Longitudinal studies of dependent heroin users in Australia: Feasibility and benefits

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Key Points

- Over the past decade heroin use and its associated harms have emerged as a major public health issue in Australia.

- About one in four heroin users will go on to develop dependence on the drug. Heroin dependence adversely affects public health and order out of all proportion to the number of people who use the drug. The major harms associated with heroin dependence include heroin overdose, blood borne viruses, psychopathology, and the effects of prescription drugs.

- Longitudinal studies of treatment outcome for heroin users in Australia are needed to guide more effective treatment interventions and public health responses.

- Longitudinal designs provide the optimal strategy for examining the effectiveness of treatment interventions and determining the influence of key variables on outcomes. Recent advances in longitudinal research methodology have made high quality treatment outcome studies with long term follow-ups feasible.

- Longitudinal studies conducted overseas have shown that existing treatments for heroin and other drug users can effectively reduce drug use and dependence. These studies have established that it is feasible to conduct longitudinal research with dependent heroin users, in that longitudinal cohorts can be maintained over several years.

- Methodological issues and differences between different settings limit the generalisability of previous cohort studies. To gain an understanding of the burden imposed by heroin use in Australia, longitudinal studies of Australian heroin users are essential.

- Heroin use and dependence are associated with a constellation of problems, each of which is of interest when assessing treatment outcome. Longitudinal data on heroin and other drug use, route of administration, criminality, psychiatric comorbidity, mortality, physical health status, and the economic burden of heroin use are essential to determine the impact of treatment and the long term patterns and consequences of heroin use.

- ATOS offers an unparalleled opportunity to maintain a large cohort of Australian heroin users, and improves significantly on the research methodologies used in previous treatment outcome studies. Extending the ATOS follow-up period beyond 12 months would allow essential data on longer term treatment outcomes and the burden imposed by heroin use in Australia to be obtained.

Executive Summary

AIMS

The aims of the current report were:

- To examine the feasibility of conducting longitudinal research with heroin users in the Australian context; and

- To provide a review of key research domains for longitudinal studies of heroin users.

HEROIN USE IN AUSTRALIA

Over the past ten years, there have been substantially heightened concerns in Australia about the increased use of heroin and the harms associated with its use. Heroin dependence is associated with major health risks, and accounts for a significant proportion of the total burden of disease and injury due to illicit drugs in Australia. There are, to date, no prospective studies of the natural history of Australian heroin users.

Prevalence of heroin use

In household surveys of alcohol and illicit drug use in Australia between 1985 and 2001, 1 to 2 percent of the adult Australian population report that they have used heroin at some time in their lives.

Prevalence of heroin dependence

Heroin dependence is one of the major health risks associated with heroin use. Approximately 25 percent of those who report ever having used heroin will go on to develop dependence on the drug. The development of heroin dependence is likely to require daily heroin use over several weeks or months.

The number of dependent heroin users in Australia is estimated at 74,000 (range from 67,000 to 92,000). This estimate (for 1997) represents a doubling of the 34,000 estimated in 1984 to 1987, and a 25 percent increase on the estimate of 59,000 in the period 1988 to 1993.

Characteristics of heroin users

Australian studies have repeatedly reported a ratio of male to female heroin users of approximately 2:1. The mean age of heroin users in cross-sectional studies has typically been approximately 30 years, with ages ranging from the late teens to the late 40s. The majority of the heroin using population lies in the 25 to 35 year age range. Among new heroin users, the age of onset of heroin use appears to be falling.

Drug use careers of heroin users

Dependent heroin users frequently continue to use heroin for decades. Among this group, periods of daily heroin use are interrupted by detoxification, drug treatment, and incarceration. No longitudinal data are available on the natural history of heroin use careers in an Australian cohort. There are, however, important differences between different countries in government policies and in the health care delivery systems available to heroin users. Treatment provision in countries such as the USA and UK is markedly different from that provided in Australia. In view of these differences, it would be unwise to generalise findings from overseas studies to the Australian context.

Harms associated with heroin use

The major harms associated with heroin use in Australia broadly include fatal and non-fatal heroin overdose, blood borne viruses, psychopathology, and the effects of prescription drugs.

Heroin overdose

There has been a dramatic increase in heroin overdose deaths in Australia in recent years. Non-fatal overdose is also extremely common among heroin users. There are no prospective data on the prevalence and patterns of heroin overdose, or the impact of treatment on its incidence among Australian heroin users.

Blood borne viruses

Blood borne viruses (primarily HIV, HBV, and HCV) represent a major harm associated with the injection of heroin and other drugs. In Australia, approximately 8 percent of new HIV diagnoses occur in individuals with a history of injecting drug use. Australia's HIV prevalence among IDU is estimated at less than 2 percent.

Australia's HCV prevalence among IDU is estimated at between 50 and 60 percent. It is estimated that 30 to 60 percent of IDU have been infected with HBV.

<u>Psychopathology</u>

Heroin users have high rates of psychiatric morbidity, with the most common diagnoses being mood disorders, anxiety disorders, and ASPD. Psychopathology has been strongly related to poorer treatment outcome among heroin users, although this is rarely measured in long term outcome studies. Longitudinal research in the Australian context will address the issue of how psychopathology relates to treatment outcome among heroin users.

<u>Effects of prescription drugs</u>

The widespread use of benzodiazepines among Australian heroin users is associated with higher rates of HIV risk-taking behaviour and psychopathology, poorer social functioning, poorer health, an increased risk of heroin overdose, and higher levels of criminality. Similarly, the injection of methadone syrup has been associated with poorer health, higher levels of psychiatric distress, and a history of heroin overdose.

Trends in heroin use

In 2001, there was a major national decline in the prevalence and frequency of heroin use in Australia. The 2001 national IDRS IDU survey revealed a sharp decline in the proportion of IDU who reported heroin as their drug of choice (63 percent in 2000 to 48 percent in 2001), and the proportion of IDU who had used heroin in the previous six months declined from 78 percent in 2000 to 66 percent in 2001. This decline is likely to be short lived, with anecdotal evidence indicating that the supply and use of heroin in Australia have been on the increase since early 2002. These data stand in sharp contrast to those of the previous decade, during which the use of heroin in Australia appeared to increase.

Significance of longitudinal research in Australia

There have been no prospective studies of the natural history of Australian heroin users. Thus, no longitudinal data are available on the patterns and consequences of heroin use, or long term treatment outcomes among this group.

Longitudinal data on the natural history of Australian heroin users would inform the development of more effective harm reduction strategies and public health responses. Such data would also provide a measure of the burden imposed by heroin use in Australia, and a baseline for measuring the effectiveness of treatment interventions.

ATOS

ATOS is a longitudinal cohort study of treatment outcome for heroin dependence that commenced data collection in February 2001. It is currently recruiting 600 consecutive entrants to treatment for opioid dependence, and a group of active heroin users who are not in treatment. Follow-up is at 3 and 12 months after study entrance. ATOS is using a range of outcome measures to determine the effectiveness of treatment and examine the natural history of Australian heroin users.

WHY LONGITUDINAL RESEARCH?

The longitudinal research design offers the optimal methodology to examine the effectiveness of treatment interventions, and to determine the influence of key variables on outcomes. Longitudinal studies enable the impact of multiple factors on subsequent behaviour to be assessed, including client characteristics, treatment factors, and factors external to treatment. Cross-sectional designs do not allow the separation of these types of effects. Longitudinal designs also provide strong support for evaluative and causal inferences. The development of new, multivariate longitudinal data analytic techniques and models has made high quality treatment outcome studies with long term follow-ups feasible.

Longitudinal research versus clinical trial methodology

The gold standard for obtaining data on treatment outcomes has historically been the randomised controlled clinical trial. Clinical trial methodology is not appropriate for examining the naturally occurring variation in treatment and the natural history of drug use careers. While the findings from clinical trials can inform policy responses by clarifying the potential therapeutic value of treatment, policy makers increasingly require information that is directly applicable to community patient samples and relevant to important societal outcomes such as long term morbidity and costs.

Benefits of longitudinal research methodology

The longitudinal research design yields a number of advantages over cross-sectional designs. These include its ability to provide a natural history account of behaviours and events as they occur over time, and its capacity to provide tests of causality based on temporal sequencing.

A major benefit of longitudinal research is its relative cost-efficiency, because many different topics may be examined within the longitudinal design framework. Another advantage is its flexibility to address emerging research themes and issues.

Methodological issues in longitudinal research

Longitudinal studies of heroin and other drug users involve a number of important methodological issues, including the potential for biases due to self-selection into treatment and subject attrition.

A major issue concerns the source of the initial study cohort. While it would be ideal to conduct a prospective cohort study in which the natural history of heroin use and dependence was assessed from before the onset of heroin use, this approach is not feasible. To conduct such a study would require an initial longitudinal study of approximately 70,000 individuals (assuming that 0.7% of the population is dependent on heroin). Sampling from dependent heroin users entering treatment is therefore the most common and practical method.

A limitation of this approach is that the populations of drug users who enter and/or remain in treatment are likely to be distinctive. The inclusion of a comparison group of active drug users who are not in treatment would thus enhance the validity of the conclusions of any longitudinal study of treatment outcome for heroin and other drug users. Moreover, it would also allow the role of treatment in the natural history of drug use to be examined.

Subject attrition is a salient issue in studies of drug users. Sample losses can threaten the validity of longitudinal studies by reducing the generalisability of their findings. Recent work on follow-up methodology has identified a number of effective procedures for maximising follow-up rates in studies of drug users. One of the basic strategies is to collect detailed locator information at the start of the study, and to update these locator data at each follow-up point.

The development of methods to correct for sample selection biases is a particular strength of longitudinal research methodology. These methods include the use of the sample selection hazard proposed by Heckman, the use of missing data estimation methods, and the use of sample weights to re-weight the sample to correct for systematic sample loss. These procedures may be used to examine the potential effects of sample selection biases on the validity of a study's conclusions.

Significance of the longitudinal design

Longitudinal studies have the potential to examine a wide range of issues relating to the assessment and prevalence of disorder, treatment seeking, continuity and change in disorders, and the long term consequences of drug use and other psychiatric disorders. The major advantages of a longitudinal design are its ability to provide a natural history account of behaviours and events as they occur over time, its ability to provide tests of causality based on temporal sequencing, its cost-efficiency, and its flexibility to address emerging research questions.

FEASIBILITY OF LONGITUDINAL STUDIES OF TREATMENT OUTCOME FOR HEROIN AND OTHER DRUG USERS

Much of what is known about typical treatment outcomes comes from a series of large scale longitudinal cohort studies conducted overseas over the past 30 years. The most widely published and influential of these studies are the US DARP, TOPS, and DATOS, and the UK NTORS. These treatment outcome studies have shown that existing behavioural, psychosocial, and pharmacological treatments can effectively reduce drug use and dependence, in the context of adequate treatment lengths. Moreover, they have established that prospective treatment outcome research can be successfully conducted with dependent heroin users, in that longitudinal cohorts can be maintained. DARP, TOPS, DATOS, and NTORS obtained high follow-up rates, and initial follow-up rates were highly predictive of later follow-up rates, even after considerable periods of time (Table 1). On the basis of overseas experience, it is feasible to conduct longitudinal research with dependent heroin users.

Table 1. Follow-up rates obtained by DARP, TOPS, DATOS, and NTORS

Study	Intake year(s)	Follow-up time points	Follow-up rates
Drug Abuse Reporting Program (DARP)	1969 – 1974	3 years 6 years 12 years	77% 73% 70%
Treatment Outcome Prospective Study (TOPS)	1979 – 1981	3 months 12 months 2 years 3-5 years	80% 79% 76% 65%
Drug Abuse Treatment Outcome Study (DATOS)	1991 – 1993	12 months	70%
National Treatment Outcome Research Study (NTORS)	1995	6 months 12 months	75% 72%

Limitations of previous studies

A limitation of the previous longitudinal treatment outcome studies is that they used treatment entrants from purposely selected treatment programs, with no attempt at representative sampling. In addition, none of the studies included a comparison group of active heroin users who were not in treatment at admission to the study. Another serious limitation is that these studies did not comprehensively assess psychiatric morbidity using valid and reliable instruments.

DOMAINS FOR LONGITUDINAL RESEARCH

Heroin use and dependence are associated with a constellation of problems, each of which is of relevance when assessing treatment outcome and drug use career history. There are a number of key research domains that should be addressed by longitudinal studies of treatment outcome for heroin users. These include patterns of heroin and other drug use, route of administration, criminality, psychiatric comorbidity, mortality, physical health status, and the economic burden imposed by heroin use.

Patterns of drug use

Factors that precede the onset and escalation of heroin use careers are likely to have an impact on the nature and severity of drug use and other problems that may be

experienced by heroin users. In addition to examining current patterns of drug use, it is vital that longitudinal studies of heroin users take into account their previous drug use behaviours, including comprehensive drug use histories, injecting drug use histories, routes of heroin use, polydrug use, and the drug use careers of heroin users.

<u>Measuring illicit drug consumption</u>

The accurate measurement of recent drug use is an essential component of treatment and research among illicit drug users.

One method of determining recent drug consumption is the use of urinalysis. There are a number of problems in relying on urinalysis results for clinical or research purposes:

i.   Urinalysis may not detect drug use where the client is using irregularly;

ii.   Some drugs (for example, hallucinogens) are typically not detected due to the small amounts ingested; and

iii.   Urinalysis is not able to detect levels of drug use, meaning that it is a relatively insensitive measure of behaviour change.

These limitations apply equally to other existing biochemical markers of drug use, namely hair and venous blood samples.

Given the limitations of the existing biochemical indicators, clinicians and researchers must rely on the self-reported drug use of clients to obtain detailed information on current consumption. There is a large literature on the legitimacy of the behavioural self-reports of drug users. Overall, these studies indicate that, in research contexts, IDU typically provide reliable and valid responses to questions about their drug use, even at long recall periods.

The Drug Use Section of the OTI provides an estimate of drug use in the preceding month. This measure has been widely used in studies of illicit drug users, and has excellent psychometric properties. The major advantage of this measure is that it enables reliable and valid data on drug consumption to be quickly obtained over a large range of drug classes.

Route of administration

Route of administration is known to influence the immediacy, intensity, and duration of the pharmacological effect of heroin. The route of heroin use also has

important implications for the nature and severity of problems that may be experienced by the user.

Over the past decade, increases in non-injecting heroin use have been reported in England, Ireland, The Netherlands, Spain, Switzerland, and the USA. Recent Australian research has documented the emergence of smoking or "chasing" as a popular route of administration among young, recent recruits to heroin use. Heroin injecting has been associated with more severe dependence than heroin smoking, but some studies have found no significant differences in severity of dependence between heroin smokers and heroin injectors. Others have suggested that the relationship between route of heroin use and severity of heroin dependence is produced only in the early stages of heroin use careers. After a certain length of time, most heroin users converge to a very high level of dependence irrespective of the route of administration. Longitudinal studies are needed to assess how heroin dependence and route of administration evolve during the user's drug career.

While heroin overdose is more commonly associated with injecting, both fatal and non-fatal overdoses have been reported in relation to non-injecting routes of administration.

Transitions to and from injecting have major clinical and public health implications with regards to blood borne virus transmission through needle sharing. Heroin injectors are at greater risk than non-injectors of contracting or transmitting blood borne viruses, notably HBV, HCV, and HIV.

The act of injecting per se also carries inherent health risks. Frequent injections may cause vascular damage, irrespective of safe injecting practices, particularly with the injection of oral preparations such as benzodiazepines and methadone syrup.

Overseas treatment outcome studies have not examined the relationship between route of heroin use and treatment outcome. As such, no longitudinal data are available on the processes underlying transitions between routes of administration, and the possible role of treatment in making transitions.

Criminality

The existence of an association between heroin use and crime has been widely documented. A large proportion of the heroin dependent population regularly engages in criminal activity, most commonly drug dealing and acquisitive property

crime. The question of how interventions for heroin and other drug users impact on criminal behaviour is important for the implementation and evaluation of treatment services, and for the development of effective policy responses.

Large scale treatment outcome studies have reported substantial post-treatment reductions in the numbers of crimes committed and the rates of criminal involvement among illicit drug users.

An estimate of overall criminal involvement, such as that obtained in the Crime Scale of the OTI, provides the optimal measure of criminality among heroin users. The OTI Crime Scale measures the occurrence of criminal behaviours in the preceding month, not just those that resulted in an arrest, and has been widely used in studies of heroin and other drug users.

Psychiatric comorbidity

Epidemiological surveys of the prevalence of psychiatric disorders from around the world have established that psychiatric disorders and drug use disorders frequently co-occur. Up to 80 percent of treatment-seeking heroin users satisfy the criteria for at least one other psychiatric disorder, with rates of mood disorders and ASPD that far exceed general population estimates.

The major psychiatric diagnoses among dependent heroin users include depression, ASPD, PTSD, and BPD.

Depression

An association between heroin use and depression has been well documented. Prevalence estimates for lifetime major depressive disorder among heroin users have ranged from 38 to 56 percent, and for current major depressive disorder from 16 to 30 percent.

Anti-social personality disorder

A diagnosis of ASPD is one of the most common psychiatric diagnoses made among IDU. The prevalence of ASPD among heroin users has been reported to range from 35 to 65 percent. In all studies conducted to date, the prevalence of ASPD among heroin users has exceeded the 4 percent population prevalence by several orders of magnitude. Heroin users with ASPD have been found to have an earlier

onset of drug use and injecting, and to be more likely to meet the criteria for diagnoses of drug abuse and dependence for drugs other than heroin.

While there is no demonstrated treatment for ASPD per se, there is evidence that heroin users with ASPD may be successfully retained in MMT, and perform as well in MMT as other patients. Important research questions concern the performance of ASPD patients in other forms of treatment relative to other patients, and the effect of a diagnosis of ASPD on treatment outcome.

Post-traumatic stress disorder

PTSD is highly prevalent among patients with drug use disorders, and has consistently been associated with poorer treatment outcomes. Relatively little is known about effective treatment for dependent heroin users with comorbid PTSD, or the impact of comorbid PTSD on treatment outcome.

Recent findings suggest that the negative consequences of a comorbid PTSD diagnosis are greater than the effects of other comorbid psychiatric diagnoses, and that these effects intensify over time and encompass drug use, psychological, and social areas of functioning. Longitudinal research is needed to understand the natural course of PTSD among heroin users, and to clarify the relationship between PTSD status and treatment outcomes.

Borderline personality disorder

BPD is characterised by substantial levels of impairment, and appears to be a strong and independent risk factor for suicidal behaviour. Among treatment-seeking heroin users, the prevalence of BPD has been found to range from 9 percent to 65 percent.

The high prevalence of psychopathology among heroin users has direct implications for treatment outcome and clinical practice. Psychopathology has consistently emerged as a salient predictor of poor treatment outcome, and has been associated with higher levels of HIV risk-taking and HIV infection, greater severity of substance use, and higher levels of psychosocial impairment.

Relatively little longitudinal research has examined the influence of co-existing psychiatric disorders on the outcome of treatment for drug use disorders. Better understanding of the effects of comorbid psychiatric disorders on treatment outcome, and the impact of treatment on such disorders, is of major clinical relevance.

Prospective studies should examine the relationships between heroin use and depression, ASPD, PTSD, and BPD, given the high prevalence of these diagnoses among dependent heroin users.

Mortality

Heroin users are at substantially greater risk of premature mortality than their non-heroin using peers. The annual mortality rates reported by longitudinal studies of heroin users have ranged from less than 1 percent to 8 percent, with most studies reporting rates of 1 to 3 percent. A recent meta-analysis of mortality rates reported by longitudinal studies of heroin users reported a mortality rate for regular heroin users 13 times greater than that of the general population.

The major causes of death among heroin users are overdose, medical condition, trauma, and suicide. Deaths attributed to overdose are the largest contributor to excess mortality associated with heroin use, and account for 30 to 45 percent of total mortality reported by longitudinal studies of heroin users. Deaths attributed to medical conditions commonly account for 20 to 35 percent of overall mortality reported by longitudinal studies of heroin users. Deaths related to violence and accident/injury have been reported to account for 10 to 25 percent of total mortality among heroin users. Most studies of heroin-related mortality report that between 3 percent and 10 percent of heroin users die by suicide. Studies that have specifically examined the relative risk of completed suicide among heroin users have reported excess mortality of 6 times to 8 times that expected among matched peers.

The risk of death is substantially reduced among heroin users who are enrolled in treatment. Enrolment in MMT has been found to reduce patients' risk of death by nearly 75 percent.

Patterns of mortality reported by overseas studies are unlikely to be applicable to the Australian context. The health care delivery systems available to heroin users differ significantly between different countries. There are no longitudinal studies of Australian heroin users, and therefore, no longitudinal data on heroin-related mortality among this group. Prospective cohort studies provide an excellent framework in which to report the deaths that occur within the cohort, to examine the circumstances and causes of death, and to identify specific factors that put heroin users at increased risk of death.

Physical health status

The overall physical health of heroin users is poor, relative to the non-heroin using population. The most common physical complications among heroin users include: infections resulting from needle sharing and unhygienic injecting practices, foreign body emboli, inflamed lesions due to the injection of contaminants, and a variety of neurological, musculoskeletal, and other lesions resulting from toxic impurities in drugs produced in illicit laboratories.

In Australia, the major physical health risks associated with heroin use are fatal and non-fatal heroin overdose, blood borne virus transmission through the sharing of injecting equipment, and vascular damage.

The measurement of health status has both clinical and research relevance. Few large scale treatment outcome studies, however, have measured health outcomes using reliable and valid instruments.

A global estimate of current health status such as the OTI Health Scale provides the optimal measure of health status among heroin users. This measure is oriented towards the specific problems associated with heroin use, and it contains a specific section on injection-related health problems. The SF-12 and SF-36 also yield valid and reliable assessments of health status. The SF-36 has been specifically demonstrated to be a reliable and sensitive measure of general health among dependent heroin users.

Burden of heroin use

Heroin use and dependence impose a significant clinical and social burden on individuals, families, and communities that includes an economic dimension. Policy makers and treatment providers are increasingly concerned with not only the effectiveness, but also the cost-effectiveness of treatment. For that reason, there is a need for health economics contributions to policy responses and clinical practice. Costs include health care costs, patient and family costs, and other sector costs.

Economic evaluation can provide estimates of service outcomes, including changes in health status, clinical outcomes, and quality of life measures. Studies of treatment for heroin and other drug use problems usually express health outcomes in terms of days drug free or abstinent. One problem with this approach is that there are likely to be other outcomes of concern that may not correlate highly with reductions in drug use or abstinence. Moreover, changes in domains such as psychiatric

morbidity, social functioning, and employment status are of independent interest when assessing treatment outcome.

Cost-consequence analysis is a method of economic evaluation that enables the cost of delivering treatment to be examined in relation to multiple outcome areas. This method is able to address the interests of multiple consumer audiences, and is therefore highly suitable for longitudinal studies of treatment outcome for heroin and other drug users.

SUMMARY

Prospective studies conducted in a number of countries have established that longitudinal treatment outcome research can be conducted with dependent heroin users, in that longitudinal cohorts can be maintained over several years. The data indicate that it is possible to follow up cohorts of heroin users, even after 12 years. Clearly, it is feasible to conduct longitudinal research with this population.

