Carter & F. Shann, Royal Children’s Hospital, Parkville, Victoria, Australia) to derive an optimal cutoff point for the PS that would distinguish cases from non-cases as diagnosed by a ‘gold standard’. The screener was validated against three diagnostic systems, the ‘gold standards’, namely, the
ICD-9 diagnosis recorded in the patient’s case file (in the case of sample 1) and the DSM-III-R and ICD-10 diagnoses derived from OPCRIT items (in the case of sample 2).

ROC curves plot a scale’s ability to predict true positives (i.e. persons classified as cases who had actually received a diagnosis of a psychotic disorder) against the rate of false positives (i.e. persons classified as cases who were actually diagnosed as non-cases) for each point along the scale. The optimal cut-off point used to distinguish cases and non-cases diagnosed by the ‘gold standard’ method in this analysis was defined as that which maximised both the sensitivity (the ability to accurately identify persons who were diagnosed as a psychotic case) and the specificity (the ability of the screener to accurately classify persons who were non-cases) of the screener. Hence, the sensitivity and specificity of the different scores were calculated. In addition, Chi square ($\chi^2$) analyses were conducted and an estimate was calculated of the area under the curve (AUC). The point at which the Chi square value was largest determined the chosen ‘optimal’ cut-off for the screener. The Positive Predictive Value (PPV) and the Negative Predictive Value (NPV) of the cut-off points were also calculated. The PPV of a cut-off refers to the proportion of persons classified as cases who have received the diagnosis, while the NPV refers to the proportion of persons classified as non-cases who do not receive the diagnosis of interest.

Separate analyses were conducted for the broad and narrow definitions of psychosis.

In analysing the internal consistency of the screener, Cronbach’s coefficient Alpha ($\alpha$) was used; calculation of $\alpha$ was carried out using SPSS for Windows version 6.1. Analyses of the sensitivity and specificity of each item were also carried out.
RESULTS

PSYCHOSIS: BROAD DEFINITION

Table B2 shows the results of the ROC analyses using the broad definition of psychosis. The ROC analysis involving sample 1 (ICD-9 diagnoses) produced an AUC of 0.55, which was not significantly better than chance.

The screener performed significantly better than chance when using sample 2 (Table B2). The AUC for the screener was 0.79 when using ICD-10 as the standard, and was 0.77 when using DSM-III-R as the standard. For both diagnostic systems, the optimal cut-off was 1, indicating that a score of 1 or more on the screener identified a likely psychotic case. The screener showed high sensitivity and poor specificity according to both standards (Table B2). This meant that when using this broad definition of psychosis, the screener was well able to identify true psychotic cases, but had a poor ability to identify non-cases. The PPV of the screener at this cut-off was 86% for DSM-III-R and 88% for ICD-10, indicating that around 17 in 20 persons classified by the screener as cases actually had a diagnosis of psychosis according to the broad definition. The NPV of the screener at this point was 83% for ICD-10 and 78% for DSM-III-R, indicating that around 8 in 10 persons classified as non-cases at this cut-off level were correctly identified.
Table B2: Results of ROC analyses using the broad definition of psychosis

<table>
<thead>
<tr>
<th></th>
<th>Cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value (PPV)</th>
<th>Negative Predictive Value (NPV)</th>
<th>AUC (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample 1</td>
<td>3</td>
<td>25.4</td>
<td>85.7</td>
<td>68.4</td>
<td>82.4</td>
<td>.55 (.42, .68)</td>
</tr>
<tr>
<td>(N = 87)$^1$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sample 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(N = 259)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICD-10$^2$</td>
<td>1</td>
<td>98.1</td>
<td>39.6</td>
<td>87.7</td>
<td>82.6</td>
<td>.79 (.73, .85)</td>
</tr>
<tr>
<td>DSM-III-R$^3$</td>
<td>1</td>
<td>97.6</td>
<td>35.3</td>
<td>86.0</td>
<td>78.3</td>
<td>.77 (.71, .83)</td>
</tr>
</tbody>
</table>

$^1$ ICD-9 diagnosis of schizophrenia or affective psychosis

$^2$ ICD-10 diagnosis of schizophrenia, mania, bipolar disorder or other non-organic psychosis

$^3$ DSM-III-R diagnosis of schizophrenia, mania, bipolar disorder, or atypical psychosis

**Psychosis: Narrow definition**

The narrow definition of psychosis - that is, a diagnosis of schizophrenia or schizoaffective disorder only - produced the same cut-off score of 3 for all ‘gold standards’. This indicated that persons with a score of 3 or more on the screener should be classified as cases. For ICD-9 diagnoses (sample 1), the AUC was 0.78, which indicated that the screener predicted significantly better than chance (Table B3). The sensitivity at this cut-off was moderate, with a higher level of specificity. At this cut-off point, 42% of persons classed as cases had actually been diagnosed with a psychotic disorder (PPV), while 92% of persons classed as non-cases did not have a diagnosis of psychosis (NPV).

The screener discriminated significantly better than chance according to both ICD-10 and DSM-III-R diagnostic systems: the AUC was 0.73 according to ICD-10 (95%CI: 0.67,
0.79), and an AUC of 0.74 according to DSM-III-R (95%CI: 0.68, 0.80). When compared against either diagnostic system, 2 was the cut-off score that maximised sensitivity and specificity. For both ‘gold standards’, the screener was more effective at correctly identifying positive cases (sensitivity) than it was at correctly identifying non-cases (sensitivity). The PPV for the screener was around 71% according to both diagnostic systems, with an NPV of around 70% (Table B3), indicating that around 7 in 10 persons classified as cases and non-cases were given the correct classification.

Table B3: Results of ROC analyses using the narrow definition of psychosis

<table>
<thead>
<tr>
<th></th>
<th>Cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value (PPV)</th>
<th>Negative Predictive Value (NPV)</th>
<th>AUC (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample 1</td>
<td>3</td>
<td>57.1</td>
<td>84.9</td>
<td>42.1</td>
<td>91.2</td>
<td>.78 (.53, .93)</td>
</tr>
<tr>
<td>(N = 87)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sample 2</td>
<td>3</td>
<td>82.1</td>
<td>57.0</td>
<td>70.8</td>
<td>71.4</td>
<td>.73 (.67, .79)</td>
</tr>
<tr>
<td>(N = 259)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICD-10</td>
<td>3</td>
<td>81.5</td>
<td>56.6</td>
<td>70.8</td>
<td>70.3</td>
<td>.74 (.68, .80)</td>
</tr>
<tr>
<td>DSM-III-R</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The ROC curves for sample 1 and sample 2 are shown in Figure B1. For clarity of presentation, the standard used for sample 2 here was a diagnosis of schizophrenia or schizoaffective disorder by either DSM-III-R or ICD-10 systems. As can be seen, for both samples, the screener discriminated between cases and non-cases better than chance (which is indicated by the straight diagonal line).
ITEM ANALYSIS

Table B4 shows the pattern of results of the item analysis for sample 1. The screener had good internal consistency, with an alpha reliability coefficient ($\alpha$) of 0.74. Just over one fifth (22%) of the sample received a score of three or more on the screener, thus meeting the cut-off for the narrow definition of psychosis. The most frequently endorsed items were those concerning delusions of persecution (Question 2 and 2a); these items were also among those most highly correlated with the total score. The items concerning delusions of thought interference (Question 1 and 1a) were also strongly correlated with the total score. For all these items, there was a high level of specificity, with more moderate sensitivity levels. Reports of having received a diagnosis of schizophrenia correlated less highly with the total score (0.57), but the item showed high specificity (89%) and sensitivity (71.4%). The items addressing grandiose delusions (Question 3 and 3a) were endorsed by only a minority of the sample, correlated poorly with the total score, and lacked sensitivity.
Table B4: Item analysis for items administered to sample 1

<table>
<thead>
<tr>
<th>Item</th>
<th>% yes</th>
<th>Item-score correlation</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qu. 1: Thoughts controlled or interfered with by others</td>
<td>29</td>
<td>.70</td>
<td>50.0</td>
<td>75.3</td>
</tr>
<tr>
<td>Qu. 1a: Came about in a way others find hard to believe</td>
<td>18</td>
<td>.72</td>
<td>35.7</td>
<td>84.9</td>
</tr>
<tr>
<td>Qu. 2: People too interested</td>
<td>32</td>
<td>.72</td>
<td>50.0</td>
<td>71.2</td>
</tr>
<tr>
<td>Qu. 2a: Things arranged specially</td>
<td>22</td>
<td>.80</td>
<td>42.9</td>
<td>82.2</td>
</tr>
<tr>
<td>Qu. 3: Special powers others lack</td>
<td>8</td>
<td>.38</td>
<td>7.1</td>
<td>91.8</td>
</tr>
<tr>
<td>Qu. 3a: Belong to a group with special powers</td>
<td>2</td>
<td>.22</td>
<td>-</td>
<td>97.3</td>
</tr>
<tr>
<td>Qu. 4: Diagnosis of schizophrenia</td>
<td>21</td>
<td>.57</td>
<td>71.4</td>
<td>89.0</td>
</tr>
<tr>
<td>Total</td>
<td>22</td>
<td>57.1</td>
<td>84.9</td>
<td></td>
</tr>
</tbody>
</table>

1 Those with a total of three or more on the screener.

A similar pattern was found for sample 2: the screener showed good internal consistency, with a reliability coefficient of $\alpha = 0.75$. The items concerning delusions of reference (Question 2 and 2a) and delusions of control (Questions 1 and 1a) were again the most highly correlated with the total score, and all showed moderate sensitivity with slightly lower sensitivity (Table B5). Again, the items concerning grandiose delusions (Question 3 and 3a) were the least correlated with the total score, and showed the poorest levels of sensitivity and specificity. In contrast to sample 1, a much higher proportion of the sample positively endorsed the question concerning their receipt of a diagnosis of psychosis (it must be noted that the wording of this question differed from that used in sample 1). Over four fifths (83%) of the sample reported having been diagnosed with a psychotic disorder.
or receiving psychotic medication; this item correlated moderately with the total, and showed moderate sensitivity and specificity (65.7% and 76.7%, respectively). In further contrast to sample 1, the majority - two thirds of the sample (65%) - met the cut-off of three or more on the screener (meeting criteria for the stringent definition of psychosis).

