INVESTING IN DRUG & ALCOHOL TREATMENT

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EXECUTIVE SUMMARY

There are two obvious trends in the drug abuse treatment field. The general public and many clinicians are of the opinion that treatment for drug and alcohol use is ineffective. In contrast, there is a growing consensus among the research community that treatment does work (Nathan & Gorman, 1998). The aim of this document is to demonstrate the benefit in investing in treatment for alcohol and drug problems. The review of the literature has led to the following conclusions and recommendations.

ALCOHOL

Assessment

- It is recommended that routine screening for alcohol abuse is carried out in primary care settings, where standard screening measures such as AUDIT should be used.
- Assessment for treatment for dependence should measure: level of drinking, level of dependence, physical effects of alcohol use, and psychiatric comorbidity. Reliable and valid assessment instruments exist and should be used in the treatment setting.

Detoxification

- Detoxification alone is of benefit to the individual as it provides respite from the physical damage which is a direct consequence of heavy alcohol usage.
- In order to maintain this benefit, detoxification needs to be augmented by treatment to prevent relapse to drinking.
- Appropriately supported home detoxification appears to be as effective as inpatient detoxification even for severely dependent alcoholics. Home detoxification has been rated as 4 to nearly 20 times less expensive and is the preferred treatment setting for those undergoing detoxification.
- Where outpatient care is not feasible, specialised detoxification units providing ambulatory and non-medicated care are cheaper and at least as effective as standard hospital inpatient care

Pharmacotherapies

- More research is needed on the appropriate applications of all pharmacotherapies currently being reviewed for the treatment of alcoholism. This research needs to be more rigorous.
- The risks associated with disulfiram, along with the poor research findings for this drug indicate that there is a need to replace it in the repertoire of treatments for alcohol dependence.
- Pharmacotherapies should only be used in conjunction with psychotherapies in the prevention of relapse for detoxified alcoholics.
- Acamprosate is the most promising pharmacotherapy. Support for naltrexone is poor at this stage, but it may prove useful for particular sub-samples of alcoholics.

- Evidence that antianxiety and antidepressant drugs help reduce drinking is poor. However SSRIs may have a role to play with depressed alcoholics.

Brief Interventions

- Brief interventions are effective in reducing alcohol consumption in those with mild to moderate problems with alcohol.
- Brief interventions of a motivational, non-confronting style appear most effective.
- A positive attitude towards change by both those who abuse alcohol and those who implement interventions at primary care centres is essential for their success. General practitionerss need to be convinced of the efficacy of brief interventions, trained in their implementation, and able to identify when to implement them. Patients need to be ready to change, or at least amenable to consider change.
- More research is required to clarify which are the most effective brief interventions and in which circumstances they are most effective. In particular, outcomes for women and those with concomitant physical and psychological problems need to be better researched.
- Brief interventions have the potential to provide a low cost approach to the problems of alcohol abuse in the general population especially where patients are self-referred. However, this does not deny the importance of greater research efforts to assist those who are unable or unwilling to change their alcohol use which is causing harm for the individual or other significant social costs. More intensive and costly approaches may prove more appropriate for this group.

Social Skills Training

- There is consistent evidence that social skills training is an important and effective component of alcohol treatment.
- Given the complexity of alcoholism, social skills training is not expected to be effective on its own, but rather seen as a component of broad spectrum treatment programs. Additional investigation is warranted to explore the unique contribution of social skills training to treatment outcome.
- There is inconsistent evidence as to the effectiveness of social skills based programs in the prevention and reduction of alcohol use in school based populations.

Behaviourally-oriented marital, family and community interventions

- Research has shown that family/marital behavioural interventions are effective but no more effective than individual therapy. The community reinforcement approach has shown greater promise but requires further research.
- The effectiveness of the community reinforcement approach package needs further assessment and clarification as to which parts are effective and which are not.
- The possible interaction of family/community reinforcement with degree of dependence and social dysfunction needs to be more thoroughly explored.
- The influence of supervised disulfiram on outcomes in trials of behavioural marital therapy and community reinforcement approach needs to be assessed. Given the suggestions made by experts in pharmacotherapies (see Section 2.5.1) that the use of disulfiram should be

curtailed, the effect of its removal or replacement in behavioural marital therapy and community reinforcement approach treatment programs needs clarification.

Cue Exposure

- Cue exposure is an effective treatment which may be most effective as one facet of controlled drinking programs.
- Because it directly addresses cues for drinking it may prove a cost-effective addition to programs which would normally require additional relapse prevention training.

Cognitive Behavioural Interventions

- Current research and expert opinion agree that behavioural self-control as taught through cognitive-behavioural therapy is an effective treatment for alcohol abuse.
- It appears that cognitive behavioural therapy may be most effective with problem drinkers who are nondependent.
- Cognitive behavioural therapy is particularly adaptable for non-direct interventions such as correspondence and computer training.
- Cognitive behavioural therapy for depression has the potential to improve drinking outcomes, which reflects the interdependence of these two psychiatric conditions.

Other Interventions

- The Quality Assurance Project in 1993 (QAP, Mattick & Jarvis, 1993) concluded that some other interventions had potential but insufficient evidence to recommend them at that time. Examples in this category are covert sensitisation, AA and acupuncture. The status of these other interventions has not changed since the completion of the QAP.

General Commentary

- It is important that those treatments which have evidence of effectiveness are implemented. To date little heed has been paid to evidence of effectiveness.
- It is likely that implementing most effective treatments will cost no more than those currently favoured, and, being more effective will prove to be more cost-effective.
- The notion of matching patients to treatments requires further investigation.

OPIATES

Assessment

- Patients presenting for treatment for opiate dependence should be assessed for: motivation to change; drug use and dependence; HIV/Hepatitis risk behaviour; mental health status; social functioning and criminality.
- Such an assessment process may be lengthy and this may discourage patients who are often ambivalent about treatment for their dependence. Hence it is recommended that a brief screen for drug use is used at first interview, and that other information is obtained in later sessions as rapport is established with the patient.

- Standard protocols such as the Severity of Dependence Questionnaire, the Opiate Treatment Index and the Addiction Severity Index have been developed and validated and should be used to assist in the assessment process.

Detoxification

- Detoxification is not of itself a treatment for opiate dependence. However reviewers agree that the process of detoxification does have intrinsic benefits for the individual, whether followed by treatment or not, because it provides a respite from the risks associated with daily drug use.
- Counselling and psychotherapy may be useful in allaying the apprehension associated with withdrawal from opiates but are not effective alone. More research is needed on non-drug adjuncts to assist detoxification.
- Treating patients with individualised tapering doses of methadone has tended to be the standard effective detoxification procedure, although other drugs are currently being assessed which may prove as effective, or better, for certain sub-groups of dependent individuals.
- Alpha adrenergic agents such as clonidine, guanfacine and lofexidine have been compared with methadone and, although effective, they have been found to have more side-effects and lesser effects on withdrawal symptoms.
- The opioid antagonists naloxone and naltrexone (unassisted or with clonidine) may be useful for those individuals who are willing to tolerate a shorter but more intense withdrawal period.
- Buprenorphine has been found to effectively assist in the process of opiate detoxification. Patients show few symptoms and signs of withdrawal from this medication and its usefulness is enhanced by the fact that it is less vulnerable to abuse than methadone. Further research is recommended to specify appropriate dosing regimes for opiate detoxification.
- Use of ultrarapid detoxification using naltrexone aided by heavy sedation or anaesthesia has received much publicity but has yet to be properly evaluated. There is also a slightly increased risk of harm associated with the use of general anaesthesia.

Methadone Replacement Therapy

- There is strong support, from the few randomised controlled trials that have been carried out, for the superior effectiveness of methadone maintenance over placebo/no treatment.
- Observational studies have also shown positive relationships between time in treatment and such outcome variables as opiate and other drug use, criminal behaviour and sexual risk-taking.
- Dose of methadone is of crucial importance to outcome. Methadone dose is positively related to retention and negatively related to illicit opioid use. It is recommended that dose is individualised to suit the patients' psychological and physiological needs.
- Methadone is only effective whilst the patient remains in treatment. Once a patient leaves treatment he/she will return to pre-treatment drug taking.

- Methadone maintenance reduces the risk of the spread of HIV/AIDS due to the decrease in injecting activity. No effects on rates of hepatitis infection have been found, probably due to the fact that most patients have these highly infectious diseases on admission to treatment.
- Clinic policies have a significant influence on the outcomes of methadone maintenance treatment. Clinics should: be maintenance-oriented; pay special attention to patients' individual needs and problems as they arise; be more accessible by providing take-home dosing; and willing to provide psychological counselling as required.
- The evidence regarding the effectiveness of methadone maintenance on cocaine use in heroin users remains equivocal.
- There are particular sub-groups of heroin users who may have better outcomes on methadone maintenance. These include older users, those who have attempted methadone maintenance before and those who have lower dependence. Those who do not do as well on methadone maintenance include patients with a high level of pre-treatment criminal activity and alcohol abuse.
- Patients with comorbid psychiatric conditions such as antisocial personality disorder or mood disorders, although often the most severely addicted, can benefit from methadone maintenance treatment and cessation of illicit opiate use.

LAAM

- LAAM is an effective alternative to methadone for opioid maintenance treatment.
- The longer half-life of LAAM yields advantages of less frequent clinic visits which have both social and cost benefits. It has the disadvantage of increased risk of toxicity.
- Higher doses of LAAM effectively block opiate receptors and lead to reduced illicit opiate use, whilst lower doses are ineffective in this regard.
- As with new treatments for alcohol dependence, greater enthusiasm and belief in its treatment effectiveness needs to be encouraged through improved communication of relevant evidence on LAAM to consumers and other stakeholders.

Buprenorphine

- Buprenorphine is a partial opioid agonist that has shown considerable potential for treating heroin dependence. It has the advantages of being safer in overdose than pure opiates, amenability to thrice-weekly dosing and reduced withdrawal symptoms on cessation. It warrants inclusion as an alternative maintenance pharmacotherapy for patients presenting for treatment for opioid dependence.
- Research has shown buprenorphine to be as effective as methadone in retaining patients in treatment and reducing illegal opioid use. It may also prove more effective in assisting patients to become abstinent because of its cross-tolerance to pure opioids and less severe withdrawal symptoms.
- At least three groups of researchers have proposed that a sequential pharmacological treatment strategy, which commences with rapid induction directly onto buprenorphine from heroin may prove most effective in ascertaining the best treatment program for patients presenting for treatment for their opioid dependence.

- The use of a buprenorphine-naloxone mix may help improve patient compliance in allowing take-home doses without increasing the risk of diversion.
- Studies which have compared addiction clinic settings with primary care settings have indicated that both are amenable to buprenorphine maintenance programs and a suitable mix in the availability of both settings is likely to cater best for the range of clients who present for treatment.
- Much recent research has tended to use quite low doses of buprenorphine, given its safety profile and its advantages both clinically and pharmacologically. Many studies have been initiated on the premise that 8mg is an effective mean dose but it appears that it is in effect a low to average effective dose. Individualised dosing may prove most effective in ensuring best treatment response and doses up to 32mg may be well tolerated and lead to optimal outcomes for some individuals.
- There has been some suggestion from research that buprenorphine maintenance may lead to reduced usage of cocaine. The issue of the relative accuracy and validity of self-report drug use and urinalysis requires further investigation.

Naltrexone

- Naltrexone is an opioid antagonist that effectively blocks opiate receptors so that opiates are unable to have their usual analgesic and euphoric effects.
- Naltrexone maintenance programs tend to have high dropout rates compared with opiate maintenance programs, but naltrexone has been found to be particularly effective for those patients who are highly motivated to cease their opiate abuse. These include health care workers and those who pay large amounts of money for their treatment. Legally mandated naltrexone treatment may also be effective, but the evidence is equivocal. It has not been established whether these sub-samples are responding specifically to naltrexone or whether they would do well with any plausible intervention.
- Comparisons of naltrexone with methadone need to be clear about achievable outcomes, as expected outcomes for these groups may turn out to be different. Whereas retention in treatment is a primary goal of methadone maintenance, it appears that an abstinence goal after relatively brief (less than 6 months) treatment with naltrexone may be appropriate. Illicit opioid use at any particular time post treatment initiation may be a more appropriate comparison measure.
- Good long-term follow-up studies of those who become abstinent following naltrexone treatment have not been completed to date. It is most important that post-treatment mortality and morbidity is closely monitored for patients who have undertaken naltrexone treatment. More research is needed on this matter.
- The evidence regarding adding antidepressants to naltrexone treatment remains equivocal.