Specialist reviews of follow-up methodology have identified a number of strategies for maintaining contact with participants and obtaining high response rates in longitudinal studies of drug users. It is vital to collect comprehensive locator information from participants at the beginning of the study, and to update the locator form at each follow-up point. Because heroin and other drug users tend to be mobile, it is important to conduct follow-up interviews in convenient locations, and to provide adequate resources for travel. The development and maintenance of rapport with participants is another essential feature of successful follow-up.

There are a number of key research domains that a longitudinal study of treatment outcome for heroin users should measure: heroin and other drug use, route of administration, criminality, psychiatric comorbidity, mortality, physical health status, and the economic burden imposed by heroin use. A major advantage of longitudinal research methodology is that it enables researchers to determine the impact of multiple factors on subsequent behaviour. Where possible, reliable and valid instruments should be used to measure the predictor and outcome variables of interest, so that the findings are comparable with those of previous studies.

Overseas experience has shown that it is feasible to carry out longitudinal research with dependent heroin users. There are a number of reasons why it is essential to conduct prospective treatment outcome studies of heroin users in

Australia. First, there are substantial differences between different countries in government policies and in the health care delivery systems available to heroin users. The characteristics of heroin users and their patterns of drug use are also likely to differ in many respects between a country such as the USA and Australia. Given these differences, it would be unwise to generalise findings from overseas studies to the Australian context.

Second, the major overseas studies of treatment outcome are methodologically flawed in that they have used treatment entrants from purposely selected treatment programs, with no attempt at representative sampling. None of these cohort studies included a comparison group of active heroin users who were not in treatment. In addition, these studies did not comprehensively assess psychiatric morbidity using reliable and valid diagnostic instruments.

ATOS improves significantly on the research methodologies used in previous drug treatment outcome studies. The treatment agencies from which the ATOS treatment sample is being recruited were selected randomly, stratified by geographical area and treatment modality, to provide a representative sample of treatment agencies. A comparison group of active heroin users who are not in treatment is being recruited from the same regions as the treatment sample, predominantly through NSPs. The research instruments used in ATOS are of demonstrated reliability and validity, which will enable effective comparisons to be made across time and across treatment modalities. ATOS is also collecting comprehensive data on levels of psychiatric morbidity. To date, follow-up rates of 91 percent and 82 percent have been obtained at 3 months and 12 months, respectively. On the basis of overseas studies, these data indicate that high follow-up rates can be maintained at 12 months and beyond.

ATOS offers an unparalleled opportunity to maintain a large cohort of Australian heroin users. Extending the ATOS follow-up period beyond 12 months would enable essential data on longer term treatment outcomes to be obtained. ATOS can make a significant contribution to the research literature on treatment outcomes for heroin users and the natural history of heroin use in Australia.

1.0   Introduction

Heroin use and its associated harms present a serious, disabling, and growing problem in Australia. Heroin use is likely to be a chronic, relapsing problem, and long term outcome is likely to be poor. Nonetheless, longitudinal studies of heroin users are rare, and there have been no longitudinal studies of heroin users in Australia.

In 1999 the National Health and Medical Research Council (NH&MRC) awarded funding to the National Drug and Alcohol Research Centre (NDARC) to conduct the Australian Treatment Outcome Study (ATOS), a longitudinal study of treatment outcome for heroin dependence. The study is currently recruiting a sample of 600 entrants to treatment for opioid dependence, and active heroin users who are not in treatment, and is collecting data on heroin and other drug use, criminality, psychopathology, and health over 12 months.

The ATOS cohort provides the opportunity for long term follow-up. This is a potentially costly exercise, so it is important to address its feasibility and to ensure that appropriate measures are used. This is the focus of the current report, which examines the feasibility of conducting a longer term follow-up of the ATOS cohort. More specifically, a comprehensive review of the international literature on longitudinal studies of treatment outcome for heroin and other drug users, and appropriate areas of outcome assessment in longitudinal research on heroin users, was undertaken.   In addition, the current report also examines the Australian epidemiology, use patterns, and associated harm of heroin, and methodological issues of relevance to longitudinal research.

1.1   Aims

- To examine the feasibility of conducting longitudinal research with heroin users in the Australian context; and
- To provide a review of key research domains for longitudinal studies of heroin users.

2.0   Heroin use in Australia

Over the past ten years, there have been substantially heightened concerns in Australia about the increased use of heroin and the harms associated with its use. These concerns have been motivated, at least in part, by evidence of dramatic increases in the rate of fatal heroin overdoses in recent years, an increase in the number of people enrolled in methadone maintenance treatment (MMT), increased amounts and availability of heroin in Australia, and increases in the number of heroin users (Darke, Kaye, & Topp, 2002; Darke, Topp, Kaye, & Hall, 2002). Heroin dependence is associated with major health risks, and accounts for a significant proportion of the total burden of disease and injury due to illicit drugs in Australia (Mathers, Vos, & Stevenson, 1999). Overseas studies have shown that long term treatment outcome and abstinence from heroin are poor, and that mortality is high (Bargagli, Sperati, Davoli, Forastiere, & Perucci, 2001; Hser, Hoffman, Grella, & Anglin, 2001). Nonetheless, there are no prospective studies of the natural history of Australian heroin users.

2.1   Prevalence of heroin use

In household surveys of alcohol and illicit drug use conducted in Australia between 1985 and 1995, 1 to 2 percent of the adult Australian population report that they have used heroin at some time in their lives (Makkai & McAllister, 1998). In the 2001 National Household Survey, 1.6 percent of the population over the age of 14 (2.2 percent of males and 1.0 percent of females) reported that they had used heroin. The prevalence of heroin use was highest among young adults aged 20 to 29 years, with 5.2 percent of males and 2.0 percent of females reporting lifetime heroin use, and 0.6 percent and 0.5 percent respectively reporting that they had used heroin in the past year (Australian Institute of Health and Welfare (AIHW), 2002).

These figures are likely to underestimate heroin use for a number of reasons. First, heroin users are probably under-represented in household survey samples. Their lifestyle makes them less likely to live in conventional households, and the distribution of heroin use tends to be concentrated in particular localities, making it likely that household surveys will underestimate use. Second, if heroin users are interviewed, their heroin use may be under-reported because it is an illegal and socially stigmatised behaviour.

2.2   Prevalence of heroin dependence

Heroin dependence is one of the major health risks associated with heroin use. In terms of clinical importance and public health, it is long term, dependent heroin users who present the primary target group. Heroin dependence is distinguished from heroin use by a number of behavioural characteristics. The Fourth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (American Psychiatric Association, 1994) defines opioid dependence as opioid use accompanied by signs and symptoms of compulsive prolonged self-administration without legitimate medical purpose. These signs include tolerance, withdrawal, using in larger amounts or for a longer time than was intended, a persistent desire or unsuccessful efforts to control use, and continued use despite recognition of adverse effects.

Large scale community surveys of mental disorders in the USA, such as the National Comorbidity Survey (Warner, Kessler, Hughes, Anthony, & Nelson, 1995), indicate that approximately 25 percent of those who report ever having used heroin will go on to develop dependence on the drug. The estimated one in four heroin users who become dependent on heroin typically report a one to two year period between their first use of heroin and their first period of sustained daily use (a reasonable indicator of dependent use). As is the case for other types of drug dependence, therefore, the development of heroin dependence is likely to require daily heroin use over several weeks or months (Hall, Lynskey, & Degenhardt, 1999).

A variety of data sources have been used to estimate the number of dependent heroin users in Australia. These include data on national overdose deaths compiled by the Australian Bureau of Statistics (ABS), data on MMT entrants from the NSW Department of Health, and data on arrests for heroin-related offences from the NSW police service (Hall, Ross, Lynskey, Law, & Degenhardt, 2000). A convergence of estimates from these sources gives a best estimate of 74,000 dependent users (range from 67,000 to 92,000). This estimate for 1997 represents a doubling of the 34,000 estimated in 1984 to 1987 (National Drug Abuse Data System, 1988), and a 25 percent increase on the estimate of 59,000 in the period 1988 to 1993 (Hall, 1995), and gives a population prevalence of heroin dependence in Australia of 6.9 per 1000 adults aged 15 to 54 years (range from 4.6 to 8.2) (Hall et al., 2000). The evidence indicates that not only is the use of heroin increasing in Australia, so is dependence on the drug.

The Australian prevalence is within the range of recent European estimates of the population prevalence of "problem drug use" in the 15 to 64 year age group, that is, 3 (Germany and The Netherlands) to 8 (Italy, Luxembourg, and Portugal) per 1000 (European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), 2001). The majority of these European "problem drug users" are heroin dependent polydrug users (EMCDDA, 2001). The Australian data do not differ significantly from the estimated rate of heroin dependence in the UK of 7 per 1000 (with a range of 3 to 11 per 1000). In addition, the Australian rate is only marginally higher than the estimated prevalence of heroin dependence in the USA from household surveys, that is, between 4 (Kessler, McGonagle, Zhao, Nelson et al., 1994) and 7 per 1000 (Anthony & Helzer, 1991).

Thus, heroin use and dependence are significant clinical and public health problems in Australia. Consistent with data from other countries, there is good evidence that the use of heroin is becoming more common among the Australian population, as is dependence on the drug.

2.3   Characteristics of heroin users

An extensive body of research has examined the characteristics of Australian heroin users (Darke, Ross, Hando, Hall, & Degenhardt, 2000; Hando, Darke, Degenhardt, Cormack, & Rumbold, 1998; Maher, Dixon, Lynskey, & Hall, 1998).

Australian studies have repeatedly reported a ratio of male to female heroin users of approximately 2:1 (Darke & Ross, 1997; Hando et al., 1998; Loxley, Carruthers, & Bevan, 1995; Topp, Darke, Bruno, Fry et al., 2001; Topp, Kaye, Bruno, Longo et al., 2002; Swift, Maher, & Sunjic, 1999).

The mean age of heroin users in cross-sectional studies has typically been approximately 30 years, with ages ranging from the late teens to the late 40s (Darke, Ross, & Hall, 1996a; Loxley et al., 1995; Topp et al., 2001). Female heroin users are, on average, significantly younger than their male counterparts (McKetin, Darke, Humeniuk, Dwyer et al., 2000; Topp et al., 2001), which may reflect an earlier initiation into heroin use among women by older, male sexual partners. Female heroin users are also more likely than males to have a sexual partner who injects drugs (Loxley et al., 1995).

There is some evidence that, in recent years, the demographic characteristics of heroin users have changed (McKetin, Darke, Hayes, & Rumbold, 1999; McKetin et

al., 2000). Among new heroin users, the age of onset of heroin use appears to be falling (Lynskey & Hall, 1998; Darke et al., 2002). Lynskey and Hall (1998) reanalysed the Australian National AIDS and Injecting Drug Use Study (ANAIDUS) and the Australian Study of HIV and Injecting Drug Use (ASHIDU) by birth cohort, and revealed a significant decrease in age of heroin initiation by birth cohort, with the age of first use being 20.5 years for the cohort born in 1940 to 1949, and 16.5 years for those born in 1970 to 1979. A pattern of earlier initiation into injecting drug use has also been reported over the period of the Illicit Drug Reporting System (IDRS), which monitors national trends in the use of heroin and other illicit drugs (Darke et al., 2002). Recent studies in south western Sydney have identified a new cohort of younger, Indochinese heroin users (Maher et al., 1998; Maher, Sargent, Higgs, Crofts et al., 2001; Swift et al., 1999).

The overwhelming majority (approximately 70 percent) of heroin users in Australia are unemployed (McKetin et al., 1999; McKetin et al., 2000; Topp et al., 2001; Topp et al., 2002). Consistent with that finding, heroin-related fatalities are also overwhelmingly unemployed at the time of death (Darke & Ross, 1999; Darke & Zador, 1996; Zador, Sunjic, & Darke, 1996).

The picture presented here is that of the dependent heroin user. In the popular media, much is made of a hidden population of recreational heroin users that is assumed to be larger than the population of dependent users (Darke et al., 2000). Although such people exist (Lenton & Tan-Quigley, 1997), some doubt about the extent of recreational heroin use is warranted. Such users are rarely represented in Australia among overdose fatalities (Darke & Ross, 1999; Zador et al., 1996), prison heroin users (Darke, Kaye, & Finlay-Jones, 1998a; Dolan, Wodak, & Hall, 1996), or treatment entrants (Hall, Bell, & Carless, 1993).

There is a large literature on the characteristics of Australian heroin users. These cross-sectional studies, however, have typically used purposive samples from particular geographical regions. So, it is unclear to what extent the findings are applicable to the heroin using population. To obtain reliable and valid data on Australian heroin users, representative samples are required. The low population prevalence of heroin use makes it very difficult to study heroin users in general population surveys. For that reason, representative treatment samples with non-treatment comparison groups provide the optimal sampling frame for studies of heroin users.

2.4   Drug use careers of heroin users

Dependent heroin users frequently continue to use heroin for decades (Goldstein & Herrera, 1995; Hser, Anglin, & Powers, 1993). Among this group, periods of daily heroin use are interrupted by detoxification, drug treatment, and incarceration for drug-related offences. The proportion that achieves enduring abstinence from heroin after any treatment encounter appears small, although it gradually increases with age (Goldstein & Herrera, 1995; Hser et al., 1993).

Overseas studies have shown that over twenty years or more, the chances of treated dependent heroin users becoming and remaining abstinent are approximately equal to their chances of dying prematurely (approximately one third in each case). The remaining third cycles through prison, drug treatment, and active heroin use well into their 40s and 50s (Goldstein & Herrera, 1995; Hser et al., 1993, 2001). When periods of voluntary and involuntary abstinence during treatment or imprisonment are included, dependent heroin users are daily heroin users for between 40 percent (Maddux & Desmond, 1992) and 60 percent (Ball, Shaffer, & Nurco, 1983) of their drug use careers.

To date, there have been no prospective studies of Australian heroin users. As such, no longitudinal data are available on the natural history of heroin use careers in an Australian cohort. There are important differences between different countries in government policies and in the health care delivery systems available to heroin users. Treatment provision in countries such as the USA and UK, for instance, is markedly different from that provided in Australia (see Section 5.5 for more detail). In view of these differences, it would be unwise to generalise findings from overseas studies to the Australian context. Clearly, there is a need for longitudinal data on the natural history of heroin use careers in Australia.

2.5   Harms associated with heroin use

The major harms associated with heroin use in Australia broadly include fatal and non-fatal heroin overdose, blood borne viruses, psychopathology, and the effects of prescription drugs.

2.5.1   Heroin overdose

There has been a dramatic increase in heroin overdose deaths in recent years, whether this is assessed by rate per million of population at risk, or as the proportion of all deaths attributed to heroin overdose. The number of deaths attributed to heroin overdose among Australian adults aged 15 to 44 years increased from 6 in 1964 to 725 in 2000. The rate (per million adults aged 15 to 44 years) increased 65-fold from approximately 1.3 in 1964 to 84.8 in 2000, while the proportion of all deaths among adults aged 15 to 44 years attributed to heroin overdose increased from 0.08 percent in 1964 to 9.05 percent in 2000 (Degenhardt, 2001).

Victoria had the highest rate of overdose fatalities in Australia in 2000, with a rate of 122.9 per million adults aged 15 to 44 years. Overdose fatalities in Victoria accounted for 36 percent of all fatal overdoses in Australia in 2000. From 1988 to 1999, NSW consistently had the highest rate of overdose deaths in Australia. In 2000, the NSW rate was 87.1 per million adults aged 15 to 44 years (Degenhardt, 2001).

Non-fatal overdose is highly prevalent among heroin users. Darke et al. (1996a), for instance, reported that 68 percent of a sample of Sydney heroin users had experienced at least one overdose, and that 20 percent had done so in the previous year.

The typical fatal overdose victim is a single, unemployed male of approximately 30 years, who is a long term dependent heroin user and was not in treatment at the time of death (Darke & Ross, 1999; Darke & Zador, 1996, Zador et al., 1996). Whereas male and female heroin users are equally likely to have experienced a non-fatal overdose (Darke, Hall, Weatherburn, & Lind, 1999; Darke et al., 1996a), men are consistently over-represented among overdose fatalities. In 2000, men accounted for 79 percent of all opioid overdose deaths in Australia (Degenhardt, 2001). In NSW between 1992 and 1996, men accounted for 85 percent of heroin overdose fatalities (Darke, Ross, Zador, & Sunjic, 2000). The average age of those dying from overdose in Australia in 2000 was 30 years (Degenhardt, 2001). Contrary to popular perception, young, relatively inexperienced heroin users comprise only a small minority of overdose deaths. The first experience of a non-fatal overdose typically occurs several years after the initiation of heroin use (Darke et al., 1996a).

There are no prospective data on the prevalence and patterns of heroin overdose, or the impact of treatment on its incidence among Australian heroin users. Previous Australian studies of overdose have been either cross-sectional or

retrospective, and have not examined the relationship between drug treatment and the incidence of fatal and non-fatal overdose. Longitudinal data on the prevalence and patterns of overdose in an Australian cohort are essential to develop strategies to prevent or reduce its occurrence among heroin users.

2.5.2   Blood borne viruses

Blood borne viruses (primarily HIV and the hepatitises) represent a major harm associated with the injection of heroin and other drugs. In the USA and parts of Europe, sharing contaminated needles, syringes, and other injecting equipment accounts for 50 percent of new HIV notifications. In Australia, approximately 8 percent of new HIV diagnoses occur in individuals with a history of injecting drug use (National Centre in HIV Epidemiology and Clinical Research (NCHECR), 2001). The prevalence of HIV infection among people attending needle and syringe programs (NSPs) in Australia has been estimated at less than 2 percent (NCHECR, 2001). Australia's HIV prevalence among injecting drug users (IDU) is low compared to that of other countries, such as Italy and the USA.

The prevalence of hepatitis C virus (HCV) among Australian IDU is much higher than that of HIV. Among IDU attending NSPs, between 50 and 60 percent have been infected with HCV (NCHECR, 2001). During 2000, over 20,000 new cases were reported, bringing the total number of notified cases of HCV in Australia to more than 160,000 since antibody testing became available in 1990 (NCHECR, 2001). Eighty percent of new infections are considered to be the result of injecting drug use (Loxley, 2000).

HCV is spread through blood contact. In IDU populations, it is spread primarily via the shared use of injecting equipment. It is a more robust virus than HIV, and more easily spread (Crofts, Aitken, & Kaldor, 1999). The rate of needle sharing among Australian IDU has decreased since 1995, although it is still common (16 percent of IDU per month) (NCHECR, 2001). Moreover, environmental contamination with infected blood during an injecting occasion may be sufficient for the transmission of HCV, and these are contaminations of which most IDU are largely unaware (Loxley, 2000).

Comprehensive data on hepatitis B virus (HBV) prevalence, incidence, morbidity, and mortality among Australian IDU are not available. It is estimated that 30 to 60 percent of IDU have been infected with HBV (Kaldor, Plant, Thompson,

Longbottom, & Rowbottom, 1996). Over 20 years ago, the NH&MRC called for all IDU to be vaccinated against HBV because of their high risk status, but it is clear that this has not occurred. Loxley and colleagues (2000) recently reported that 70 percent of a large sample of IDU had been tested for HBV, but only 24 percent had been vaccinated. Many of those who had not been vaccinated reported that they had never heard of vaccination or been offered it (Loxley, Davidson, Heale, & Sullivan, 2000).

It is important that longitudinal studies of treatment outcome for heroin and other drug users measure health risk behaviours such as needle sharing. It is not feasible, however, to examine blood borne virus incidence and transmission within a longitudinal treatment outcome study. Samples of blood are difficult to collect among non-treatment street-recruited samples of drug users, and the cost of blood testing is prohibitive for many researchers.

2.5.3   Psychopathology

Heroin users have high rates of psychiatric morbidity, with the most common diagnoses being mood disorders, anxiety disorders, and anti-social personality disorder (ASPD) (Darke & Ross, 1997; Darke, Swift, & Hall, 1994; Swift, Williams, Neill, & Grenyer, 1990). Few Australian studies have examined the prevalence of co-existing psychiatric disorders among heroin users or the relationship between psychopathology and treatment outcome. Two studies used the General Health Questionnaire (GHQ) to estimate the prevalence of psychiatric morbidity among heroin users (Darke et al. 1994; Swift et al., 1990). Swift et al. (1990) reported that 61 percent of a sample of treatment entrants scored highly enough on the GHQ to warrant psychiatric attention. Darke et al. (1994) reported a comparable figure (58 percent) among methadone maintenance patients. Darke and Ross (1997) examined polydrug dependence and psychiatric comorbidity among heroin injectors, and revealed high levels of polydrug dependence and lifetime anxiety and mood disorders that did not vary by treatment status or gender.

Psychopathology has been strongly related to poorer treatment outcome among heroin users (Darke & Ross, 1997), although this is rarely measured in long term outcome studies (see Section 5.4 for more detail). Longitudinal research in the Australian context will address the issue of how psychopathology relates to heroin use, that is, whether levels of psychopathology decline with reductions in heroin use, or whether heroin use is a result of pre-existing psychopathology. The answers to

questions such as these have important implications for the allocation of treatment resources for heroin users, and the benefits that may be expected from interventions among this group.

2.5.4   Effects of prescription drugs

The widespread use of benzodiazepines among Australian heroin users (Ross, Darke, & Hall, 1997) is associated with higher rates of HIV risk-taking behaviour and psychopathology, poorer social functioning, poorer health, and higher levels of criminal involvement (Darke, 1994; Ross et al., 1997). Benzodiazepine use has also been linked to both fatal (Darke et al., 2000; Zador et al., 1996) and non-fatal heroin overdose (Darke et al., 1996a). The injection of benzodiazepine tablets substantially increases these elevated risks (Ross et al., 1997), with greater harm reported by those who inject benzodiazepines compared to oral users of benzodiazepines, who in turn report greater harm than non-benzodiazepine users.

Similarly, the injection of methadone syrup has been associated with abscesses and infections in injection sites, venous thrombosis, poorer general health, higher levels of psychiatric distress, and a history of heroin overdose (Darke et al., 1996c).

2.6   Trends in heroin use

In 2001, there was a major national decline in the prevalence and frequency of heroin use in Australia. The 2001 national IDRS IDU survey revealed a sharp decline in the proportion of IDU who reported heroin as their drug of choice, from 63 percent in 2000 to 48 percent in 2001. Consistent with that finding, the proportion of IDU who had used heroin in the preceding six months declined from 78 percent in 2000 to 66 percent in 2001, and the proportion of IDU who were daily users of heroin decreased from 29 percent in 2000 to 13 percent in 2001 (Topp et al., 2002). This state of affairs is likely to be short lived, however, with anecdotal evidence indicating that the supply and use of heroin in Australia have been on the increase since early 2002.

The above findings stand in sharp contrast to those of the previous decade, during which the use of heroin in Australia appeared to increase. Over the first five years of the IDRS (1996 to 2000), heroin use among IDU in NSW and Victoria increased, while key informants and IDU in these States reported increases in the number of heroin users (Darke et al., 2000). These perceived increases in heroin use

are consistent with other, independent indicators. The number of arrests for narcotic possession in Australia has increased yearly since 1996 (Darke et al., 2000), and Police and Customs have reported increased amounts and availability of heroin in Australia (Australian Bureau of Criminal Intelligence, 1999). As stated earlier, there has been a substantial increase in heroin overdose deaths, whether this is assessed by rate per million of population at risk, or as the proportion of all deaths in the 15 to 44 year age group attributed to heroin overdose. The decrease in the average age of heroin users in some recent studies, and a fall in the age at which overdose mortality peaks are consistent with an influx of new, younger heroin users (Lynskey & Hall, 1998). The earlier onset of heroin use among younger cohorts also suggests an increase in use.