**Table B5: Item analyses for screener items administered to sample 2**

<table>
<thead>
<tr>
<th>Item</th>
<th>% yes</th>
<th>Item-score correlation</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qu. 1: Thoughts controlled or interfered with by others</td>
<td>39</td>
<td>.74</td>
<td>76.5</td>
<td>52.9</td>
</tr>
<tr>
<td>Qu. 1a: Came about in a way others find hard to believe</td>
<td>34</td>
<td>.75</td>
<td>77.5</td>
<td>51.2</td>
</tr>
<tr>
<td>Qu. 2: People too interested</td>
<td>65</td>
<td>.68</td>
<td>71.4</td>
<td>64.8</td>
</tr>
<tr>
<td>Qu. 2a: Things arranged specially</td>
<td>55</td>
<td>.73</td>
<td>72.5</td>
<td>58.1</td>
</tr>
<tr>
<td>Qu. 3: Special powers others lack</td>
<td>44</td>
<td>.49</td>
<td>63.2</td>
<td>44.8</td>
</tr>
<tr>
<td>Qu. 3a: Belong to a group with special powers</td>
<td>1</td>
<td>-.03</td>
<td>-</td>
<td>40.9</td>
</tr>
<tr>
<td>Qu. 4: Prescribed psychotic medicine or diagnosed with a psychotic disorder</td>
<td>83</td>
<td>.51</td>
<td>65.7</td>
<td>76.7</td>
</tr>
<tr>
<td>Total</td>
<td>65</td>
<td>81.5</td>
<td>58.9</td>
<td></td>
</tr>
</tbody>
</table>

1 Those with a total of three or more on the screener.
2 Sensitivity and specificity of the screener when participants had received a diagnosis of schizophrenia or schizoaffective disorder according to either DSM-III-R or ICD-10 classifications.
**DISCUSSION**

This analysis represents one of few attempts to validate a short screening instrument designed for the detection of psychosis in a general population sample. Analyses revealed that the instrument was internally consistent, and with the exception of the items assessing grandiose delusions, all items correlated well with the total score, and exhibited moderate predictive ability.

Two definitions of psychosis were used in the ROC analyses, and these affected the findings quite markedly. The broad definition of psychosis classed schizophrenia, schizoaffective disorder, and affective psychosis as psychotic disorders. When this broad definition of psychosis was used with ICD-9 diagnoses as the standard (in sample 1), the screener did not fare better than chance. However, this may have been related to the fact that diagnoses for sample 1 were obtained from clinical records which are coded using ICD-9-CM codes. This may have lead to some incorrect categorisation of patients as cases due to discrepancies between ICD-9 and ICD-9-CM codes, particularly for affective psychoses. This possibility is supported by the finding that when using two other diagnostic systems as ‘gold standards’, the screener was able to discriminate adequately between cases and non-cases, as assessed by the area under the ROC curve (the AUC). For both ICD-10 and DSM-III-R diagnostic systems (using sample 2), the optimal cut-off point was zero, indicating that a score of 1 or more on the screener indicated a case according to this definition of psychosis.

Using the narrow definition of psychosis, in which only those with a diagnosis of schizophrenia or schizoaffective disorder were classified as cases, the screener was able to discriminate between cases and non-cases using any of the three diagnostic systems as the standard. A score of three or more on the screener was the optimal score for indicating a case for all three ‘gold standards’. As might be expected, the cut-off for the narrower definition of psychosis was higher than that for the broader definition.
It is interesting that although the two samples were distinctly different in their composition, the same cut-off point was obtained for the stringent definition of psychosis used in the analysis. The two samples showed different patterns of specificity and sensitivity at this cut-off, as well as different patterns of positive predictive value and negative predictive value. This may have been due to several reasons.

First, the characteristics of the two samples were quite different. Those in sample 1 came from an inpatient setting, whereas those from sample 2 came from a variety of mental health service settings. Further, those in sample 1 were much less likely to have received a diagnosis of schizophrenia or schizoaffective disorder, and much more likely to have received a diagnosis of affective psychosis, than those in sample 2. Those in sample 2 were more likely to have met criteria for schizophrenia or schizoaffective disorder.

Second, the way in which the ‘gold standard’ diagnoses were derived was markedly different for the two samples. The standard used in sample 1 was the diagnosis recorded on the patients’ case records, while the diagnoses in sample 2 were derived from structured diagnostic interviews. This may have involved different classification biases for the different ‘gold standards’, and so there may have been systematic differences between the way in which a diagnosis of psychosis was made in each sample.

Third, the standard for sample 1 was derived from the ICD-9 diagnostic classification system, while sample 2 used ICD-10 and DSM-III-R systems. The different operationalisation of disorders in these classification systems may have affected the pattern of diagnosis. This highlights another issue in the use of ‘gold standards’: they are assumed to be valid and accurate. Any limitations in the ability of these diagnostic systems to discriminate between actual cases and non-cases necessarily attenuates the distinction between true cases and non-cases used in the ROC analyses, and hence reduces the ability of the analysis to estimate the true discriminant power of the screener (Fombonne, 1991).

The screener demonstrated moderate sensitivity and specificity levels at the cut-off score obtained. However, it must be remembered that non-cases for both samples were composed almost exclusively of persons who had received some other psychiatric diagnosis, often with psychotic symptoms (such as major depression). This raises two
possibilities. First, if the characteristics of schizophreniform psychosis are not be completely distinct from other forms of mental illness, then the screener may not be as effective at discriminating between cases and non-cases. Second, the screener may be more discriminating when used in populations that include individuals who do not have a mental illness.

This paper has used the point at which both the sensitivity and specificity are maximised as the optimal cut-off point for the screener. However, when using any cut-off for a screening test, three important issues must be considered. First, the sensitivity and specificity of a screening test vary with the prevalence of a disorder in the population (Brenner & Gefeller, 1997). For example, the sensitivity and positive predictive power of a test decrease as the prevalence of a disorder in the population decreases, while the specificity and negative predictive power of a test increases. In the samples used in this analysis, the prevalence of psychotic disorders was considerably higher than would be expected in a general population sample. Hence, the sensitivity of the test in the general population would be lower than that obtained here, while the specificity would be higher. This needs to be kept in mind when applying the test to groups in which the base rate of psychosis might be expected to be significantly different (Brenner & Gefeller, 1997).

Second, the use to which a screener is to be put also determines the relative importance of a particular rate of sensitivity and specificity, and so influences the choice of cut-off (Meehl, 1973; Rey, Morris-Yates, & Stanislaw, 1992). For instance, if a screener is to be used with a clinical population for screening purposes, with further assessment following a positive result, it may be considered more important to correctly identify true cases. In this case a liberal cut-off would be more appropriate, at the expense of a higher rate of false positives (Fombonne, 1991; Rey et al., 1992). On the other hand, if the screener is to be used to determine who should receive an expensive treatment, a more conservative criterion might be used to avoid treating those who do not require attention (thus increasing the specificity of the cut-off point). However, if a test is being used for epidemiological research with the aim of identifying prevalence rates in a general population, it may be more appropriate to strike a balance between sensitivity and specificity (as has been done in the present paper) (Rey et al., 1992).
With these concerns in mind, Table B6 presents the sensitivity and specificity of all cut-off points on the screener, using the narrow definition of psychosis, from both samples. These might be used to estimate the most appropriate cut-off point to be used for the screener in a given situation.

Table B6: Sensitivity and specificity of the Psychosis Screener in two samples

| Cut-off | Sample 1 | | | Sample 2 |
| --- | --- | --- | --- | --- | --- |
|  | Sensitivity | Specificity | Chi square | Sensitivity | Specificity | Chi square |
| 1 | 92.8 | 54.8 | 8.9 | 99.3 | 20.6 | 28.3 |
| 2 | 64.3 | 72.6 | 5.6 | 91.4 | 36.4 | 28.7 |
| 3 | 57.1 | 84.9 | 9.8 | 81.6 | 58.9 | 43.4 |
| 4 | 35.7 | 87.7 | 3.2 | 52.6 | 75.7 | 19.7 |
| 5 | 7.1 | 97.3 | .001 | 36.2 | 86.9 | 16.0 |
| 6 | 0 | 100 | - | 23.0 | 92.5 | 9.9 |

*Persons categorised as having psychosis if they met either ICD-10 or DSM-III-R criteria for schizophrenia or schizoaffective disorder

The analyses carried out here have revealed that the psychosis screener developed as a brief screening instrument for the presence of psychosis has a moderate ability to discriminate between those who meet diagnostic criteria for psychotic disorders, and those who do not. This represents an advance in efforts to develop a measure that will be an effective screen for these low prevalence disorders. Consideration must be given to the nature of the population with which a screening test is to be used before a cut-off point is selected.
REFERENCES
**APPENDIX C - EPQ NEUROTICISM SCALE USED IN THE NSMHWB**

The next questions are about your nature, how you usually are. There are no right or wrong answers, and no trick questions.

1. Does your mood often go up and down?
2. Do you ever feel “just miserable” for no reason?
3. Are you an irritable person?
4. Are your feelings easily hurt?
5. Do you often feel “fed-up”?
6. Would you call yourself a nervous person?
7. Are you a worrier?
8. Would you call yourself “highly strung”?
9. Do you worry too long after an embarrassing experience?
10. Do you suffer from “nerves”?
11. Do you often feel lonely?
12. Are you often troubled by feelings of guilt?
**APPENDIX D - PREVALENCE ESTIMATES OF MENTAL DISORDERS BY DEMOGRAPHIC CHARACTERISTICS**

Table D1: Weighted prevalence of DSM-IV mental disorders, psychosis “cases”, and tobacco use according to gender