Prescribed Heroin

- The issue of provision of prescribed heroin for those individuals for whom conventional treatments have repeatedly failed should be subjected to further investigation. The area has not been adequately researched and definitive conclusions cannot be drawn regarding the efficacy of this particular therapy.

Drug-Free Treatment

- No randomised controlled trials have been conducted to ascertain the effectiveness of Narcotics Anonymous, therapeutic communities and outpatient drug counselling. Observational studies have found that reduced heroin usage can result for those who remain within non-drug treatment programs.

CANNABIS

Specific Interventions

- Although results from pre-post studies do not adequately demonstrate specific treatment effects, outcomes for marijuana from these types of studies have been positive, and of a similar magnitude to those for other drugs. In particular, the demonstration of treatment dosage effects in the DATOS study lends credence to the conclusion that current treatment programs are reducing marijuana use and abuse.
- Comprehensive prevention programs delivered in early adolescence may have potential to reduce initiation to marijuana use. Further research is needed to specify the best model and intervention implementation procedures.
- Insufficient recognition has been given to the need for treatment for marijuana abuse and dependence. This is evidenced in the paucity of research on specific interventions and the high response rates when volunteers are sought for marijuana treatment research programs.
- There is some evidence that the community reinforcement approach, relapse prevention, marijuana-focussed supportive social interaction groups and brief motivational interventions, or combinations of these, are likely to be effective in clinical treatment for marijuana abuse and dependence.
- The few controlled studies completed to date have not demonstrated conclusively the superiority of any one of these interventions and further research is required.

COCAINE

Treatment Setting

- Intensive outpatient treatment is less expensive and generally more effective than inpatient treatment. However, inpatient treatment should be available for more intractable patients for whom outpatient programs are unlikely to succeed.

Assessment

- The aims of assessment are to reveal the level of dependence and psychosocial impairment of the patient, as well as establishing a rapport to serve as a basis for positive treatment interaction.

- Standard measures of dependence, motivation and psychosocial impairment are available and should be used.

Detoxification & Withdrawal

- There is some disagreement in the literature regarding the course of withdrawal from cocaine, with some theorists arguing that there are three stages beginning with the highly aversive "crash". Others claim that there is a gradual decline of withdrawal symptom severity which is not initially excessive.
- Due to the relatively low intensity of withdrawal symptoms, medicated assistance is not recommended.

Pharmacotherapies

- Desipramine, although showing early potential for improving treatment outcomes, has not been found to be generally effective in treating cocaine addicts. Further research is needed into its usefulness particularly as a part of a broader behavioural program and with patients with lower levels of dependence.
- The specific serotonin reuptake inhibitor fluoxetine has shown some positive outcomes with cocaine abusing subjects, especially for those patients also addicted to opiates. However it needs to be further assessed in randomised controlled trials.
- Antidepressant medications have shown little potential to assist with treatment for cocaine abuse.
- There is little research support for the use of lithium to control cocaine use with individuals with bipolar disorder; nor for the use of stimulant drugs used in general treatment of ADD for cocaine use in ADD.
- There is little research evidence to support the use of dopamimetic agents, dopamine precursors, anticonvulsants nor diazepam to treat cocaine abuse. However, if these classes of drugs are to be investigated further, it is recommended that individualised rather than fixed dosing is used, along with monitoring of serum levels.
- Treatment with the blocking agents flupenthixol and buprenorphine may be effective in reducing cocaine use, especially in psychotic and opiate-abusing patients respectively. Further controlled research is warranted on these drugs and for these sub-groups of cocaine abusers.
- No aversive medication has been identified to treat cocaine abuse, although the neuroleptic flupenthixol decanoate should be further studied for its aversive effects.
- Consideration should be given to placebo-controlled trials of oral amphetamine replacement therapy to ascertain the safety and efficacy of such interventions.
- Further research on pharmacotherapies for cocaine (and other stimulants) needs to factor in complementary psychosocial therapies, but also to demonstrate that specific pharmacotherapies add to overall treatment effectiveness.
- Because the safety of cocaine use is unpredictable and considering the poor retention rates achieved in this area of research, caution should be exercised when trialling new medications because of the possibility of additive negative effects of the trial drug and cocaine.

Nonpharmacological Interventions

- High early dropout rates are related to waiting list time, and therefore experts recommend rapid induction to treatment.
- There is consensus that more intensive programs (sessions at least once per week) are more likely to be effective. No clear-cut treatment period has been specified, but research suggests that for patients with medium to severe disability, a minimum of 3 months is recommended. Further research is required on these issues, taking into account both the severity of disability and the nature of the treatment being offered.
- There is little research evidence to support use of psychodynamic therapy, while the efficacy of the 12 step approach requires further investigation.
- The use of vouchers to reward abstinence, either alone or within a broader treatment program such as CRA, has been demonstrated to be effective in treating cocaine abuse. Further research is needed to establish appropriate schedules and most fitting contexts for these.
- Recent research has lent support to the use of cognitive-behavioural techniques for treating cocaine abuse. In particular, manualised interventions which address coping skills and dealing with risky drug-taking situations have shown promise. However, the few RCTs to date have not clearly demonstrated the effectiveness of this intervention.
- Results from various studies have suggested future directions for research especially in terms of matching patients to treatment on the basis of personal interests, abilities and level of disability.

AMPHETAMINES

Specific Interventions

- There is a need for greater recognition of the prevalence and harms associated with amphetamine abuse.
- It is recommended that the feasibility of a shared care approach to treatments for amphetamine abuse is investigated, with greater intervention by GPs at the primary level and improved specialised referral services.
- Treatments for amphetamine abuse have been poorly researched. To date no pharmacological interventions have been found to be effective. One possible area of research is the use of replacement amphetamines based on harm minimisation principles. However other pharmacotherapies may emerge once there is appropriate recognition of the extent of the problem.
- As with cocaine, care is needed in applying pharmacotherapies in a situation where a potentially very harmful drug is being abused. Pharmacotherapies should be supported by effective psychosocial interventions.
- Manualised contingency management and cognitive-behavioural therapy incorporating relapse prevention have been recommended as the best available therapies for amphetamine abuse. There are no published trials of these interventions and there is a need for more

formal controlled research on these approaches. Similarly the efficacy of 12-step and therapeutic community approaches should be assessed.

1.0 INTRODUCTION

This document provides a summary of research on treatment outcome in drug and alcohol. There have been a number of extensive reviews in the area of treatment outcome in this area and more recently a number of large studies. Three of the most extensive reviews which this report aims to build on are:

- Heather, N., & Tebbut, J. (Eds.) (1989). *An Overview of the Effectiveness of Treatment for Drug and Alcohol Problems*. National Campaign Against Drug Abuse Monograph Series Number 11. Australian Government Publishing Service.
- Mattick, R.P., & Jarvis, T. (Eds.) (1993). *An Outline for the Management of Alcohol Dependence and Abuse*. Quality Assurance Project. National Drug Strategy Monograph.
- Mattick, R.P., & Hall, W. (1993). *A treatment outline for approaches to opioid dependence: Quality Assurance Project*. NDS Monograph No. 21. Canberra: AGPS.

Summaries of more recent large-scale studies and reviews are presented at the end of the report (Appendix). The report takes each treatment area in turn, firstly for alcohol, then opiates, cannabis, cocaine and amphetamines. The existing reviews are summarised and any new research is critically assessed and summarised. The report therefore provides both a summary of the existing reviews in the area and a thorough review of research since 1993. The aim of the document is to outline what has been shown to work and to highlight recent research completed since the above major reviews in the area.

1.1 BACKGROUND AND CONTEXT

The impetus for this review came from an increased awareness at the international level of the importance of a balanced approach to drug use, including both supply and demand reduction. The United Nations convened a Special Session of the General Assembly on the World Drug Problem in New York, 8-10 June 1998 (United Nations, 1998a). The overwhelming message from the Special Session is that all countries now recognise the importance of adopting a balanced approach, one that places equal priority on measures to reduce demand for drugs and those to reduce supply of drugs.

The shift in emphasis is evidenced by the Special Session's adoption of the Declaration on the Guiding Principles of Demand Reduction. Through the Declaration, nations are committed to investing in demand reduction programs that will, inter alia, contribute towards reducing public health problems and improve health and well being. The Special Session also established the Year 2008 as a target date for achieving significant and measurable results in the field of demand reduction.

The challenge upon which the Declaration on the Guiding Principles of Demand Reduction was based is expressed in the following quote:

1. All countries are affected by the devastating consequences of drug abuse and illicit trafficking: adverse effects on health; an upsurge in crime; violence and corruption; the draining of human, natural and financial resources that might otherwise be used for social and economic development; the destruction of individuals, families and communities; and the undermining of political, cultural, social and economic structures.
2. Drug abuse affects all sectors of society and countries at all levels of development. Therefore drug demand reduction policies and programs should address all sectors of society.
3. A rapidly changing social and economic climate coupled with increased availability and promotion of drugs and the demand for them have contributed to the increasing magnitude of the global drug abuse problem. Changing patterns of drug abuse, supply and distribution has compounded the complexity of the problem. There has been an increase in social and economic factors which make people, especially the young, more vulnerable and likely to engage in drug use and drug-related risk-taking behaviour.
4. Extensive efforts have been and continue to be made by Governments at all levels to suppress the illicit production, trafficking and distribution of drugs. The most effective approach towards the drug problem consists of a comprehensive, balanced and coordinated approach; encompassing supply control and demand reduction reinforcing each other, together with the appropriate application of the principles of shared responsibility. There is now a need to intensify our efforts towards demand reduction and to provide adequate resources towards that end.
5. Programs to reduce the demand for drugs should be part of a comprehensive strategy to reduce the demand for all substances of abuse. Such programs should be integrated to promote cooperation between all concerned, should include a wide variety of appropriate interventions, should promote health and social wellbeing among individuals, families and communities and should reduce adverse consequences of drug abuse for the individual and for society as a whole.

   (Reproduced from the Declaration on the Guiding Principles of Drug Demand Reduction (United Nations, 1998a)

Through the Declaration, countries are committed to intensify efforts to reduce the demand for drugs. The Declaration states as one of its guiding principles that "Demand reduction should incorporate knowledge from research as well as lessons derived from past programs."

The 38th Session of the Commission on Narcotic Drugs requested the United Nations International Drug Control Program (UNDCP) to update the 'Resource Book on Measures to Reduce Illicit Demand for Drugs' (United Nations, 1979). This updated series is intended to further define the principles of the Declaration and assist countries to identify a set of programs and policies which would reduce the demand for illicit drugs.

In 1996, an informal international working group was established under the auspices of UNDCP to develop a new set of demand reduction resource materials which would reflect new knowledge gained over the past twenty years. In 1997, the Australian Government convened

the informal international working group, who agreed to the development of a glossary of demand reduction terms and a monograph entitled "Investing in Demand Reduction". The "Glossary of Demand Reduction Terms" was provided to the UNDCP for consideration in June 1998.

Treatment for drug use is one of the main demand reduction strategies outlined in this present document: "Investing in Demand Reduction". This document outlines the evidence for effective treatment options in both alcohol and illicit drug use. In doing so it outlines the case for effectively investing in treatment.

1.2 AIMS OF THE PROJECT

This project examines the recent research-based knowledge on the effectiveness of treatment for drug and alcohol use disorders. There continues to be substantiated and ever increasing interest from the national policy makers and their advisers, clinicians and service providers, user groups and the lay population as to the efficacy and necessity of drug and alcohol treatment services.

Much recent research has indicated that successful management and treatment of drug and alcohol abuse can be achieved and that the economic gains made in doing so are beneficial to society at a number of levels. However, this view is not widely accepted by the general public. Despite extensive evidence that treatment for drug and alcohol abuse does work, questions continue to be raised regarding its effectiveness.