Recent Australian studies have documented a diffusion of non-injecting routes of heroin use, particularly among Indochinese populations in Sydney and Melbourne (Maher et al., 1998; Maher et al., 2001; Swift et al., 1999). Heroin smoking has increased substantially among Australian heroin users. This may be a factor in an overall increase in heroin use, and can be expected to result in an increase in the number of heroin injectors (Swift et al., 1999).

The number of clients seeking treatment for opioids is greater than that for alcohol, based on the most recent census of clients from Australian treatment agencies (Shand & Mattick, in press). This is a large over-representation of opioid users, given the relative prevalence of recent alcohol use (82 percent) and heroin use (0.2 percent) in the general population (AIHW, 2002). There has also been a steady increase in the number of new entrants to MMT in NSW since 1991 (Hall et al., 2000).

2.7   Significance of longitudinal research in Australia

There have been no prospective studies of the natural history of Australian heroin users. Thus, no longitudinal data are available on the patterns and consequences of heroin use, or long term treatment outcomes among this group. Better understanding of the natural history of heroin users in terms of abstinence, drug use and treatment careers, mortality, psychiatric comorbidity, health, and criminality would inform the development of more effective harm reduction strategies and public health responses. Longitudinal data on the patterns and consequences of heroin use in an Australian cohort would also provide a measure of the burden imposed by heroin

use in Australia, and a baseline for measuring the effectiveness of treatment interventions.

2.8   ATOS

ATOS, funded by the NH&MRC, is a longitudinal cohort study of treatment outcome for heroin dependence that commenced data collection in February 2001. It is currently recruiting 600 consecutive entrants to treatment for opioid dependence from three major treatment modalities: pharmacotherapy maintenance treatment (methadone and buprenorphine), drug free residential treatment, and detoxification. A group of active heroin users who are not in treatment are also being recruited. Follow-up is at 3 months and 12 months after admission to the study. ATOS is using a range of outcome measures including heroin and other drug use, criminality, levels of psychopathology, and health status to determine the effectiveness of treatment and examine the natural history of Australian heroin users.

Key points:

- The use of heroin in Australia has increased over the past decade.
- About one in four heroin users will go on to develop dependence on the drug.
- Heroin dependence adversely affects public health and order out of all proportion to the number of people who use the drug.
- The major harms associated with dependent heroin use are heroin overdose, blood borne viruses, psychopathology, and the effects of prescription drugs.
- Longitudinal studies of treatment outcome for heroin users in Australia are essential to guide more effective treatment interventions and public health responses.
- ATOS will provide longitudinal data on treatment outcomes and the natural history of heroin users in an Australian cohort.

3.0 Why longitudinal research?

Data on the natural history of Australian heroin users are essential to better inform policy makers and providers of treatment services for heroin and other drug users. The need for treatment outcome research to improve treatment for heroin and other drug use problems has also been emphasised in several recent reports (Desmond, Maddux, Johnson, & Confer, 1995; Fletcher, Tims, & Inciardi, 1993). There is consensus among clinicians who provide or evaluate treatments for heroin and other drug users that drug dependence is often a chronic condition, characterised by cycles of increasingly heavy use, treatment, abstinence, and eventual relapse (Anglin, Hser, & Grella, 1997). McLellan and colleagues (2000), for example, have argued that drug dependence shares many of the essential features of other chronic diseases such as asthma, hypertension, depression, and diabetes. Studies of treatment outcome for heroin and other drug users should therefore reflect the chronic nature of dependent drug use.

The longitudinal research design offers the optimal strategy to evaluate the effectiveness of treatment interventions, and to determine the influence of key variables on outcomes. Longitudinal studies enable the impact of multiple factors on subsequent behaviour to be assessed, including client characteristics, treatment factors, and factors external to treatment. Cross-sectional designs do not allow the separation of these types of effects, particularly the effects of historical and social changes occurring outside treatment (Hubbard, Marsden, Rachal, & Harwood, 1989). In addition, longitudinal designs also provide strong support for evaluative and causal inferences (Flynn, Craddock, Hubbard, Anderson, & Etheridge, 1997). The development of new, multivariate longitudinal data analytic techniques and models has made high quality treatment outcome studies with long term follow-ups feasible (Horton & McKay, 2001).

3.1 Longitudinal research versus clinical trial methodology

The gold standard for obtaining data on how treatments for drug use and other psychiatric disorders affect health outcomes has historically been the randomised controlled clinical trial (Wells, 1999). Clinical trials assess efficacy, that is, whether a given treatment per se improves outcomes relative to a control or comparison condition. Achieving this goal often requires examining treatments under ideal or best practice conditions that minimise variation in treatment. To examine the

naturally occurring variation in treatment, and the natural history of drug use careers, this methodology is not appropriate. Clinical trials are likely to create artificial selection conditions and atypical treatment settings that are not directly applicable to treatments as delivered in the community, and are therefore of limited value for clinical practice and policy decisions about treatments. While the findings from clinical trials can inform policy responses by clarifying the potential therapeutic value of treatment, policy makers increasingly require information that is directly applicable to community patient samples and relevant to important societal outcomes such as long term morbidity and costs (Wells, 1999). An important feature of longitudinal treatment outcome studies is their ability to address the interests of multiple consumer audiences, including policy makers, treatment providers, and the scientific community (Fergusson & Horwood, 2001). Longitudinal studies of treatment outcome for heroin and other drug users are able to address a broad range of research questions in addition to treatment efficacy.

3.2   Benefits of longitudinal research methodology

The longitudinal research design yields a number of conceptual and analytic advantages over cross-sectional designs (Fergusson & Horwood, 2001). These include its ability to provide a natural history account of behaviours and events as they occur over time, and its capacity to provide tests of causality based on temporal sequencing. The longitudinal design also makes it possible to examine patterns of continuity and change in behaviours over time, and to examine the linkages between antecedent risk factors and consequent outcomes. In turn, this feature opens the way for the development of causal models and for tests of causal hypotheses.

In recent years, there have been many significant developments in statistical techniques for the multivariate analysis of longitudinal data (Horton & McKay, 2001). Data analytic approaches such as structural equation modelling, hierarchical linear modelling, latent growth curve modelling, and survival/event history analysis allow for the complex modelling of treatment effects, mediators and moderators of those effects, and drug use trajectories over prolonged time periods. In addition, the effects of time-varying covariates such as subsequent treatment episodes can also be determined. These recent advances in longitudinal modelling approaches offer great flexibility in examining long term treatment effects using longitudinal data with

varying numbers and intervals of assessment, and a range of different measures (Horton & McKay, 2001; Hser, Shen, Chou, Messer, & Anglin, 2001).

One of the major benefits of longitudinal research is its relative cost-efficiency, because a large number of different topics may be examined within the framework of a longitudinal design. The knowledge gained in longitudinal studies tends to be accumulative, with findings from earlier stages of research laying the foundations for future research. An additional advantage is the flexibility of longitudinal designs to address emerging research themes and issues (Fergusson & Horwood, 2001).

3.3   Methodological issues in longitudinal research

Longitudinal studies of heroin and other drug users involve a number of important methodological issues, including the potential for biases due to self-selection into treatment and subject attrition (Gerstein & Johnson, 2000). It is important to note, however, that these issues will have an impact on any study involving human subjects, and are therefore not exclusive to longitudinal studies of drug users.

3.3.1   <u>Self-selection bias</u>

A major issue concerns the source of the initial study cohort. While it would be ideal to conduct a prospective cohort study in which the natural history of heroin use and dependence was assessed from before the onset of heroin use, this approach is not feasible. To conduct such a study would require an initial longitudinal study of approximately 70,000 individuals (assuming that 0.7% of the population is dependent on heroin). Sampling from dependent heroin users entering treatment is therefore the most common and practical method.

A limitation of this approach is that individuals who enter treatment for heroin and other drug use problems are not a random sample of the general population, of the drug using population, or of the population who have drug use disorders according to standard diagnostic criteria (Gerstein & Johnson, 2000). The populations of drug users who enter and/or remain in treatment are likely to be distinctive, that is, they may be more motivated to change, or their problems may have a severity that necessitates treatment. Without a randomly assigned comparison group, it is difficult to separate a treatment effect from the effect of self-selection and unmeasured factors

extraneous to treatment (Cook & Campbell, 1979). Clearly, the inclusion of a comparison group of active drug users who are not in treatment would enhance the validity of the conclusions of any longitudinal study of treatment outcome for heroin and other drug use problems. Moreover, it would also allow the role of treatment in the natural history of drug use to be examined.

3.3.2 Non-response bias

Subject attrition is a salient issue in studies of illicit drug users, because subjects who are lost to follow-up are considered likely to be different from those who are easily located and interviewed (Desmond et al., 1995). A common assumption is that non-responders (subjects who cannot be located and interviewed at follow-up) tend to have poorer outcomes. On the other hand, it may be argued that subjects with more positive outcomes are more difficult to locate, particularly if the follow-up period exceeds one year, because relapsing subjects often return to treatment or are incarcerated, and may be interviewed relatively easily in these settings (Desmond et al., 1995). In either case, sample losses can threaten the validity of longitudinal studies by reducing the generalisability of their findings. Recent work on follow-up methodology has identified a number of effective procedures for maximising follow-up rates in studies of illicit drug users (Cottler, Compton, Ben-Abdallah, Horne, & Claverie, 1996; Dennis, Perl, Huebner, & McLellan, 2000; Desmond et al., 1995). One of the basic strategies involves the collection of detailed locator information at the start of the study, and updating these locator data at each follow-up point. Nonetheless, an important question concerns the extent to which sample losses introduce a sample selection bias that may compromise the validity of a study. Data on follow-up rates obtained by large scale longitudinal treatment outcome studies conducted overseas are presented in Section 4.0.

3.3.3 Correcting sample selection biases

A particular advantage of longitudinal research designs is that because the characteristics of subjects at the first point of observation are known, it becomes possible to test for potential sample selection biases (Fergusson & Horwood, 2001). In recent years, there has been a growing literature on methods for correcting biases introduced by sample losses in longitudinal studies (Carlin, Wolfe, Coffey, & Patton, 1999). These methods of correction have included the use of the sample selection

hazard proposed by Heckman (Berk, 1983; Heckman, 1976), the use of missing data estimation methods (Little & Rubin, 1987), and the use of sample weights to re-weight the sample to correct for systematic sample loss (Carlin et al., 1999). These procedures may be used to examine the potential effects of sample selection biases in a longitudinal study on the validity of its conclusions.

3.4   Significance of the longitudinal design

Longitudinal studies have the potential to examine a wide range of issues relating to the assessment and prevalence of disorder, treatment seeking, continuity and change in disorders, and the long term consequences of drug use and other psychiatric disorders. The major advantages of a longitudinal design are its ability to provide a natural history account of behaviours and events as they occur over time, its ability to provide tests of causality based on temporal sequencing, its cost-efficiency, and its flexibility to address emerging research questions. Moreover, longitudinal research is able to address the interests and needs of multiple consumer audiences. Improved analytic methods for examining longitudinal data can provide more accurate tests of the trajectories of drug use over time. Some of these methods are also able to accommodate time-varying covariates, which allows for the modelling of potential mediating variables over repeated assessment points. The development of specific procedures to correct for possible sample selection biases has also enhanced longitudinal research methodology.

Key points:

- Longitudinal designs offer the optimal strategy for examining the effectiveness of treatment interventions, and for determining the influence of key variables on outcomes.
- The gold standard for obtaining data on treatment outcomes has historically been the randomised controlled clinical trial. This methodology is not appropriate for examining the naturally occurring variation in treatment and the natural history of drug use careers.
- Longitudinal designs yield several advantages over cross-sectional designs, the most significant of which is their ability to provide tests of causality based on temporal sequencing.
- Recent advances in longitudinal modelling approaches have made high quality treatment outcome studies with long term follow-ups feasible.
- The development of methods to correct for sample selection biases is a particular strength of longitudinal research methodology.

4.0 Feasibility and major findings of longitudinal studies of treatment outcome for heroin and other drug users

Drug use and dependence are of great community concern, but remain among the least understood of human problems. Similarly, there is little general understanding of what can reasonably be expected from effective drug treatment interventions, or of the essential features of effective treatment. Much of what is known about typical treatment outcomes comes from a series of large scale longitudinal cohort studies conducted overseas over the past 30 years (Table 2). These treatment outcome studies have shown that existing behavioural, psychosocial, and pharmacological treatments can effectively reduce drug use and help manage drug dependence (Simpson, 1997).

To date, there have been no longitudinal cohort studies of treatment outcome or the natural history of drug use careers in the Australian context. There are, however, inherent difficulties in generalising from studies carried out in other countries. The characteristics of drug users are likely to differ in many respects from those in Australia, as are the types of treatment provided.

This section presents an overview of the research methods and key findings from four major large scale follow-up studies of drug treatment: the Drug Abuse Reporting Program (DARP), Treatment Outcome Prospective Study (TOPS), Drug Abuse Treatment Outcome Study (DATOS), and the UK National Treatment Outcome Research Study (NTORS). These studies were chosen for detailed discussion because they are the most widely published and influential studies of drug treatment evaluation. They have made significant contributions to the state of knowledge on treatment effectiveness, and to treatment policy, programming, and research in the USA and UK.

Table 2. Follow-up rates obtained by large scale longitudinal treatment outcome studies

Study	Country	Description	Modality	Follow-up time points	Follow-up rates	Intake sample (N)
De Leon et al. (1982)	USA	Longitudinal cohort study of admissions to treatment in 1970-1971 and 1974-1975	TC	2 years 5 years	75% 84%[a]	N = 424 N = 307
Goldstein & Herrera (1995)	USA	Evaluation of the long term patterns and consequences of heroin use among admissions to treatment in 1969-1971	MMT, MRT	22 years	24%	N = 1019
California Civil Addict Program (CAP) McGlothlin et al. (1977) Hser et al. (1993, 2001)	USA	Evaluation of the long term patterns and consequences of drug use among admissions to CAP in 1962-1964	Intensive parole supervision	10 years 24 years 33 years	76% 61% 42%	N = 581
Drug Abuse Reporting Program (DARP) Simpson & Sells (1982, 1990)	USA	Longitudinal cohort study of admissions to treatment from 1969-1974	MMT, TC, ODF, ODT	3 years 6 years 12 years	77%[b] 73% 70%	N = 6402 N = 6402 N = 697
Treatment Outcome Prospective Study (TOPS) Hubbard et al. (1989)	USA	Longitudinal cohort study of admissions to treatment from 1979-1981	MMT, TC, ODF	3 months 12 months 2 years 3-5 years	80%[c] 79% 76% 65%	N = 2111 N = 3270 N = 1159 N = 1000
Services Research Outcomes Study (SROS) Schildhaus et al. (2000)	USA	Longitudinal study of admissions to treatment from 1989-1990	MMT, TC, ODF, IDT	5 years	59%	N = 3047
Drug Abuse Treatment for AIDS-Risk Reduction (DATAR) Simpson et al. (1997)	USA	Longitudinal study of admissions to treatment from 1990-1993	MMT	12 months	61%[d]	N = 711

Drug Abuse Treatment Outcome Study (DATOS) Hubbard et al. (1997)	USA	Longitudinal cohort study of admissions to treatment from 1991-1993	MMT, TC, ODF, STI	12 months	70%[e]	N = 4229
California Drug and Alcohol Treatment Assessment (CALDATA) Gerstein et al. (1994)	USA	Longitudinal study of admissions to treatment from 1991-1992	MMT, MRT, TC, ODF	15 months	61%	N = 3055
National Treatment Improvement Evaluation Study (NTIES) Gerstein et al. (1997)	USA	Longitudinal study of admissions to treatment from 1992-1995	MMT, ODF, TC, CF	12 months	83%	N = 6593
National Treatment Outcome Research Study (NTORS) Gossop et al. (1997)	UK	Longitudinal study of admissions to treatment in 1995	MMT, MRT, TC, IDT	6 months 12 months	75% 72%	N = 1075

MMT = methadone maintenance treatment, MRT = methadone reduction treatment, TC = therapeutic community, ODF = outpatient drug-free, ODT = outpatient detoxification, IDT = inpatient detoxification, STI = short-term inpatient treatment, CF = correctional facilities.

The follow-up rates presented in this table refer to the percentage of clients who *completed interviews* at the relevant follow-up time points.
For studies in which selected samples of clients were targeted for follow-up, N = the size of the target sample.

a. The 1974-75 (N = 424) cohort was followed up 2 years after treatment entry, and the 1970-71 cohort (N = 307) was followed up 5 years after treatment entry.
b. Samples of DARP treatment clients were *selected* for follow-up.
c. Samples of TOPS treatment clients were *selected* for follow-up.
d. 61% of a *selected* DATAR follow-up sample was successfully interviewed at 12 month follow-up.
e. 70% of a *selected* DATOS follow-up sample was successfully interviewed at 12 month follow-up.

4.1   DARP

DARP was the first comprehensive national evaluation of drug treatment effectiveness to be carried out in the USA. Between 1969 and 1974, data were collected on over 44,000 primarily heroin dependent clients from treatment programs representing four treatment modalities (MMT, therapeutic communities, outpatient drug free treatment, and detoxification). Data were also collected on individuals who applied for admission but did not return for treatment. DARP included intake measures of client demographic and background variables, and pre-treatment, during treatment, and post-treatment measures of heroin and other drug use, criminal involvement, and employment. Data were collected at intake, during treatment, and at a series of follow-ups from 3 to 12 years after treatment (Simpson & Sells, 1990).

The first series of DARP post-treatment follow-up studies was conducted an average of 6 years after admission to treatment, and focused on outcomes in the first 1 to 3 years following DARP treatment (Simpson, 1993; Simpson & Sells, 1982, 1990). A total of 6,402 clients admitted in three successive years were selected for follow-up, of whom 73 percent were successfully located and interviewed. The second wave of DARP follow-up interviews occurred an average of 12 years after treatment admission, and focused on long term outcomes and drug use careers. A sample of 697 clients, all of whom were daily heroin users at intake to DARP treatment, were selected for 12 year follow-up from the sample of completed 6 year interviews. Seventy percent of this target group was successfully located and interviewed.

4.1.1   <u>DARP: Major findings</u>

DARP produced many research findings of relevance to US drug policies. Positive treatment outcomes, in terms of reductions in drug use and criminal activity, were produced in the MMT, therapeutic community, and outpatient drug free treatment modalities, but not in detoxification programs or among those who enrolled but did not return for treatment (cf. TOPS, DATOS, and NTORS). There were no significant differences in outcomes among the three major modalities. In the year following treatment, abstinence from daily heroin use was reported by 64 percent of clients in methadone programs, 61 percent of those in therapeutic communities, and 56 percent of those in outpatient drug free programs. In the first 3 years after treatment, 63 percent of pre-treatment daily heroin users reported any heroin use, and 47 percent reported daily use. There was no significant change in the percentage of

subjects reporting daily heroin use between the 6 and 12 year follow-up interviews (Simpson & Savage, 1980).

Positive outcomes were predicted by the length of time spent in treatment. A minimum of 90 days was needed to produce reductions in drug use and criminal activity; beyond the first 90 days, outcomes improved with time spent in treatment. When the criteria of no drug use and no criminality in the 12 months after treatment were used, none of the treatment modalities was significantly different to the intake only group for clients in treatment less than 90 days (Simpson & Sells, 1982).

DARP demonstrated that methodologically sound longitudinal research could be successfully carried out with dependent heroin users to determine the effectiveness of treatment (Fletcher, Tims, & Brown, 1997). In addition, DARP studies also identified outcome patterns related to subsequent treatment episodes (Simpson & Savage, 1980), criminal activity (Savage & Simpson, 1981), and employment (Simpson, 1981), and provided data on the natural history of heroin use careers in a treated population (Joe, Chastain, & Simpson, 1990).

4.2   TOPS

The primary goal of TOPS was to provide longitudinal data on clients entering US drug treatment programs, to determine short and long term treatment outcomes. TOPS was intended to expand on DARP by obtaining more data on client attributes, program environments, and services delivered in treatment. In its design and core data elements, it built directly on the methodological progress made by DARP (Fletcher et al., 1997).

TOPS used a prospective cohort design based on more than 11,000 clients who entered treatment in 1979, 1980, and 1981. Treatment programs representing three treatment modalities (MMT, outpatient drug free, and long term residential treatment) were purposely selected for participation in TOPS. The three annual admission cohorts were interviewed at intake and one month after entry to treatment, then at three month intervals during treatment. Samples of clients in each admission cohort and each modality were selected to be interviewed at specific intervals after *termination* of treatment: 3 months, 12 months, 2 years, and 3 to 5 years after termination (Hubbard et al., 1989).

Client data included intake measures of demographic and background variables, drug use history, and previous treatment experience, and pre-treatment,

during treatment, and post-treatment measures of drug use, criminality, depression, social and community support, and employment. TOPS provided a framework for studies of changing drug use patterns, psychiatric comorbidity, criminal behaviour and the impact of legal involvement, and cost-effectiveness (Hubbard, 1992).

TOPS follow-up rates were found to vary slightly by treatment modality, although they were high in all modalities. Three month follow-up interviews were completed with 75 percent of methadone, 81 percent of residential, and 84 percent of outpatient drug free clients. Similar rates were obtained at 12 month follow-up: 75 percent, 81 percent, and 82 percent, respectively. The rates decreased to 70 percent, 78 percent, and 79 percent for the 2 year follow-up, and to about 65 percent for the 3 to 5 year follow-up (Hubbard et al., 1989).

4.2.1 TOPS: Major findings

As in DARP, TOPS showed that treatment was effective in reducing the use of heroin and other illicit drugs during and after treatment. Significant reductions in the prevalence of heroin use were reported for clients who remained in treatment for at least three months, and were most substantial for clients in MMT and residential programs, 70 percent of whom either decreased their level of use or ceased heroin use in the year after treatment. TOPS also revealed that patterns of drug use had changed substantially from DARP, with less daily use of heroin and greater polydrug use. Nevertheless, heroin was the primary drug used by 77 percent of TOPS admissions (Hubbard et al., 1989).

TOPS treatment was associated with a significant decline in criminal activity. In each of the modalities, levels of acquisitive crime declined substantially during treatment, and remained substantially lower than intake levels following treatment. Those clients who reported legal involvement (including legal pressure to enter treatment) at admission remained in treatment longer than those without legal involvement. Thus, TOPS showed that legal coercion to enter treatment could be effective in interrupting early criminal and drug use careers (Hubbard et al., 1989).