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Males</th>
<th>Females</th>
<th>Persons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Substance use disorder</td>
<td>11.5 (1.0)</td>
<td>4.4 (0.4)</td>
<td>7.9 (0.4)</td>
</tr>
<tr>
<td>Anxiety disorder</td>
<td>4.4 (0.6)</td>
<td>6.8 (0.3)</td>
<td>5.6 (0.3)</td>
</tr>
<tr>
<td>Mood disorder</td>
<td>4.9 (0.3)</td>
<td>8.5 (0.5)</td>
<td>6.7 (0.3)</td>
</tr>
<tr>
<td>Psychosis “case”</td>
<td>0.9 (0.2)</td>
<td>1.0 (0.1)</td>
<td>0.9 (0.1)</td>
</tr>
<tr>
<td>Tobacco use</td>
<td>26.9 (0.9)</td>
<td>23.0 (0.6)</td>
<td>24.9 (0.6)</td>
</tr>
<tr>
<td>No alcohol use</td>
<td>Alcohol use</td>
<td>Alcohol Abuse</td>
<td>Alcohol dependence</td>
</tr>
<tr>
<td>----------------</td>
<td>-------------</td>
<td>---------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>% (SE)</td>
<td>% (SE)</td>
<td>% (SE)</td>
<td>% (SE)</td>
</tr>
<tr>
<td>Prevalence</td>
<td>26.5 (0.5)</td>
<td>67.5 (0.6)</td>
<td>1.9 (0.2)</td>
</tr>
<tr>
<td>(population N)</td>
<td>(3,562,000)</td>
<td>(9,089,000)</td>
<td>(256,000)</td>
</tr>
<tr>
<td>Female</td>
<td>36.1 (0.7)</td>
<td>60.7 (0.8)</td>
<td>0.9 (0.1)</td>
</tr>
<tr>
<td>Male</td>
<td>16.6 (0.7)</td>
<td>74.4 (1.2)</td>
<td>2.9 (0.3)</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>20.4 (1.7)</td>
<td>65.1 (1.9)</td>
<td>5.2 (0.8)</td>
</tr>
<tr>
<td>25-34</td>
<td>21.2 (1.0)</td>
<td>70.7 (1.1)</td>
<td>2.4 (0.4)</td>
</tr>
<tr>
<td>35-44</td>
<td>23.4 (1.0)</td>
<td>70.6 (0.9)</td>
<td>1.9 (0.6)</td>
</tr>
<tr>
<td>45-54</td>
<td>24.2 (3.5)</td>
<td>71.7 (3.4)</td>
<td>1.1 (0.6)</td>
</tr>
<tr>
<td>55-64</td>
<td>31.7 (2.2)</td>
<td>66.3 (2.2)</td>
<td>0.3 (0.2)</td>
</tr>
<tr>
<td>65-74</td>
<td>35.2 (1.5)</td>
<td>63.7 (1.6)</td>
<td>0.3 (0.2)</td>
</tr>
<tr>
<td>75+</td>
<td>52.2 (4.2)</td>
<td>47.0 (4.2)</td>
<td>0.1 (0.1)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than secondary</td>
<td>34.9 (0.9)</td>
<td>59.5 (0.8)</td>
<td>2.0 (0.5)</td>
</tr>
<tr>
<td>Secondary</td>
<td>26.7 (1.3)</td>
<td>65.4 (3.2)</td>
<td>2.6 (1.0)</td>
</tr>
<tr>
<td>Post-secondary</td>
<td>20.8 (0.6)</td>
<td>73.4 (0.7)</td>
<td>1.6 (0.2)</td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Employed full-time</td>
<td>15.6 (1.2)</td>
<td>76.6 (0.9)</td>
<td>2.7 (0.4)</td>
</tr>
<tr>
<td>Employed part-time</td>
<td>25.7 (2.6)</td>
<td>69.1 (1.9)</td>
<td>1.2 (0.3)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>27.7 (3.0)</td>
<td>57.5 (3.1)</td>
<td>4.6 (1.0)</td>
</tr>
<tr>
<td>Not in labour force</td>
<td>41.9 (1.2)</td>
<td>55.2 (1.2)</td>
<td>0.8 (0.3)</td>
</tr>
<tr>
<td>Relationship status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Widowed</td>
<td>55.0 (2.3)</td>
<td>43.5 (2.1)</td>
<td>0.4 (0.3)</td>
</tr>
<tr>
<td>Married/ de facto</td>
<td>25.7 (0.5)</td>
<td>70.5 (0.5)</td>
<td>1.2 (0.2)</td>
</tr>
<tr>
<td>Separated/ divorced</td>
<td>28.9 (1.6)</td>
<td>63.4 (1.5)</td>
<td>1.9 (0.8)</td>
</tr>
<tr>
<td>Never married</td>
<td>20.2 (1.4)</td>
<td>66.2 (1.8)</td>
<td>4.3 (0.6)</td>
</tr>
<tr>
<td>Neuroticism (M)</td>
<td>2.7 (0.05)</td>
<td>2.4 (0.03)</td>
<td>3.3 (0.20)</td>
</tr>
</tbody>
</table>
Table D3: Weighted prevalence of tobacco use by demographic characteristics

<table>
<thead>
<tr>
<th></th>
<th>Never smoker</th>
<th>Former smoker</th>
<th>Current smoker</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (SE)</td>
<td>% (SE)</td>
<td>% (SE)</td>
</tr>
<tr>
<td>(n = 4976)</td>
<td>(n = 2898)</td>
<td>(n = 2767)</td>
<td></td>
</tr>
<tr>
<td>Prevalence</td>
<td>48.2 (0.5)</td>
<td>26.9 (0.4)</td>
<td>24.9 (0.6)</td>
</tr>
<tr>
<td>Weighted N</td>
<td>(6,485,000)</td>
<td>(3,623,000)</td>
<td>(3,358,000)</td>
</tr>
<tr>
<td>Female</td>
<td>55.1 (0.8)</td>
<td>21.8 (0.6)</td>
<td>23.0 (0.6)</td>
</tr>
<tr>
<td>Male</td>
<td>41.0 (0.9)</td>
<td>32.1 (0.7)</td>
<td>26.9 (0.9)</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>55.5 (3.2)</td>
<td>10.4 (1.5)</td>
<td>34.1 (2.7)</td>
</tr>
<tr>
<td>25-34</td>
<td>49.7 (2.2)</td>
<td>17.7 (1.0)</td>
<td>32.7 (1.7)</td>
</tr>
<tr>
<td>35-44</td>
<td>44.6 (0.9)</td>
<td>27.4 (0.9)</td>
<td>28.0 (1.0)</td>
</tr>
<tr>
<td>45-54</td>
<td>44.9 (2.0)</td>
<td>32.8 (2.4)</td>
<td>22.3 (1.1)</td>
</tr>
<tr>
<td>55-64</td>
<td>46.7 (1.6)</td>
<td>36.7 (1.4)</td>
<td>16.7 (1.4)</td>
</tr>
<tr>
<td>65-74</td>
<td>45.6 (1.3)</td>
<td>40.7 (1.4)</td>
<td>13.7 (1.3)</td>
</tr>
<tr>
<td>75+</td>
<td>55.0 (4.4)</td>
<td>37.1 (4.4)</td>
<td>8.0 (1.2)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than secondary</td>
<td>42.1 (1.2)</td>
<td>28.3 (0.9)</td>
<td>29.6 (1.1)</td>
</tr>
<tr>
<td>Secondary only</td>
<td>53.0 (1.3)</td>
<td>21.8 (1.0)</td>
<td>25.3 (1.3)</td>
</tr>
<tr>
<td>Post-secondary</td>
<td>50.6 (1.3)</td>
<td>27.6 (0.6)</td>
<td>21.7 (1.0)</td>
</tr>
<tr>
<td>Relationship status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never married</td>
<td>54.5 (1.9)</td>
<td>21.1 (1.2)</td>
<td>33.3 (1.7)</td>
</tr>
<tr>
<td>Married/ defacto</td>
<td>47.0 (0.8)</td>
<td>31.5 (0.7)</td>
<td>21.6 (0.7)</td>
</tr>
<tr>
<td>Separated/ divorced</td>
<td>33.8 (1.9)</td>
<td>28.6 (2.5)</td>
<td>37.6 (2.2)</td>
</tr>
<tr>
<td>Widowed</td>
<td>58.8 (2.4)</td>
<td>27.0 (1.6)</td>
<td>14.2 (2.4)</td>
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<td>Employment status</td>
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</tr>
<tr>
<td>Unemployed</td>
<td>33.6 (4.2)</td>
<td>18.8 (1.8)</td>
<td>47.6 (3.7)</td>
</tr>
<tr>
<td>Employed/ not in force</td>
<td>48.8 (0.6)</td>
<td>27.3 (0.4)</td>
<td>24.0 (0.6)</td>
</tr>
<tr>
<td>Neuroticism</td>
<td>2.4 (0.03)</td>
<td>2.6 (0.05)</td>
<td>3.1 (0.05)</td>
</tr>
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</table>
Table D4: Weighted prevalence of cannabis use, DSM-IV abuse and dependence, by demographic characteristics

<table>
<thead>
<tr>
<th></th>
<th>No Cannabis use</th>
<th>Cannabis use</th>
<th>Cannabis abuse</th>
<th>Cannabis dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>% (SE)</td>
<td>% (SE)</td>
<td>% (SE)</td>
</tr>
<tr>
<td>Prevalence</td>
<td>92.8</td>
<td>4.8</td>
<td>0.8</td>
<td>1.5</td>
</tr>
<tr>
<td>Weighted N</td>
<td>(12,511,000)</td>
<td>(652,000)</td>
<td>(102,000)</td>
<td>(200,000)</td>
</tr>
<tr>
<td>Female</td>
<td>95.8 (0.6)</td>
<td>3.3 (0.4)</td>
<td>0.2 (0.07)</td>
<td>0.7 (0.2)</td>
</tr>
<tr>
<td>Male</td>
<td>89.9 (0.5)</td>
<td>6.5 (0.4)</td>
<td>1.3 (0.2)</td>
<td>2.3 (0.4)</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>80.2 (1.9)</td>
<td>11.8 (1.5)</td>
<td>2.1 (0.6)</td>
<td>5.9 (0.8)</td>
</tr>
<tr>
<td>25-34</td>
<td>87.6 (1.0)</td>
<td>8.4 (0.7)</td>
<td>1.6 (0.4)</td>
<td>2.4 (0.4)</td>
</tr>
<tr>
<td>35 +</td>
<td>97.2 (0.3)</td>
<td>2.3 (0.4)</td>
<td>0.2 (0.06)</td>
<td>0.3 (0.06)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than secondary</td>
<td>93.3 (0.5)</td>
<td>4.0 (0.4)</td>
<td>0.8 (0.2)</td>
<td>1.9 (0.3)</td>
</tr>
<tr>
<td>Secondary only</td>
<td>91.2 (1.0)</td>
<td>6.3 (1.0)</td>
<td>0.7 (0.2)</td>
<td>1.8 (0.6)</td>
</tr>
<tr>
<td>Post-secondary</td>
<td>93.2 (0.6)</td>
<td>4.9 (0.5)</td>
<td>0.8 (0.2)</td>
<td>1.1 (0.2)</td>
</tr>
<tr>
<td>Relationship status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not married/ de facto</td>
<td>87.4 (1.4)</td>
<td>8.2 (0.9)</td>
<td>1.4 (0.3)</td>
<td>3.0 (0.5)</td>
</tr>
<tr>
<td>Married/ de facto</td>
<td>95.9 (0.3)</td>
<td>3.1 (0.3)</td>
<td>0.4 (0.1)</td>
<td>0.7 (0.2)</td>
</tr>
<tr>
<td>Employment status</td>
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</tr>
<tr>
<td>Employed</td>
<td>91.8 (0.7)</td>
<td>5.8 (0.4)</td>
<td>0.9 (0.2)</td>
<td>1.5 (0.3)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>74.5 (2.7)</td>
<td>13.0 (2.3)</td>
<td>3.8 (1.2)</td>
<td>8.8 (2.6)</td>
</tr>
<tr>
<td>Not in labour force</td>
<td>97.4 (0.4)</td>
<td>2.0 (0.4)</td>
<td>0.13 (0.07)</td>
<td>0.5 (0.2)</td>
</tr>
<tr>
<td>Neuroticism</td>
<td>2.5 (0.03)</td>
<td>3.1 (0.13)</td>
<td>3.6 (0.33)</td>
<td>4.1 (0.25)</td>
</tr>
</tbody>
</table>
Table D5: Weighted prevalence of other substance use, DSM-IV abuse and dependence, by demographic characteristics