1.3 REVIEW METHOD

Searches of Psychinfo, Medline and Embase databases were conducted. These searches were supplemented by scanning the reference lists of review articles and treatment outcome studies for further treatment outcome studies. Major reviews of treatment outcome research were identified. Large treatment outcome studies were also identified. A study was included in the review if:

1. it was a randomised controlled trial involving a clinically relevant intervention group (e.g.brief advice) and a comparison group (e.g. no treatment, minimal treatment); or
2. it used a quasi-experiment design and there were few randomised controlled studies in the area.

The methodologies of the various large-scale reviews which have provided data throughout this review are summarised in Appendix 1. Appendix 2 summarises both methodologies and outcomes for recent large-scale studies, which warranted mention due to their size, but did not fit the inclusion criteria listed above.

A critical analysis of the method used was included for all studies reviewed.

1.4 DEFINITION OF DRUG AND ALCOHOL PROBLEMS

Substance abuse and dependence are conditions defined by a set of cognitive, behavioural, physiological and neurobiological changes in the body, whereby the individual will continue substance use despite the co-occurrence of significant problems. Substance abuse is defined according to DSM-IV (American Psychiatric Association, 1994) as a maladaptive pattern of drug use manifested by recurrent and significant adverse consequences related to repeated use. In particular, an individual abusing drugs may repeatedly fail to fulfil major role obligations and continue to use drugs in the face of adverse social, legal, physical, financial and interpersonal problems arising form the recurrent use. Unlike dependence, abuse is not characterised by withdrawal, tolerance or a pattern of compulsive use, only the adverse consequences of intermittent and repeated use.

Dependence on the other hand, is defined (DSM-IV) as a characteristic set of cognitive, behavioural and physiological signs in which the individual will continue to use the substances despite considerable related problems. There is also the presence of tolerance and withdrawal symptoms upon cessation of the drug. The actual criteria for dependence are summarised as follows:

TABLE 1: DSM-IV Criteria for Substance Dependence

The pattern of substance use, which leads to significant distress/ impairment manifested by three or more of the following in a period of 12 months.
(1) Tolerance - the need for larger amounts of the drug in order to achieve the same effect.
(2) Withdrawal; characteristic syndrome present upon cessation of the drug or the drug is taken to relieve withdrawal symptoms.
(3) The substance is taken over a longer period of time than initially intended.
(4) A persistent desire to decrease use, however attempts may be unsuccessful.
(5) Social and personal interests are given up or decreased due to the substance use.
(6) Considerable time spent acquiring the substance/using or recovering from use.
(7) Continuation of substance use despite awareness of recurrent problems associated with use.

In addition to these criteria, the World Health Organisation (WHO) International Classification of Diseases, 10th Edition (ICD-10) suggests that another essential characteristic of dependence is that the individual must possess a strong desire to take the substance and is indeed consuming it.

1.5 THE MAGNITUDE OF DRUG PROBLEMS

Recently, significant advances have been made in the quantification of the burden of disease by the World Bank (Murray & Lopez, 1997). This new approach simultaneously considers the fatal and non-fatal consequences of disease. This incidence-based burden of disease approach provides an estimate of the number of years lost due to premature death and the number of years of life lived with a disability. Importantly, for the first time, this method allowed the calculation of the number of disability adjusted life years (DALYs) lost from any disease by combining the two separate measures of disability or death.

In late 1996 the World Health Organisation (Murray & Lopez, 1996) published a table of causes of disability adjusted life years (DALYs) lost in the developed nations. Substance use disorders contributed 5.3% of the total burden of human disease. These preliminary data, while undergoing revision, provide a strong indicator of the worldwide burden of substance use disorders. The authors themselves indicate that the burden due to illicit drug use would be under-reported in the study. Indeed, relative to use, illicit drugs cause a disproportionate number of deaths. Furthermore, deaths caused by illicit drug use occur at a much younger age than those caused by tobacco and alcohol. The population health consequences of drug use are of greatest concern for intravenous drug use. Intravenous drug use is the primary vector for the transmission of HIV (AIDS) and hepatitis. It is predicted that in the year 2020, HIV will cause 1.2 million deaths worldwide and will be one of the world's top ten leading causes of death (Murray & Lopez, 1997).

Of the substance use disorders, alcohol dependence produces a considerable burden of disease in men. In developed regions, it is the third highest cause of DALYs lost in men aged 45-59 and the second highest cause in men aged 15-44. It is the 5th highest cause of DALYs lost overall for both sexes across all ages.

1.6 THE EPIDEMIOLOGY OF DRUG PROBLEMS

Substance use disorders are among the most prevalent mental disorders in the general community. There have been a number of large epidemiological studies, first in the US and later in other countries which have all consistently demonstrated the pervasive nature of drug and alcohol use disorders (Hall, 1996).

One of the first epidemiological studies was the Epidemiologic Catchment Area (ECA) study. The ECA involved personal interviews with over 20,000 Americans (Regier et al., 1990; Regier et al., 1993). The results indicated that alcohol use disorders were the second most common mental disorder among the major diagnoses that were assessed (Helzer, Burnam, & McEvoy, 1991). A total of just under 14% of the population suffered from alcohol use disorders at some time in their lives, (with 8% meeting criteria for alcohol dependence) comparable to the 14% who had phobias at some time in their lives (Robins & Regier, 1991).

The prevalence of alcohol use disorders was strongly related to gender: 24% of men and 5% of women had suffered from such disorders at some time in their lives, while 12% of men and 2% of women had experienced these disorders in the year before they were interviewed. Just under a third of the ECA sample (31% overall, 36% of men and 25% of women) had used at least one drug. Drug use disorders were diagnosed in 6% of the sample. Cannabis use disorders affected 4% of the sample, followed by stimulants (2%), sedatives (1%) and opioid (0.7%) use disorders.

The National Comorbidity Survey (NCS) is the most recent population survey undertaken between 1990 and 1992 to examine the extent of comorbidity between substance use and non-substance use disorders in the USA (Kessler et al., 1994). The survey used a modified version of the Composite International Diagnostic Interview (CIDI) schedule to make the same diagnoses as in the ECA.

The prevalence of alcohol use disorders was higher in the NCS than the ECA. The NCS differed from the ECA in assessing dependence symptoms in any person who had ever used alcohol 12 or more times in a year (Anthony, Warner, & Kessler, 1994). The proportion of the population that met lifetime criteria for alcohol dependence was 24%. Men were more likely than women to become dependent on alcohol (Anthony et al., 1994). At some time in their lives 12 % had a drug use disorder (15% for men and 9% for women). In the NCS this figure was 4% (5% among men and 2% among women).

The National Survey of Mental Health and Well-Being (Hall, Teesson, Lynskey, & Degenhardt, 1999; McLennan, 1997) was the first national survey of the prevalence of common mental disorders including substance use disorders in the Australian adult general population. The survey interviewed a representative sample of 10,641 adults (aged 18 years or older) from throughout Australia and assessed symptoms of the affective, anxiety, and substance use disorders. Disorders were defined in terms of ICD-10 and DSM-IV diagnostic criteria. Substance use disorders included harmful use and dependence on alcohol, and the harmful use and dependence on four classes of drug: cannabis, stimulants, sedatives, and opioids. The method of the survey allowed direct comparisons with both the ECA and NCS studies.

In the past 12 months, 6.5% of Australians 18 years and over had an ICD-10 alcohol use disorder, and 2.2% had another drug use disorder. More males than females had an alcohol and other drug use disorder: 9.4% of males and 3.7% of females met criteria for an alcohol use disorder, and 3.2% of males and 1.3% of females met criteria for another drug use disorder within the past 12 months. The prevalence of substance use disorders decreased with increasing age: 10.6% of respondents aged 18-34 years met criteria for an alcohol use disorder and 4.9% met criteria for a drug use disorder. The rates of these disorders among those aged 55 years or older were 4.4% and 0.8%, respectively.

Alcohol was the most widely used of any drug but more users of other drugs had a use disorder in the past year. Specifically, only 8.9% of those who used alcohol in the previous 12 months had an alcohol use disorder while 22.7% of those who used other drugs had a co-occuring drug use disorder.

1.7 AIMS OF TREATMENT

Treatment has been defined as

> *The medical, surgical or psychiatric management of a patient or client. Any specific procedure used for the cure or amelioration of a disease, disorder, or pathological condition. In a public health context treatment may be described as secondary prevention.*
> *(Reproduced from the draft UNDCP Glossary of Demand Reduction Terms (United Nations, 1998b)*

Treatment aims to assist the individual to control or manage their drug use and responds to the physiological, psychological and social consequences arising from an individual's drug use.

What are the aims of treatment?

- To reduce illicit and licit drug use
- To reduce the hazard, harm and disability associated with an individual's illicit and licit drug use
- To decrease the population health, social burden and public safety threats associated with illicit and licit drug use.
- To provide an economically viable means of reducing the overall use of illicit and licit drugs and their associated disability.

Treatment activities cover a range of strategies including brief interventions, self help programs, psychological therapies, counselling, pharmacotherapies, social skills training and relapse prevention.

2.0 ALCOHOL

2.1 GENERAL INTRODUCTION

Alcohol is the second most widely used psychoactive substance in the western world (after caffeine) and because of this, it has created special problems for individuals and society as a whole. Alcohol is a sedative hypnotic: the main difference between it and other central nervous system depressants is that it is used recreationally rather than for medical purposes.

Alcohol is a simple molecule containing two carbon atoms and a hydroxyl group attached to one of them. It is both water and fat soluble and can therefore cross biological membranes easily. Ethanol is rapidly absorbed from the stomach, small intestine and colon and between 90-98 % is completely oxidised in the liver at a constant rate with respect to time. The remainder is excreted unchanged from the lungs and breath. The rate of metabolism of ethanol does not depend on the amount present in the blood (zero order kinetics). The oxidation process is catalysed by the enzyme alcohol dehydrogenase and occurs in the liver at a rate of approximately 120 mg/kg/hour or 10 ml of 100% ethanol are metabolized each hour regardless of the blood alcohol level (Sytkowski & Vallee, 1979).

Short-term exposure to ethanol and the resultant behavioural and cognitive impairment depend on the person's age, weight, sex, prior exposure to ethanol, level of tolerance and genetic vulnerability. The effects range from minimal coordination impairment and slight euphoria for blood alcohol levels below 50 mg/dl to stage one anaesthesia at blood alcohol levels of 300mg alcohol per 100 ml blood (30 mg %). Levels of 300-700 mg % result in respiratory failure, coma and death.
Note: 100 mg % = 0.1g ethanol/ 100 ml. The average drink contains 8-12 g of absolute ethanol per 100 ml.

2.2 TREATMENT SETTING

Previous reviews of treatment setting for alcohol treatment have concluded that there is no evidence for the superiority of inpatient over outpatient treatment of alcohol abuse (Mattick & Jarvis, 1993). The exception is that there are some types of patients, particularly those who are itinerant, who might be more effectively treated in inpatient settings. A recent review by Finney et al (1996) found that of the 14 research studies in this area, five favoured inpatient treatment, two found day hospital to be more effective than inpatient care and seven found no significant differences. They point out that in all but one of the studies showing superiority for inpatient, the inpatient care was more intensive than the comparison group. The review used a "box-score" to gauge treatment effectiveness, that is tallying the number of studies which did and didn't show an effect. This method has limitations and the calculation of effect sizes is the preferred approach.

Unfortunately, as the authors point out, the information available in the 14 studies did not allow the calculation of effect sizes. The authors conclude that given the overall pattern of results for the 14 studies reviewed it is likely that the effect sizes would favour inpatient care but their magnitude would be modest. This is consistent with the review by Mattick and Jarvis (1993).

The Finney et al (1996) review highlights the point that the setting of treatment for alcohol abuse is a very "distal" variable in relation to treatment outcome. The mixed results of the 14 studies and the fact that only seven showed treatment setting effects indicated that other variables such as modality, amount and duration of treatment are more likely to have an impact on outcome.

2.3 ASSESSMENT

Assessment for alcohol problems can range from brief screening interviews by general health care workers which may then lead to early intervention; to in-depth measures of a broad range of psychosocial functioning which are required to formulate and evaluate ongoing structured treatment programs.