Cost-benefit studies were carried out on each of the TOPS modalities based on a cost of illness framework. Within cost of illness methodology, costs refer to the tangible consequences of drug use disorders that can be assigned monetary values. The findings indicated that when the crime-related costs of drug use (costs to victims, criminal justice costs, crime career – productivity costs, and losses from theft) were

calculated, treatment was cost-effective. In most cases, the cost of treatment was recovered during treatment, and further cost-benefits accrued as a result of reductions in post-treatment drug use (Harwood, Collins, Hubbard, Marsden, & Rachal, 1988). It is important to note, however, that these studies estimated the economic benefits of treatment only in terms of crime reduction. They did not consider the potential benefits associated with improvements in other behaviours during and after treatment, such as an increase in the legitimate productivity of drug users who were not criminally active, or a reduction in the need for other social services. Moreover, these analyses did not consider the health-related benefits of treatment or the intangible costs of drug-related crime.

4.3   DATOS

DATOS is a prospective cohort study of over 10,000 adults who entered US drug treatment programs between 1991 and 1993. It examined treatment outcomes in four modalities (MMT, long term residential, outpatient drug free, and short term inpatient treatment). Participating treatment programs were purposely selected to represent treatment as delivered in typical stable programs. In comparison to the focus of DARP and TOPS on overall treatment effectiveness and the relationship between treatment retention and outcomes, DATOS sought to determine the complex relationships between psychiatric impairment, treatment process, service environment, and treatment outcome (Hubbard, Craddock, Flynn, Anderson, & Etheridge, 1997).

Client data were collected at intake, during treatment, and at 12 months following treatment *termination*. DATOS included intake measures of drug use history, severity of dependence, health status, psychiatric status, social functioning, criminal involvement, employment status, income and expenditures, and demographics. Nine outcome measures were chosen to describe changes in drug use and behavioural functioning between the pre-treatment and follow-up years. Drug use was assessed in terms of self-reported weekly or more frequent heroin, cocaine, cannabis, and alcohol use during the follow-up period. Behavioural functioning was measured in terms of self-reported criminal involvement, suicidal thoughts – attempts, health status, employment status, and sexual risk-taking during the follow-up year. The DATOS admission cohort consisted of 10,010 clients, almost 50 percent of whom were randomly selected (with stratification) for interview 12 months after treatment termination. Seventy percent of the target follow-up sample was successfully located

and interviewed (Flynn, Craddock, Hubbard, Anderson, & Etheridge, 1997). An extended follow-up is in progress to collect data on clients over a 4 year period.

4.3.1   <u>DATOS: Major findings</u>

DATOS reported significant reductions in heroin, cocaine, and cannabis use between the pre-treatment and follow-up years, in each of the treatment modalities. The proportion of MMT clients reporting weekly or more frequent use of heroin during the preceding year, for instance, declined from 89 percent at intake to 28 percent at 12 month follow-up. Among long term residential and outpatient drug free clients, the prevalence of weekly or more frequent cocaine use fell by 50 percent from intake to follow-up. The most substantial reductions in drug use were found among clients who remained in treatment for at least 3 months (Hubbard et al., 1997).

Among MMT clients, the rates of criminal involvement and sexual risk-taking in the follow-up year fell to 50 percent of the rates reported at treatment entry. No significant changes in employment, health status, or suicidal thoughts or attempts were found among this group. In the residential, outpatient drug free, and short term inpatient treatment modalities, substantial reductions in criminal involvement, sexual risk-taking, and suicidal thoughts or attempts from intake to 12 month follow-up were reported, but there were no significant changes in employment or health status.

An important focus of DATOS was the drug use and treatment histories of clients. DATOS revealed considerable heterogeneity of drug use and treatment career characteristics among clients in each of the modalities. In particular, individuals who were dependent on heroin, cocaine, and alcohol demonstrated substantial variability in their histories of treatment use. Heroin dependence was associated with the longest treatment careers, while alcohol dependence was associated with the shortest treatment careers. Clients across the dependence groups had received treatment from a diverse range of modalities (Anglin et al., 1997).

Multiple drug use and an early onset of heroin and/or cocaine use were significantly related to greater levels of prior treatment exposure. More extensive prior treatment exposure was also associated with higher levels of injecting drug use, sex work, and criminal involvement. Many DATOS clients had multiple previous treatment admissions, and many subsequently re-entered treatment during the follow-up year. In general, the data indicated that many drug users do not enter treatment until they are well into a lifestyle committed to drug use (Anglin et al., 1997).

4.4   NTORS

NTORS is the first large scale prospective study of treatment outcomes for drug use problems to be conducted in the UK. It follows a cohort of more than 1,000 clients treated for drug use problems in four treatment modalities during 1995. NTORS was designed to provide longitudinal data on the impact of treatment in terms of drug use, psychological, social, and health changes among clients.

Fifty-four treatment programs across England were purposely selected to participate in NTORS. Residential treatment modalities comprised inpatient detoxification units and residential rehabilitation agencies, and community modalities comprised methadone maintenance and methadone reduction programs. The four modalities were chosen as being representative of the main national treatment types in the UK, both in terms of the numbers of patients receiving such treatments and/or the resources allocated to them. The NTORS admission cohort consisted of 1,075 clients who entered treatment during 1995 (Gossop, Marsden, Stewart, Edwards et al., 1997).

NTORS uses a prospective cohort design to assess treatment outcome and the natural history of drug use careers. Data on the whole NTORS cohort have been collected at admission to treatment, and at 6 and 12 months after treatment *entry*. NTORS reported follow-up rates of 75 percent and 72 percent at 6 and 12 months, respectively. Since its inception, NTORS has been extended to follow-up clients at 2 to 3 years and 4 to 5 years after treatment entry. Intake and follow-up data on patterns of drug use, health risk behaviour, readiness for treatment and motivation to change, physical health problems, psychiatric symptoms, criminality, and treatment history have been collected via structured interviews.

4.4.1   NTORS: Major findings

Reductions in drug use from intake to 6 month follow-up were found in terms of the percentage of clients who were using drugs, and the quantity and frequency of drug use. In all modalities, there was a significant reduction in the proportion of clients regularly using heroin and non-prescribed methadone, and in the frequency and amount of illicit opiates being used. A significant reduction in the use of cocaine was also observed at 6 month follow-up. There was a substantial reduction in the proportion of clients who were injecting drugs at 6 month follow-up, and in the sharing of injecting equipment among drug injectors (Gossop et al., 1997).

At 6 month follow-up, improvements were reported in the number and severity of physical and psychological problems among the cohort. Criminal activity was also significantly reduced, particularly among clients who had completed residential treatments and those who were still receiving methadone treatments. Clients who were still in treatment at 6 month follow-up showed more positive outcomes than those who had left treatment, in terms of improvements in their drug use, physical and psychological health, and criminal activity (Gossop et al., 1997).

From intake to 12 month follow-up, there were significant reductions in drug use in terms of the percentage of clients who were using drugs, and in terms of the frequency of use. In all treatment modalities, abstinence rates for illicit opiate use more than doubled. The proportion of clients who were injecting drugs, and the rate of sharing of injecting equipment among drug injectors also declined significantly. There was a strong positive association between length of time in treatment and improved post-treatment outcome, which is consistent with the findings of earlier treatment outcome studies (Gossop, Marsden, & Stewart, 1998).

NTORS reported substantial improvements in the overall health status of the cohort at 12 months, and reduced rates of specific symptoms. In addition, improvements in psychiatric symptoms were found among clients in all modalities. At 12 month follow-up, there were substantial reductions in the number of crimes committed and in the number of clients who engaged in crime. A strong positive association was found between reductions in drug use, particularly heroin use, and reductions in acquisitive property crime and drug selling. The savings to society in terms of reduced criminal behaviour and reduced demands on the criminal justice system were estimated to be worth £5.2 million per year. It was also estimated that for every extra £1 spent on treatment, there is a return of more than £3 in terms of cost savings associated with lower levels of victim costs of crime, and reduced demands on the criminal justice system (Gossop et al., 1998).

The findings from NTORS show substantial post-treatment improvements in drug use, criminality, and physical and psychological health made by people entering treatment for drug use problems in the UK. Recent NTORS studies have also specifically examined outcome patterns in relation to rates of non-fatal overdose (Stewart, Gossop, & Marsden, 2002), mortality rates (Gossop, Marsden, Stewart, & Treacy, 2002), and alcohol use (Gossop, Marsden, Stewart, & Rolfe, 2000).

4.5   Limitations of previous studies

The major large scale treatment outcome studies have shown that existing treatments can effectively reduce drug use and dependence. They have also demonstrated that longitudinal research can be successfully conducted with dependent heroin users to determine treatment effectiveness and outcomes. These cohort studies obtained high follow-up rates, and initial follow-up rates were highly predictive of later follow-up rates, even after considerable periods of time.

A limitation of the studies reviewed here, however, is that they used treatment entrants from purposely selected treatment programs, with no attempt at representative sampling. None of these studies included a comparison group of active heroin users who were not in treatment at admission to the study. Moreover, these studies did not comprehensively examine psychiatric morbidity using valid and reliable instruments. For instance, TOPS included only three indicators of depression: one general indicator of depression, one measure of suicidal thoughts, and one measure of suicide attempts. This is a serious omission, in view of the high prevalence of psychiatric morbidity among heroin users (see Section 5.4).

It would be unwise to generalise findings from one country to another, given the differences between different countries in government policies and health care delivery systems. The US system of social service provision, for example, is considerably more restrictive than the Australian system, with access to benefits being very limited for dependent heroin and other drug users. Similarly, treatment provision in the USA and UK is substantially different from that provided in Australia. Longitudinal studies in the Australian context are needed to determine treatment effectiveness and the burden imposed by heroin use in Australia.

Key points:

- Much of what is known about treatment outcomes for heroin and other drug use problems comes from a series of large scale studies conducted overseas.
- Overseas cohort studies have shown that existing treatments for drug use problems can be effective.
- These studies have obtained high follow-up rates, and initial follow-up rates have been highly predictive of later follow-up rates.
- Methodological issues and differences between different settings limit the generalisability of previous cohort studies.
- To gain an understanding of the burden of heroin use in Australia, longitudinal cohort studies of Australian heroin users are essential.

5.0 Domains for longitudinal research

Heroin use and dependence are associated with a constellation of problems, each of which is of relevance when assessing treatment outcome. Thus, there are a number of key research domains that should be addressed by longitudinal studies of treatment outcome for heroin users. These include patterns of heroin and other drug use, route of administration, criminality, psychiatric comorbidity, mortality, physical health status, and the economic burden imposed by heroin use. Longitudinal data on these areas of assessment are essential to determine the impact of treatment and the long term patterns and consequences of heroin use.

5.1 Patterns of drug use

Factors that precede the onset and escalation of heroin use careers are likely to have an impact on the nature and severity of drug use and other problems that may be experienced by heroin users. In addition to examining current patterns of drug use, it is vital that longitudinal studies of treatment outcome for heroin users take into account their previous drug use behaviours. These should include the age of onset of heroin and other drug use, the age of onset of injecting drug use, and their drug use and injecting histories.

5.1.1 Antecedents of heroin use

Few studies have examined the risk factors and life pathways that lead people to use and become dependent on heroin, because the relatively small number of heroin users in the population makes it difficult to study these processes (Hall et al., 1999). There is, however, a large literature on risk factors for early alcohol and cannabis use in adolescence and early adulthood. While these studies have typically examined heavy alcohol and cannabis users, there is good evidence that young people who are the earliest initiators and heaviest users of alcohol and cannabis are those who are most likely to use heroin and cocaine (Kandel, 1993). These studies have identified a wide range of factors that predict an increased risk of early illicit drug use, such as parental and sibling drug use, impulsive or problem behaviour during childhood, and affiliating with delinquent or drug using peers (Hawkins, Catalano, & Miller, 1992). Exposure to these risk factors puts young people at an increased risk of commencing illicit drug use at an early age, and of developing serious problems related to their drug use (Hall et al., 1999). The initiation of heroin use usually occurs after a long

history of drug use, with early intoxication with alcohol at age 12 or 13 being the most common starting point of the heroin use career (Darke et al., 1998a).

5.1.2 Initiation of illicit drug use

Cross-sectional studies have consistently reported that the first use of heroin typically occurs in the late teen years, with regular use commencing within 12 to 24 months of the first use (Crofts, Louie, Rosenthal, & Jolley, 1996; Darke et al., 1998a; Swift et al., 1999; Topp et al., 2001).

In Australia, the age of initiation of illicit drug use appears to be declining. Degenhardt and colleagues (2000) recently examined birth cohort trends in the prevalence of use and the age of initiation to use of cannabis, amphetamines, LSD, and heroin, and revealed that more recent cohorts are more likely to have used these drugs at some point in their lives, and more likely to have done so at an earlier age than young people in earlier birth cohorts. In addition, there is evidence that, among new heroin users, the age of first use of heroin is falling (Lynskey & Hall, 1998). There is considerable consistency between this pattern and those observed for cannabis, amphetamines, and LSD. Individuals born in more recent cohorts are much more likely to report using these drugs by the age of 15 years, and report a lower mean age of first use (Degenhardt et al., 2000). These data are similar to those of a recent US study of population cohort trends in the use of alcohol, tobacco, cannabis, and LSD (Johnson & Gerstein, 1998).

These findings have important implications for public health, in that a greater number of young Australians may be at an increased risk of experiencing a range of adverse consequences. Early initiation of heroin and other drug use has been linked to an increased likelihood of negative outcomes including escalating drug use, poorer psychological functioning, criminal involvement, and reduced life opportunities (Anthony & Petronis, 1995; Chen & Kandel, 1995; Fergusson & Horwood, 1997).

5.1.3 Initiation of injecting drug use

Consistent with the above findings, a pattern of earlier initiation into injecting drug use has been identified by recent Australian studies (Darke et al., 2002; Lynskey & Hall, 1998; McKetin et al., 2000; Topp et al., 2001; Topp et al., 2002). In the 2001 national IDRS, for instance, the mean age of first injecting drug use was 20 years for IDU aged older than 25 years, and 16 years for those aged 25 years or younger. There

was a significant correlation between age at the time of interview and age at the time of first injection, indicating that successive cohorts of IDU are initiating injecting at an earlier age (Topp et al., 2002). These data are consistent with analyses of initiation into injecting from the National Household Surveys (Lynskey & Hall, 1998), and with the declining age of onset of heroin overdose deaths in Australia over successive birth cohorts (Hall, Degenhardt, & Lynskey, 1999).

It should not be assumed that heroin is the first drug injected by regular heroin injectors (Crofts et al., 1996; Darke, Kaye, & Ross, 1999; Swift et al., 1999). Large proportions of heroin users in Australia have injected amphetamines prior to the commencement of heroin use. Crofts et al. (1996) reported that 77 percent of a sample of young IDU had first injected amphetamines (mean age 16 years), with a steady movement thereafter to heroin as their most commonly injected drug. More recently, Darke et al. (1999) reported that 40 percent of a sample of current primary heroin users had first injected amphetamines, while Swift et al. (1999) reported a figure of 46 percent among Caucasian heroin users in south western Sydney. Regional and ethnic patterns appear to influence transitions between the injection of amphetamines and heroin, in that all of the Indochinese heroin users in the Swift et al. (1999) sample had first injected heroin.

Over the period of the IDRS, the proportion of IDU in NSW nominating heroin as the first drug injected has steadily increased (Darke et al., 2002). In 1996, 45 percent of NSW IDU reported heroin as the first drug they had injected, while 46 percent reported amphetamines. By 2001, the corresponding figures were 64 percent and 33 percent. Moreover, younger IDU are significantly more likely to commence injecting with heroin. In the 2001 NSW IDRS IDU sample, 81 percent of respondents aged 25 years or younger reported heroin as the first drug injected, compared to 60 percent of those aged over 25 years. Conversely, a significantly greater proportion of those aged over 25 years had initiated injecting with amphetamines (Topp et al., 2002).

5.1.4   <u>Route of heroin use</u>

A major change in patterns of heroin use in recent years has been in the route of administration. As stated in Section 2.6, heroin smoking has become more common among many Australian heroin users. Heroin smokers, however, are at high risk of making the transition to injecting heroin (Swift et al., 1999) as their

dependence increases. It is important to note that the smoking of heroin can induce dependence (Swift et al., 1999), and can result in fatal overdose (Darke & Ross, 1999) (see Section 5.2 for more detail).

5.1.5   Polydrug use

Polydrug use is the norm among heroin users, and among illicit drug users in general (Darke & Hall, 1995; Darke & Ross, 1997; Loxley et al., 1995). Darke and Hall (1995) specifically examined polydrug use among illicit drug users, and revealed that primary heroin users had used an average of 8.5 different drug classes in their lives, and 5.2 different drug classes in the previous 6 months. Among primary heroin users, the most widely used drugs other than heroin were tobacco (94 percent), cannabis (84 percent), alcohol (78 percent), and benzodiazepines (64 percent). Similarly, recent national IDRS IDU surveys have reported patterns of extensive polydrug use among Australian drug users (Topp et al., 2001; Topp et al., 2002).

Large proportions of Australian heroin users also meet criteria for dependence on other drugs, including alcohol, amphetamines, and benzodiazepines (Darke & Ross, 1997; Ross, Darke, & Hall, 1996; Ross et al., 1997). Of particular concern is the widespread oral and parenteral use of benzodiazepines (Ross et al., 1997). Concomitant use of benzodiazepines, and in particular their injection, is associated with substantially higher levels of harm. Of further concern is the widespread injection of methadone syrup among Australian heroin users (Darke et al., 1996c; Darke, Topp, & Ross, 2002).

Polydrug use has been strongly related to an increased risk of overdose among primary heroin users (Darke & Ross, 1999; Darke & Zador, 1996; Zador et al., 1996). Concomitant use of heroin with other central nervous system (CNS) depressant drugs predominates among heroin overdose deaths. The evidence of polydrug use in fatal heroin overdose is consistent with the experience of non-fatal overdose victims, especially in terms of alcohol and benzodiazepine use (Darke et al., 1996a). Overall, overdoses involving heroin use alone are in the minority.

In addition to an increased risk of heroin overdose, multiple drug use among primary heroin users has been associated with higher rates of needle sharing, poorer psychological and social functioning, poorer health, and higher levels of criminality (Darke & Hall, 1995; Darke et al., 1994; Ross et al., 1997).

5.1.6   Drug use careers

Dependent heroin users frequently go through repeated cycles of treatment, abstinence, and relapse over the course of their drug use careers (Hser, Anglin, Grella, Longshore, & Prendergast, 1997; Hser et al., 1993). Data from long term follow-up studies conducted in the USA indicate that achieving long term abstinence from heroin is a very slow process, and that, for many heroin users, heroin dependence is a lifelong condition.   Hser and colleagues (1993, 2001), for instance, examined longitudinal patterns of heroin and other drug use, health, criminal involvement, and mortality in a large cohort of dependent heroin users who were admitted to the California CAP from 1962 to 1964. The sample was first interviewed 10 years after program admission as part of an evaluation of the CAP (McGlothlin et al., 1977), and was subsequently interviewed 24 years (Hser et al., 1993) and 33 years (Hser et al., 2001) after treatment entry. The follow-up studies revealed marked reductions in daily heroin use and incarceration, and increases in abstinence after CAP admission up to the 10 year follow-up interview. Thereafter, the sample showed little treatment participation and essentially no changes in heroin use status. Between the 24 and 33 year follow-up interviews, 7 to 9 percent of the sample used heroin daily, 2 to 3 percent engaged in occasional heroin use, and 20 to 22 percent reported abstinence. The remainder of the cohort was deceased (49 percent), incarcerated (4 to 7 percent), in MMT (2 to 6 percent), or lost to follow-up (12 percent). While a minimum of five years of abstinence was found to considerably reduce the likelihood of future relapse, 25 percent of those who reported more than fifteen years of abstinence still relapsed.

In addition to very high mortality rates, the CAP sample showed high overall rates of disability, hepatitis, excessive drinking, cigarette smoking, and other drug-related problems. Even among the surviving members of the cohort, problems associated with long term heroin use and dependence were severe (Hser et al., 2001). Consistent with the findings from earlier studies (Goldstein & Herrera, 1995; Simpson, Joe, Lehman, & Sells, 1986), these results reveal a cyclical pattern of treatment, abstinence, and relapse in the natural history of heroin use careers.

More severe drug use career characteristics and risk behaviours, including early onset of heroin use, polydrug use, injecting drug use, engagement in sex work, and criminal involvement, have been associated with poorer treatment outcomes in terms of continued or resumed drug use (Hubbard et al., 1989; Simpson et al., 1986). Drug use career profiles have important implications for clinical practice. Developing

an understanding of the drug use career patterns of Australian heroin users is essential to better inform providers of treatment services and interventions.

5.1.7   Measuring illicit drug consumption

The accurate measurement of recent drug use is an essential component of treatment and research among illicit drug users. Accurate consumption data are necessary for clinical purposes, and to determine the effectiveness of treatment. Because clinicians and researchers require information on recent use across a wide range of drug classes, any method of collecting such data must also be efficient (Darke, Heather, Hall, Ward, & Wodak, 1991).

One method of determining recent drug consumption is the use of urinalysis. This method has the advantage of not relying on the self-report of the client. There are, however, a number of problems in relying on urinalysis results for clinical or research purposes. First, urinalysis may not detect drug use where the client is using irregularly. Typically, the client must have used the drug in the 72 hours prior to providing a urine specimen (Kilpatrick, Howlett, Sedgwick, & Ghodse, 2000; Schwartz, 1998). This is particularly evident in the case of cocaine, where use must have occurred in the 12 hours prior to testing. A second limitation is that some drugs (for example, hallucinogens) are typically not detected due to the small amounts ingested. Third, urinalysis is not able to detect levels of drug use, meaning that it is a relatively insensitive measure of behaviour change (Darke et al., 1991).

These limitations apply equally to other existing biochemical markers of drug use, namely hair and venous blood samples. These biochemical markers cannot assess drug use histories, drug use frequency over extended time frames, levels of drug use, or patterns of concomitant use. Samples of urine and blood are also difficult to collect among non-treatment street-recruited samples of drug users, and the cost of such analyses is prohibitive for many researchers (Darke, 1998).

Given the limitations of the existing biochemical indicators, clinicians and researchers must rely on the self-reported drug use of clients to obtain detailed information on current consumption. In contrast to biochemical methods, self-report is both efficient and convenient (Kilpatrick et al., 2000). There is a large literature on the legitimacy of the behavioural self-reports of drug users (cf. Darke, 1998). Overall, these studies indicate that, in research contexts, IDU typically provide reliable and valid responses to questions about their drug use, even at long recall periods. While

inconsistencies do occur, in many cases these are in the direction of self-report giving higher levels of drug use than detected by independent measures such as urinalysis. An additional benefit of self-report is that researchers are able to guarantee the confidentiality of the respondent, and to ensure that any disclosure of drug use will have no legal consequences and will not affect their treatment.

The Drug Use Section of the Opiate Treatment Index (OTI) provides an estimate of drug use in the preceding month. This measure has been widely used in studies of illicit drug users, and has excellent psychometric properties. It has 0.90 test-retest reliability, a kappa of 0.70 between self-reported drug use and urinalysis, and a kappa of 0.83 between self-reported drug use and collateral reports (Darke et al., 1991). Moreover, it is easily administered, and has both clinical and research applications. The major advantage of this measure is that it enables reliable and valid data on drug consumption to be quickly obtained over a large range of drug classes. When used in conjunction with other indicators such as hair analysis, it can provide clinicians and researchers with an accurate picture of the degree of drug involvement of the respondent (Darke et al., 1991).