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<th></th>
<th>No other substance use</th>
<th>Other substance use</th>
<th>Other substance abuse</th>
<th>Other substance dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (SE)</td>
<td>% (SE)</td>
<td>% (SE)</td>
<td>% (SE)</td>
</tr>
<tr>
<td>Prevalence</td>
<td>96.4 (12,979,000)</td>
<td>2.7 (365,000)</td>
<td>0.6 (86,000)</td>
<td>0.3 (35,000)</td>
</tr>
<tr>
<td>Weighted N</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Female</td>
<td>96.6 (0.3)</td>
<td>2.6 (0.2)</td>
<td>0.5 (0.1)</td>
<td>0.2 (0.1)</td>
</tr>
<tr>
<td>Male</td>
<td>96.2 (0.4)</td>
<td>2.8 (0.3)</td>
<td>0.8 (0.1)</td>
<td>0.3 (0.16)</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>94.6 (1.5)</td>
<td>3.5 (1.2)</td>
<td>0.9 (0.3)</td>
<td>1.0 (0.4)</td>
</tr>
<tr>
<td>25-34</td>
<td>95.8 (0.5)</td>
<td>2.8 (0.4)</td>
<td>1.3 (0.3)</td>
<td>0.2 (0.1)</td>
</tr>
<tr>
<td>35 +</td>
<td>96.9 (0.3)</td>
<td>2.5 (0.2)</td>
<td>0.4 (0.1)</td>
<td>0.1 (0.06)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Less than secondary</td>
<td>96.3 (0.4)</td>
<td>2.7 (0.3)</td>
<td>0.8 (0.1)</td>
<td>0.3 (0.2)</td>
</tr>
<tr>
<td>Secondary only</td>
<td>97.2 (0.4)</td>
<td>2.0 (0.3)</td>
<td>0.4 (0.2)</td>
<td>0.4 (0.3)</td>
</tr>
<tr>
<td>Post-secondary</td>
<td>96.2 (0.3)</td>
<td>2.9 (0.3)</td>
<td>0.4 (0.3)</td>
<td>0.2 (0.1)</td>
</tr>
<tr>
<td>Relationship status</td>
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</tr>
<tr>
<td>Not married/ de facto</td>
<td>94.8 (0.7)</td>
<td>3.5 (0.7)</td>
<td>1.2 (0.2)</td>
<td>0.5 (0.1)</td>
</tr>
<tr>
<td>Married/ de facto</td>
<td>97.2 (0.4)</td>
<td>2.3 (0.3)</td>
<td>0.3 (0.1)</td>
<td>0.1 (0.05)</td>
</tr>
<tr>
<td>Employment status</td>
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<td></td>
</tr>
<tr>
<td>Employed/ not in force</td>
<td>96.4 (0.2)</td>
<td>2.7 (0.2)</td>
<td>0.6 (0.1)</td>
<td>0.3 (0.07)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>95.4 (1.1)</td>
<td>2.7 (1.1)</td>
<td>1.9 (0.6)</td>
<td>-</td>
</tr>
<tr>
<td>Neuroticism (M)</td>
<td>2.5 (0.03)</td>
<td>4.1 (0.19)</td>
<td>6.1 (0.37)</td>
<td>4.3 (0.55)</td>
</tr>
</tbody>
</table>

1. Other substances: sedatives, stimulants or opiates
Table D6: Association between cannabis, alcohol, other drug and tobacco involvement; and demographics and neuroticism

<table>
<thead>
<tr>
<th></th>
<th>Cannabis involvement</th>
<th>Alcohol involvement</th>
<th>Other drug involvement</th>
<th>Regular tobacco use involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>25-34</td>
<td>0.53 (0.44, 0.65)</td>
<td>0.75 (0.64, 0.89)</td>
<td>0.72 (0.51, 1.00)</td>
<td>0.95 (0.82, 1.11)</td>
</tr>
<tr>
<td>35+</td>
<td>0.12 (0.10, 0.15)</td>
<td>0.46 (0.39, 0.53)</td>
<td>0.55 (0.41, 0.73)</td>
<td>0.52 (0.45, 0.60)</td>
</tr>
<tr>
<td><strong>Less than secondary education</strong></td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Secondary education</td>
<td>1.28 (1.02, 1.60)</td>
<td>1.46 (1.29, 1.66)</td>
<td>0.86 (0.62, 1.20)</td>
<td>0.74 (0.65, 0.85)</td>
</tr>
<tr>
<td>Postsecondary education</td>
<td>1.09 (0.92, 1.29)</td>
<td>1.86 (1.70, 2.03)</td>
<td>0.99 (0.80, 1.24)</td>
<td>0.66 (0.60, 0.72)</td>
</tr>
<tr>
<td><strong>Married/ defacto</strong></td>
<td>0.37 (0.31, 0.43)</td>
<td>1.03 (0.95, 1.12)</td>
<td>0.53 (0.43, 0.65)</td>
<td>0.60 (0.55, 0.66)</td>
</tr>
<tr>
<td><strong>Unemployed</strong></td>
<td>1.37 (1.13, 1.60)</td>
<td>1.42 (1.14, 1.76)</td>
<td>1.75 (1.16, 2.63)</td>
<td>2.92 (2.41, 3.54)</td>
</tr>
<tr>
<td><strong>Neuroticism</strong></td>
<td>1.16 (1.11, 1.16)</td>
<td>1.03 (1.02, 1.06)</td>
<td>1.28 (1.24, 1.32)</td>
<td>1.10 (1.08, 1.12)</td>
</tr>
</tbody>
</table>

Note: Odds ratios reported for alcohol, cannabis and other drugs refer to the average odds ratio from moving one level up the ordinal scale (e.g. from no use to use). Odds ratios for tobacco use refer to the change in odds when moving from no use to use.

1. Reference: female
2. Reference: never married/ widowed/ separated/ divorced
3. Reference: employed/ not in the labour force.
Table D7: Weighted prevalence of DSM-IV anxiety disorders by demographic characteristics

<table>
<thead>
<tr>
<th>No anxiety disorder</th>
<th>Anxiety disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>% (SE)</td>
<td>% (SE)</td>
</tr>
<tr>
<td>Prevalence</td>
<td>94.4 (0.3)</td>
</tr>
<tr>
<td>Weighted N</td>
<td>(12,708,000)</td>
</tr>
<tr>
<td>Female</td>
<td>93.2 (0.3)</td>
</tr>
<tr>
<td>Male</td>
<td>95.6 (0.6)</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>94.1 (0.7)</td>
</tr>
<tr>
<td>25-34</td>
<td>93.0 (0.7)</td>
</tr>
<tr>
<td>35-44</td>
<td>93.1 (0.7)</td>
</tr>
<tr>
<td>45-54</td>
<td>93.3 (0.6)</td>
</tr>
<tr>
<td>55-64</td>
<td>96.1 (0.9)</td>
</tr>
<tr>
<td>65-74</td>
<td>98.0 (0.4)</td>
</tr>
<tr>
<td>75+</td>
<td>98.8 (0.5)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Less than secondary</td>
<td>93.9 (0.4)</td>
</tr>
<tr>
<td>Secondary only</td>
<td>94.8 (0.6)</td>
</tr>
<tr>
<td>Post-secondary</td>
<td>94.6 (0.4)</td>
</tr>
<tr>
<td>Relationship status</td>
<td></td>
</tr>
<tr>
<td>Not married/ defacto</td>
<td>92.6 (0.6)</td>
</tr>
<tr>
<td>Married/ defacto</td>
<td>95.3 (0.3)</td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>87.0 (2.6)</td>
</tr>
<tr>
<td>Employed/ not in labour force</td>
<td>94.7 (0.3)</td>
</tr>
<tr>
<td>Neuroticism (M)</td>
<td>2.4 (0.02)</td>
</tr>
<tr>
<td></td>
<td>No mood disorder</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-----------------</td>
</tr>
<tr>
<td></td>
<td>% (SE)</td>
</tr>
<tr>
<td>Prevalence</td>
<td>93.3 (0.3)</td>
</tr>
<tr>
<td>Weighted N</td>
<td>(12,561,000)</td>
</tr>
<tr>
<td>Female</td>
<td>91.5 (0.5)</td>
</tr>
<tr>
<td>Male</td>
<td>95.1 (0.3)</td>
</tr>
<tr>
<td>Age group</td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>92.1 (0.9)</td>
</tr>
<tr>
<td>25-34</td>
<td>92.5 (0.6)</td>
</tr>
<tr>
<td>35-44</td>
<td>92.0 (0.5)</td>
</tr>
<tr>
<td>45-54</td>
<td>92.3 (1.0)</td>
</tr>
<tr>
<td>55-64</td>
<td>94.05 (1.0)</td>
</tr>
<tr>
<td>65-74</td>
<td>97.0 (0.7)</td>
</tr>
<tr>
<td>75+</td>
<td>98.95 (0.5)</td>
</tr>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Less than secondary</td>
<td>92.9 (0.4)</td>
</tr>
<tr>
<td>Secondary only</td>
<td>92.3 (1.0)</td>
</tr>
<tr>
<td>Post-secondary</td>
<td>93.9 (0.4)</td>
</tr>
<tr>
<td>Relationship status</td>
<td></td>
</tr>
<tr>
<td>Not married/ de facto</td>
<td>90.9 (0.9)</td>
</tr>
<tr>
<td>Married/ defacto</td>
<td>94.6 (0.4)</td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>87.7 (2.4)</td>
</tr>
<tr>
<td>Employed/ not in labour force</td>
<td>93.5 (0.3)</td>
</tr>
<tr>
<td>Neuroticism (M)</td>
<td>2.4 (0.02)</td>
</tr>
<tr>
<td></td>
<td>Non-cases</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-----------</td>
</tr>
<tr>
<td></td>
<td>% (SE)</td>
</tr>
<tr>
<td><strong>Prevalence</strong></td>
<td>99.1 (0.2)</td>
</tr>
<tr>
<td><strong>Weighted N</strong></td>
<td>(13,340,000)</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>99.0 (0.1)</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>99.1 (0.2)</td>
</tr>
<tr>
<td><strong>Age group</strong></td>
<td></td>
</tr>
<tr>
<td>18-24</td>
<td>98.7 (0.5)</td>
</tr>
<tr>
<td>25-34</td>
<td>98.7 (0.3)</td>
</tr>
<tr>
<td>35-44</td>
<td>98.6 (0.3)</td>
</tr>
<tr>
<td>45-54</td>
<td>99.2 (0.3)</td>
</tr>
<tr>
<td>55-64</td>
<td>99.7 (0.2)</td>
</tr>
<tr>
<td>65-74</td>
<td>99.9 (0.1)</td>
</tr>
<tr>
<td>75+</td>
<td>99.8 (0.2)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
</tr>
<tr>
<td>Less than secondary</td>
<td>99.0 (0.2)</td>
</tr>
<tr>
<td>Secondary only</td>
<td>99.4 (0.2)</td>
</tr>
<tr>
<td>Post-secondary</td>
<td>99.0 (0.2)</td>
</tr>
<tr>
<td><strong>Relationship status</strong></td>
<td></td>
</tr>
<tr>
<td>Not married/ defacto</td>
<td>98.4 (0.2)</td>
</tr>
<tr>
<td>Married/ defacto</td>
<td>99.4 (0.1)</td>
</tr>
<tr>
<td><strong>Employment status</strong></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>96.7 (1.0)</td>
</tr>
<tr>
<td>Employed/ not in labour force</td>
<td>99.2 (0.1)</td>
</tr>
<tr>
<td><strong>Neuroticism (M)</strong></td>
<td>2.6 (0.03)</td>
</tr>
</tbody>
</table>
Table D10: Association (odds ratios and 95% confidence intervals) between mood disorders, anxiety disorders, and psychosis “caseness”; and demographics and neuroticism