2.3.1 Screening

Because excessive alcohol consumption is so pervasive, and has significant implications in terms of health care and other costs to society, it is widely agreed that routine screening should occur in primary health care settings (Gomel, Saunders, Burns, Hardcastle, & Sumich, 1994; Moore, 1994). It has been argued in reviews that there will be significant cost-benefits if screening is routinely carried out in settings where prevalence of excessive drinkers is likely to be highest. The following settings have been highlighted, in order of salience, with medical settings most likely to have the highest rate of identification, and recommendations are made regarding the role of each:

- *Medical practices*: In Australia at least 80% of the population consult with general practitioners (GPs) each year. GPs are thus ideally situated to detect drug and alcohol problems and offer advice and help to at-risk patients. Despite this, it appears that they are still somewhat reluctant to take on this role (Gomel et al., 1994; Roche, Guray, & Saunders, 1991). This points to the need for more research aimed at removing the barriers to GPs being involved in screening.
- *General hospitals*: Hospitals should be encouraged to undertake screening for excessive alcohol consumption and to provide advice and referral as needed. Hospital accreditation should routinely assess whether such procedures are in place (Mattick & Jarvis, 1993).
- *The workplace*: In workplaces where high rates of drinking occur, detection and treatment would improve health and safety and should be regarded as a cost-reducing exercise by employers.
- *Welfare and general counselling*: As it is likely that excessive alcohol intake has contributed to presenting problems at such services, routine screening and follow-up for alcohol abuse should increase the likelihood of a good outcome.

In general, diagnostic tests for a condition are assessed on their ability to discriminate accurately between those who have the condition and those who have not. The term sensitivity describes the proportion of individuals with the condition who test positive on that test, while the specificity of a test is the proportion of those without the condition who test negative. However, it is not only the detection of the condition of alcohol dependence which is the legitimate subject of screening programs. In fact, the costs to the community from lost productivity and the provision of health, welfare and legal services for people who are neither dependent nor consume large amounts of alcohol, far outweigh the costs of chronic alcoholism (Rydon, Redman, & Sanson-Fisher, 1988). Hence there has been a realisation in recent years that screening for hazardous but non-dependent alcohol use will lead to considerable benefits both economically and in terms of the well-being of individuals in society.

Standardised methods of screening for excessive drinking include use of clinical examinations, testing for biological markers and use of standard questionnaires. **Standard clinical examinations** which involve identifying physical signs of excessive alcohol consumption such as dilated facial capillaries, bloodshot eyes and coating of the tongue, have been found to be accurate for detecting alcohol dependence but are not sensitive enough for detecting signs of hazardous, non-dependent drinking (Mattick & Jarvis, 1993). The most widely used **biological marker** for alcohol abuse is serum gamma glutamyltransferase (GGT), a liver enzyme which tends to be detected in around 55%-80% of people with alcohol disorders. Detection rates are lower for hazardous, non-dependent drinkers. Overall, reviews of relevant research have concluded that standard questionnaires most accurately screen for both hazardous alcohol use and alcohol dependence (Mattick & Jarvis, 1993; Schorling & Buchsbaum, 1997).

A range of **standard questionnaires** has been designed to screen for alcohol abuse. Such questionnaires as the 24-item Michigan Alcoholism Screening Test (MAST, (Selzer, 1971)) and its shortened 13-item version, and the 4-item CAGE (Mayfield, McLeod, & Hall, 1974) have been shown to be valid in identifying alcohol dependence in males, but their ability to detect non-dependent hazardous drinking in females and a broad ethnic mix has not been established (Cherpitel, 1995). The TWEAK is a 5-item version of CAGE designed to assess at-risk drinking in pregnant women (Russell & Bigler, 1979). The Alcohol Use Disorders Identification Test (AUDIT) was developed as part of a WHO study of brief alcohol interventions and was based on research carried out in six countries. It is short; comprising only 10 questions, measures alcohol consumption, drinking behaviour and alcohol-related problems during the past year, and has been shown to validly detect at-risk drinking behaviour cross-nationally (Saunders, Aasland, Babor, Fuente, & Grant, 1993).

Recent Research

- Saunders et al (1993) document the development of the AUDIT brief screening questionnaire. AUDIT was developed following administration of a composite 150-item

schedule to a representative sample of 1888 persons attending primary health care facilities in six countries (Australia, Bulgaria, Kenya, Mexico, Norway and USA). The subjects were classified on the basis of a structured interview as 'non-drinkers' (less than 4 drinks per year), 'drinkers' (4 or more drinks per year and never treated for alcohol problems) and 'alcoholics' (had been diagnosed and treated for alcoholism in the past or are seeking treatment). Only the'drinkers' group was used to select items for the AUDIT questionnaire - the other two groups were used for validation of the instrument. The AUDIT questionnaire thus developed was found to have a sensitivity of .92 and specificity of .94, using a cut-off score of 8 (maximum score is 40). The authors concluded that AUDIT is superior to other screening instruments, currently in use, because:

- it detects persons at risk of becoming addicted, as well as those already dependent;
- it has more relevance for assessment of current drinking status as it refers to the past year, whereas other instruments refer to lifetime practice;
- by requesting frequencies rather than yes/no responses, it does not require the respondent to identify as a problem drinker;
- it is relatively short and can be disguised amongst other questions of a more general clinical nature so that respondents do not feel threatened; and
- it is valid cross-culturally.

- Bohn, Babor & Kranzler (1995) evaluated the validity of the AUDIT by assessing a sample of known alcoholics (n = 65) and general medical patients (n = 187) on several self-report questionnaires (AUDIT, MAST and MacAndrew screening test (MacAndrew, 1965)), and comparing outcomes with those from diagnostic interview, physical examination and laboratory tests. They found that the AUDIT correlated significantly with: scores on the other two screening tests used; both questionnaire and physical measures of recent heavy drinking; measures of alcoholism vulnerability such as familial alcoholism and sociopathy, and somatic and affective consequences of drinking. They found that AUDIT was superior to MAST in discriminating hazardous from non-hazardous drinkers.

- Cherpitel (1995) looked at the relative effectiveness of CAGE, short MAST, AUDIT and TWEAK for screening for alcohol abuse, by comparing scores on these instruments with scores on the Composite International Diagnostic Interview (CIDI, (Wittchen, 1994)) alcohol disorder measure. CIDI is a standardised interview for the independent assessment of alcohol intake and related disorders and has to be administered by trained personnel. The study used a random sample of 1330 emergency room patients from a university medical centre, and considered harmful drinking and dependence separately. Overall TWEAK and AUDIT performed best in identifying both hazardous and dependent drinkers, using standard cut-off points. However it was also found that different tests performed better with different population sub-groups depending on the cut-off used. The author noted a problem with the design of this study, in that all subjects were asked several questions related to quantity and frequency of drinking, and then given all questionnaires in the same order i.e. CAGE, then TWEAK, short MAST, AUDIT and finally the diagnostic interview. A randomised administration order would eliminate serial order effects which are likely to have occurred in this design. Furthermore, Cherpitel noted that other research had found that

asking questions about quantity and frequency of drinking prior to administering a screening questionnaire can reduce the sensitivity of the screening instrument.

- Hays et al (1995) screened 832 individuals in 6 West Coast treatment programs, who were compulsorily attending the programs as a consequence of arrest for alcohol-impaired driving. They were administered a 112-item questionnaire by computer. The questionnaire consisted of various sociodemographic measures, questions about frequency of drug use and various screening measures including CAGE, AUDIT and Short MAST. They randomly varied order of presentation of questions about frequency of use but presented the rest of the questionnaire in constant order. This would eliminate the problem mentioned for the Cherpitel study described above where prior questions about quantity and frequency of use may have confounded results. This study found that, with only 4 items, the response time was quicker for CAGE, but because of its shortness, CAGE was also least reliable (.69 cf. .84 and .83 for Short MAST and AUDIT respectively) with the largest standard error of measurement. Furthermore, the AUDIT and Short MAST were found to have greater relative validity based on various measures of drinking behaviour. They concluded that CAGE provides considerable relevant data quickly, but MAST and AUDIT provide more reliable and valid information with the additional time burden of only 1-2 minutes. The Short MAST was found to be most sensitive to long-term drinking patterns, while the AUDIT is more sensitive to recent drinking experience.

- Piccinelli et al (1997) compared scores on AUDIT with scores on the CIDI, for 482 subjects attending 10 primary care centres in Verona, Italy. They concluded that AUDIT performed as well as other screening instruments such as MAST and CAGE in detecting dependent drinking, but had higher sensitivity and specificity for detecting hazardous non-dependent drinking. Other advantages of AUDIT noted in the study are that it is short, easy to administer, and can be administered by health workers with no formal training. They also found that a shortened (5-item) version of AUDIT showed acceptable accuracy. They noted the potential usefulness of this shortened version of AUDIT for screening in busy medical practices.

- Volk et al (1997) studied the effectiveness of AUDIT in a sample of 1333 primary care patients of different racial/ethnic backgrounds. The sample was selected in a randomised fashion with the constraint that sufficient minority group (African-American and Mexican-American) patients and women were included for testing race and gender effects amongst the dependent and non-dependent categories of drinkers. AUDIT scores were compared with Alcohol Use Disorders and Associated Disabilities Interview Schedule (AUDADIS) diagnoses. The study found strong support for the efficacy of AUDIT in screening male and female white and minority primary care patients with little variation between sub-groups. Gender and racial/alcohol use effects were accounted for by differences in prevalence of alcohol use problems in the various sub-groups. The authors pointed out the need to critically examine cut-off points which may need to be varied in order to optimise the use of

AUDIT as a screen for a particular level of alcohol use or to reflect different prevalence levels in the population of interest.

- In their review of the literature on screening tests for alcohol, Schorling and Buchsbaum (1997) noted that the National Institute of Alcohol Abuse and Alcoholism (NIAAA) in the U.S. recommended that CAGE is used to routinely screen for alcohol abuse in general practice. They pointed out that neither MAST nor CAGE is time-sensitive but that CAGE has only 4 items and is thus easy to administer. They referred to research studies quoting sensitivity and specificity of various alcohol screening instruments and reported that AUDIT has only medium sensitivity (.38-.63) in research on outpatients in various parts of the US. They also refer to the low specificity of AUDIT found with college students in one study. However they do not refer to better outcomes for AUDIT found in the WHO study (Saunders et al., 1993), nor to its broader applicability and greater reliability and validity found in the studies quoted herein.

Other studies which tend to support use of AUDIT in preference to CAGE or MAST include the following:

- Heck and Williams (1995) surveyed 1000 students, randomly selected at one Midwestern university in 1988 (response rate = 58.2%) and another 1000 in 1992 (response rate = 49.8%). Part of their studies involved examining the screening characteristics of CAGE. Problem drinkers were identified by a composite scale incorporating self-reported quantity-frequency data and negative effects. They found CAGE had low predictive validity overall and tended to be lower still for women.
- Hiro and Shima (1996 - abstract only read) administered Japanese translations of AUDIT and CAGE to 93 applicants attending for health checks. Level of alcohol abuse was assessed by semi-structured interview. They found that AUDIT had good sensitivity and specificity for detecting both alcoholics (n=10) and problem drinkers (n=23), although sample size was low. They also found that AUDIT was superior to CAGE in discriminating between these two groups of drinkers.
- Skipsey et al (1997) examined the usefulness of AUDIT in identifying hazardous and harmful drinking in a sample of 82 patients who were dependent on other drugs. They found that AUDIT was equivalent to MAST in identifying current alcohol dependence but better than MAST in identifying hazardous drinkers.

SUMMARY POINTS

1. It is recommended that routine screening for alcohol abuse is carried out in primary care settings.

2. Standard screening measures such as AUDIT should be used for screening purposes.

2.3.2 Assessment and Treatment Planning

Whilst brief screening devices are useful for early detection and proactive intervention in general health care settings, more comprehensive assessment procedures are needed in specialised treatment settings for chronic alcoholics. In this context the assessment interview is seen as serving two functions. The first is to obtain information on specific client problems which will assist in planning treatment goals and strategies and the second is to establish a rapport between therapist and client. It is recommended that assessment be done in a semi-structured, yet non-threatening and non-judgmental way. The therapist should establish a sense of hope and optimism and allow the interview to proceed in such a way as to obtain the needed information without significant digression. Although it is not recommended that the interview is strictly structured, a checklist of important areas should be used as a guide (Mattick & Jarvis, 1993).