Key points:

- The age of onset of injecting drug use is declining, with initiation of injecting among younger cohorts occurring in the mid-teen years.
- Polydrug use is the norm among illicit drug users, and is strongly associated with an increased risk of overdose and other harms.
- Dependent heroin users frequently continue to use heroin for decades, and go through repeated cycles of treatment, abstinence, and active heroin use throughout their drug use careers.
- There are a number of serious problems in relying on biochemical indicators for the measurement of illicit drug consumption.
- Self-report yields reliable and valid data on the use of licit and illicit drugs.

5.2   Route of administration

With the advent of the HIV pandemic, the emphasis of treatment interventions for drug users shifted from drug use per se to the methods by which people use drugs (Strang, Des Jarlais, Griffiths, & Gossop, 1992). Route of administration is known to influence the immediacy, intensity, and duration of the pharmacological effect of heroin (Jenkins, Keenan, Henningfield, & Cone, 1994). The route of heroin use also has important implications for the nature and severity of problems that may be experienced by the user. Heroin injecting has been associated with a higher level of dependence (Gossop, Griffiths, Powis, & Strang, 1992) and risk of overdose than other routes of administration (Gossop, Griffiths, Powis, Williamson, & Strang, 1996). Blood borne virus transmission through the sharing of injecting equipment has also been well documented. Moreover, the act of injecting per se carries the risk of vascular damage (Darke, Ross, & Kaye, 2001).

5.2.1   <u>Non-injecting routes of heroin administration</u>

Over the past decade, increases in non-injecting heroin use have been reported in England (Griffiths, Gossop, Powis, & Strang, 1994), Ireland (Smyth, O'Brien, & Barry, 2000), The Netherlands (van Ameijden, van den Hoek, Hartgers, & Coutinho, 1994), Spain (de la Fuente, Lardelli, Barrio, Vicente, & Luna, 1997; de la Fuente, Saavedra, Barrio, Royuela et al., 1996), Switzerland (Stohler, Dursteler-Mac Farland, Gramespacher, Petitjean et al., 2000), and the USA (Des Jarlais, Casriel, Friedman, & Rosenblum, 1992).

In Australia, injection has historically been considered the dominant route of heroin administration (Darke, Cohen, Ross, Hando, & Hall, 1994). Recent research on out-of-treatment heroin users in Cabramatta, however, has documented the emergence of smoking or "chasing" as a popular route of administration among young, recent recruits to heroin use (Maher & Dixon, 1999). Chasing involves inhaling the vapours produced when heroin is heated to a level at which it sublimates; this is typically achieved by heating the drug on tin foil above a flame (Strang, Griffiths, & Gossop, 1997). Fifty-nine percent of a multi-ethnic, street-based sample commenced heroin use by smoking. New injectors (70 percent) were more likely than experienced injectors (28 percent) to report a transition from smoking to intravenous use (Maher & Dixon, 1999).

Swift et al. (1999) have also reported the existence of heroin chasing as a popular route of administration among Indochinese and Caucasian heroin users in south western Sydney. Sixty-one percent of the Swift et al. (1999) sample had smoked heroin at least once. More than one quarter of the sample (29 percent) had made a transition from smoking to injecting heroin. Indochinese heroin users were more likely than Caucasians to commence heroin use by smoking the drug, and to smoke heroin on an exclusive or regular basis.

Very little attention has been given to the differences in characteristics and drug taking patterns between heroin chasers and injectors. Strang et al. (1999) recently reported major differences between heroin chasers and injectors in terms of the quantity and frequency of heroin intake, severity of dependence, and demographic characteristics. Injectors were using higher daily doses, and were significantly more likely to be using heroin on a daily basis. Studies are needed to examine the differences in characteristics and patterns of drug use between heroin chasers and injectors in Australia.

5.2.2   <u>Factors influencing route of administration</u>

Many parts of the developed world have seen recent increases in the purity of heroin available for sale at the street level, and a corresponding reduction in price (Swift et al., 1999). While these changes could potentially alter the perception that administering heroin by injection is the only economically viable method of using the drug, the type of heroin sold will also impact on how the drug is administered.

Heroin sold in street markets is generally available in two forms: as a heroin salt, such as hydrochloride, which is freely soluble in water, or as heroin free base which is insoluble in water. Heroin that is injected or snorted takes the form of heroin hydrochloride (or some other salt), whereas heroin that is smoked is usually the free base. In their analysis of the properties of heroin available for retail sale in Sydney, Maher et al. (2001) encountered no heroin free base. All the samples analysed for the study contained heroin as hydrochloride salt. While heroin in Sydney is not readily available in a form that can be easily and efficiently smoked, heroin in the base form has become increasingly available in Europe and the UK since the late 1970s (Strang et al., 1997).

Recent studies have documented reasons for transitions to injecting heroin, including the perceived superior effect of injecting (a better rush), and beliefs that

injecting is more cost-effective and that smoking is a "waste" (Maher, Sargent, Higgs, Crofts et al., 2001; Maher & Swift, 1997; Swift et al., 1999). In contrast to the stable smoking patterns reported by heroin users since the late 1980s and early 1990s in Europe and the UK (de la Fuente et al., 1996; Grund & Blanken, 1993; Strang et al., 1997), transitions from injecting to smoking appear to be relatively rare in Australia (although the reverse transition is common) (Maher et al., 2001; Swift et al., 1999). This is likely to be due to heroin in Europe and the UK being more amenable to smoking.

5.2.3 Route of administration and severity of dependence

The route of administration used by a naive heroin user is likely to condition the rate of progression to heroin dependence and the level of dependence reached. Similarly, a change in severity of heroin dependence may influence the transition between routes of administration (Barrio, de la Fuente, Lew, Royuela et al., 2001). Gossop et al. (1992) reported that heroin injecting was associated with more severe dependence than heroin smoking. In contrast, Swift et al. (1997) found no significant differences in severity of dependence between heroin smokers and heroin injectors. Similarly, Stohler et al. (2000) found no differences in severity of dependence between heroin chasers and heroin injectors in a Swiss cohort.

Others have suggested that the relationship between route of administration and severity of heroin dependence is produced only in the early stages of heroin use careers. After a certain length of time, most heroin users converge to a very high level of dependence irrespective of the route of administration (Barrio et al., 2001). Longitudinal research is needed to assess how heroin dependence and route of administration evolve during the user's drug career, and how these variables interact.

5.2.4 Route of administration and overdose risk

While heroin overdose is more commonly associated with injecting, both fatal and non-fatal overdoses have been reported in relation to non-injecting routes of administration. Gossop et al. (1996) reported that an overdose had been experienced by 2 percent of heroin smokers, compared to 31 percent of injectors.

In Australia, Swift et al. (1999) found that 43 percent of heroin users had experienced a non-fatal heroin overdose, of which only 2 percent had smoked heroin immediately prior to the overdose. A recent study of the 953 heroin-related fatalities

that occurred in NSW between 1992 and 1996 found injection to be the route of final heroin administration in 99 percent of cases (Darke, Ross, Zador, & Sunjic, 2000). In ten cases, alternative routes of administration had been used. In three cases the route of administration was by inhalation, in five cases by nasal administration, and in two cases by swallowing. The small proportion of heroin-related fatalities attributable to non-injecting routes of administration is consistent with the view that injecting is a substantially more dangerous route. If interventions are to encourage heroin users away from injecting, better understanding of the circumstances surrounding transitions to and from injecting is needed.

5.2.5   Route of administration and health risks

Transitions to and from injecting have major clinical and public health implications with regards to blood borne virus transmission through needle sharing. Heroin injectors are at greater risk than non-injectors of contracting or transmitting blood borne viruses, notably HBV, HCV, and HIV (Garfein, Vlahov, Galai, Doherty, & Nelson, 1996; Gossop, Powis, Griffiths, & Strang, 1994). Whereas transmission of HIV in Australia occurs mainly through sexual contact between men, HBV and HCV are transmitted primarily through the sharing of contaminated injecting equipment (NCHECR, 2001). Harm reduction efforts directed towards changing the risk behaviours of heroin users should take account of their current routes of administration and the potential for future transitions with continued drug use.

The act of injecting per se also carries inherent health risks. Frequent injections may cause vascular damage, irrespective of safe injecting practices. Damage to a favourite injection site commonly leads to the use of other, potentially more dangerous injection sites. Darke et al. (2001) recently interviewed IDU about their bodily injection sites, and revealed widespread use of multiple sites. A significant proportion of the sample had injected in sites such as the hand, foot, and leg, and 10 percent of subjects had injected in the neck. The use of more injection sites was independently associated with a greater number of injection-related health problems such as prominent scarring, lumps, and swelling. In addition, most subjects continued to use earlier injection sites, such as the arm, but added other sites to their repertoire. Regular vascular damage was therefore assumed to be occurring in a wide variety of sites (Darke et al., 2001). The risk of injecting in sites such as the groin and neck is substantially greater than in sites such as the cubital fossa (crook of the arm).

It is difficult for the drug user to see what they are doing in these sites, increasing the risk of vascular damage. Moreover, because the veins in these sites are considerably larger, damage to them may result in serious circulatory problems and an increased risk of infections such as endocarditis (Darke et al., 2001).

There are also health implications concerning the types of drugs injected into injection sites. Heroin injectors are typically polydrug users who inject other drugs in addition to heroin. The injection of oral preparations such as benzodiazepines and methadone syrup is common among Australian IDU (Darke et al., 1996c; Darke, Topp, & Ross, 2002; Ross, Darke, & Hall, 1997), and is associated with serious health consequences such as abscesses/infections, fistulas, venous thrombosis, amputations, and death (Darke et al., 1996c; Ralston & Taylor, 1993).

5.2.6   Impact of treatment on route of administration

Prospective treatment outcome studies conducted overseas have not examined the relationship between route of heroin use and treatment outcome. As such, no longitudinal data are available on the processes underlying transitions between routes of administration, and the possible role of treatment in making transitions. In the NTORS cohort, there were significant post-treatment reductions in injecting and in the sharing of injecting equipment (Gossop et al., 1998). NTORS, however, did not examine the influence of route of administration on treatment outcome, or the potential role of treatment in making transitions between routes of administration. Given the impact that route of administration has on heroin dependence, overdose risk, and general and vascular health, the role of transitions requires greater attention in future longitudinal research.

Key points:

- Increases in non-injecting heroin use have been reported in many parts of the developed world in recent years.
- In Australia, injecting has historically been the dominant route of heroin use. Recently, chasing has emerged as a popular route of administration.
- Street level heroin in Australia is available in a form that is most amenable to injecting.
- The route of administration has important implications for the nature and severity of problems that may be experienced by heroin users.
- Longitudinal studies should examine the processes involved in transitions between routes of heroin use, and the relationship between route of administration and treatment outcome.

5.3   Criminality

The existence of an association between heroin use and crime has been widely documented (Ball, Rosen, Flueck, & Nurco, 1981; Ball, Shaffer, & Nurco, 1983; Best, Sidwell, Gossop, Harris, & Strang, 2001; Hall, Bell, & Carless, 1993; Nurco, Ball, Shaffer, & Hanlon, 1985; Patterson, Lennings, & Davey, 2000). A large proportion of the heroin dependent population regularly engages in criminal activity, most commonly drug dealing and acquisitive property crime (Gossop, Marsden, Stewart, & Rolfe, 2000). Kokkevi and colleagues (1993) reported that 79 percent of a sample of dependent heroin users had been arrested, 60 percent had been convicted for a criminal offence, and the number of arrests and convictions increased with the frequency of heroin use. Lehman and Simpson (1990) found that 99 percent of a large US cohort of dependent heroin users had engaged in some form of illegal activity during a 12 year period after treatment, with 60 percent having spent at least one year in gaol. High rates of convictions have also been reported in an Australian sample of MMT applicants (Hall et al., 1993): 90 percent had one or more convictions, with 76 percent for drug offences, and 78 percent for property offences. Similarly, studies of criminal populations have revealed significant proportions to be heroin users prior to incarceration (Chaiken & Chaiken, 1982; Dobinson & Ward, 1985). The question of how interventions for heroin and other drug use problems impact on criminal behaviour is important for the implementation and evaluation of treatment services, and for the development of effective policy responses.

5.3.1   Models of heroin use and criminality

Although there is widespread agreement about the existence of a direct relationship between heroin use and crime, there is a lack of consensus as to its nature. Three primary models of the heroin use – crime relationship have been proposed. These may be characterised as:

  i.   An economic view, which regards the economic burden imposed by heroin use as engendering drug-related crime.
  ii.   A subcultural model, according to which criminality leads to drug use as a result of association with deviant subcultures in which drug users form a subgroup of criminals.

iii.   A common causes approach, which regards the heroin using population as a heterogeneous group within which drug use may be either a cause or a consequence of criminality.

The economic model

The economic model states that the economic burden imposed by dependent heroin use leads to crime. Indirect evidence consistent with this position is provided by the over-representation of heroin users in samples of incarcerated property crime offenders (Dobinson & Ward, 1985). More importantly, studies of the criminality of heroin users have found that the frequency of crime increases substantially during periods of dependence (Ball et al., 1981, 1983), and that there is a strong association between the frequency of crime and both the length of dependence periods and level of heroin use (Ball et al., 1981; Ball & Ross, 1991; Best et al., 2001).

Of major importance to the economic model are the types of crimes committed by heroin users. In the studies conducted by Ball and colleagues (1981, 1983), theft and drug dealing were the most common types of offences, indicating that heroin users engage in criminal activity for the purpose of obtaining money. Similarly, property offences and drug dealing were the most common crimes committed by heroin users in the Best et al. (2001) and Patterson et al. (2000) samples. These findings support the view that any causal association between heroin use and crime may be explained by the fact that heroin is an illegal, and therefore, expensive drug. To maintain a heroin habit, users need a constant supply of money, and may therefore be forced to commit lucrative crimes such as theft and drug dealing.

There is good evidence that dependent heroin use is a contributory cause of the *frequency* of criminal offences, in that the frequency of heroin use is positively correlated with the frequency of criminal activity (Hall et al., 1999). McGlothlin and colleagues (1978) examined the criminal and drug use careers of dependent heroin users in California, and revealed a much higher rate of self-reported crime when users were using heroin daily than when they were abstinent in the community. Ball et al. (1983) found substantial differences in the reported rates of criminal activity between periods of active heroin use and abstinence in a sample of Baltimore heroin users. When they were abstinent, there was a 75 percent reduction in the number of days that heroin users engaged in crime. These data are consistent with the results of

ethnographic research on drug use and criminality among heroin users (Maher, Dixon, Lynskey, & Hall, 1998).

The subcultural model

An alternative explanation for the heroin use – crime relationship is that criminality leads to drug use. Proponents of this model contend that drug use is an extension of a generally deviant lifestyle, and that drug users form a subgroup of criminals (Bean & Wilkinson, 1988). There is evidence that a significant proportion of heroin users were involved in criminal activity, typically property offences, before they first used heroin (Bean & Wilkinson, 1988; Hall et al., 1993; Kaye, Darke, & Finlay-Jones, 1998). This is especially true of male heroin users; heroin dependent women are more likely to be initiated to heroin use by a heroin using male sexual partner, so their criminal activities are more likely to follow their heroin use (Hall et al., 1993; Hser, Anglin, & McGlothlin, 1987). Nonetheless, the same studies have reported an equally significant proportion of heroin users for whom criminality succeeded drug use (Bean & Wilkinson, 1988).

The common causes model

The third model proposes that criminality and drug use have common causes. The heroin using population is a heterogeneous group in which drug use may be either a cause or a consequence of criminality (Kaye et al., 1998). Support for this model comes from longitudinal studies of drug use and criminality that indicate that common causes are at work in adolescence when drug use and criminal behaviour are initiated (Jessor & Jessor, 1977; Kandel, 1993). Kaye et al. (1998) found significant differences between those incarcerated MMT patients who committed crime prior to the initiation of heroin use and those for whom heroin use preceded the onset of criminality, in the nature and severity of crimes committed and in psychopathology.

5.3.2   Gender differences in the heroin use – crime relationship

There are gender differences in the types of criminal offences in which heroin users typically engage to support their drug use. Men are more likely to commit property offences, while women are more likely to engage in prostitution. In a large US cohort (Hser et al., 1987), 25 percent of the women and none of the men reported involvement in prostitution. Female heroin users also reported greater involvement in

fraud, while men favoured burglary and robbery. Similar patterns of criminal involvement have been reported by Australian heroin users (Patterson et al., 2000). The extent to which female IDU engage in prostitution has implications for the transmission of blood borne viruses through needle sharing and unsafe sexual practices.

5.3.3 Community impact of heroin-related crime

Only a very small proportion of adults ever become dependent on heroin. Nonetheless, the frequency with which dependent heroin users engage in crime, and the range of their criminal activity have an adverse impact on the community that is out of proportion to their small number. The results of a recent survey of heroin users in south western Sydney indicated that many were actively engaged in some form of criminal activity, primarily acquisitive property crime (70 percent) and drug dealing (70 percent) (Maher et al., 1998). Illegally obtained income accounted for 82 percent of the sample's total income in the week before interview. From these data it was estimated that the total costs of heroin-related crime in Australia were between A$535 million and $1.6 billion per annum.

5.3.4 Impact of treatment on criminality

In general, MMT has been shown to lead to reductions in criminal involvement among heroin users (Hall, Ward, & Mattick, 1998). Ball and Ross (1991), for instance, reported substantial reductions in property and drug dealing offences after admission to MMT, with the mean number of crime days per year decreasing from 238 in the year prior to treatment entry to 69 during the early months of treatment. In the Australian context, Bell and colleagues (1995) followed a cohort of Sydney methadone patients over a 12 month period, and revealed substantial reductions in the self-reported rates of both property and drug dealing offences during treatment. Others have suggested, however, that treatment alone has little impact on criminal behaviour (French, Zarkin, Hubbard, & Rachal, 1993).

Large scale overseas treatment outcome studies have reported substantial post-treatment reductions in the numbers of crimes committed and the rates of criminal involvement among illicit drug users. In both residential and community treatment modalities, the proportion of TOPS patients committing property crimes during treatment was reduced to 10 percent of pre-treatment levels, and to about one third in

the year after treatment (Hubbard et al., 1989). In the NTORS cohort, the number of acquisitive property crimes was reduced to one third of intake levels, and the rate of involvement in acquisitive crime was reduced to about half of intake levels at 12 month follow-up (Gossop et al., 2000). Similar post-treatment reductions were reported for drug dealing offences. Overall, the number of reported dealing offences was reduced to less than one fifth of intake levels, and the rate of involvement in drug dealing was reduced to less than two thirds of intake levels at 12 month follow-up (Gossop, Marsden, & Stewart, 2000). Reductions in property crime and drug dealing were strongly associated with reductions in the regular use of heroin and benzodiazepines (Gossop et al., 2000).

Overseas studies have identified a number of key variables that moderate the impact of treatment on criminality among heroin users. Continued use of heroin and other drugs is a significant predictor of continued criminal activity (Gossop et al., 2000), as is lack of social support (Hammersley, Forsyth, & Lavelle, 1990). Treatment length also plays a role, with retention in treatment being associated with better outcomes. Studies of a range of treatment modalities in different countries have shown that the impact of treatment on drug use and criminality is affected primarily not by admission to treatment, but by retaining clients in treatment for sufficient periods of time to permit treatment processes to have an effect (Ball & Ross, 1991; French et al., 1993; Gossop et al., 2000; Simpson & Sells, 1982). The presence of psychopathology is also known to affect treatment outcome, and may therefore impact on criminality (Corty, Ball, & Myers, 1988).

These findings have important policy implications, in that reducing heroin use among heroin dependent individuals may produce significant reductions in criminal activity. Given the differences between different countries in government policies and health care delivery systems, however, it would be unwise to generalise findings from one country to another. Longitudinal studies in the Australian context are needed to shed further light on the issue of how crime relates to heroin use, and the impact of treatment on criminality among heroin users.

5.3.5   Measurement of criminality among heroin users

An important methodological issue concerns the measurement of criminality. Data on the relationship between self-reported crime and official arrest statistics indicate great discrepancies between these two measures (Dobinson & Poletti, 1989;

Inciardi, 1979). For that reason, a measure sensitive to changes in the criminal behaviour of heroin users cannot be based solely on the number of arrests and incarcerations in the cohort. An estimate of overall criminal involvement, such as the Crime Scale of the OTI (Darke, Hall, Wodak, Heather, & Ward, 1992), provides the optimal measure of criminality among this group. The OTI Crime Scale measures the occurrence of criminal behaviours in the preceding month, not just those that resulted in an arrest, and has been widely used in studies of heroin and other drug users. It has very good test-retest reliability (0.96), and correlates 0.54 with Addiction Severity Index crime days (Darke et al., 1992). The OTI Crime Scale is therefore a reliable and valid measure of criminal involvement.

A related issue is the legitimacy of behavioural self-reports of drug users. Reliance on self-reported behaviours by drug users is widespread in studies of illicit drug use, because self-report is often the only feasible methodology that can address the research questions of interest to the investigators (Darke, 1998). Investigations of undetected criminal behaviour inevitably involve a reliance on self-report from respondents. Darke (1998) reviewed the literature on the reliability and validity of self-reported drug use, criminality, and HIV risk-taking among illicit drug users, and concluded that self-report is a legitimate methodology for studying these behaviours. In the case of criminality, the concordance of official arrest and conviction records with self-reported criminal histories was very good. Presumably, therefore, reports of undetected crime are also valid (Darke, 1998).

Key points:

- The existence of a direct relationship between heroin use and crime has been widely documented.
- The most common offences committed by heroin users are drug dealing and acquisitive property crimes.
- There is widespread agreement about the existence of a direct relationship between heroin use and crime, but disagreement as to its nature.
- Studies have shown that the frequency of criminal activity among heroin users is directly proportional to the frequency of heroin use and severity of dependence.
- Overseas treatment outcome studies have shown that drug treatment interventions lead to reductions in criminality among heroin users.
- Longitudinal research is needed to examine the issue of how crime relates to heroin use in Australia.

5.4   Psychiatric comorbidity

The US Epidemiologic Catchment Area (ECA) studies (Robins & Regier, 1991) and similar epidemiological surveys of the prevalence of psychiatric disorders from around the world (Farrell, Howes, Taylor, Lewis et al., 1998; Merikangas, Mehta, Molnar, Walters et al., 1998) have established that psychiatric disorders and drug use disorders frequently co-occur. In the ECA studies, 50 percent of individuals with a drug use disorder had experienced another psychiatric disorder. Among this group, the most prevalent comorbid psychiatric disorders were anxiety disorders (28 percent), mood disorders (26 percent), ASPD (18 percent), and schizophrenia (7 percent) (Regier, Farmer, Rae, Locke et al., 1990). In the recent Australian National Survey of Mental Health and Wellbeing (NSMH&WB), 65 percent of females with a drug use disorder met criteria for an anxiety, mood, or alcohol use disorder. These rates were considerably elevated compared to females without drug use disorders, 12 percent of whom had a psychiatric disorder. Similarly, whereas 64 percent of males with a drug use disorder met criteria for another disorder, only 11 percent of males without a drug use disorder had a psychiatric disorder (Andrews, Henderson, & Hall, 2001). Such comorbidity is likely to increase, because younger cohorts are at greater risk of early onset of drug use and the development of drug use disorders (Grant, 1997).