<table>
<thead>
<tr>
<th></th>
<th>Mood disorder</th>
<th>Anxiety disorder</th>
<th>Psychosis “case”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male¹</td>
<td>0.57 (0.49, 0.66)</td>
<td>0.64 (0.54, 0.75)</td>
<td>0.70 (0.48, 1.03)</td>
</tr>
<tr>
<td>18-24</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>25-34</td>
<td>0.96 (0.75, 1.24)</td>
<td>1.11 (0.85, 1.47)</td>
<td>1.00 (0.57, 1.77)</td>
</tr>
<tr>
<td>35 +</td>
<td>0.71 (0.57, 0.88)</td>
<td>0.74 (0.57, 0.94)</td>
<td>0.49 (0.29, 0.84)</td>
</tr>
<tr>
<td>Less than secondary education</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Secondary education</td>
<td>1.04 (0.84, 1.29)</td>
<td>0.90 (0.71, 1.15)</td>
<td>0.81 (0.45, 1.45)</td>
</tr>
<tr>
<td>Postsecondary education</td>
<td>0.88 (0.75, 1.03)</td>
<td>0.90 (0.76, 1.07)</td>
<td>0.91 (0.61, 1.35)</td>
</tr>
<tr>
<td>Married/defacto²</td>
<td>0.50 (0.43, 0.57)</td>
<td>0.58 (0.49, 0.68)</td>
<td>0.31 (0.21, 0.46)</td>
</tr>
<tr>
<td>Unemployed³</td>
<td>2.08 (1.58, 2.75)</td>
<td>2.63 (1.99, 3.47)</td>
<td>4.08 (2.42, 6.88)</td>
</tr>
<tr>
<td>Neuroticism</td>
<td>2.23 (1.92, 2.58)</td>
<td>2.41 (2.06, 2.83)</td>
<td>1.42 (1.34, 1.05)</td>
</tr>
</tbody>
</table>

2. Reference: never married/ widowed/ separated/ divorced
3. Reference: employed/ not in the labour force
### APPENDIX E - ADDITIONAL STATISTICS FROM ANALYSES OF COMORBIDITY BETWEEN ALCOHOL USE AND MENTAL HEALTH

Table E1: Odds ratios (OR) and 95% confidence intervals (95%CI) of other substance use according to alcohol use, after adjusting for demographics

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Regular tobacco use</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1.80</td>
<td>1.60, 2.03</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>4.33</td>
<td>3.15, 5.95</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>4.81</td>
<td>3.84, 6.02</td>
</tr>
<tr>
<td><strong>Cannabis use</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>2.87</td>
<td>2.15, 3.84</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>7.72</td>
<td>4.91, 12.12</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>10.61</td>
<td>7.44, 15.13</td>
</tr>
<tr>
<td><strong>Other drug use</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1.36</td>
<td>1.03, 1.80</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>4.15</td>
<td>.237, 7.26</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>7.05</td>
<td>4.87, 10.21</td>
</tr>
</tbody>
</table>
Table E2: Odds ratios (OR) and 95% confidence intervals (95%CI) of other substance use disorders according to alcohol use, after adjusting for demographics

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cannabis use disorder</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1.39</td>
<td>0.89, 2.18</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>3.68</td>
<td>1.88, 7.22</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>7.15</td>
<td>4.31, 11.85</td>
</tr>
</tbody>
</table>

<p>| <strong>Other drug use disorder</strong> |     |              |
| No alcohol use          | 1.00| --           |
| Alcohol use             | 0.85| 0.49, 1.48   |
| Alcohol abuse           | 2.52| 0.82, 7.68   |
| Alcohol dependence      | 8.38| 4.52, 15.54  |</p>
<table>
<thead>
<tr>
<th></th>
<th>OR - 1</th>
<th>95%CI - 1</th>
<th>OR-2</th>
<th>95%CI-2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mood disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>0.95</td>
<td>0.80, 1.14</td>
<td>0.86</td>
<td>0.72, 1.03</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>1.04</td>
<td>0.57, 1.88</td>
<td>0.71</td>
<td>0.39, 1.31</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>4.89</td>
<td>3.73, 6.42</td>
<td>3.16</td>
<td>2.37, 4.23</td>
</tr>
<tr>
<td><strong>Anxiety disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>0.93</td>
<td>0.77, 1.12</td>
<td>0.83</td>
<td>0.68, 1.01</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>0.85</td>
<td>0.42, 1.71</td>
<td>0.57</td>
<td>0.28, 1.17</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>4.85</td>
<td>3.64, 6.46</td>
<td>1.24</td>
<td>2.29, 4.24</td>
</tr>
<tr>
<td><strong>Psychosis “case”</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1.29</td>
<td>0.80, 2.10</td>
<td>1.04</td>
<td>0.63, 1.70</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>2.59</td>
<td>0.86, 7.79</td>
<td>1.41</td>
<td>0.46, 4.38</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>5.64</td>
<td>3.02, 10.55</td>
<td>2.57</td>
<td>1.32, 4.99</td>
</tr>
</tbody>
</table>
### APPENDIX F - ADDITIONAL STATISTICS FROM ANALYSES OF COMORBIDITY BETWEEN TOBACCO USE AND MENTAL HEALTH

Table F1: Odds ratios (OR) and 95% confidence intervals (95%CI) of other substance use according to tobacco use, after adjusting for demographics

<table>
<thead>
<tr>
<th>Substance</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>1.95</td>
<td>1.74, 2.19</td>
</tr>
<tr>
<td>Current smoker</td>
<td>2.50</td>
<td>2.22, 2.83</td>
</tr>
<tr>
<td>Cannabis use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>2.76</td>
<td>2.12, 3.58</td>
</tr>
<tr>
<td>Current smoker</td>
<td>6.66</td>
<td>5.38, 8.26</td>
</tr>
<tr>
<td>Other drug use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>1.54</td>
<td>1.17, 2.04</td>
</tr>
<tr>
<td>Current smoker</td>
<td>2.45</td>
<td>1.91, 3.13</td>
</tr>
<tr>
<td>Substance Use Disorder</td>
<td>OR</td>
<td>95%CI</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>--------</td>
<td>------------</td>
</tr>
<tr>
<td>Alcohol use disorder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>2.07</td>
<td>1.61, 2.66</td>
</tr>
<tr>
<td>Current smoker</td>
<td>4.15</td>
<td>3.36, 5.12</td>
</tr>
<tr>
<td>Cannabis use disorder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>2.32</td>
<td>1.39, 3.87</td>
</tr>
<tr>
<td>Current smoker</td>
<td>6.47</td>
<td>4.40, 9.53</td>
</tr>
<tr>
<td>Other drug use disorder</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>1.70</td>
<td>0.88, 3.29</td>
</tr>
<tr>
<td>Current smoker</td>
<td>4.72</td>
<td>2.81, 7.94</td>
</tr>
</tbody>
</table>
Table F3: Odds ratios (OR) and 95% confidence intervals (95%CI) of other mental health problems according to tobacco use, adjusted for demographics (OR-1); and adjusted for demographics and other drug use (OR-2)

<table>
<thead>
<tr>
<th></th>
<th>OR - 1</th>
<th>95%CI - 1</th>
<th>OR-2</th>
<th>95%CI-2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mood disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>1.32</td>
<td>1.09, 1.60</td>
<td>1.22</td>
<td>1.00, 1.48</td>
</tr>
<tr>
<td>Current smoker</td>
<td>2.19</td>
<td>1.85, 2.60</td>
<td>1.80</td>
<td>1.51, 2.16</td>
</tr>
<tr>
<td><strong>Anxiety disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>1.25</td>
<td>1.01, 1.55</td>
<td>1.17</td>
<td>0.94, 1.45</td>
</tr>
<tr>
<td>Current smoker</td>
<td>2.38</td>
<td>1.98, 2.87</td>
<td>2.01</td>
<td>1.66, 2.44</td>
</tr>
<tr>
<td><strong>Psychosis “case”</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Former smoker</td>
<td>1.74</td>
<td>0.96, 3.16</td>
<td>1.55</td>
<td>0.85, 2.81</td>
</tr>
<tr>
<td>Current smoker</td>
<td>4.63</td>
<td>2.88, 7.46</td>
<td>3.51</td>
<td>2.14, 5.75</td>
</tr>
</tbody>
</table>
## APPENDIX G - ADDITIONAL STATISTICS FROM ANALYSES OF COMORBIDITY BETWEEN CANNABIS USE AND MENTAL HEALTH

Table G1: Odds ratios (OR) and 95% confidence intervals (95%CI) of other substance use according to cannabis use, after adjusting for demographics