It is important that the individual's **motivation to change** is assessed and, if motivation is not adequate, treatment may involve clarifying the benefits of change to the drinker, with the express purpose of preparing for change. A widely-quoted model for preparedness for change is Prochaska and Climente's Stages of Change Model (Prochaska & DiClemente, 1986) which has been applied to a broad range of addictive behaviors. This model proposes that the dependent person who successfully becomes non-dependent will go through four stages of change, namely precontemplation, contemplation, action and maintenance. So, according to this model, the individual needs to be brought to the stage of contemplation in order to be ready to change.

The client's history of drinking should be taken as well as an assessment of daily routine which gives information on **levels of drinking** as well as antecedents and consequences of drinking. Careful probing of drinking patterns, including both quantity and frequency of drinking, is needed in order to distinguish daily drinking from binge drinking. This can be done through diary or questionnaire. **Other drug use** (including nicotine - (Sobell, Toneatto, & Sobell, 1994)) should be assessed at the same time.

Measuring **level of dependence** allows for planning of realistic goals for treatment. Seven factors are regarded as symptoms of dependence. They are: narrowing of drinking style or repertoire; salience or importance of drinking; subjective awareness of a compulsion to drink; increased tolerance to the effects of alcohol; repeated withdrawal symptoms; relief or avoidance of withdrawal symptoms by further drinking; and reinstatement of dependent drinking after abstinence.

Research has suggested that less dependent drinkers may achieve controlled drinking, whereas severely dependent drinkers should aim for abstinence (Mattick & Jarvis, 1993). Sobell and

Sobell (1995) argued similarly that from the available research, irrespective of stated treatment goals or amount of drinking skills training, the most likely positive outcome of treatment for low dependence drinkers is controlled drinking while, for high dependence drinkers, it is abstinence. This same editorial also pointed out that other background factors such as lack of social support and poor vocational history, may be more important in deciding treatment aims than considerations of levels of dependence - that level of dependence may be an epiphenomenon of such other life circumstances.

Several scales have been developed to assess level of dependence derived in general from operationalising DSM-IIIR (and later DSM-IV) criteria. These scales include the Severity of Alcohol Dependence Questionnaire Form C (SADQ-C, (Stockwell, Sitharthan, McGrath, & Lang, 1994)), the Severity of Alcohol Dependence Data questionnaire (SADD, (Raistrick, Dunbar, & Davidson, 1983)) and the Alcohol Dependence Scale (ADS, (Skinner, 1982)). Mattick and Jarvis (1993) emphasised that no test or measure should be used alone to determine treatment outlines. Such measures can serve as useful guides to check progress, to determine the amount of attention that may be needed by the individual, length of treatment or treatment focus.

In order to assess the validity of these and the short screening devices mentioned in the previous section, it is important that the accepted classificatory systems, which set out diagnostic criteria for drug and alcohol use, are operationalised through valid and reliable assessment instruments. Larger diagnostic interviews, such as CIDI (Wittchen, 1994), Schedules for Assessment in Neuropsychiatry (SCAN, (World Health Organization, 1993b) and the alcohol/drug-revised version of AUDADIS (AUDADIS-ADR, (World Health Organization, 1992) have been developed and revised on the basis of criteria for mental disorders as specified by the American Psychiatric Association's most recent version of the Diagnostic and Statistical manual of mental disorders (DSM-IV, (American Psychiatric Association, 1994)) and the WHO International Classification of Diseases (ICD-10, (World Health Organization, 1993a)).

The CIDI, SCAN and AUDADIS-ADR are all being assessed in a large-scale international WHO-funded study, the first results of which were recently published (Ustun et al., 1997). This study has found that the instruments reliably and validly diagnose drug and alcohol dependence. However, this research also found that the instruments were not as reliable for assessing non-dependent but hazardous use of alcohol and drugs. Hence there is a need for caution when interpreting the above-described studies which assessed the validity of screening instruments such as AUDIT and CAGE for detecting hazardous alcohol use against CIDI interview results.

Physical well-being as indicated by liver function, blood pressure, withdrawal symptoms and organic brain damage should be included in the overall assessment prior to treatment. Results may prove useful in counselling against continued hazardous drinking. Cognitive dysfunction should also be assessed by use of neuropsychological tests.

Because **comorbid psychiatric conditions** such as depression have been found to influence treatment outcome, it is important that these also are assessed at the initial assessment stage. Such conditions may need to be addressed as part of the treatment program. This is again likely to involve other specialist services and it is important that contacts are established with these. Brief psychiatric screening devices such as the Beck Depression Inventory (BDI, (Beck & Steer, 1987)), the Beck Anxiety Inventory (BAI, (Beck & Steer, 1990)) and the SCL-90 (Derogatis, 1983) can be administered and responses used as the basis for further probing for possible comorbid conditions which may then lead to referral to specialist services. Childhood sexual abuse and sub-clinical emotional problems (e.g. stress, social skills) should be probed through non-threatening discussion and referred on to appropriate specialists as required. It may be prudent to wait until the client is settled into the treatment relationship before broaching such issues.

Family issues may have an important bearing on treatment compliance and outcome. Such factors as how the individual's drinking affects family relations, the quality of family relations in general, the presence of violence and abuse and the commitment of the family to the rehabilitation of the individual all bear heavily on outcomes. Interviews with significant other family members may help clarify levels of dysfunction, expectations and/or commitment. **Other problems** such as those which may arise at work, in other social situations and financially should also be addressed.

Recent Research

In an editorial in the British Journal of Addiction, Davidson (1992) pointed out that, despite its popularity, Prochaska and DiClimente's Stages of Change model has found very little support in the research literature. Among the criticisms enumerated by Davidson are the facts that (1) there appears to be no evidence that people who defeat their addiction actually proceed in order through the stages; (2) there is a singular lack of support for the factors in the model outside of the US; (3) it is more logical to think of relapse as a part of the process of change, and not as a stage; (4) successful individuals are often not aware of proceeding through other stages in readiness for change; and (5) there has been little support for the model from matching treatment to stage. Evidence relating to motivation to change (including stages of change) and family relationships is discussed later under relevant sections on particular types of interventions.

- The WHO collaborative study (Ustun et al., 1997) on the reliability and validity of the drug use disorder instruments assessed a total of 1825 subjects drawn from 12 international centres. Each centre contributed between 131 and 197 cases of alcohol and/or drug users, but focused especially on one or two principle drugs as well as being responsible for one or more sub-studies (test-retest for one instrument or comparison between two instruments). Samples were selected from both treatment and other general non-treatment groups and were enriched to ensure adequate distribution across substance, gender and non-treatment respondents. The researchers concluded that the three instruments used in the study, the

SCAN, CIDI and AUDADIS-ADR, reliably diagnose alcohol and drug dependence. All three instruments showed high inter-scale agreement for assessing dependence which indicates that the translation from diagnostic criteria to operational assessment is reliable. The test-retest reliability coefficients for alcohol dependence were strong for each instrument for ICD-10 and DSM-IV formulations, ranging from .66 to .76. However, reliability was poor for assessing harmful use and abuse, ranging from .17 to .60. They comment on areas of possible improvement in operationalisation based on a careful breakdown of the statistical findings.

No further recent research was found in the literature review which compared the reliabilities and validities of the alcohol dependence measures.

SUMMARY POINTS

1. Assessment for treatment for dependence should measure: level of drinking; level of dependence; physical effects of alcohol use; and psychiatric comorbidity.

2. Reliable and valid assessment instruments exist and should be used.

2.4. DETOXIFICATION

Detoxification is the term given to the process by which alcohol and drug dependent persons recover from intoxication in a supervised way so that withdrawal symptoms are minimised. The symptoms of withdrawal are generally opposite to the action of the drug and, in the case of alcohol can be life-threatening. The severity of alcohol and drug withdrawal depends on such factors as level and duration of use, concomitant other drug use, the general health and nutritional state of the person and the detoxification setting (Mattick & Jarvis, 1993).

Alcohol detoxification can be medicated or unmedicated. Unmedicated withdrawal involves withdrawing from alcohol use without drugs to assist the process. However, thiamine and multivitamins should be administered to moderate to heavy drinkers in order to correct nutritional deficits and prevent the development of Wernicke's encephalopathy. Medicated withdrawal involves substitution for uncontrolled drug use by a controlled drug which has a similar action to the abused drug. In the case of alcohol, benzodiazapines such as diazepam, chlordiazapoxide and chlormethiazole are recommended to combat the symptoms of withdrawal (Mayo-Smith, 1997). The dosage of sedative used to combat withdrawal should be carefully calibrated against severity of symptoms and fluid status needs to be monitored and stabilised.

Detoxification can be home-based or inpatient. Where a person is considered likely to suffer mild to moderate withdrawal, is not in need of sedative medication and has no medical or psychiatric history which may complicate the process, then home medication may be

appropriate (Hayashida et al., 1989). Even in cases of severe and medicated withdrawal, home medication may be chosen where conditions permit (Stockwell, Bolt, Milner, Pugh, & Young, 1990). There must be close liaison between GP, patient and responsible caregivers and preferably a community drug and alcohol counselor and/or a community nurse should be involved.

Where inpatient detoxification is warranted i.e. where the severity of dependence (and thus complications) is likely to be high, or where there are no supportive relatives or friends to assist with home monitoring, purpose-built detoxification units rather than acute medical wards, provide the best conditions for inpatient withdrawal (Alterman, Hayashida, & O'Brien, 1988; Pedersen, 1986). These units are increasingly adopting a non-medicated approach, using instead counselling in a non-threatening and non-stimulating environment. In fact, it is now agreed that unless the patient routinely experiences tremors, sweating, nausea and feelings of apprehension or shows symptoms of withdrawal convulsions and delerium, then they are more likely to be harmed than helped by use of medication for detoxification (Shaw, 1995). Medication is thus reserved for these most severe cases, preferably administered in the more relaxed environment of the detoxification unit.

Although detoxification is an important component of treatment for addicted drinkers, especially where the degree of dependence is great, it is not appropriate to consider detoxification as a treatment in its own right. This is because people who have undergone detoxification programs are equally as likely to relapse as those who have not. As Mattick and Hall (1996) noted, the benefits of detoxification in general arise because of (1) the opportunity it provides for a change in lifestyle with the help of other interventions and (2) harm reduction effects where continued heavy drug-usage could lead to serious complications including death.

Thus the primary effectiveness of a particular detoxification procedure can be assessed in terms of retention rate, withdrawal severity, distress and medical complications arising during the program. In assessing associated costs, outpatient programs tend to cost considerably less per user than inpatient. However retention rates for outpatient programs are somewhat lower than for inpatient and they could lead to greater cost burden because they attract clients who would not normally seek treatment (Stockwell et al., 1990; Stockwell et al., 1991).

The cost-effectiveness of detoxification can be assessed in terms of the probability that the client will proceed to treatment, and thus detoxification costs would be incorporated into overall program costs, which are in turn balanced against the ability of the particular program to reduce addiction-related deficits. However, in the situation where detoxification is used to temporarily prolong life or improve quality of life, there may be no general economic benefit. Yet it is considered incumbent upon a modern humane society to finance many uneconomical medical interventions, especially with the elderly and severely disabled.

Recent Research

There has been very little research in this area since 1991. Important research is described below.

- Mayo-Smith (1997) completed a meta-analysis of all trials of the pharmacological management of alcohol withdrawal reported through MEDLINE up to July 1, 1995. Original data from 65 prospective controlled trials involving 42 different medications were analysed. Overall benzodiazapines were found to be most effective of all agents studied, and more effective than placebo, in reducing the incidence of delirium or seizures associated with alcohol withdrawal. All benzodiazapines appear equally effective although there is some evidence that longer acting agents may be more effective in reducing seizures. As well as having the greatest documented efficacy, benzodiazapines were also found to be safer and had lower abuse potential than other agents studied. The author also recommended use of individualized dosing regimens wherever feasible, based on patient withdrawal history and standardized assessment of current needs.

- Stockwell and co-workers (1991) contrasted rates of treatment completion and complications for 41 severely dependent alcoholics treated medically at home, with a retrospectively-matched group treated on an inpatient basis. This study found that, for those suffering from severe alcohol dependence, medicated home detoxification was as safe and effective as inpatient detoxification.