An important research question concerns the prevalence of comorbid disorders among individuals seeking treatment for one or other disorder (Lynskey, 1998). Studies of psychiatric comorbidity among people seeking treatment for heroin dependence have reported that up to 80 percent of treatment seekers satisfy the criteria for at least one other psychiatric disorder, with rates of mood disorders and ASPD that far exceed general population estimates (Abbott, Weller, & Walker, 1994; Khantzian & Treece, 1985; Rounsaville, Weissman, Kleber, & Wilber, 1982; Woody, McLellan, Luborsky, & O'Brien, 1985). Previous Australian studies have also documented high rates of psychiatric comorbidity among heroin users, with the three most common diagnoses being mood disorders, anxiety disorders, and ASPD (Darke & Ross, 1997; Darke et al., 1994; Darke et al., 1992; Swift et al., 1990). In addition to these diagnoses, high rates of post-traumatic stress disorder (PTSD) and borderline personality disorder (BPD) have also been reported among dependent heroin users (Clark, Masson, Delucchi, Hall, & Sees, 2001; Trull, Sher, Minks-Brown, Durbin, & Burr, 2000; Villagomez, Meyer, Lin, & Brown, 1995).

The high prevalence of psychopathology among heroin users has direct implications for treatment outcome and clinical practice. Psychopathology has consistently emerged as a salient predictor of poor treatment outcome (Eland-Goossensen, van de Goor, Garretsen, & Schudel, 1997), and has been associated with higher levels of HIV risk-taking and HIV infection (Brooner, Greenfield, Schmidt, & Bigelow, 1993; Metzger, Woody, DePhilipis, McLellan et al., 1991), greater severity of substance use, and higher levels of psychosocial impairment (Brooner, King, Kidorf, Schmidt, & Bigelow, 1997).

Relatively little is known about differences in psychopathology between heroin users in and outside treatment, because most research has been carried out in the treatment setting (Eland-Goossensen et al., 1997). Questions have been raised as to the generalisability of the results of studies of heroin users in one treatment modality to heroin users not in treatment, and to those in other treatment settings. Van Limbeek and colleagues (1992) examined the prevalence of psychopathology in a sample of dependent heroin users in two different treatment settings (inpatient detoxification and MMT). Fifty-three percent of the total sample reported at least one lifetime psychiatric disorder. The prevalence of psychopathology was significantly greater in the inpatient detoxification group (68 percent) than the methadone maintenance group (40 percent). More recently, Eland-Goossensen et al. (1997) examined the prevalence of psychiatric comorbidity in a sample of heroin users in either methadone maintenance or inpatient treatment programs, and a non-treatment group. Over 90 percent of inpatient treatment clients reported at least one lifetime psychiatric disorder, compared with 68 percent of methadone maintenance clients and 76 percent of those not in treatment. The prevalence of recent psychiatric disorders was also significantly higher among inpatient treatment clients than in the other two groups.

Despite widespread interest in the study of psychiatric comorbidity, relatively little longitudinal research has examined the influence of co-existing psychiatric disorders on the outcome of treatment for drug use disorders. Better understanding of the effects of comorbid psychiatric disorders on treatment outcome, and the impact of treatment on such disorders, is of major clinical relevance.

5.4.1   <u>Depression</u>

Depression and drug use disorders are highly prevalent in the general population, and are widely implicated in comorbid relationships across the life span (Swendsen & Merikangas, 2000). Over the past 20 years, an association between heroin use and depression has been well documented (Brienza, Stein, Chen, Gogineni et al., 2000; Brooner et al., 1997; Milby, Sims, Khuder, Schumacher et al., 1996). Studies of treatment-seeking heroin users have revealed high rates of lifetime and current major depressive disorder at entry to MMT, that far exceed general population estimates (Kessler et al., 1994). Prevalence estimates for lifetime major depressive disorder among heroin users have ranged from 38 to 56 percent, and for current major depressive disorder from 16 to 30 percent (Brienza et al., 2000; Kosten & Rounsaville, 1988).

In a non-treatment cohort of heroin users, lower rates of depression were found in comparison to heroin users enrolled in MMT (Rounsaville & Kleber, 1985). The rates of lifetime dysphoric disorder (defined as major depression, minor depression, cyclothymia, labile personality, chronic depression, and intermittent depression) for the community and treatment samples were 56 percent and 73 percent respectively, and the rates of current major depressive disorder in these groups were 14 percent and 34 percent (Rounsaville & Kleber, 1985). To explain the higher rates among methadone maintenance clients, the authors suggested that the presence of depression itself might motivate heroin users to seek treatment. In a more recent study, however, the mean Beck Depression Inventory (BDI) scores of non-treatment heroin users were found to be higher than those of heroin dependent MMT patients (Steer, Iguchi, & Platt, 1992). Similarly, Brienza et al. (2000) found a significantly higher rate of recent major depressive disorder among non-treatment heroin users recruited from a needle exchange program than among heroin users enrolled in MMT.

The significance of the high rate of depression among heroin dependent individuals concerns the relationship of depression to poorer treatment outcome. Comorbid depression appears to confer a poor long term prognosis for heroin users in terms of continued drug use, failure to enter treatment, and relapse rates (Brienza et al., 2000). In a 2.5 year follow-up study, for example, Kosten and colleagues (1986) reported that heroin users who were diagnosed as depressed at entry to treatment were less likely to be abstinent at follow-up than other heroin users with normal affect. McLellan and colleagues (1983) reported that treatment outcome for heroin users at 6

month follow-up was associated with psychiatric severity: high severity patients showed poor outcome performance irrespective of treatment modality, whereas low severity patients improved regardless of modality. Metzger et al. (1991) found that among current methadone maintenance patients, needle sharing in the previous six months was related to higher levels of depression, as measured by the BDI. Higher BDI scores have also been associated with continued injecting among Australian methadone maintenance patients (Darke, Swift, Hall, & Ross, 1994).

These data indicate that depression is prevalent among heroin users, and is associated with poorer treatment performance. Large scale treatment outcome studies conducted in the USA and UK, however, have not comprehensively assessed depression to determine lifetime or current diagnoses (cf. Flynn et al., 1997). TOPS included only three indicators of depression: one general indicator of depression, one measure of suicidal thoughts, and one measure of suicide attempts (Hubbard et al., 1989). Among TOPS clients, the frequency of depressive and suicidal symptoms was found to decrease significantly from intake to 3 month follow-up, and to increase slightly in the first year after treatment. By 3 to 5 years after treatment, the prevalence of depressive and suicidal symptoms was considerably reduced in comparison to pre-treatment levels. These changes in depressive symptoms were also reflected in 12 month abstinence and improvement rates. For those clients who reported symptoms of depression in the year before treatment, 12 month abstinence rates indicate the percentage who reported no symptoms in the year after treatment, and 12 month improvement rates indicate the percentage who reported either no symptoms or a less severe symptom in the year after treatment. Abstinence rates were high relative to other treatment outcomes, ranging from 63 percent for residential clients to 51 percent for outpatient drug-free clients and 52 percent for methadone maintenance clients. One year improvement rates were also high, ranging from 79 percent for both residential and methadone maintenance clients to 61 percent for outpatient drug-free clients. In general, post-treatment depressive and suicidal symptoms were more likely among clients with pre-treatment symptoms, those with previous treatment experience, and those who re-entered treatment in the year after TOPS treatment.

NTORS assessed psychiatric symptoms with the anxiety, depression, paranoid ideation, and psychoticism subscales of the Brief Symptom Inventory (BSI) (Derogatis, 1993). At intake to treatment, depressed mood was frequently reported by

NTORS clients. Sixty-two percent of clients reported feeling hopeless about the future in the three months prior to treatment entry, 29 percent reported having thoughts of suicide, and 10 percent reported being extremely troubled by suicidal thoughts. At 6 month follow-up, significant improvements were observed in the frequency and severity of depression. Forty-four percent of clients reported feeling hopeless about the future, and 16 percent of clients reported having suicidal thoughts. Moreover, the proportion of clients who were extremely troubled by suicidal thoughts fell to 4 percent. Significant reductions in the psychiatric problems of the NTORS cohort were also observed at 12 month follow-up (Gossop et al., 1997, 1998).

In DATOS, lifetime DSM-III-R diagnoses of major depression were made based on items taken from the Diagnostic Interview Schedule (DIS) (Robins, Helzer, Croughan, & Ratcliff, 1981). To measure current depressive symptomatology, the depression scale of the Symptom Checklist 90 (SCL-90) (Derogatis, Lipman, & Covi, 1973) was also administered at intake. Depression was not assessed at follow-up, although clients' self-reported suicidal ideation was included as a dichotomous outcome measure. The proportions of DATOS clients who reported having suicidal thoughts or attempts during the pre-admission year ranged from 17 percent of methadone maintenance clients to 19 percent of outpatient drug free clients, 24 percent of long term residential clients, and 31 percent of short term inpatient treatment clients. In the residential, outpatient drug-free, and short term inpatient treatment modalities, significant reductions were found in the number of clients reporting suicidal ideation from intake to 12 month follow-up. By contrast, there was little change in the prevalence of suicidal thoughts and attempts among MMT clients (Hubbard, Craddock, Flynn, Anderson, & Etheridge, 1997).

5.4.2   Anti-social personality disorder

A diagnosis of ASPD is one of the most common psychiatric diagnoses made among IDU. The prevalence of ASPD among heroin users has been reported to range from 35 to 65 percent (Brooner, Schmidt, Felch, & Bigelow, 1992; Darke et al., 1994; Darke, Finlay-Jones, Kaye, & Blatt, 1996; Darke, Kaye, & Finlay-Jones, 1998b). In contrast, the lifetime prevalence of ASPD in the US general population has been estimated to be 4 percent (Robins, Tipp, & Pryzbeck, 1991). In all studies conducted to date, the prevalence of ASPD among heroin users has exceeded the 4 percent population prevalence by several orders of magnitude (Darke, 1998).

Heroin users with ASPD have been found to have an earlier onset of drug use and injecting, and to be more likely to meet the criteria for diagnoses of drug abuse and dependence for drugs other than heroin (Brooner et al., 1992; Darke et al., 1994). The primary clinical significance of the diagnosis of ASPD, however, concerns the reported association between ASPD and higher levels of HIV risk-taking (Darke, 1998). In US studies, ASPD has been associated with higher levels of injecting and sexual risk-taking, as well as higher HIV seroprevalence (Brooner, Bigelow, Strain, & Schmidt, 1990; Brooner et al., 1993). Heroin users with a diagnosis of ASPD have been reported in these studies to share injecting equipment more frequently, have more needle sharing partners, and have more sexual partners than other heroin users.

The evidence for the broader effects of a diagnosis of ASPD on treatment outcome is currently ambiguous. Woody and colleagues (1985) reported that methadone maintenance patients with ASPD performed more poorly at 7 month follow-up than other patients over a range of outcome measures. More recent studies have indicated, however, that heroin users with ASPD respond as well as other heroin users to pharmacotherapy (Darke et al., l996; Darke et al., 1994; Gill, Nolimal, & Crowley, 1992; Rouser, Brooner, Regier, & Bigelow, 1994). Gill et al. (1992) found no differences in retention, methadone dosage, or drug use at 12 month follow-up between ASPD and other methadone maintenance patients. Rouser et al. (1994) also reported no differences between ASPD patients and others in retention in MMT. Darke et al. (1994) reported no significant differences in retention or drug use between MMT patients with a current diagnosis of ASPD and other patients, although the social functioning of ASPD patients was significantly poorer than other patients. Similarly, Darke et al. (1996) reported no differences in retention, methadone dosage, or heroin use between heroin dependent ASPD patients and others.

Clinically, heroin users with a diagnosis of ASPD may enter treatment with higher overall risk-taking and longer standing drug use problems (Darke, 1998). While there is no demonstrated treatment for ASPD per se, there is evidence that heroin users with ASPD may be successfully retained in MMT, and perform as well in MMT as other patients. Important research questions concern the performance of ASPD patients in other forms of treatment relative to other patients, and the effect of a diagnosis of ASPD on treatment outcome. To date, however, those questions have not been examined within a large scale treatment outcome study.

5.4.3   Post-traumatic stress disorder

PTSD is highly prevalent among patients with drug use disorders (Ouimette, Brown, & Najavits, 1998), and has consistently been associated with poorer treatment outcomes (Brown, Stout, & Mueller, 1996; Brown & Wolfe, 1994; Ouimette, Ahrens, Moos, & Finney, 1997).   In treatment-seeking samples of drug dependent patients, lifetime prevalence of PTSD is estimated at about 50 percent, and approximately 30 percent of patients meet criteria for a current diagnosis (Brown, Recupero, & Stout, 1995; Triffleman, Marmar, Delucchi, & Ronfeldt, 1995).   In a general population study, Cottler and colleagues (1992) reported that heroin and cocaine users were significantly more likely to meet DSM-III criteria for PTSD than individuals without a drug use disorder.   Villagomez et al. (1995) examined the relationship between violent traumatic events and PTSD among MMT entrants, and reported that 14 percent of the sample met diagnostic criteria for current PTSD.   More recently, Clark et al. (2001) reported that 29 percent of a sample of dependent heroin users met DSM-III-R criteria for a current diagnosis of PTSD.   The prevalence of PTSD in general population samples has been estimated to range from 1 to 9 percent, which is substantially lower than the rates reported in studies of heroin and other drug users (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; Wasserman, Havassy, & Boles, 1997).   In the NSMH&WB, 3 percent of Australian adults met criteria for a diagnosis of PTSD in the preceding 12 months (Henderson, Andrews, & Hall, 2000).   Relatively little is known about effective treatment for dependent heroin users with comorbid PTSD, or the impact of comorbid PTSD on treatment outcome.

Few longitudinal studies have examined treatment outcomes in drug dependent patients with PTSD.   Brown et al. (1996) compared drug dependent women with and without a comorbid diagnosis of PTSD on their alcohol and drug use 3 months after inpatient treatment.   Although rates of relapse (defined as any alcohol or drug use) at 3 month follow-up did not differ by PTSD status, women with a diagnosis of PTSD were found to relapse more quickly than women without PTSD. In addition, PTSD emerged as a significant predictor of relapse, even after controlling for general psychiatric distress.

As part of a multi-site investigation of inpatient drug treatment, Ouimette and colleagues (1997) have followed the post-treatment course of drug dependent patients with PTSD (SUD-PTSD) relative to drug dependent patients with another psychiatric disorder (SUD-PSY), and drug dependent only patients (SUD-only).   Patients in this

sample were assessed 12 months and 2 years following treatment on drug use, psychological, and social functioning outcomes. At 12 month follow-up, SUD-PTSD patients reported more drug-related problems, greater psychological distress, and less social support than patients in the other two groups. In comparison to SUD-only patients, SUD-PTSD patients were also more likely to re-enter inpatient treatment and less likely to be employed during the follow-up year. By 2 year follow-up, the differences between the three groups on drug use, psychological, and social functioning had markedly increased (Ouimette et al., 1998). SUD-PTSD patients reported more drug-related problems, more psychological distress, less social support, and less employment than patients in the other two groups. SUD-PTSD patients were also less likely to report remission (abstinence from illicit drug use) than patients without PTSD. Comparisons of the 12 month to the 2 year follow-up revealed that SUD-PTSD patients deteriorated at a greater rate on remission status than patients in the other two groups (Ouimette et al., 1998). These results suggest that poorer treatment outcomes were largely specific to PTSD, rather than to psychiatric morbidity in general. A major limitation of this study, however, is that PTSD was not assessed via structured clinical interview. A second limitation is the lack of a control group of drug dependent patients with comorbid PTSD who did not receive treatment.

Studies of PTSD among heroin users have revealed high rates of depressive symptoms and diagnoses (Clark et al., 2001; Villagomez et al., 1995). Villagomez et al. (1995) reported that heroin dependent patients who met diagnostic criteria for PTSD at some point in their lives were more likely than those without PTSD to experience depression and suicidal thoughts, and to make suicide attempts. In the study by Clark et al. (2001), heroin users with a history of PTSD were more likely than those without PTSD to be diagnosed with depression, and to have higher levels of depressive symptoms and a higher rate of suicide attempts. The strong association between PTSD and depressive symptomatology among heroin users indicates that it would be useful to assess PTSD and comorbid psychiatric disorders at entry to treatment (Dansky, Roitzsch, Brady, & Saladin, 1997). Trauma-related psychological distress has been associated with more severe drug use, and more risky injecting and sexual behaviours among heroin users (Clark et al., 2001). So, psychological distress associated with exposure to trauma may be a risk factor for the progression of more severe drug use (Clark et al., 2001).

There is evidence that PTSD renders drug users more vulnerable to poor treatment outcomes. The findings also suggest that the negative consequences of a comorbid PTSD diagnosis are greater than the effects of other comorbid psychiatric diagnoses, and that these effects intensify over time and encompass drug use, psychological, and social areas of functioning. The extent to which these findings are applicable to dependent heroin users, however, is unknown. Longitudinal research is needed to understand the natural course of PTSD among heroin users, and to clarify the relationship between PTSD status and treatment outcomes.

5.4.4   <u>Borderline personality disorder</u>

BPD is the most commonly diagnosed personality disorder in both inpatient and outpatient settings (Schaar & Öjehagen, 2001; Widiger & Trull, 1993). In addition to its high prevalence in clinical populations, recent reports indicate that BPD is also common in non-clinical populations, with prevalence estimates ranging from 2 percent to 4 percent (Trull et al., 2000). BPD is characterised by substantial levels of impairment. Individuals diagnosed with BPD are prone to seek out and utilise health care services, to report significant levels of functional impairment, and to attempt suicide (Trull et al., 2000). Rates of completed suicide among BPD patients are estimated at between 5 percent and 7 percent (Duberstein & Conwell, 1997), and there is evidence that BPD is a strong and independent risk factor for suicidal behaviour (Brodsky, Malone, Ellis, Dulit, & Mann, 1997).

Several studies have shown high comorbidity between BPD and drug use disorders (Trull et al., 2000; van den Bosch, Verheul, & van den Brink, 2001). Within drug use disordered populations, the prevalence of BPD has been reported to range from 14 percent to 62 percent (Alnaes & Torgersen, 1988; Grilo, Martino, Walker, Becker et al., 1997; Sansone, Fine, & Nunn, 1994). Among treatment-seeking heroin users, the prevalence of BPD has been found to range from 9 percent to 65 percent (Brooner, Herbst, Schmidt, Bigelow, & Costa, 1993; DeJong, van den Brink, Harteveld, & van der Wielen, 1993; Kosten, Kosten, & Rounsaville, 1989; Malow & West, 1989). The observed comorbidity can partly be accounted for by overlapping diagnostic criteria, but prevalence rates remain high even when drug-related characteristics are not considered in the diagnosis of BPD (Grilo et al., 1997).

It has been suggested that comorbidity between drug use disorders and BPD occurs because these conditions share common aetiologies (Verheul, Ball, & van den

Brink, 1997), and are part of the same domain of psychopathology, that is, impulse control disorders (Siever & Davis, 1991). Drug use is often viewed as a manifestation of impulsivity, which is one of the defining features of BPD (Links, Heslegrave, & van Reekum, 1999). Another central feature of borderline pathology is affective instability. Because extreme affective changes are often seen as unpredictable and undesirable, individuals with BPD may be especially prone to drug use in order to cope with unwanted negative emotional states (Trull et al., 2000). Kruedelbach and colleagues (1993) found, for example, that dependent drug users with comorbid BPD reported drug craving and use in response to negative emotional states and anxiety significantly more often than patients without BPD.

Further research is needed to examine the comorbidity between drug use and other psychiatric disorders, and the influence of co-existing psychiatric diagnoses on the outcomes of treatment for heroin and other drug use problems. To delineate the nature of the relationship between psychiatric morbidity and treatment outcome, longitudinal studies are required. Prospective cohort studies should examine the relationships between heroin use and depression, ASPD, PTSD, and BPD, given the high prevalence of these diagnoses among dependent heroin users.

Key points:

- Psychiatric morbidity is widespread among heroin users, with the most common diagnoses being depression and ASPD. High rates of PTSD and BPD are also found among this group.
- Psychopathology is an important predictor of poor treatment outcome among heroin users.
- Psychopathology is an important treatment outcome variable, in that levels of psychopathology have been found to decline following treatment for heroin and other drug use problems.
- Prospective cohort studies are needed to examine the relationships between heroin dependence and depression, ASPD, PTSD, and BPD.
- Longitudinal research on the impact of comorbid psychopathology on treatment outcome is required.

5.5 Mortality

Heroin users are at substantially greater risk of premature mortality than their non-heroin using peers. The annual mortality rates reported by longitudinal studies of heroin users have ranged from less than 1 percent (Frischer, Goldberg, Rahman, & Berney, 1997) to 8 percent (Zanis & Woody, 1998), with most studies reporting rates of 1 to 3 percent (Table 3). The standardised mortality ratios (SMRs) in these studies have ranged from 2 times that of the general population (Dukes, Robinson, & Robinson, 1992) to 55 times (Gronbladh, Ohland, & Gunne, 1990). A recent meta-analysis of mortality rates reported by longitudinal studies of heroin users (Hulse, English, Milne, & Holman, 1999) reported a mortality rate for regular heroin users 13 times greater than that of the general population.

The excess mortality associated with heroin use is further illustrated by the cumulative risk of death among heroin users. Hser et al. (2001) reported, for example, that 48 percent of their American cohort was dead at 33 year follow-up. In a large Italian cohort, the cumulative risk of death was 29 percent by age 40, and 53 percent by age 50 (Davoli, Perucci, Rapiti, Bargagli et al., 1997).

The major causes of death among heroin users are overdose, medical condition, trauma, and suicide (Hulse et al., 1999). The relative contribution of these causes has varied from study to study, over time, and across countries. AIDS, for instance, overtook overdose as the leading cause of death among heroin users in Italy during the late 1980s, but has declined in relative contribution since the early 1990s (Bargagli, Sperati, Davoli, Forastiere, & Perucci, 2001).