<table>
<thead>
<tr>
<th>Substance Type</th>
<th>OR</th>
<th>95%CI</th>
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<tbody>
<tr>
<td><strong>Regular tobacco use</strong></td>
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</tr>
<tr>
<td>No cannabis use</td>
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</tr>
<tr>
<td>Cannabis use</td>
<td>3.45</td>
<td>2.85, 4.18</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>3.56</td>
<td>2.21, 5.73</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>5.69</td>
<td>3.93, 8.25</td>
</tr>
<tr>
<td><strong>Alcohol use</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cannabis use</td>
<td>1.00</td>
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</tr>
<tr>
<td>Cannabis use</td>
<td>4.62</td>
<td>3.17, 6.73</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>3.57</td>
<td>1.41, 9.03</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>1.86</td>
<td>1.15, 3.02</td>
</tr>
<tr>
<td><strong>Other drug use</strong></td>
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<td></td>
</tr>
<tr>
<td>No cannabis use</td>
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<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>5.91</td>
<td>4.37, 8.00</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>5.54</td>
<td>2.75, 11.16</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>11.54</td>
<td>7.49, 17.78</td>
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<td>Substance Use Disorder</td>
<td>No cannabis use</td>
<td>Cannabis use</td>
</tr>
<tr>
<td>------------------------</td>
<td>-----------------</td>
<td>---------------</td>
</tr>
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<tr>
<td>Alcohol dependence</td>
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</tr>
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</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>Other drug abuse</td>
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<td>6.23</td>
</tr>
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</tr>
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<td>Other drug dependence</td>
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Table G2: Odds ratios (OR) and 95% confidence intervals (95%CI) of other substance use disorders according to cannabis use, after adjusting for demographics.
Table G3: Odds ratios (OR) and 95% confidence intervals (95%CI) of DSM-IV mood and anxiety disorders according to cannabis use, adjusted for demographics (OR-1); demographics and other drug use (OR-2)

<table>
<thead>
<tr>
<th></th>
<th>OR - 1</th>
<th>95%CI-1</th>
<th>OR - 2</th>
<th>95%CI-2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mood disorder</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cannabis use</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>2.11</td>
<td>1.61, 2.77</td>
<td>1.25</td>
<td>0.93, 1.68</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>2.75</td>
<td>1.50, 5.04</td>
<td>1.53</td>
<td>0.81, 2.89</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>2.44</td>
<td>1.56, 3.81</td>
<td>1.07</td>
<td>0.66, 1.73</td>
</tr>
<tr>
<td><strong>Anxiety disorder</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No cannabis use</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>1.62</td>
<td>1.18, 2.23</td>
<td>0.88</td>
<td>0.62, 1.24</td>
</tr>
<tr>
<td>Cannabis abuse</td>
<td>0.94</td>
<td>0.37, 2.38</td>
<td>0.47</td>
<td>0.18, 1.22</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>3.49</td>
<td>2.27, 5.35</td>
<td>1.51</td>
<td>0.95, 2.40</td>
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<tr>
<td><strong>Psychosis “case”</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>No cannabis use</td>
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<td>1.00</td>
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<tr>
<td>Cannabis use</td>
<td>2.88</td>
<td>1.60, 5.19</td>
<td>1.48</td>
<td>0.79, 2.75</td>
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<tr>
<td>Cannabis abuse</td>
<td>3.38</td>
<td>0.99, 11.49</td>
<td>1.87</td>
<td>0.54, 6.47</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>7.41</td>
<td>3.76, 14.61</td>
<td>3.11</td>
<td>1.51, 6.41</td>
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</table>
**APPENDIX H - ADDITIONAL STATISTICS FROM COMPARISON OF COMORBIDITY BETWEEN ALCOHOL, TOBACCO AND CANNABIS AND MENTAL HEALTH**

Table H1: Odds ratios and 95% confidence intervals (95%CI) of other substance use and substance use disorders according to alcohol, cannabis and tobacco use, considered simultaneously (OR-1); and adjusted for demographics (OR-2)

<table>
<thead>
<tr>
<th></th>
<th>OR-1</th>
<th>95%CI-1</th>
<th>OR-2</th>
<th>95%CI-2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Other substance use</strong></td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>No alcohol use</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>1.04</td>
<td>0.79, 1.37</td>
<td>1.21</td>
<td>0.91, 1.61</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>2.17</td>
<td>1.23, 3.84</td>
<td>2.68</td>
<td>1.49, 4.82</td>
</tr>
<tr>
<td>Alcohol dependence</td>
<td>3.62</td>
<td>2.48, 5.29</td>
<td>4.23</td>
<td>2.85, 6.29</td>
</tr>
<tr>
<td>No cannabis use</td>
<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>4.16</td>
<td>3.07, 5.63</td>
<td>4.45</td>
<td>3.24, 6.11</td>
</tr>
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<td>Cannabis abuse</td>
<td>2.94</td>
<td>1.45, 5.96</td>
<td>3.43</td>
<td>1.67, 7.08</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>6.48</td>
<td>4.21, 9.96</td>
<td>7.41</td>
<td>4.69, 11.72</td>
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<tr>
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<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Tobacco use</td>
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<td>1.08, 1.71</td>
<td>1.35</td>
<td>1.07, 1.71</td>
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<tr>
<td><strong>Other substance use disorder</strong></td>
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</tr>
<tr>
<td>Alcohol use</td>
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<td>0.34, 0.99</td>
<td>0.71</td>
<td>0.40, 1.23</td>
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<tr>
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<td>0.34, 3.27</td>
<td>1.32</td>
<td>0.41, 4.24</td>
</tr>
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<td>Alcohol dependence</td>
<td>3.24</td>
<td>1.72, 6.11</td>
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<td>1.97, 7.56</td>
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<td>No cannabis use</td>
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<td>1.00</td>
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</tr>
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<td>Cannabis use</td>
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<td>1.74, 6.28</td>
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<td>3.32</td>
<td>0.93, 11.80</td>
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<td>Cannabis dependence</td>
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<tr>
<td>No tobacco use</td>
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<tr>
<td>Tobacco use</td>
<td>1.52</td>
<td>3.85</td>
<td>2.32</td>
<td>1.45, 3.72</td>
</tr>
</tbody>
</table>
Table H2: Odds ratios and 95% confidence intervals (95%CI) of DSM-IV mood and anxiety disorders according to alcohol, cannabis and tobacco use, considered simultaneously (OR-1); adjusted for demographics (OR-2); and adjusted for demographics and other drug use (OR-3)

<table>
<thead>
<tr>
<th></th>
<th>OR-1</th>
<th>95%CI-1</th>
<th>OR-2</th>
<th>95%CI-2</th>
<th>OR-3</th>
<th>95%CI-3</th>
</tr>
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<tbody>
<tr>
<td><strong>Mood disorder</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>No alcohol use</td>
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<td>1.00</td>
<td>--</td>
<td>1.00</td>
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</tr>
<tr>
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<td>0.63, 0.88</td>
<td>0.87</td>
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<td>0.85</td>
<td>0.71, 1.02</td>
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<td>0.62</td>
<td>0.34, 1.12</td>
<td>0.80</td>
<td>0.44, 1.46</td>
<td>0.72</td>
<td>0.39, 1.32</td>
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<tr>
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<td>2.36, 4.04</td>
<td>3.69</td>
<td>2.78, 4.90</td>
<td>3.16</td>
<td>2.36, 4.23</td>
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<tr>
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<td>1.00</td>
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<td>1.00</td>
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</tr>
<tr>
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<td>1.18, 2.05</td>
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<td>1.17, 2.08</td>
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<td>0.94, 1.71</td>
</tr>
<tr>
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<td>0.81, 2.80</td>
<td>1.65</td>
<td>0.88, 3.11</td>
<td>1.46</td>
<td>0.77, 2.76</td>
</tr>
<tr>
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<td>0.88, 2.19</td>
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<tr>
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<td>1.00</td>
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</tr>
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<td>1.62, 2.21</td>
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<td>1.48, 2.04</td>
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<td>1.45, 2.00</td>
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<td><strong>Anxiety disorder</strong></td>
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</tr>
<tr>
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</tr>
<tr>
<td>Alcohol use</td>
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<td>0.59, 0.85</td>
<td>0.85</td>
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<td>0.69, 1.01</td>
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<td>0.29, 1.19</td>
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<td>Alcohol dependence</td>
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<td>2.31, 4.08</td>
<td>3.69</td>
<td>2.73, 4.99</td>
<td>3.12</td>
<td>2.29, 4.25</td>
</tr>
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<td>1.00</td>
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<td>1.00</td>
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<tr>
<td>Cannabis use</td>
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<td>0.16, 1.13</td>
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<tr>
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<td>1.97</td>
<td>1.25, 3.11</td>
<td>1.43</td>
<td>0.89, 2.29</td>
</tr>
<tr>
<td>No tobacco use</td>
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<td>1.00</td>
<td>--</td>
<td>1.00</td>
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</tr>
<tr>
<td>Tobacco use</td>
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<td>1.64, 2.32</td>
<td>1.92</td>
<td>1.61, 2.28</td>
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</tbody>
</table>

422
Table H3: Odds ratios and 95% confidence intervals (95%CI) of psychosis according to alcohol, cannabis and tobacco use, considered simultaneously (OR-1); adjusted for demographics (OR-2); and adjusted for demographics and other drug use (OR-3)

<table>
<thead>
<tr>
<th>Psychosis “case”</th>
<th>OR-1</th>
<th>95%CI-1</th>
<th>OR-2</th>
<th>95%CI-2</th>
<th>OR-3</th>
<th>95%CI-3</th>
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</thead>
<tbody>
<tr>
<td>No alcohol use</td>
<td>1.00</td>
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<td>1.00</td>
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<td>1.00</td>
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</tr>
<tr>
<td>Alcohol use</td>
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<td>0.53, 1.36</td>
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<td>0.65, 1.75</td>
<td>1.05</td>
<td>0.64, 1.72</td>
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<td>0.48, 4.55</td>
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<td>1.40, 4.93</td>
<td>3.02</td>
<td>1.56, 5.83</td>
<td>2.47</td>
<td>1.27, 4.82</td>
</tr>
<tr>
<td>No cannabis use</td>
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<td>1.00</td>
<td>--</td>
<td>1.00</td>
<td>--</td>
</tr>
<tr>
<td>Cannabis use</td>
<td>1.97</td>
<td>1.10, 3.54*</td>
<td>1.83</td>
<td>1.00, 3.34</td>
<td>1.45</td>
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<td>0.59, 6.68</td>
<td>2.01</td>
<td>0.58, 6.95</td>
<td>1.80</td>
<td>0.52, 6.24</td>
</tr>
<tr>
<td>Cannabis dependence</td>
<td>4.26</td>
<td>2.19, 6.68</td>
<td>3.93</td>
<td>1.94, 7.97</td>
<td>2.95</td>
<td>1.43, 6.12</td>
</tr>
<tr>
<td>No tobacco use</td>
<td>1.00</td>
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<td>1.00</td>
<td>--</td>
<td>1.00</td>
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</tr>
<tr>
<td>Tobacco use</td>
<td>3.42</td>
<td>2.29, 5.11</td>
<td>2.96</td>
<td>1.96, 4.46</td>
<td>2.88</td>
<td>1.91, 4.36</td>
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</tbody>
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* p<.05
# Appendix I - Additional Details of Ordinal Logistic Regression Predicting Increased Numbers of Psychotic Symptoms

Table I1: Additional results of ordinal logistic regression - demographic variables