- In another report from this same treatment program (Stockwell et al., 1990), use of community nursing services to supervise medication at home was found to be a very effective and cheap alternative to inpatient detoxification, with costs about 1/4 those of inpatient care. Both clients and relatives rated support from the community nurse as being more important than the medication. Furthermore this research found that home treatment was preferred by the great majority of patients, with half claiming they would not accept hospital care.

- Pedersen (1986) analysed various aspects of a social setting alcohol detoxification unit established in Sydney in 1981. The unit was set up as an alternative to acute medical care and did not use drug-assisted withdrawal therapies. Patients were ambulatory rather than bed-based and the units were organised to encourage a domestic rather than a clinical atmosphere. Of particular research interest was whether such units do decrease demands on hospital care and whether their use is associated with increased risk to heavy drinkers. Pedersen followed up all 4192 admissions to the unit between October, 1981 and July, 1984 and found that despite the fact that the unit dealt with a population with chronic and major alcohol impairment problems, only 1.2% required transfer to acute hospital care with only .5% being transferred for symptoms associated with alcohol withdrawal management. The author concluded that, given that the daily bed cost in one of these units is approximately 1/4 of hospital acute care bed cost, such detoxification units appear to be both cheaper and better for the large proportion of those in need of the service.

- Hayashida et al (1989) compared the effectiveness, safety and costs of medicated outpatient and inpatient detoxification from alcohol in a randomized, prospective trial using 164 males of low socioeconomic status. Their procedure for treatment of outpatients was to require them to attend an outpatient unit for evaluation each week day when blood samples and reported usage of medication and alcohol were recorded. Inpatient treatment was a standard procedure administered in a closed ward. The importance of proceeding to rehabilitation treatment following detoxification was emphasised to both groups. A period of no more than two calendar weeks was allowed for completion. Using a stringent test for completion of detoxification which involved physiological as well as self-report measures they found that:
    - significantly more inpatients than outpatients successfully completed detoxification (95% cf. 72%;$p<.0001$);
    - outpatients took significantly less time to complete (mean of 6.5 days cf. 9 days for inpatients; $p<.001$);
    - no patients in either group showed severe medical consequences from alcohol withdrawal whether they completed or not;
    - there was no significant difference between the two groups in terms of the rates of entry to rehabilitation treatment (59% for outpatients and 65% for inpatients);
    - there were no differences between the two groups in need for redetoxification in the 1 month and 6 month follow-up periods;
    - inpatient treatment was markedly more costly than outpatient, with average costs, based on a low estimate, 19 times that of outpatient and, based on a high estimate, of 9.5 times outpatient costs; and
    - outcome measures at 1 month and 6 month found no differences between the two groups, with approximately 50% of both groups abstinent for the month preceding the 6 month follow-up.

  The authors concluded that outpatient detoxification should be regarded as an effective, safe and cost-saving alternative to inpatient care for those with mild- to-moderate symptoms of alcohol withdrawal.

SUMMARY POINTS

1. Detoxification alone is of benefit to the individual as it provides respite from the physical damage which is a direct consequence of heavy alcohol usage.

2. In order to maintain this benefit, detoxification needs to be augmented by treatment to prevent relapse to drinking.

3. Appropriately supported home detoxification appears to be as effective as inpatient detoxification even for severely dependent alcoholics. Home detoxification has been rated as 4 to nearly 20 times less expensive and is the preferred treatment setting for those undergoing detoxification.

4. Where outpatient care is not feasible, specialised detoxification units providing ambulatory and non-medicated care are cheaper and at least as effective as standard hospital inpatient care

2.5. SPECIFIC INTERVENTIONS

2.5.1. Pharmacotherapies

Definition and applicability of pharmacotherapies:

Pharmacotherapies in this context refer to drug therapies used as part of the treatment and rehabilitation of alcohol abusers. Hence drugs used specifically to offset the symptoms of withdrawal during detoxification are not included here (see section 2.4). The individuals for whom pharmacotherapies are being trialled tends to be those who are dependent on alcohol and recovering following detoxification. In general there is little research on the use of pharmacotherapies in treating those who abuse alcohol but are not dependent.

Over the past 40 years, drug therapy for the treatment of alcohol abuse has typically involved use of antidipsotropic drugs such as disulfiram and calcium carbamide. These drugs inhibit the enzyme that catalyzes the breakdown of acetaldehyde in the blood. Ingestion of alcohol raises acetaldehyde levels which, if allowed to build up in the system, causes unpleasant symptoms such as nausea, vomiting, dizziness and shortness of breath.

More recently and with the improved understanding of brain neurobiology, new pharmacological treatments for alcohol abuse have been proposed and tested. Use of these medications is based on theories regarding the relevance of various neurotransmitter systems in establishing dependence. These treatments include use of dopaminergic agents (e.g.

bromocriptine), selective serotonin reuptake inhibitors (e.g. citalopram), a glutamate antagonist (acamprosate), and opiate antagonists (e.g. naltrexone). Because of the high incidence of anxiety and depression with alcohol dependence, anti-anxiety drugs such as buspirone and antidepressants such as imipramine and desipramine have also been applied to the treatment of individuals with alcohol dependence and comorbid depression or anxiety.

Two large-scale critical reviews, one of disulfiram (Hughes & Cook, 1997) and the other of the newer pharmacotherapies (Moncrieff & Drummond, 1997), were published in 1997. Both of these reviews concluded that research in the area is methodologically poor and that there is little evidence that pharmacotherapy is an effective treatment for alcohol abuse. However, commentaries on these reviews, especially that by Moncrieff and Drummond, have criticised them for being too harsh. Ritson (1998) provides an update on the newer pharmacotherapies which is more optimistic than the review by Moncrieff and Drummond, but does not provide a critical analysis of the research reviewed.

Disulfiram

Hughes and Cook (1997) pointed out that studies of oral disulfiram provide equivocal evidence of efficacy due to problems with methodology. For instance, it is difficult to carry out a double blind study on disulfiram, because ingestion of a small amount of alcohol will result in nausea, which then clearly indicates to participants whether they are part of the treatment or placebo group. Because the effects of disulfiram are so direct and aversive, unsupervised administration has particularly poor efficacy - if patients want a drink, then they can skip the medication for a period. However, this drawback with regard to long-term abstinence has been found to be more beneficial in terms of controlled drinking outcomes. Hughes and Cook reported that there was some evidence that oral disulfiram can reduce the number of drinking days and amounts drunk in compliant patients, but this needed further evaluation.

Maintenance of compliance is a significant problem with the use of oral disulfiram. Thus disulfiram implants have been proposed and tested in various studies (Hughes & Cook, 1997). However, these studies have found that it is not feasible, with current technology, to use disulfiram implants to assist in reduction of alcohol use. Hughes and Cook conclude that further research is warranted into the efficacy of injectable long-acting disulfiram metabolites, as well as identifying patient characteristics which may increase the efficacy of oral disulfiram treatment.

In their large-scale methodological review of treatments for alcohol problems, Miller et al (1995) found that treatments using disulfiram had equivocal outcomes. Schuckit (1996), in reviewing recent developments in this area, concluded that evidence for clinical effectiveness of disulfiram is modest at best; and that the use of this treatment needs to be carefully considered in view of the risks, although low, of various dangerous side-effects such as peripheral neuropathy and hepatitis. In their review of pharmacotherapies for alcohol dependence, Zernig et al (1997) also advocate against the routine use of disulfiram because of the dangerous side effects of this drug.

New pharmacotherapies

Moncrieff & Drummond (1997) provided a penetrating and highly critical review of research on the newer drug treatments for alcohol abuse. As they stated, research on these new drugs is based on the premise that central biochemical mechanisms modulate drinking behaviour which is therefore susceptible to modification by centrally acting agents. They criticized the methodology of the randomized controlled trials (RCTs) completed in the area and many of these criticisms have been reiterated with regard to outcome studies for other treatments (see section 2.5.2 on brief interventions). Such problems as lack of generalisability, variable outcome specification, failure of double-blinding and substantial unspecified withdrawals from studies led them to conclude that to date there was no clear evidence of the efficacy of any of the new drug treatments.

Furthermore, Moncrieff and Drummond sounded a timely warning that pharmacotherapies may be promoted in a biased fashion because they may appear to provide a quick fix for what is an intrinsically psychosocial problem. They claimed that such therapies may undermine self-efficacy which is important in relapse prevention and thus in the long-term recovery of alcohol abusers. In this context they commented on the plausible advantages of incorporating alcohol-sensitizing drugs such as disulfiram in an overall cognitive-behavioural program, compared with centrally-acting drugs which are intended to replace or counter psychological mechanisms such as craving. There are also strong commercial factors operating and drug companies were generally seen as having considerable political influence.

The review by Moncrieff and Drummond drew considerable expert comment and criticism (Chick, 1997; Kranzler & Babor, 1997; Littleton, 1997; Nutt, 1997; O'Malley, 1997; Soyka, 1997). In particular, most experts who commented felt that Moncrieff and Drummond were being too negative and expected greater rigor of pharmacological trials than had been achieved in testing psychosocial interventions for alcohol abuse. For instance, it is difficult to deliver psychosocial interventions in a double-blind paradigm, and the notion of testing whether subjects believe that they are in a treatment group or non-treatment group is not generally addressed in such research. So, to require trials of pharmacotherapies to have such rigor is somewhat harsh. However, because good control is not achievable in one area of research, does not mean that it is not possible in other areas.

Perhaps more plausibly, the comparison made by Nutt (1997) with ECT treatment for depression demonstrates why it is important not to dismiss treatments for alcohol abuse because they are not found to be generally applicable in RCTs. RCTs for ECT when administered to the broad range of depression sufferers would undoubtedly have large dropout rates and thus ECT would not be found to be effective in an intention-to-treat analysis. However, it has been found to be a most valuable and effective treatment for a particular sub-group of depressives.

Expert critics of the review by Moncrieff and Drummond argue that specific combinations of psycho - and pharmacotherapies, designed for particular sub-samples of drinkers, are likely,

ultimately, to prove more efficacious in the treatment of alcohol abuse than either therapy alone. It would be inappropriate to dismiss these promising treatments simply because, to date, the appropriate research has not been completed.

Below is a summary of the findings of the review by Moncrieff and Drummond and of more recent RCTs carried out for particular pharmacotherapies.

(a) Naltrexone

The research studies on naltrexone which were reviewed by Moncrieff and Drummond (1997), tended to be of short duration and equivocal in outcome. They conclude that although the studies reviewed appeared to show a positive effect for naltrexone, they may have been biased and that evidence is accumulating from more recent trials that naltrexone may be of limited effectiveness.

- Two reports from one study have been published since that review, which assessed the effects of a combination of naltrexone and intensive relapse prevention therapy in order to clarify issues regarding patient-treatment matching. One report was published immediately following treatment (Jaffe, Rounsaville, Chang, Schottenfeld, & et al., 1996) and at 6 months follow-up (O'Malley et al., 1996). There were four treatment categories within a 2x2 factorial design: naltrexone and intensive relapse prevention treatment (coping skills therapy); naltrexone and supportive therapy (minimal treatment); placebo and relapse prevention; and placebo and supportive therapy. Treatment was provided for 12 weeks for a sample of 104 subjects.

  They found a significant decrease in average daily drinking during the 12 week treatment period for those treated with naltrexone compared with placebo, but no difference in drinks per occasion (Jaffe et al., 1996). Although only exploratory, examination of interaction effects suggested that patients with higher levels of craving and poorer cognitive functioning might benefit most from naltrexone treatment. There was no main effect for psychotherapy but there were interaction effects in that higher levels of verbal learning were associated with better outcomes for intensive psychotherapy but not for supportive therapy; while lower levels of verbal learning were associated with poorer outcomes for intensive relapse prevention but not for supportive therapy.