Table 3. Annual mortality rates and SMRs reported by studies of heroin users

Study	Country/Period	Annual mortality rate (%)	SMR
Bargagli et al. (2001)	Italy 1980-1997	-	15.4
Bewley et al. (1968)	UK 1947-1966	2.7	28.0
Bucknall & Robertson (1986)	UK 1981-1985	1	11.6
Cherubin et al. (1972)	US 1964-1968	7	-
Cottrell et al. (1985)	UK 1971-1982	1.9	-
Davoli et al. (1997)	Italy 1980-1992	0.8-2.8	M 9.3-21.2 F 18.1-38.6
Dukes et al. (1992)	NZ 1971-1989	-	2.4
Engstrom et al. (1991)	Sweden 1973-1984	2.3	18.3
Eskild et al. (1993)	Norway 1985-1991	2.7	31.0
Frischer et al. (1997)	UK 1982-1994	0.5	22.0
Fugelstad et al. (1997)	Sweden 1981-1992	2.2	-
Goldstein & Herrera (1995)	US 1979-1993	-	M 4.0 F 6.8
Gossop et al. (2002)	UK 1995-1999	1.2	6.0
Gronbladh et al. (1990)	Sweden 1967-1988	1.4 (MMT) 7.2 (non-Rx)	8.4 (MMT) 55.3 (non-Rx)
Haarstrep & Jepson (1988)	Denmark 1973-1984	2	-
Joe & Simpson (1987)	US 1978-1984	1.4	6.9
McAnulty et al. (1995)	US 1989-1991	1.1	8.3
Oppenheimer et al. (1994)	UK 1969-1991	1.8	11.9
Oyefeso et al. (1999)	UK 1974-1993	0.05	M 10.7 F 21.2
Perucci et al. (1991)	Italy 1980-1988	-	M 10.1 F 20.0
Quaglio et al. (2001)	Italy 1985-1998	-	13
Rossow (1994)	Norway 1968-1992	2.3	-
Sanchez-Carbonell & Seus (2000)	Spain 1985-1995	3.4	28.6
Segest et al. (1990)	Denmark 1978-1986	3.3	-
Tunving (1988)	Sweden 1970-1984	2.1	M 5.4 F 8.0
Vaillant (1973)	US 1952-1970	1.0	-
Watterson et al. (1975)	US 1970-1974	1.3	-
Zanis & Woody (1998)	US 1993-1994	8.2	-

5.5.1   Heroin overdose

Deaths attributed to overdose are the largest contributor to excess mortality associated with heroin use (Darke, Hall, Weatherburn, & Lind, 1999), and account for 30 to 45 percent of total mortality reported by longitudinal studies of heroin users (Hulse et al., 1999). While male and female heroin users are equally likely to have experienced a non-fatal overdose (Darke et al., 1999), men are consistently over-represented in overdose fatalities. The incidence of fatal heroin overdose in Australia has increased dramatically over the past 30 years (Degenhardt, 2001). Recent increases in the rate of fatal heroin overdose have been reported in Italy (Davoli et al., 1997), Spain (Fuente, Barrio, Vicente, Bravo et al., 1995), Austria (Risser, Uhl, Stichenwirth, Honigschnabl et al., 2000), England (Hall, Lynskey, & Degenhardt, 2000), and the USA (Drucker, 1999).

There is a need to develop effective strategies to prevent or reduce the occurrence of overdose among heroin users. Longitudinal data on the prevalence and patterns of overdose in an Australian cohort would provide a baseline for measuring the effectiveness of such interventions.

5.5.2   Medical condition and trauma

Deaths attributed to medical conditions commonly account for 20 to 35 percent of overall mortality reported by longitudinal studies of heroin users (Hulse et al., 1999). In the Hser et al. (2001) cohort, 40 percent of all deaths were caused by medical conditions including chronic liver disease (15 percent), cancer (12 percent), cardiovascular diseases (12 percent), and AIDS (1 percent). In a large Italian cohort (Bargagli et al., 2001), deaths related to medical conditions (notably AIDS, infectious diseases, and cirrhosis) were found to account for more than 50 percent of total mortality over an 18 year follow-up. Similarly, in a Spanish cohort (Sanchez-Carbonell & Seus, 2000), nutritional, endocrine, and immune system disorders (including AIDS) accounted for 50 percent of all deaths over a 10 year follow-up.

Deaths related to violence and accident/injury have been reported to account for 10 to 25 percent of total mortality among heroin users (Hulse et al., 1999). Goldstein and Herrera (1995) reported that 17 percent of deaths in their American cohort were attributable to violence. In the Bargagli et al. (2001) cohort, 12 percent of deaths were caused by injuries and poisoning. Quaglio and colleagues (2001) reported that 10 percent of overall mortality in their large Italian cohort was

attributable to road accident. In addition, road accident consistently emerged as a major cause of death during the 14 year period of this study.

5.5.3   Suicide

The proportion of deaths among heroin users attributed to suicide has been found to range from 3 percent (O'Doherty & Farrington, 1997) to 35 percent (Engstrom, Adamsson, Allebeck, & Rydberg, 1991), with most studies reporting rates between 3 percent and 10 percent (Darke & Ross, in press). Studies that have specifically examined the relative risk of completed suicide among heroin users have reported excess mortality of 6 times (Perucci, Davoli, Rapiti, Abeni, & Forastieri, 1991) to 8 times (Pokorny, 1983) that expected among matched peers. Harris and Barraclough (1997) calculated suicide specific SMRs for longitudinal studies in which these ratios were not reported. Overall, the suicide specific SMR for heroin users was 14 times that expected of matched peers.

Suicide represents a major risk for heroin users, and a major clinical issue for treatment providers. To reduce the rate of suicide in this group, targeted interventions are required. Better understanding of the role of suicide in overall mortality among heroin users would enable us to develop more effective prevention and treatment strategies.

5.5.4   Impact of treatment on mortality

The risk of death is substantially reduced among heroin users who are enrolled in treatment (Caplehorn & Drummer, 1999). In a cohort study of Australian heroin users, Caplehorn and colleagues (1996) found that heroin users not in treatment were four times more likely to die than methadone maintenance patients, and that the reduction in mortality risk for these patients was wholly attributable to a reduction in the risk of fatal heroin overdose. When these findings were combined in a meta-analysis with the results of overseas cohort studies that examined mortality rates among dependent heroin users, Caplehorn et al. (1996) concluded that enrolment in methadone maintenance reduced patients' risk of death by nearly 75 percent.

A number of studies have indicated that overdose fatalities are less likely to have been in treatment at the time of death than living heroin users (Caplehorn, Dalton, Cluff, & Petrenas, 1994; Davoli, Perucci, Forastiere, Doyle et al., 1993; Fugelstad, Rajs, Bottiger, & Gerhardsson de Verdier, 1995; Perucci et al., 1991).

Davoli et al. (1993) found that heroin users who left methadone maintenance were eight times more likely to die from overdose in the 12 months after treatment, and three times more likely to die in the period 12 to 36 months after treatment, relative to patients who remained in treatment. Fugelstad et al. (1995) reported a three times relative risk of death attributed to overdose for heroin users who had never been in MMT, relative to those currently in treatment.

In support of these findings, only 2 percent of heroin-related deaths in NSW in 1992 were receiving MMT at the time of death, and 75 percent had never been in methadone treatment (Zador, Sunjic, & Darke, 1996). Recent studies conducted in Austria (Risser, Honigschnabl, Stichenwirth, Pfudl et al., 2001) and the Netherlands (Langendam, van Brussel, Coutinho, & van Ameijden, 2001) have also reported that MMT is strongly associated with decreased overall and overdose specific mortality among heroin users.

5.5.5 The need for mortality data in an Australian cohort

The overall high mortality rates reported by overseas studies provide evidence of the severe consequences of heroin use. Patterns of mortality reported by overseas studies, however, are unlikely to be applicable to the Australian context. The health care delivery systems available to heroin users differ significantly between different countries. In particular, treatment provision in countries such as the UK and USA is markedly different from that provided in Australia. The British system of methadone prescription is less tightly regulated than in Australia, with methadone and other opiates (including heroin) being prescribed by general practitioners, with little or no supervision of drug administration. The US system is considerably more restrictive, with access to methadone being very limited. The system in Australia appears to lie somewhere between these models in terms of access to treatment and restrictions placed on those in treatment.

There are no longitudinal studies of the natural history of Australian heroin users, and therefore, no longitudinal data on heroin-related mortality among this group. Prospective cohort studies provide an excellent framework in which to report the deaths that occur within the cohort, to examine the circumstances and causes of death, and to identify specific factors that put heroin users at increased risk of death. Future research should examine the factors that influence the transition to eventual

cessation of heroin use, so that intervention strategies may be developed to promote earlier cessation and to minimise heroin-related mortality.

Key points:

- The mortality rate for regular heroin users is estimated at 13 times that of the general population.
- The leading causes of death among heroin users are overdose, medical condition, trauma, and suicide.
- The risk of death is significantly reduced among heroin users who are enrolled in treatment.
- Patterns of mortality reported by overseas studies are unlikely to generalise to the Australian context. Prospective cohort studies are required to elucidate the prevalence and patterns of mortality among Australian heroin users.

5.6   Physical health status

The overall physical health of heroin users is poor, relative to the non-heroin using population (Ryan & White, 1996). Webster and colleagues (1977) reported a poor level of general health in a sample of dependent heroin users, many of whom suffered from liver disease, menstrual difficulties, and poor nutritional status. More recently, Ryan and White (1996) found considerable physical and psychological health problems among a sample of South Australian methadone treatment entrants.

The most common physical complications among heroin users include: infections resulting from needle sharing and unhygienic injecting practices (septicaemia, endocarditis, HIV, HBV, HCV, tetanus, and cerebral and subcutaneous abscesses), foreign body emboli, inflamed lesions due to the injection of contaminants, and a variety of neurological, musculoskeletal, and other lesions resulting from toxic impurities in drugs produced in illicit laboratories (Jaffe, 1990). Many aspects of the heroin using lifestyle are known to impair immune function, including malnutrition, stress, reversed sleep-wake cycles, sleep deprivation, and excessive alcohol intake (McLachlan, Crofts, Wodak, & Crowe, 1993). The likely widespread exposure to violence inherent in the heroin using lifestyle also places heroin users at an increased risk of traumatic brain injury (Darke, Sims, McDonald, & Wickes, 2000).

In Australia, the major physical health risks associated with heroin use are fatal and non-fatal heroin overdose, blood borne virus transmission through the sharing of injecting equipment, and vascular damage.

5.6.1   Heroin overdose

Heroin overdose has emerged as a major public health issue in Australia. As stated in Section 2.5, there has been a dramatic increase in heroin overdose deaths in recent years, whether this is assessed by rate per million of population at risk, or as the proportion of all deaths attributed to heroin overdose.

The recent marked increases in heroin overdose deaths do not appear to be confined to Australia. The EMCDDA (2001) reports that drug-related deaths in Ireland, Greece, and Germany have increased steadily over the past decade, but cautions that previous under-reporting may be contributing to these trends. Recent increases in the rate of fatal heroin overdose have also been reported in Spain (Fuente

et al., 1995), Italy (Davoli et al., 1997), Austria (Risser et al., 2000), the USA (Drucker, 1999), and the UK (Hall et al., 2000; Neeleman & Farrell, 1997).

Non-fatal overdoses are extremely common among heroin users (Darke et al., 1996a). Recent studies of non-fatal overdose report that about 60 percent of the heroin using population has experienced at least one non-fatal overdose (Bennett & Higgins, 1999; Darke et al., 1996a; McGregor et al., 1998).

Health consequences of heroin overdose

Approximately one in ten overdoses ends fatally (Darke et al., 1996b). Those who die from overdose are usually in their early 30s, unlike, for example, deaths arising from alcohol or nicotine dependence. As such, while heroin overdose deaths are grossly outnumbered by deaths from licit drug use, they represent a significant number of potential life years lost (Warner-Smith et al., 2001).

While non-fatal overdose is highly prevalent among heroin users, there is a dearth of epidemiological literature on the medical morbidity arising from overdose. Case reports describing complications of overdose provide little indication of the incidence and prevalence of overdose-related morbidity. They do suggest, however, that there is a significant burden of morbidity associated with heroin overdose.

Sequelae of heroin overdose include a variety of pulmonary, cardiac, muscular, and neurological complications. Pulmonary conditions appear to be the most common complications of overdose (Duberstein & Kaufman, 1971; Schachter & Basta, 1973), of which the most widely reported is oedema, a build up of fluid in the lung. Pulmonary oedema usually resolves within days of treatment, but may leave residual impairment (Schachter & Basta, 1973). Heroin induced pulmonary oedema has also been associated with chronic lung disease (Schachter & Basta, 1973).

The cardiac complications associated with heroin overdose include profound cardiovascular collapse, arrhythmia, and acute cardiomyopathy (Ghuran & Nolan, 2000). Although these conditions are potentially life threatening in the acute phase, there is no evidence of ongoing morbidity as a result of these complications.

The primary muscular complication associated with heroin overdose is rhabdomyolysis, the disintegration or dissolution of muscle cells (Taylor, 1988). Rhabdomyolysis is associated with a significant burden of morbidity, leading to muscular necrosis, severe neurological complications, and potentially fatal renal failure (Crowe, Howse, Bell, & Henry, 2000).

A number of neurological complications may result from heroin use, including toxic spongiform encephalopathy (McCann & Ricaurte, 2000), stroke (Vila & Chamorro, 1997), and seizure (Alldredge, Lowenstein, & Simon, 1989). These conditions have the potential to cause significant cognitive and other neurological morbidity. Moreover, heroin overdose may cause substantial neurological impairment through prolonged hypoxia. Darke et al. (2000) recently found significantly greater levels of cognitive impairment among methadone maintenance patients compared to matched non-heroin using controls, despite there being no differences in premorbid cognitive functioning. The number of overdoses experienced by a patient was a significant predictor of poorer cognitive performance. So, long term heroin users are likely to suffer from a significant burden of cognitive morbidity that is proportional to their overdose experience.

Warner-Smith and colleagues (in press) recently examined the nature and extent of overdose-related morbidity in a large sample of Sydney heroin users, and found that 79 percent of those who had ever overdosed had experienced at least one overdose-related morbidity symptom. The most commonly reported symptom was peripheral neuropathy, resulting from prolonged pressure on a limb while unconscious (49 percent). Similarly, temporary paralysis from prolonged pressure on limbs was reported by 26 percent of those who had ever overdosed. Overdose-related morbidity was not limited to direct physiological morbidity, with many subjects reporting injuries resulting from falls (40 percent) and burns (24 percent).

The findings indicate a significant burden of overdose-related morbidity in the heroin using population. Further research is needed to quantify the risk and degree of morbidity arising from heroin overdose, and to inform the development of interventions to prevent or reduce its occurrence.

5.6.2   Blood borne viruses

HIV and HCV are the two blood borne pathogens most commonly transmitted by drug users through the sharing of injecting equipment, and are likely to be responsible for the highest infectious disease morbidity and mortality rates among IDU (Hagan & Des Jarlais, 2000).

Natural history of HIV among IDU

Persistent infection occurs in virtually all persons infected with HIV. In the absence of effective treatment, HIV infection eventually le ads to severe immunodeficiency that promotes opportunistic infections, certain malignancies, and other fatal diseases (Phair, 1999). Epidemiological research has not shown that continuing to inject heroin has any consistent effect on the rate of progression of HIV infection (Krol, Flynn, Vlahov, Miedema et al., 1999; Ronald, Robertson, & Elton, 1994).

HIV prevalence and incidence among IDU vary greatly throughout the world. In some IDU populations, such as Australia and Sweden, HIV seroprevalence has stabilised at low levels (less than 5 percent). Incidence is also typically low in these settings, with rates of 1 per 100 person years at risk or less (Crofts & Aitken, 1997). In other regions, such as New York, Bangkok and Amsterdam, seroprevalence has stabilised at high levels, from 20 to 50 percent. In these conditions, HIV incidence is generally in the range of 4 to 8 per 100 person years at risk (van Ameijden & Coutinho, 1998). There are other populations (China, Myanmar, and north east India) in which more than 80 percent of IDU are HIV positive, and incidence rates are 10 per 100 person years at risk or higher (Hagan & Des Jarlais, 2000).

Natural history of HCV among IDU

Following infection with HCV, 25 to 50 percent of IDU typically develop acute hepatitis. More than 60 percent of chronic HCV infections result in chronic liver disease, with cirrhosis or chronic active hepatitis occurring within several years after infection in most of these cases (Liang, Rehermann, Seeff, & Hoofnagle, 2000). Few natural history studies have examined the influence of ongoing drug use on the course of persistent HCV infection, but alcohol use has been associated with more rapid progression and greater severity of liver disease in patients with HCV infection (Imperial, 1999).

In Australia, HCV prevalence among IDU is about 65 percent (Crofts et al., 1999). The incidence of HCV infection among IDU is generally 10 to 100 times higher than HIV incidence in the same group, in the range of 10 to 30 percent per year (Hagan, 1998). HCV incidence among Australian IDU is estimated at 15 percent per year (Crofts et al., 1999).

How can we explain the discrepancy between the low incidence of HIV and the high incidence of HCV among Australian IDU? First, the risk associated with exposure to infected blood during an injecting occasion is greater for HCV than HIV, because smaller amounts of blood are required to efficiently transmit the infection. Second, Australia's HCV prevalence among IDU is now so high that even very occasional sharing of injecting equipment carries an extreme risk of HCV infection. Given the higher infectiousness of HCV per contact episode, and its higher prevalence among IDU relative to HIV, the difference in incidence comes down to "the force of numbers" (Crofts et al., 1999, p. 221).

5.6.3 Vascular health

As stated in Section 5.2, the act of injecting per se also carries inherent health risks. Frequent injections may cause vascular damage, and damage to a favourite injection site commonly leads to the use of other, potentially more dangerous injection sites. Heroin injectors are therefore at high risk of injection-related health problems such as prominent scarring, lumps, and swelling, serious circulatory problems, and life threatening infections. Darke et al. (2001) recently reported that 97 percent of a sample of Sydney IDU had experienced injection-related health problems. The most commonly reported problems were prominent scarring/bruising (88 percent), lumps/swelling (86 percent), and difficulty injecting (vascular scarring) (61 percent), all of which denote vascular damage.

There are also clear health implications regarding the types of drugs injected into injection sites. The injection of temazepam has been associated with amputations and death (Ralston & Taylor, 1993), while the injection of methadone syrup has been associated with fistulas, abscesses/infections, and venous thrombosis (Darke et al., 1996c).

5.6.4 Impact of treatment on health status
Overdose risk

The risk of overdose death is substantially reduced among heroin users who are enrolled in treatment, of which MMT is the dominant modality in Australia (Caplehorn & Drummer, 1999; Caplehorn et al., 1996). As discussed in Section 5.5, several studies have shown that overdose fatalities are less likely to have been in treatment at the time of death than living heroin users. The reduced risk of heroin

overdose observed among methadone patients is likely to reflect reduced heroin use while in treatment and/or a higher tolerance to opioids while being maintained on methadone (Warner-Smith et al., 2001).

Blood borne virus infection

There is good evidence that MMT provides protection against HIV infection among heroin injectors. Longitudinal cohort studies conducted in the USA (Metzger, Woody, McLellan, O'Brien et al., 1993; Moss, Vranizan, Gorter, Bacchetti et al., 1994) and Italy (Serpelloni, Carrieri, Rezza, Morganti et al., 1994) have shown that participation in MMT is negatively associated with risk for HIV infection. Nonetheless, data from a series of longitudinal cohort studies from The Netherlands indicate that MMT may only be effective in preventing HIV infection when it is delivered at an adequate dose level (Hartgers, van den Hoek, Krijnen, & Coutinho, 1992; van Ameijden, van den Hoek, Mientjes, & Coutinho, 1993; van Ameijden, van den Hoek, Hartgers, & Coutinho, 1994).

Few studies have examined the relationship between exposure to MMT and HBV and HCV, and the evidence from these studies is contradictory (Ward, Mattick, & Hall, 1998). To the extent that the transmission characteristics of HBV and HCV are the same as HIV among IDU, the evidence that MMT protects against HIV infection may be applicable to HBV and HCV. Relative to HIV, however, HBV and HCV are more readily transmitted and more highly prevalent among Australian IDU. By the time heroin injectors enter treatment, they have typically been injecting for a number of years, and have already been exposed to HBV and HCV infections. For that reason, it is too late for MMT to protect a significant proportion of patients. In principle, therefore, any protective effect of MMT would apply only to those patients who have not been exposed to HBV and HCV (Ward et al., 1998).

Health risk behaviours

There is good evidence that MMT is associated with reductions in the sharing of injecting equipment (for a recent review, see Sorensen & Copeland, 2000). Longshore and colleagues (1993), for instance, examined needle sharing in a large US cohort of heroin injectors, 41 percent of whom were in MMT at the time of interview. Even after adjusting for frequency of injection, being in MMT was significantly related to reduced needle sharing. Similar findings have been reported by studies in

the UK (Gossop, Marsden, Stewart, & Treacy, 2002; Klee, Faugier, Hayes, & Morris, 1991) and Germany (Stark & Müller, 1993). In the Australian context, Darke and colleagues (1990) found that 20 percent of a sample of IDU who were in treatment at the time of interview reported needle sharing, compared with 68 percent of the subjects who were not in treatment. More recently, Caplehorn and Ross (1995) reported that being enrolled in MMT was associated with less needle sharing among a large cohort of Sydney IDU. They estimated the odds of needle sharing to be almost halved among MMT patients compared with IDU who were not in treatment.

In their review of the literature on the utility of drug treatment in preventing HIV infection among IDU, Sorensen and Copeland (2000) noted that what is known about the protective effect of treatment against HIV infection is largely based upon studies of MMT. Much less is known about changes in health risk behaviours after treatment in other modalities such as residential or outpatient drug free treatment. Hubbard et al. (1989) reported reductions in injecting drug use that were associated with participation in both residential and outpatient drug free treatment programs. McCusker and colleagues (1997) compared the effectiveness of two residential programs (a therapeutic community and a relapse prevention program) in changing HIV risk behaviour among drug users, and found that both programs produced substantial reductions in injection-related and sexual risk behaviours. More recently, Gossop et al. (2002) reported significant reductions from intake to 12 month follow-up in the injection-related and sexual risk behaviours of the NTORS cohort. Injecting, needle sharing, and having unprotected sex were substantially reduced among MMT clients and among those admitted to residential treatments. Nonetheless, in view of the relative paucity of studies of the impact of treatment other than MMT on the health risk behaviours of heroin and other drug users, there is a need for further research on this issue.

5.6.5   Measuring the health status of heroin users

Clearly, health assessment has an important clinical role, both in order to ascertain the initial health status of heroin users, and to measure the impact of treatment on health outcomes. Health status is also an important variable in studies of treatment outcome for heroin and other drug use problems. Few large scale treatment outcome studies, however, have measured health outcomes using reliable and valid instruments (cf. Gossop et al., 1998).

General health status

The focus of many health assessment instruments, such as the Sickness Impact Profile (Bergner, Bobbott, Kressel, Pollard et al., 1976) and the OARS Multidimensional Functional Assessment Questionnaire (Fillenbaum & Smyer, 1981), is the impact of illness on lifestyle, gross morbidity, and/or elderly people. Given that, in general, heroin users are young and ambulatory, and because these instruments are not oriented towards the particular health problems associated with heroin use, they are not appropriate for measuring the health status of heroin users. A global estimate of current health status such as the OTI Health Scale (Darke, Ward, Zador, & Swift, 1991) provides the optimal measure of health status among heroin users. The OTI Health Scale is oriented towards the specific problems associated with heroin use, and therefore provides clinically relevant information. It also contains a specific section on injection-related health problems. It is useful for research purposes, as it does not require diagnoses or assessments of severity on the part of the interviewer. The Health Scale has very good test-retest reliability (0.86), and correlates 0.57 with the Addiction Severity Index medical total (Darke et al., 1991). Thus, it provides a reliable and valid assessment of current health status.