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<thead>
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<th></th>
<th>Coefficient</th>
<th>SE</th>
<th>Z</th>
<th>p</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male^1</td>
<td>0.039</td>
<td>0.081</td>
<td>0.49</td>
<td>ns</td>
<td>1.04</td>
<td>0.89, 1.22</td>
</tr>
<tr>
<td>25-34 years^2</td>
<td>0.021</td>
<td>0.109</td>
<td>0.19</td>
<td>ns</td>
<td>1.02</td>
<td>0.83, 1.26</td>
</tr>
<tr>
<td>35-44 years^2</td>
<td>-0.334</td>
<td>0.121</td>
<td>-2.76</td>
<td>&lt;.01</td>
<td>0.72</td>
<td>0.56, 0.91</td>
</tr>
<tr>
<td>45-49 years^2</td>
<td>-0.381</td>
<td>0.149</td>
<td>-2.55</td>
<td>&lt;.01</td>
<td>0.68</td>
<td>0.51, 0.92</td>
</tr>
<tr>
<td>Secondary education^3</td>
<td>0.028</td>
<td>0.115</td>
<td>0.34</td>
<td>ns</td>
<td>1.03</td>
<td>0.82, 1.29</td>
</tr>
<tr>
<td>Postsecondary^3</td>
<td>0.206</td>
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<td>2.37</td>
<td>&lt;.05</td>
<td>1.23</td>
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<tr>
<td>Separated/divorced^4</td>
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<td>7.41</td>
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<td>2.16</td>
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<td>Widowed^4</td>
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<td>0.558</td>
<td>-0.31</td>
<td>ns</td>
<td>0.84</td>
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<tr>
<td>Never married^4</td>
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<td>4.89</td>
<td>&lt;.001</td>
<td>1.57</td>
<td>1.31, 1.89</td>
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<tr>
<td>Part-time employed^5</td>
<td>0.134</td>
<td>0.098</td>
<td>1.37</td>
<td>ns</td>
<td>1.14</td>
<td>0.94, 1.39</td>
</tr>
<tr>
<td>Unemployed^5</td>
<td>0.394</td>
<td>0.140</td>
<td>2.82</td>
<td>2.82</td>
<td>1.48</td>
<td>1.13, 1.95</td>
</tr>
<tr>
<td>Not in labour force^5</td>
<td>0.192</td>
<td>0.104</td>
<td>1.85</td>
<td>ns</td>
<td>1.21</td>
<td>0.99, 1.49</td>
</tr>
</tbody>
</table>

1. reference “female”
2. reference “18-24 years”
3. reference “less than secondary completed”
4. reference “married”
5. reference “employed full time”
APPENDIX J - REVIEW OF LITERATURE EXAMINING COMORBIDITY BETWEEN CANNABIS USE AND PSYCHOSIS

DOES CANNABIS USE CAUSE PSYCHOSIS?

Given what is known about the psychotomimetic effects of cannabis (Hall, Solowij, & Lemon, 1994), it is plausible that high doses of cannabis may produce psychotic symptoms. It is less clear whether cannabis plays a causal role in the development of lasting psychotic disorders that would not otherwise have occurred.

The evidence on this issue will be examined by considering two sources of information:

a) Studies examining the issue of a putative “cannabis psychosis”, which is taken here to indicate a psychotic episode caused by cannabis use and that would not have occurred otherwise; and

b) Literature examining whether cannabis use is associated with an increased likelihood of psychosis or psychotic symptoms.

CASES OF “CANNABIS PSYCHOSIS”

There has been a series of case reports of psychosis occurring among persons who had recently used cannabis. In one study, the authors outlined a series of patients over a 5-year period who were admitted to a psychiatric hospital with psychotic symptoms following the use of a large amount of cannabis (Chopra & Smith, 1974). Among the most common symptoms were delusions, hallucinations, emotional lability, and paranoia. The authors argued that it was unlikely that excessive cannabis use was a sign of pre-existing psychopathology. This was because one-third of their cases had no prior psychiatric history, the symptoms did not differ according to psychiatric history, and those who had
used the most potent cannabis preparations experienced psychotic symptoms after the shortest period of use (Chopra & Smith, 1974).

The findings of Chopra and Smith have received some support from smaller case series from the US (Eva, 1992; Tennant & Groesbeck, 1972), the UK (Carney, Bacelle, & Robinson, 1984), India (Basu, Malhotra, Bhagat, & Varma, 1999), South Africa (Solomons et al., 1990), Sweden (Bernardson & Gunne, 1972) and New Zealand (Wylie et al., 1995).

Some commentators have criticised these studies for the poor quality of information on cannabis use and its relationship to the onset of psychosis, and of information on the person’s premorbid adjustment and their family history of psychosis (Gruber & Pope, 1994; Thornicroft, 1992). They also emphasise the wide variety of clinical pictures of psychoses reported by different observers, which reduces confidence that there is a specific clinical disorder caused by cannabis use.

A number of controlled studies have been conducted over the past 20 years (Imade & Ebie, 1991; Mathers & Ghodse, 1992; McGuire, Jones, Harvey, & al, 1994; McGuire et al., 1995; Rolfe et al., 1993; Rottanburg, Robins, Ben-Arie, Teegin, & Elk, 1982; Thacore & Shukla, 1976). Some case-control studies have either compared persons with “cannabis-induced” psychoses with persons who have schizophrenia, or compared psychoses occurring in persons who do and do not have evidence of cannabis use prior to presenting for treatment. Perhaps because of small sample sizes and varied research methods, results have differed: associations in some studies have not been replicated in others.

**Psychotic Symptoms Among Cannabis Users**

As noted in Chapter Ten, there has been a paucity of epidemiological research on the comorbidity between psychosis and cannabis use, doubtless affected by the low prevalence of psychotic disorders in the population. The research that has been carried out has identified an association between cannabis use and reported psychotic symptoms during a follow-up year (Tien & Anthony, 1990), and higher rates of cannabis use (23%) among persons with schizophrenia (Cuffel, Heithoff, & Lawson, 1993). A community study in a
New Zealand city also found that among cannabis users in a random sample of people from a New Zealand city, one in seven (14%) cannabis users reported “strange, unpleasant experiences such as hearing voices or becoming convinced that someone is trying to harm you or that you are being persecuted” after using cannabis (Thomas, 1996). The frequency of these symptoms in non-users was not reported. The analyses in Chapter Ten also found that after adjusting for demographics, mental health and other substance use, dependent cannabis use was associated with a doubling of the odds of each additional psychotic symptom (adjusted OR = 2).

There is some longitudinal evidence supportive of an association between cannabis use and psychosis. A study of Swedish army conscripts found that the use of cannabis by age 18 years was associated with having received a diagnosis of schizophrenia 15 years later (Andreasson, Allebeck, & Rydberg, 1987). Andreasson and colleagues found that the relative risk of receiving a diagnosis of schizophrenia was 2.4 times higher among those who had tried cannabis by age 18 compared to non-users. There was also a dose–response relationship, with those who had used cannabis more than 50 times by age 18 years having a relative risk of a diagnosis of schizophrenia that was 6 times that of non-users.

These risks were substantially reduced after statistical adjustment for variables that were related to the risk of developing schizophrenia, namely, having a psychiatric diagnosis at conscription, and having parents who had divorced (as a proxy for parental psychiatric disorder). Nevertheless, the adjusted relative risk of a diagnosis of schizophrenia was 1.5 times greater for those who had smoked cannabis for one to 10 times, and 2.3 times greater for those who had used more than 10 times (Andreasson et al., 1987).

In summary, it appears that there is an association between cannabis use and reported psychotic symptoms, but the evidence is less clear about whether there is a causal role between cannabis use and the development of a lasting psychotic disorder that would not otherwise have occurred.
DOES CANNABIS PRECIPITATE PSYCHOSIS AMONG VULNERABLE INDIVIDUALS?

A second hypothesis, similar to the first, is that regular cannabis use precipitates schizophrenia only among vulnerable individuals, that is, among persons who would have developed the disorder regardless of whether they used cannabis or not. In broad terms, this would mean that if the prevalence of regular cannabis use increased in the general population, then the overall number of persons who developed psychosis would not change (i.e. the overall incidence and prevalence rates would not be altered), but that some persons would have “triggered” their psychotic illness earlier than it would otherwise have occurred.

AGE OF ONSET OF PSYCHOSIS

One of the implications of this is that among regular cannabis users who were vulnerable to developing the disorder, the average age of onset of psychosis would be reduced.

There have been a number of studies that have specifically examined whether the age of onset is different among cases of psychosis according to cannabis use. In a study of cases admitted to psychiatric hospitals over a 1-year period, cannabis users were significantly younger than non-users – mean ages of 28 years vs. 40 years, respectively (Mathers, Ghodse, Caan, & Scott, 1991). A study of similar design also found that in a sample of first-episode psychosis patients, cannabis “abusers” (those using cannabis almost daily before admission) were on average 1 year younger than non-abusers (20 years vs. 21 years) (Linszen, Dingemans, & Lenior, 1994).

While these data are consistent with the hypothesis that cannabis use may play a role in precipitating psychosis, it could well be that these younger age of cannabis users simply reflects that cannabis users in the general population are likely to be young adults anyway. In other words, this may simply be a confounding effect of the demographics of cannabis users. One way to examine this possibility is to examine the onset of cannabis use and of
psychotic symptoms among persons who report both. In order to be consistent with a precipitation hypothesis, we would expect that cannabis use would tend to precede psychotic symptoms.

This is what has been found in cases where such an issue has been examined. A study of persons who had been diagnosed with psychosis and with cannabis dependence looked at the distribution of the onset of regular cannabis use and psychotic symptoms (Allebeck, Adamsson, Engstrom, & Rydberg, 1993). In 79% of cases for which data on this aspect was provided, regular cannabis use was either in the same year or preceding years before the first psychotic symptom (Allebeck et al., 1993). In the Linszen and colleagues study, 23 out of 24 near-daily cannabis users had been using cannabis in this way for at least a year before admission.

Another study examined first-episode cases of psychosis according to “drug abuse” status (Hambrecht & Haefner, 2000). “Drug abuse” was defined as using illegal drugs more than once a week for at least a month. Psychosis cases with a history of drug abuse were much more likely to have used cannabis than those without a history of drug abuse (88% vs. 13%). They were also 4 times more likely to have the first sign of schizophrenia emerge before the age of 20 years (the average age of the first sign was 18.5 years). The onset of substance abuse preceded or was in the same month as the onset of schizophrenia in around 60% of cases. This is consistent with the possibility that cannabis use played a part in precipitating the illness among these individuals.