  At 6-months follow-up (O'Malley et al., 1996), the beneficial effects of naltrexone compared with placebo on any drinking had disappeared. However, if heavy drinking only is considered, subjects who received coping skills therapy and placebo had rates of heavy-drinking similar to the two naltrexone groups and significantly lower than the group that received supportive therapy alone. Hence the effects of naltrexone post-treatment on abstinence appear to decrease over time, but it may have a role to play in maintaining controlled drinking outcomes. Due to the small sub-sample sizes and other methodological problems, some of which were discussed by the authors, these studies do not provide

significant support for the general application of naltrexone therapy for treatment of alcohol abuse. However, they do provide some interesting leads regarding future research in the area. In particular, use of naltrexone with specific sub-samples of alcohol abusers, or for longer or intermittent periods, based on individual response, need to be further investigated.

- Studies by Kranzler et al (1997) and King, Volpicelli and co-workers (1997) also explore issues of how naltrexone should be administered and for whom it may prove most effective. Kranzler and coworkers found that allowing subjects to self-administer naltrexone to target particular high risk situations, in combination with brief coping skills training, resulted in a significant decline in alcohol abuse.

- King et al found that high risk social drinkers (first-degree relatives of alcohol abusers) showed greater decline in physiological response to alcohol following naltrexone pretreatment than did low-risk subjects. High-risk subjects were also more aware of naltrexone reducing alcohol effects. Again, although methodologically flawed, the results of this study point to areas of further research which may assist in identifying those groups most likely to benefit from naltrexone treatment for alcohol abuse.

(b) Acamprosate

Moncrieff and Drummond (1997) concluded that despite inconsistent results for acamprosate from the studies in their review, there is some evidence to suggest that it has a small but significant beneficial treatment effect compared with placebo. The studies below were not covered by this review.

- Sass et al (1995) pooled data from 11 European trials which compared acamprosate with placebo (n=3338). Although not reported in detail, the authors stated that the studies included had comparable designs, with treatment duration varying between 6 and 12 months except for 1 study of 3 months. They found that acamprosate was significantly superior using the intention to treat principle for the outcome criteria used, namely, rates of patient attendance (50% acamprosate group vs 40% placebo), abstinence rate (67% vs 54%), and longer duration of drink-free periods (49% vs 40%). No significant interaction effects were found with other variables such as psychotherapy, and outcome was also found to be positively influenced by increasing age and decreasing baseline alcoholism severity. Unfortunately, a more critical review of this meta-analysis is not possible as it has been reported in English as an abstract only.

- Poldrugo (1997a) completed a RCT for patients at 5 alcoholism treatment units in northern Italy. The total sample size was 246, with 122 randomly allocated to 6 months acamprosate treatment and 124 to placebo. The study had a high exclusion rate - 73.3% of alcohol dependent subjects who were screened were excluded; and a high dropout rate with significantly higher dropouts from the placebo group - 49.1% of the acamprosate group and 33.8% of the placebo group were retained after 6 months treatment plus 6 months follow-

up. Following detoxification, and during the treatment period, subjects in both groups received the full rehabilitation program which included group sessions, family therapy, education on alcoholism, community meetings and physical and recreational activities. The acamprosate group had significantly more positive outcomes in terms of abstinence rate, time to first relapse and cumulative abstinence duration. These outcomes were reinforced by data from biological markers. Other variables such as levels of dependence, craving, psychotherapy, involvement in self-help groups, depression and anxiety were not predictive of cumulative abstinence rate when adjusted for number of comparisons made. However, study numbers may not have provided sufficient power to obtain significant findings for the large number of t-tests carried out.

- Pelc et al (1997) randomly assigned 188 subjects to placebo and 2 levels of acamprosate (1332mg/day and 1998mg/day) following a 14-day detoxification program. The study covered a treatment period of 90 days and 119 (63%) completed with significantly more completing in the two acamprosate groups. The two acamprosate groups had significantly improved outcomes compared with placebo, for all outcome measures: cumulative days abstinent, relapse rate, number abstinent for whole treatment period (survival analysis), time to first relapse, score on Clinical Global Impression scale, craving and biological markers. Although no significant differences were found between the two acamprosate dosage groups, there was a trend for the higher dosage group to have a better outcome. Small numbers may have precluded significant findings for these comparisons. As with the study by Poldrugo reported above, there were no significant differences between groups for other psychosocial variables. As pointed out by the authors, this study cannot be considered conclusive due to the lack of information on follow-up and post-treatment relapse.

- Another recent study assessing acamprosate was carried out by Besson et al (1998). This study attempted to follow patients through 1-year treatment and a further 1-year follow-up and allowed concomitant voluntary usage of disulfiram to be included in the analysis. Patients were detoxified and randomly assigned to acamprosate or placebo (N=55 in each). The groups were stratified by disulfiram use. Only 19 in each group (35%) remained by the end of the 360 day treatment period. Results from all efficacy measures used showed acamprosate to be significantly more effective than placebo during treatment except for the last visit where the numbers were probably too low to obtain significance, even though the acamprosate group had nearly twice as many abstainers as the placebo group at that visit. The patients who used disulfiram (22 in placebo and 24 in acamprosate groups) had significantly higher levels of dependence based on several measures but had improved outcomes compared with those not on disulfiram. However they also had more frequent contact with health advisors, so that no direct comparisons can be made amongst the four disulfiram/acamprosate groups. The authors were able to conclude that no adverse interactions were found between disulfiram and acamprosate and that the group using both had a better cumulative abstinence duration than the other 3 sub-groups. The low number completing treatment meant that no statistically useful findings could be made regarding follow-up. However, the authors observed that no rebound drinking occurred following

termination of medication, although they did not clarify if this applied to both placebo and acamprosate groups. This suggests that gains made through treatment were maintained.

(c) Other pharmacotherapies and comorbid groups

Moncrieff and Drummond (1997) concluded that the dopamine agonist bromocriptine had not been found to be effective in research that they reviewed. This has been confirmed in a more recent international multicentre RCT (Naranjo, Dongier, & Bremner, 1997) using 366 subjects in 16 international centres. This study found that, following 6 months treatment, bromocriptine was no more effective than placebo in maintenance of abstinence or reducing drinking.

The review by Moncrieff and Drummond also found little support for the use of selective serotonin reuptake inhibitors (SSRIs) in treatment for alcohol abuse. No more recent large scale RCTs using SSRIs on noncomorbid alcoholics were found in the literature search. A small study comparing both fluvoxamine (n= 25) and citalopram (n=33) with placebo (n=23) (Angelone, Bellini, Di Bella, & Catalano, 1998) had positive findings with regard to continuous abstinence over the 16 week period of their study. However, they ignored dropouts and it is unlikely that the differences found between the three groups using an intention to treat analysis would be significant.

In his 1998 review of pharmacotherapies for alcohol problems, Ritson (1998) points out that there is little evidence of benefit of SSRIs, except possibly for some genetically-mediated forms of alcohol dependence relating to severe depression. Studies which compare ritanserin, another SSRI, with placebo have not been able to show a benefit for this drug.

Comelius et al (1997) report a 12-week RCT using fluoxetine (an SSRI) with alcoholics with comorbid depression. Although the sample size was low at 51 (with a further 5 dropping out) and the study period was somewhat short, the fluoxetine group showed significantly decreased depression and a significantly less alcohol consumption over the study period. There was also a strong correlation (Pearson $r \cong 0.60$) between change in level of depression and change in alcohol consumption. No follow-up was carried out.

Buspirone is an anxiolytic which has also shown some promise in treating alcoholics with comorbid anxiety. Moncrieff and Drummond reviewed four RCTs for buspirone and pointed out methodological problems associated with those with positive results and the generally negative outcome for the study which was best controlled. There is thus little current evidence to support its use to reduce alcohol abuse amongst high anxious alcoholics.

Two recent studies which tested the efficacy of tricyclic antidepressants with alcoholics with comorbid depression did not show a significant benefit of these drugs compared with placebo with this group of alcoholics (Mason, Kocsis, Ritvo, & Cutler, 1996; McGrath et al., 1996). Sample size tended to be too small and follow-up too short. Furthermore, the significant side-

effects of imipramine in the McGrath study may have alerted participants to their treatment status.

Summary of effectiveness and expert commentaries

In general, experts agree that it is important that pharmacological treatment for alcohol abuse is administered within an active and supportive psychosocial treatment program (Carroll, 1997; Hughes & Cook, 1997; Poldrugo, 1997b; Ritson, 1998; Zernig et al., 1997).

From research evidence and because of the risks associated with its use, the antidipsotropic drug, disulfiram is not recommended for routine use with recovering alcoholics. However, further research on antidipsotropics may be fruitful as there is some suggestion that self-administration may have a role to play in maintaining controlled drinking with compliant patients.

The use of naltrexone to prevent relapse in recovering alcoholics has received little empirical support to date. However, as with the other newer pharmacotherapies, it may prove to be useful for particular sub-samples of patients using more flexible schedules of administration. In particular it may assist those patients with poorer cognitive functioning who benefit least from coping skills training. Also, as with antidipsotropics, it may prove helpful in maintenance of controlled drinking in particular patients.

Acamprosate was the most promising of the pharmacotherapies reviewed here. In general, benefits over placebo have been small but significant. More research is needed on effects of dosage level as well as treatment time, post-treatment effectiveness and appropriate psychosocial backup.

There is little evidence to support the use of either the dopamine agonist bromocriptine or SSRIs with noncomorbid patients. However, SSRIs may prove valuable with the subgroup of depressed alcoholics. On the other hand tricyclics such as imipramine and desipramine appear to have little effect on drinking outcomes for depressed alcoholics. As Mason et al (1996) commented consequent upon their research on desipramine, it is more likely that the newer generation of antidepressants with their greater tolerability and lower toxicity, the SSRIs, may be more fruitfully tested for effectiveness with depressed alcoholics.

Studies to date have been equivocal regarding the effectiveness of the antianxiety drug buspirone in reducing drinking in anxious alcoholics.

SUMMARY POINTS

1. More research is needed on the appropriate applications of all pharmacotherapies currently being reviewed for the treatment of alcoholism. This research needs to be more rigorous.

2. The risks associated with disulfiram, along with the poor research findings for this drug indicate that there is a need to replace it in the repertoire of treatments for alcohol dependence.

3. Pharmacotherapies should only be used in conjunction with psychotherapies in the prevention of relapse for detoxified alcoholics.

4. Acamprosate is the most promising pharmacotherapy. Support for naltrexone is weak at this stage, but it may prove useful for particular sub-samples of alcoholics.

5. Evidence that antianxiety and antidepressant drugs help reduce drinking is poor. However SSRIs may have a role to play with depressed alcoholics.

2.5.2. Brief Interventions

Brief interventions provide short-duration treatment for clients identified by screening as drinking at hazardous or harmful levels. Babor (1994) describes a typical brief intervention as consisting of structured therapy of short duration (5-30minutes), which is offered to help the individual to cease or reduce drinking. Brief interventions encompass a variety of treatment approaches including health education, self-management training, group therapy, social skills training, simple advice (either direct or through manuals), and motivational interviewing.

It is generally agreed that brief interventions are most appropriately carried out in primary health-care settings, because these are accessed by a large proportion of the general population on a regular basis. Being unsolicited, brief interventions contrast with more intensive treatments which tend to be sought out by the client, or by others on behalf of the client.

Miller et al (1995) found that brief interventions and motivational enhancement and self-help manuals (which are included as brief interventions in the present review) were amongst the most effective and also the cheapest to implement. They tend also to be used for the less severely affected drinkers. Although several large-scale reviews of research have been undertaken in the past decade (Babor, 1994; Bien, Miller, & Tonigan, 1993; Kahan, Wilson, & Becker, 1995; Mattick & Jarvis, 1993), their findings are reflected in a recently-completed meta-analysis outlined below, and so they will not be reviewed separately here.

The most recently reported meta-analysis of brief interventions (Wilk, Jensen, & Havighurst, 1997) included those 31 treatment trials published in Medline and Psychlit between 1966 and 1995 which fitted the following inclusion criteria:

- trials with a focus on brief interventions for alcohol abuse in adults which were prospective and randomized with no alcohol-related treatment for controls;
- the sample size was greater than 30;
- the brief intervention was of a motivational self-help orientation, which included feedback, education on the harms of drinking and advice to moderate to low-risk levels; and
- interventions ranged from 10-15 minutes to 1 hour and follow-up (booster) sessions varied from 0-3 sessions.