The SF-12 (Ware, Kosinski, & Keller, 1996) and SF-36 (Ware, Kosinski, & Keller, 1994) also yield valid and reliable assessments of health status. The SF-36, of which the SF-12 is a brief version, measures three aspects of health: functional status, well-being, and an overall evaluation of health. It has been specifically demonstrated to be a reliable and sensitive measure of general health among dependent heroin users (Ryan & White, 1996). The SF-12 correlates 0.96 with the SF-36 (Ware et al., 1996). In addition, normative data have been generated for these two measures, allowing comparisons of heroin users with other clinical groups and with the general population (Jenkinson, Couter, & Wright, 1993; Ware et al., 1996).

Injection-related risk behaviour

Sharing needles and syringes is the primary means of blood borne virus transmission between IDU. To measure the extent of injection-related risk behaviour among IDU, and to determine the effectiveness of interventions aimed at reducing such behaviour, a reliable and valid measure of current injection-related risk-taking is required. The injecting subscale of the HIV risk-taking behaviour scale (HRBS)

(Darke, Hall, Heather, Ward, & Wodak, 1991) specifically measures injection-related risk behaviour. The HRBS has good psychometric properties, is easily administered, and may be used for both clinical and research purposes (Darke et al., 1991; Darke et al., 1992). Thus, it provides the optimal measure of injection-related risk behaviour among drug users.

Key points:

- The overall physical health of heroin users is poor, and heroin dependence is associated with serious medical consequences.
- In Australia, the major health risks associated with heroin use are heroin overdose, blood borne virus transmission, and vascular damage.
- The risk of overdose is substantially reduced among heroin users who are enrolled in treatment.
- Overseas studies have indicated that MMT provides protection against HIV infection among heroin injectors when it is delivered at an adequate dose level.
- There is evidence that being in treatment leads to significant reductions in needle sharing among heroin users.
- The measurement of health status has both clinical and research relevance.

5.7   Burden of heroin use

Heroin use and dependence impose a significant clinical and social burden on individuals, families, and communities that includes an economic dimension. The total cost of heroin dependence in the USA in 1996, for instance, was estimated to be US$21.9 billion (Mark, Woody, Juday, & Kleber, 2001). The total cost of illicit drug use in Australia in 1992 was estimated at A$1.7 billion (Collins & Lapsley, 1996). Heroin use and dependence exact costs at all levels of society, either directly through expenditure or unpaid time spent on providing health care, or indirectly in terms of productivity losses due to premature mortality, unemployment, and incarceration. Heroin-related crime also produces a significant economic burden in terms of policing, legal, and incarceration costs, and the economic cost to crime victims. Heroin dependence is also associated with intangible costs, such as deficits in wellbeing, family and social disruption, and community fears about heroin-related crime (Mark et al., 2001).

The large economic burden resulting from heroin dependence highlights the importance of investing in effective interventions for dependent heroin users. Overseas studies of treatment outcome have established a clear relationship between treatment participation, greater length of time in treatment, and positive outcomes. Cumulatively, these studies have demonstrated the effectiveness of treatment in the context of adequate treatment lengths (Flynn, Kristiansen, Porto, & Hubbard, 1999). Policy makers and treatment providers, however, are increasingly concerned with not only the effectiveness, but also the cost-effectiveness of treatment (Barnett, 1999). Put simply, they need to decide how to use scarce resources in a way that yields the greatest benefit. For that reason, there is a need for health economics contributions to policy responses and clinical practice. Health economic evaluation provides a means of comparing the costs and outcomes of an intervention within an explicit framework. This, in turn, enables policy makers and clinicians to assess the extent to which particular treatment approaches offer the most constructive use of scarce resources. An analysis of costs alone, or of outcomes alone, does not provide such information.

5.7.1   <u>Describing the cost of the burden of heroin use</u>

To describe the costs associated with heroin use and dependence, these need to be defined and measured. Cost of illness studies are concerned with establishing these costs (Singh, Hawthorne, & Vos, 2001). Cost of illness methodology proposes

that an illness or social problem imposes costs when resources are redirected as a result of that illness or problem from purposes to which they would otherwise have been devoted (Harwood, Fountain, & Livermore, 1999). Early cost of illness studies typically used the cost definitions proposed by Fein (1958): costs were viewed as direct, indirect, or intangible. More recently, Drummond and colleagues (1998) redefined these as costs consumed within the health care sector, costs borne by the patient and his or her family, and costs borne by other sectors of the economy.

Health care costs

Health care costs describe the resources used by health care interventions aimed at either preventing or treating illness (Singh et al., 2001). In the case of heroin dependence, health care costs include medical care expenditures for diagnosis and treatment of heroin dependence and its medical consequences (Mark et al., 2001). According to Mark et al. (2001), medical care costs accounted for 23 percent of the total economic burden of heroin dependence in the USA in 1996.

Heroin use is associated with serious medical consequences and relatively high utilisation and cost of health services, especially emergency department care (McGeary & French, 2000; Ottaway & Erickson, 1997). Among illicit drug users, those who inject drugs are the most frequent consumers of health services, due to blood borne virus transmission through needle sharing, and the elevated risk of overdose in this population (Beaufoy, 1993). French and colleagues (2000) recently examined health services utilisation in a sample of dependent heroin and/or cocaine injectors and matched non-drug users. Compared with non-drug users, heroin and/or cocaine injectors consumed significantly more inpatient services and emergency department care, but fewer outpatient services, over a 12 month period. Analyses of total annual health care costs indicated that heroin and/or cocaine injectors generated approximately US$1,000 in excess health services utilisation per individual relative to non-drug users.

Patient and family costs

Heroin dependence and its consequences are costly to the heroin user and to his or her family and friends. Dependent heroin users may be unable to perform roles that would have been undertaken in the absence of their heroin dependence, or performance in these roles may be compromised. Under these circumstances, there

may be loss of income for the heroin user, as well as loss of social or leisure activities. While these losses can, in theory, be measured, it is difficult to assign dollar values to these costs. For that reason, cost of illness studies typically include only a subset of patient and family costs, most usually lost income (Singh et al., 2001). Mark et al.'s (2001) recent analysis revealed that productivity losses accounted for 53 percent of the total cost of heroin dependence in the USA in 1996. In the Australian context, productivity losses were found to account for 43 percent of the total economic burden of illicit drug use in 1992 (Collins & Lapsley, 1996).

Other sector costs

In addition to health care costs and patient/family costs, heroin use and dependence impose social costs in terms of crime and the use of social services. Crime costs include policing, legal, and incarceration costs, and the economic cost to crime victims, while social welfare costs include social insurance, public aid, and direct human services (Mark et al., 2001). These costs do not include the intangible costs of heroin dependence, such as reductions in the quality of life of the heroin user and members of his or her social network. Almost 25 percent of the total economic burden of heroin dependence in the USA in 1996 was attributed to crime (24 percent) and social welfare costs (0.5 percent) (Mark et al., 2001). The US system of social service provision is considerably more restrictive than the Australian system, with access to benefits being very limited for drug dependent individuals. For that reason, social welfare costs are likely to account for a greater proportion of the total cost of heroin dependence in Australia than in the USA.

5.7.2   Measuring costs

Which of these costs are included in an economic evaluation depends on the perspective from which the analysis is viewed. The possible perspectives include those of the patient, the service provider (that is, the health care system), and society. The broadest perspective is the societal perspective, which incorporates all the identifiable costs and consequences arising from an intervention regardless of who incurs the costs and who obtains the outcomes. For psychiatric services the societal perspective is preferred, because many psychiatric disorders involve high patient and family and other sector costs (Singh et al., 2001). A major problem with this approach is that collecting reliable data on non-service costs is extremely difficult.

Thus, many studies focus only on costs arising from the health care system (Chisholm, 1998; Singh et al., 2001).

The health care perspective considers the costs and consequences arising from the provision of treatment for the problem or disorder of interest. From this perspective, an economic analysis would not include costs (or savings) to individuals, non-treatment related health sector expenditures, or broader social considerations such as crime-related costs.

5.7.3 Measuring health outcomes

Economic evaluation can also provide estimates of service outcomes, or consequences. These include changes in health status, clinical outcomes, and quality of life measures. Changes in health status refer to the effects of treatment on health, which are typically measured in terms of mortality or morbidity (Singh et al., 2001). Studies of treatment for heroin and other drug use problems usually express health outcomes in terms of days drug free or abstinent. One problem with this approach is that there are likely to be other outcomes of concern that may not correlate highly with reductions in drug use or abstinence (Sindelar & Fiellin, 2001). Moreover, changes in domains such as psychiatric morbidity, social functioning, and employment status are of independent interest when assessing treatment outcome for heroin and other drug users. By restricting the economic analysis to a single outcome measure such as abstinence from heroin, researchers ignore the constellation of problems that are associated with heroin use and dependence. Which outcomes should be included in a particular evaluation ultimately depends on the scope, objectives, and setting of the study (Chisolm, 1998).

5.7.4 Methods of economic evaluation

There are several ways in which data on costs and outcomes may be combined for analysis. These include cost-minimisation, cost-consequence, cost-effectiveness, and cost-benefit analyses (see Gold, Siegel, Russell, & Weinstein, 1996, for a review). Of these methods, cost-benefit analysis has been the most widely used in economic studies of treatment for heroin and other drug users (Barnett, 1999). In theory, cost-benefit analysis considers all the identifiable costs and outcomes of an intervention. These costs and outcomes are valued in monetary units, allowing researchers to assess whether the intervention is worthwhile in terms of a simple decision rule that benefits

must exceed costs. In practice, however, it is extremely difficult to measure all costs and benefits, and to reduce these to dollar values (Chisholm, 1998; Singh et al., 2001).

5.7.5   Economic studies of treatment for heroin dependence

Economic evaluation as applied to treatment for heroin and other drug use problems is a relatively new area of research (Barnett, 1999; Flynn et al., 1999). Overall, the findings from overseas treatment outcome studies support the view that treatment yields benefits that justify its cost.

Both TOPS (Harwood et al., 1988) and CALDATA (Gerstein, Johnson, Harwood, Fountain et al., 1994) examined the economic benefits of treatment in terms of crime reduction, by comparing the cost of treatment with cost savings estimated from the difference between baseline rates of crime and subsequently lower crime rates during and after treatment. Components of the social costs of crime included victim costs, criminal justice system costs, and crime career – productivity costs. These costs were estimated using data from Federal reports (Hubbard et al., 1989). Treatment cost estimates were developed for TOPS and CALDATA using data reported from the US National Drug and Alcohol Treatment Unit Survey (NDATUS) (US Department of Health and Human Services, 1992). Daily treatment costs and the cost of an average treatment episode in long term residential, outpatient drug free, and methadone maintenance treatment were analysed and reported. Overall, the ratio of benefits to costs for an average treatment episode in both TOPS and CALDATA showed that treatment leads to significant benefits above the costs of providing treatment.

More recently, DATOS examined the cost of long term residential and outpatient drug free treatment for cocaine dependent individuals in relation to the economic benefits from reduced crime during and after treatment (Flynn et al., 1999). Benefits were defined as the cost savings produced by reduced costs of crime to society. As in TOPS and CALDATA, data from NDATUS were used to estimate treatment costs. Estimated tangible costs per crime based on data from Federal reports were used to value the criminal acts reported by DATOS clients in nine crime areas (including assault, burglary, theft, robbery, forgery, and drug law violations). Costs of crime to society before, during, and after treatment were calculated by multiplying the number of individual types of crimes reported by each client by the tangible cost for each individual crime. Positive social net benefits were reported for

both modalities, indicating the value of investing in treatment for cocaine dependence (Flynn et al., 1999).

NTORS examined the cost of providing treatment during the year after admission in relation to the cost savings produced by reductions in acquisitive crime (Gossop et al., 1998). The reductions in crime among the NTORS cohort from intake to 12 month follow-up were found to represent cost savings of £5.2 million in terms of reductions in the victim costs of crime and savings to the criminal justice system. Or, for every extra £1 spent on treatment, there was a return of more than £3 in terms of cost savings associated with reduced victim costs and reduced demands on the criminal justice system (Gossop et al., 1998). It is unclear, however, how estimates of the victim costs of crime and criminal justice service costs were derived.

The significance of these studies is minimised by several methodological limitations. First, none of the studies included a comparison group of active drug users who did not receive treatment. Second, key measures of impact such as costs to victims, criminal justice system costs, and lost productivity costs were estimated from national surveys rather than measures of the actual costs attributed to clients in the study cohort. Third, these studies focused primarily on treatment costs and the tangible benefits accrued from reduced crime that can be estimated in monetary terms. Other areas of potential benefit, such as employment, health, psychiatric morbidity, and social and family functioning were not examined. The additional benefits of treatment for heroin and other drug use problems beyond reductions in the costs of crime to society require study and quantification. While factors such as increased employment and improved functioning in health and other areas have been widely reported as treatment benefits, they have not been translated into economic benefits that accrue to the community.

5.7.6 Cost-consequence analysis

Studies of treatment for heroin and other drug users are likely to involve multiple outcomes of concern to researchers, treatment providers, and policy makers. Cost-consequence analysis is a pragmatic method of economic evaluation that enables the cost of delivering treatment to be examined in relation to multiple outcome areas. In this approach, the costs and consequences of an intervention compared to one or more relevant alternatives are calculated separately and listed. The analysis itself does not combine these components, nor does it indicate the relative importance of the

various outcomes of interest. These decisions are left to the users of the study, whether they are researchers, clinicians, policy makers, or others (Gold et al., 1996). Cost-consequence analysis is therefore able to address the interests of multiple consumer audiences. Such flexibility makes this method highly suitable for longitudinal studies of treatment outcome for heroin and other drug users.

Key points:

- Heroin use and dependence impose a substantial clinical and social burden that contains an economic dimension.
- Policy makers and treatment providers are increasingly concerned with the cost-effectiveness of drug treatment.
- Economic evaluation enables policy makers and clinicians to assess the degree to which particular interventions offer the best use of scarce resources.
- The findings from overseas treatment outcome studies suggest that treatment yields benefits in terms of crime reduction that justify its cost.
- Studies of the additional economic benefits of treatment beyond reductions in the costs of crime to society are required.
- Cost-consequence analysis enables the cost of delivering treatment to be examined in relation to multiple outcome domains.

6.0   Summary

6.1   Feasibility of long term follow-up

It is commonly assumed that heroin users are a marginalised group engaging in a range of illicit activities, and therefore, that heroin using cohorts are difficult, if not impossible, to follow up. Overseas data are clearly inconsistent with this view. Prospective studies conducted in a number of countries have established that longitudinal treatment outcome research can be conducted with dependent heroin users, in that longitudinal cohorts can be maintained over several years. The US TOPS, for instance, reported 80 percent follow-up at 3 months, 79 percent at 12 months, 76 percent at 2 years, and 65 percent at 3 to 5 years. DARP had 77 percent follow-up at 3 years, 73 percent at 6 years, and 70 percent at 12 years. The UK NTORS reported follow-up rates of 75 percent and 72 percent at 6 months and 12 months, respectively. These data indicate that it is possible to follow up cohorts of heroin users, even after 12 years. Clearly, it is feasible to conduct longitudinal research with this population.

6.2   Maintenance of longitudinal cohorts

The maintenance of a cohort is essential to all longitudinal research. Specialist reviews of follow-up methodology have identified a number of strategies for maintaining contact with participants and obtaining high response rates in longitudinal studies of drug users (Cottler et al., 1996; Desmond et al., 1995). It is vital, for instance, to collect comprehensive locator information from participants at the beginning of the study, and to update the locator form at each follow-up point. The locator form should document, for example, the full legal name of the respondent, any aliases or nicknames, best mailing address and phone number, mother's and father's full names, addresses, and phone numbers, and employer information. Because heroin and other drug users tend to be mobile, it is important to conduct follow-up interviews in convenient locations, and to provide adequate resources for travel. The development and maintenance of rapport between the interviewer and participants is another essential feature of successful follow-up.

6.3 Research domains

There are a number of key research domains that a longitudinal study of treatment outcome for heroin users should examine (Table 4). As stated in Section 5.1, polydrug use is the norm among heroin users, and is strongly related to an increased risk of overdose and other harms. The accurate measurement of heroin and other drug use is essential to determine treatment effectiveness and patterns of concomitant drug use. Data on the processes involved in transitions between routes of heroin use, and the possible role of treatment in making transitions are also of relevance, given the impact that route of administration has on heroin dependence, overdose risk, and health (Section 5.2). Heroin use and dependence, however, are associated with a constellation of problems in addition to heroin and other drug use per se, each of which are of independent interest when assessing treatment outcome.

Table 4. Recommended research domains and instruments for longitudinal studies of treatment outcome for heroin users

Research domains	Possible instruments
Heroin and other drug use	OTI Drug Use Section
Route of administration	*Assessment of drug use history and current route(s) of heroin use**
Criminality	OTI Crime Scale
Psychiatric morbidity	
General psychological distress	GHQ, SF-36, SF-12
Depression	CIDI, BDI
ASPD	CIDI
PTSD	CIDI
BPD	CIDI
Mortality	*Search of Births, Deaths and Marriages**
Physical health status	
General health	OTI Health Scale, SF-36, SF-12
Injection-related risk taking	HRBS
Economic burden of heroin use	*Health economic analysis**

Recommended procedures

As discussed in Section 5.3, heroin users frequently commit crime to sustain heroin use. The question of how interventions for heroin users impact on criminal behaviour has implications for treatment providers and policy makers. Criminality (in terms of self-reported crime) is therefore an important treatment outcome variable. Similarly, there are high rates of psychiatric morbidity among heroin users, with the most common diagnoses being depression and ASPD (Section 5.4). Data on

psychiatric morbidity are essential to determine the long term consequences of heroin use, and to determine the value of treatment in reducing heroin-related harm. Psychiatric morbidity has also been strongly related to poorer treatment outcome, and is therefore an important predictor variable.

Overseas studies have shown that mortality among heroin users is high (Section 5.5). Longitudinal data on the prevalence and patterns of mortality in an Australian cohort would provide a baseline for measuring the effectiveness of interventions for heroin users. As stated in Section 5.6, the overall physical health of heroin users is poor, and heroin users are at an increased risk of a range of serious medical consequences. The assessment of overall health status and injection-related risk behaviour is essential to determine the impact of treatment on health outcomes. Similarly, analyses of the cost of delivering treatment in relation to particular outcomes are important to determine the degree to which different interventions offer the best use of scarce resources. While resources remain limited and demand for treatment high, economic analysis can provide valuable data on the most cost-efficient way to deliver services so as to maximise treatment outcomes (Section 5.7).

6.4   Research instruments

A major advantage of longitudinal research methodology is that it enables researchers to determine the impact of multiple factors on subsequent behaviour. Where possible, reliable and valid instruments should be used to measure the predictor and outcome variables of interest, so that the findings are comparable with those of previous studies (Table 4). In the case of heroin and other drug use, the Drug Use Section of the OTI provides reliable and valid data on recent drug use across a wide range of drug classes. The OTI Crime Scale provides the optimal measure of criminality among heroin users, in that it is sensitive to changes in criminal behaviour. To assess psychiatric morbidity, it is recommended that the Composite International Diagnostic Interview (CIDI) be used. This structured interview yields diagnoses of current DSM Axis I psychiatric morbidity, including depression, ASPD, PTSD, and BPD. In the case of physical health status, a global estimate of current health status such as the OTI Health Scale provides the optimal measure, because it is oriented towards the specific health problems associated with heroin use. The SF-12 and SF-36 also yield reliable and sensitive assessments of the physical and psychological

health of heroin and other drug users. Finally, the injecting subscale of the HRBS provides a reliable and valid measure of current injection-related risk behaviour.

6.5   The need for longitudinal research in Australia

Overseas experience has shown that it is feasible to carry out longitudinal research with dependent heroin users. Nonetheless, there are a number of reasons why it is essential to conduct prospective treatment outcome studies of heroin users in Australia. First, there are substantial differences between different countries in government policies and in the health care delivery systems available to heroin users. In particular, treatment provision in countries such as the USA and UK is markedly different from that provided in Australia. As stated in Section 5.5, the British system of methadone prescription is less tightly regulated than in Australia, with methadone and other opiate drugs (including heroin) being prescribed by general practitioners, with little or no supervision of drug administration. The US system is considerably more restrictive, with access to methadone being very limited. The Australian system lies somewhere between these two models in terms of access to treatment and restrictions placed on those in treatment. The characteristics of heroin users and their patterns of drug use are also likely to differ in many respects between a country such as the USA and Australia. In view of these differences, it would be unwise to generalise findings from overseas studies to the Australian context.

Second, the major overseas studies of treatment outcome are methodologically flawed in that they used treatment entrants from purposely selected treatment programs, with no attempt at representative sampling. None of these cohort studies included a comparison group of active heroin users who were not in treatment at admission to the study. In addition, these studies did not comprehensively assess psychiatric morbidity using reliable and valid diagnostic instruments. TOPS, for instance, included only three indicators of depression: one general indicator of depression, one measure of suicidal thoughts, and one measure of suicide attempts (Section 5.4). This is a serious limitation, given the high prevalence of psychiatric morbidity among heroin users.

Third, the findings from prospective studies of treatment outcome for heroin users will guide future responses and interventions for this group, with particular reference to Australia.

6.6   ATOS

ATOS improves significantly on the research methodologies used in previous studies of treatment outcome for heroin and other drug users. The treatment agencies from which the ATOS treatment sample is being recruited were selected randomly, stratified by geographical area and treatment modality, to provide a representative sample of treatment agencies. In addition, a comparison group of active heroin users who are not in treatment is being recruited from the same regions as the treatment sample, predominantly through NSPs. This has not been attempted in previous studies, and represents a significant methodological advance.   The research instruments used in ATOS are of demonstrated reliability and validity, which will enable effective comparisons to be made across time and across treatment modalities. ATOS is also collecting comprehensive data on levels of psychiatric morbidity using the CIDI, which generates DSM-IV diagnoses of depression, ASPD, PTSD, and BPD. To date, 604 participants have been recruited into the study. A total of 475 interviews have been completed at 3 month follow-up, representing a follow-up rate of 91 percent. A total of 196 interviews have been completed at 12 month follow-up, representing a follow-up rate of 82 percent. Follow-up rates are comparable across all treatment modalities and the non-treatment comparison group.   On the basis of overseas studies, these data indicate that high follow-up rates can be maintained at 12 months and beyond.

Large scale follow-up studies of heroin users are extremely labour intensive. Heroin users represent a challenging population, and obtaining high follow-up rates requires a great deal of time, effort, and persistence on the part of researchers. To maintain high follow-up rates over 3 years, ATOS must be adequately resourced. A minimum of one full-time senior research officer and two full-time research officers is required to maintain the ATOS cohort. Full-time research personnel are essential to the maintenance of respectable follow-up rates. Additional resources are needed to cover the travel costs of interviewers, subject reimbursement costs, and telephone costs.   Research has shown that reimbursement for participation is effective in maximising follow-up in longitudinal studies of drug users (Cottler et al., 1996). Similarly, the telephone is particularly important in maintaining contact with participants to achieve high follow-up rates.

6.7   Conclusion

On the basis of overseas experience, it is feasible to conduct longitudinal treatment outcome research with dependent heroin users in Australia. ATOS offers an unparalleled opportunity to maintain a large cohort of Australian heroin users. Extending the ATOS follow-up period beyond 12 months would enable essential information on longer term treatment outcomes and the burden imposed by heroin use to be obtained. Thus, ATOS can make a significant contribution to the research literature on treatment outcomes for heroin users and the natural history of heroin use in Australia.

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