**Family History of Psychosis**

Another method of assessing whether cannabis use precipitated psychosis among vulnerable individuals would be to assess whether persons who had been using cannabis prior to developing psychosis were likely to have a family history of mental illness. It would be expected that if vulnerable individuals were more likely to develop psychosis after using cannabis, then the proportion with a history of mental illness would be higher among this group.
In one study examining this possibility, McGuire and colleagues (1995) studied 23 patients admitted with acute psychosis who screened positively for cannabis upon urine testing, and compared them each with two psychotic controls who were matched for gender and who had screened negatively for all substances in urine testing. Those who screened positively for cannabis had a higher morbid risk of a family history of schizophrenia than those who did not screen positively for cannabis (7% vs. 1%) (McGuire et al., 1995). This relationship was stronger when only persons with DSM-III schizophrenia were included in the analyses (morbid risks of 9% vs. 1%). The authors concluded that the development of acute psychosis might be more likely given a genetic predisposition to the development of schizophrenia.

In the study discussed above of Chopra and Smith, it is notable that a relatively high proportion of persons (two thirds) in the sample had a prior psychiatric history (Chopra & Smith, 1974). While symptoms did not differ according to this history, this finding is consistent with the possibility that persons vulnerable to psychosis might 'trigger' the psychosis.

In summary, there is some evidence to suggest that persons with a vulnerability to developing schizophrenia might have a higher risk of developing psychosis following the use of cannabis.

**DOES CANNABIS USE WORSEN THE PROGNOSIS OF PERSONS WITH PSYCHOSIS?**

This hypothesis will be taken to mean that of the persons who do use cannabis, the likelihood that they relapse to psychotic symptoms is increased. The evidence concerning this hypothesis is outlined below.

In support of this possibility are clinical reports, which have found that schizophrenic patients who cannabis experience more psychotic symptoms (Weil, 1970), respond more poorly to neuroleptic drugs (Bowers, Mazure, Nelson, & Jatlow, 1990) and have a worse
clinical course than those patients who do not (Drake, Mueser, Clark, & Wallach, 1996; Turner & Tsuang, 1990).

These reports have been supported by controlled studies. Negrete and colleagues conducted a retrospective study of the relationship between self-reported cannabis use and symptoms using clinical records in 137 patients with schizophrenia who had a disorder of at least 6 months' duration (Negrete, Knapp, Douglas, & Smith, 1986). They compared the prevalence of hallucinations, delusions and hospitalisations among the active cannabis users with that among patients who had previously used cannabis, and those who had never used cannabis. There were higher rates of continuous hallucinations and delusions, and more hospitalisations among active cannabis users. These relationships persisted after statistical adjustment for age and sex differences between the user groups.

One study compared the symptom profiles of schizophrenic patients with histories of substance abuse, among whom cannabis was the most heavily used drug, with those who had no such history (Cleghorn et al., 1991). Drug abusers had a higher prevalence of hallucinations, delusions and positive symptoms than those who did not abuse drugs. Another study found that the continued use of cannabis over a 1-year follow up of patients with schizophrenia predicted a higher rate of relapse and poorer compliance with anti-psychotic drug treatment (Martinez-Arevalo, Calcedo-Ordonez, & Varo-Prieto, 1994).

Several prospective studies have also examined the association between cannabis use and prognosis. The World Health Organization collaborative study involved a 2-year follow up of 1202 patients with first-episode schizophrenia enrolled in 10 countries (Jablensky, Sartorius, & Ernberg, 1991). They found that the use of ‘street drugs’, including cannabis and cocaine, during the follow-up period predicted more psychotic symptoms and periods of hospitalisation.

Linszen and colleagues reported a prospective study of outcome in 93 psychotic patients whose symptoms were assessed monthly over 1 year (Linszen et al., 1994). Twenty-four of their patients were cannabis users (11 were between weekly and daily users, and 13 were daily cannabis users). Cannabis users relapsed to psychotic symptoms sooner, and had more frequent relapses in the year of follow up, than the patients who had not used
cannabis. There was also a dose–response relationship, with the daily users relapsing earlier and more often than the less than daily users who, in turn, relapsed sooner, and more often, than the patients who did not use cannabis. These relationships persisted after multivariate adjustment for premorbid adjustment, and alcohol and other substance use during the follow-up period (Linszen et al., 1994).

The major cause of uncertainty about these findings is assessing the contribution of confounding factors. It may be, for example, that the difference in psychotic symptoms between schizophrenia patients who do and do not use cannabis is due to differences in premorbid personality, family history and other characteristics. This is unlikely in the WHO schizophrenia study (Jablensky et al., 1991) and the Linszen study (Linszen et al., 1994), both of which used multivariate statistical methods to adjust for some of these confounders. The Linszen and colleagues study, in particular, specifically examined the effect of cannabis use (as opposed to “street drug” use) and adjusted for the use of alcohol, which has also been associated with higher rates of rehospitalisation (Drake, Osher, & Wallach, 1989).

In summary, there is some suggestive evidence that regular cannabis use may worsen the prognosis of persons with schizophrenia.

**ARE PERSONS WITH PSYCHOSIS MORE LIKELY TO BECOME PROBLEMATIC CANNABIS USERS?**

This hypothesis proposes that persons with psychotic disorders are more likely to become regular users of cannabis if they use it at all. There is no causal relationship between cannabis use and psychosis, so there is no effect upon the number of incident cases of schizophrenia nor upon the prevalence of schizophrenia. An increase in the general population prevalence of cannabis use, however, will see a higher increase in the prevalence among persons with psychosis.

There is some support for this possibility. Chapter Ten showed that in the Australian population, the conditional prevalence of cannabis dependence was higher among persons
who screened positively for psychosis. In other words, if they reported any use of cannabis, they were more likely than non-cases to also report dependent use of cannabis. Other research has also found that persons with psychosis may be at higher risk of cannabis related problems if they report any use of it (Mueser, Drake, & Wallach, 1998).

This lower threshold for problems related to substance use may not be surprising given that persons with psychotic disorders are likely to have a range of problems that already impair their functioning in social, occupational and other areas (Mueser, Bellack, & Blanchard, 1992). Research comparing schizophrenic persons who were problematic alcohol users with persons who had a “primary” alcohol use problem has found that while both groups had significant substance use problems, schizophrenic persons were using significantly lower amounts (Drake et al., 1990); persons with psychosis have also been found to have lower levels of physical dependence on alcohol than “primary” alcohol abusing populations (Mueser et al., 1998).

An increased vulnerability to problematic substance use has also been discussed in more biological terms (Mueser et al., 1998). Mueser and colleagues discussed the possibility that persons with psychosis might be more sensitive to the effects of psychoactive substances. This has been supported in pharmacological “challenge” tests that have shown that persons with schizophrenia are more sensitive than controls to the effects of psychostimulants (Janowsky & Davis, 1976; Lieberman, Kane, & Alvir, 1987).
REFERENCES


## APPENDIX K - ADDITIONAL STATISTICS FROM MODELLING OF RELATIONSHIPS BETWEEN CANNABIS USE AND PSYCHOSIS

**Table K1: Incidence rates of schizophrenia according to gender and age (taken from Hall et al., 1985)**

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-19</td>
<td>36.3</td>
<td>25.1</td>
</tr>
<tr>
<td>20-24</td>
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<td>41.3</td>
</tr>
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<td>57.9</td>
<td>47.3</td>
</tr>
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</tr>
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<td>45-49</td>
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<td>30.2</td>
</tr>
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<td>50-54</td>
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<td>32.6</td>
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</table>
Table K2: Estimated percentage of cases of schizophrenia relapsing according to age of onset

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<tr>
<th>Age</th>
<th>Percentage of cases relapsing</th>
</tr>
</thead>
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<tr>
<td>15</td>
<td>95.74</td>
</tr>
<tr>
<td>16</td>
<td>94.18</td>
</tr>
<tr>
<td>17</td>
<td>92.62</td>
</tr>
<tr>
<td>18</td>
<td>91.06</td>
</tr>
<tr>
<td>19</td>
<td>89.50</td>
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<tr>
<td>20</td>
<td>87.94</td>
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<tr>
<td>21</td>
<td>86.38</td>
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<td>84.82</td>
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<td>23</td>
<td>83.26</td>
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<td>58.18</td>
</tr>
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<td>54</td>
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Table K3: Prevalence of monthly cannabis use by age (estimated from Chen and Kandel, 1995)

<table>
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<th>Persons</th>
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</tr>
</thead>
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<tr>
<td>34</td>
<td>12</td>
<td>13.86</td>
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Table K4: Prevalence of lifetime cannabis use in Australia according to gender and birth cohort (NDSHS, 1998)

<table>
<thead>
<tr>
<th></th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>1940-44</td>
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<td>13.7</td>
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<tr>
<td>1945-49</td>
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</tr>
<tr>
<td>1980-84</td>
<td>42.4</td>
<td>42.2</td>
</tr>
</tbody>
</table>

Figure K1 shows the model produced of the prevalence of schizophrenia among Australian males according to year and birth cohort. Looking at the oldest birth cohort examined here, 1940-44, it is possible to see that by 1998, the prevalence of schizophrenia was 1.2%. While this may appear to be an estimate that is at the upper limits of estimates of the lifetime prevalence of schizophrenia (Jablensky, Sartorius, & Ernberg, 1991; Robins & Regier, 1991), note that if the prevalence of schizophrenia is estimated in 1998 for the whole population examined here, the estimate is 0.7%, which is very similar to previous studies that have attempted to estimated the population prevalence of schizophrenia (Jablensky et al., 2000; Jablensky et al., 1991; Robins & Regier, 1991).
Figure K1: Prevalence of schizophrenia among Australian males according to year and birth cohort

![Graph showing prevalence of schizophrenia by year and birth cohort](image)

Table K5: Mean age of first cannabis use according to birth cohort, 1998 NDSHS

<table>
<thead>
<tr>
<th>Birth Cohort</th>
<th>Mean Age of First Use</th>
</tr>
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<tbody>
<tr>
<td>1940-44</td>
<td>30</td>
</tr>
<tr>
<td>1945-49</td>
<td>26</td>
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<tr>
<td>1950-54</td>
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</tbody>
</table>
If we take the oldest and youngest birth cohorts, the prevalence of schizophrenia by age 25 years is estimated to be 0.38% among those in the 1940-1944 birth cohort, compared to 0.43% in the 1975-1979 birth cohort, a difference of 0.05%, which is a 14% increase in the prevalence. At age 20 years, the difference between the oldest and youngest birth cohorts in the number of cases of schizophrenia caused by cannabis there would be an increase of 17% (between the calendar years 1960-1964 and 1995-2000) in the number of cases aged 20 years with schizophrenia coming to the attention of treatment services.
APPENDIX L - PAPERS AND CONFERENCE PRESENTATIONS SUPPORTING THIS THESIS

PEER REVIEWED PUBLICATIONS ARISING FROM THIS THESIS


PEER REVIEWED PUBLICATIONS SUPPORTING THIS THESIS

CONFERENCE PRESENTATIONS ARISING FROM AND SUPPORTING THIS THESIS