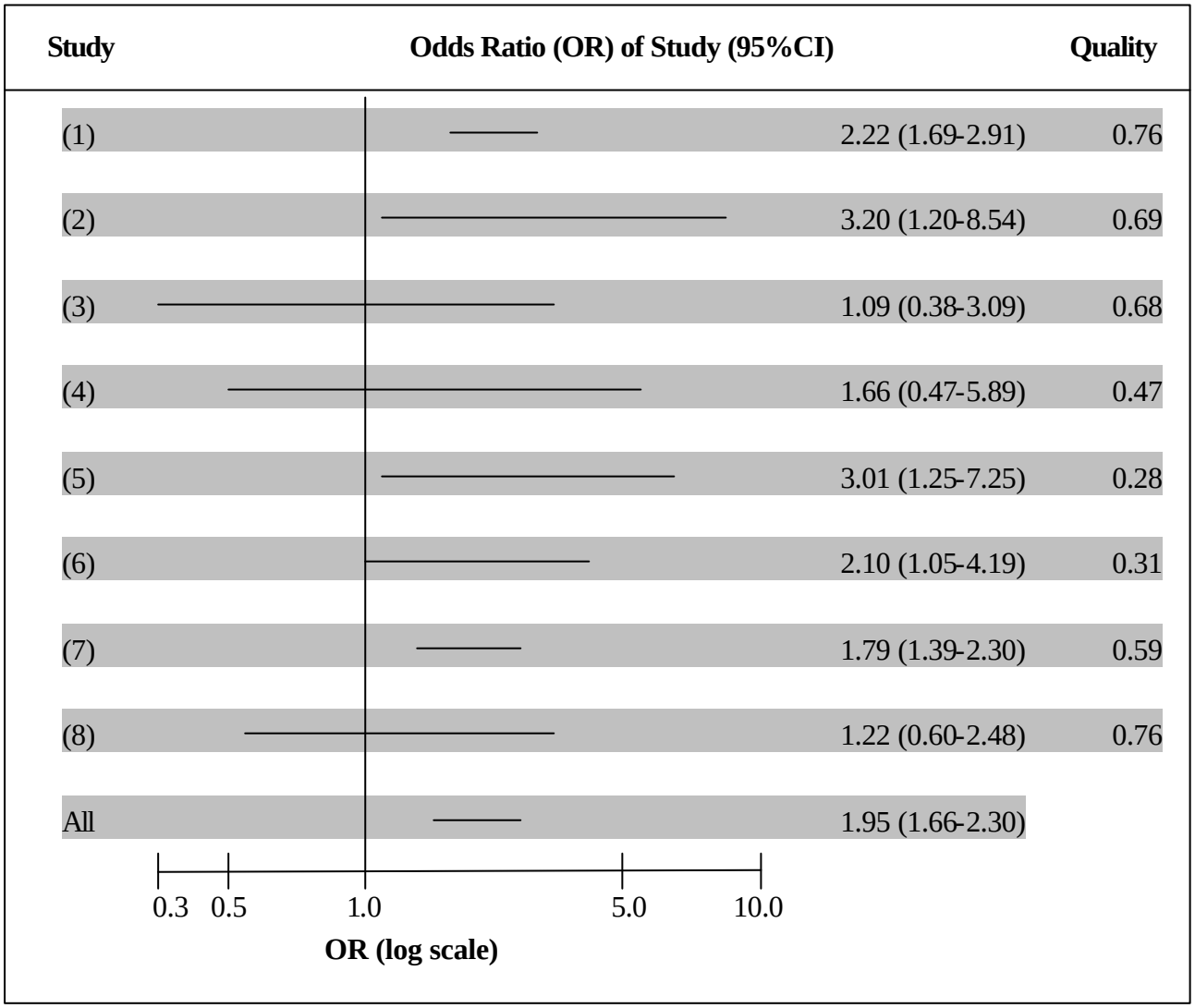
Twelve studies were found to fulfil these criteria. Some of these individual studies incorporated exclusion criteria such as level of dependence, having received previous advice to stop, and having serious medical or psychiatric disorders.

The 12 studies represented 3948 patients from outpatient, inpatient and general populations, who had been randomly assigned to intervention or control group. The studies were assessed quantitatively and qualitatively. For the quantitative analysis, odds ratios were calculated based on the estimate that heavy drinkers moderated their drinking 6 or 12 months after intervention compared with the untreated control group. Eight of the 12 studies provided adequate data to do this calculation, which represented 70% of all subjects in these studies. Although 3 of the 8 studies, had non-significant odds ratios (Figure 1), the mean pooled odds ratio was 1.95, indicating that subjects undergoing treatment were nearly twice as likely as control subjects to have moderated their drinking over the relevant time period.

The qualitative assessment was based on a widely-used scoring system developed for this purpose (Chalmers, Smith, Blackburn, & al, 1981) and, for this meta-analysis, scores in the following categories were used: selection criteria, rejection log (patients screened and rejected), testing of randomization, blinding of assessors, measurement of biological equivalents (e.g. GGT, blood pressure), statistical analyses, handling of withdrawal and data presentation. Possible ratings range from 0 for the poorest quality to 1.00 for the highest. The mean score for this study is comparable to those found in other clinical trial meta-analyses. Quality ratings for the 8 studies for which odds ratios were calculable are listed in Figure 1.
It should be noted that the mean quality rating for studies with non-significant odds ratios was .64, while for studies with significant odds ratios it was only .53. This means that the poorer quality (and presumably less accurate) studies tended to produce more positive findings, which supported some of the criticisms of the methodology and analysis of the research raised by the authors. These criticisms included:

- the randomization process was flawed in all but one study (Babor et al., 1994) and often details were not adequately reported. Hence there was a large risk of over-estimation of treatment effects across most of the studies. Tests comparing baseline characteristics of treatment and control groups carried out in more than half the trials showed insignificant differences but this does not necessarily exclude the possibility of enlarged treatment effects;

FIGURE 1: Meta-analysis results for eight randomized controlled trials whose outcome data allowed calculation of individual odds ratios (from Wilk et al 1997).



- the study selection process (literature survey) may have meant that randomised controlled trials with negative results, which tend to be under-published, may be under-represented;
- the results were only generalisable to those heavy drinkers with little or no alcohol dependence. There was thus a likelihood of failure or onset of withdrawal if brief intervention alone was used for the more severely affected dependent group. Hence the authors urged caution in applying brief interventions; and
- it was not yet clear what the impact of brief interventions was in other significant areas such as cost effectiveness, hard endpoints such as mortality and morbidity, long-term effects of treatment and health care utilization.

The authors noted that biomedical markers are unreliable measures, and recommended that in future research, other collateral information on outcomes, such as CAGE and reports of significant others, should be obtained. Also, effects on such variables as work performance, family relationships and overall quality of life indicators should be consistently included. They emphasised the need for the use of standardized outcome measures in research, and that follow-up of treatment and control groups should be carried out for 5 to 10 years after treatment. In this way the persistence of effects can be assessed and incorporated into cost-benefit analyses.

Recent Research

Randomised controlled studies since 1995

Several randomized controlled studies on the effectiveness of brief interventions have been completed since those covered by the meta-analysis by Wilk et al and reported above.

- The WHO Brief Intervention Study Group (1996) conducted a cross-national, randomized clinical trial comparing a no-treatment control condition with two treatment conditions: 5 minutes advice or 20 minutes brief counselling. The initial sample consisted of 1260 men and 399 women with no history of alcohol dependence who were identified as being at risk of alcohol-related problems. The sample was taken from Australia, Kenya, Mexico, Norway, the UK, Russia, the US and Zimbabwe. Subjects were followed up 9 months later. 75% of the sample was interviewed at follow-up and it was assumed for analysis purposes that there was no change in the drinking behaviour of those available to follow-up. Significant improvements were found for males for both treatment groups compared with the control group, but no difference was found between the two treatments. Overall, treatment led to a 17% reduction in average daily consumption and 10% reduction in intensity of drinking and this was consistent across the 8 countries. The authors noted that these findings were not due to a few patients achieving abstinence, but were distributed across many patients who reduced their drinking by small and meaningful amounts. They concluded that these results support the notion that moderate drinking goals are achievable by a substantial proportion of heavy drinkers. Even though no significant differences were found between the three groups for females, it was concluded that, overall, brief interventions are effective across health care settings and sociocultural groups. This study reinforced the notion that screening and brief interventions should be conducted in primary health care settings as a first low cost step to reducing the negative impact of excessive alcohol use.

- Burge et al (1997) found that, of 4014 Mexican-American patients screened at a public hospital in Texas, 326 were classified as heavy drinkers and randomised into 4 groups: (1) physician intervention, which involved a brief 10-15 minute confrontation and discussion which varied according to severity of problem; (2) psychoeducation with six 90-minute sessions which described the related problems and possible resolutions, followed by group discussion; (3) both interventions; and (4) no intervention (control). The treatment conditions were directed at the need for abstinence and recommended AA involvement.

They also encouraged involvement in the sessions of another family member. 175 subjects (54%) completed baseline, 12 month and 18 month assessment interviews. All groups improved significantly over time in drinking patterns, psychosocial problems and biological measures, but there were no differences between groups. The authors suggested that the long assessment sessions used in this study, the transparency of its purpose, and its low power may explain lack of differences between groups. It could also be argued that this particular ethnic group shows different responses to assessment than do European-origin groups, or that an abstention goal may not be the most effective or appropriate, or that the types of interventions used are ineffective (see comments by Rollnick et al (1997)).

- Project TrEAT (Trial for Early Alcohol Treatment, (Fleming, Barry, Manwell, Johnson, & London, 1997)) is the first large-scale brief intervention conducted in community-based primary care practices in the US. 17,695 patients were screened at 17 intervention clinics in Wisconsin. Screening took about 30 minutes and was done by a trained researcher. 2925 screened positive and 1705 (58%) of these completed a further interview to assess eligibility for the study. 774 of the 852 deemed eligible, were randomly assigned to treatment and control conditions. 723 of these were followed up at 12 months. For the purpose of analysis, those lost to follow-up were considered to have not altered their drinking behaviour over the period of the study. The treatment group was given a workbook which contained feedback about current health behaviours, a review of the prevalence of problem drinking, associated risks, list of drinking cues, drinking agreement in the form of a prescription, and diary cards. Brief intervention and reinforcement consisted of two 15-minute sessions 1 month apart with the physician; then a follow-up call from the nurse 2 weeks after each meeting. The control group was given a booklet on general health issues and followed up at 6 and 12 months. Outcome measures were average drinks per week, binge drinking and excessive drinking, as well as emergency department visits and hospital days. While both groups showed improvement, there were significant improvements in the experimental condition compared with controls for both sexes for mean drinks in past 7 days, episodes of binge-drinking during past month, and frequency of excessive drinking. There was no clear evidence of decreased use of health care services for either group.

- Senft et al (1997) used a population-based team approach to assess the effectiveness of a brief intervention in a busy primary care setting in Portland, Oregon. They identified hazardous drinkers, using AUDIT plus a frequency/quantity measure, and gathered collateral information where possible to validate self-reports. The intervention involved, firstly, delivery of a 30-second warning message by the GP, then, immediately on leaving the GP's office, they were interviewed by a trained counselor for a further 15 minutes. This interview involved: comparing individual patients' responses with national norms; explaining the damage that alcohol abuse can do; recommending a maximum of 3 drinks per day for men and 2 for women, plus 2 alcohol-free days a week, and explaining that zero alcohol means no risk; discussing tactics for reducing drinking; and confidence-building to improve self-efficacy to reduce or abstain. The control group received the usual care.

From a population sample of 10,911, 620 hazardous drinkers were ultimately identified and 516 consented to randomization to treatment (260) and control (256) conditions. Six-month follow-up data was obtained for 431 subjects (84%) and 12-month data for 414 (80%). There were no significant differences at baseline between treatment and control groups on sociodemographics, AUDIT scores, drinking frequency or drinking intensity. Significantly more of the intervention group refused to respond at 6 and 12 months. No differences were found between responders and non-responders on baseline characteristics, except that more educated subjects were more likely to respond.

The study reported that the intervention group had significantly lower total alcohol consumption and significantly fewer drinking days per week at 6 months and significantly less drinking days per week at 12 months. However, no account was taken of the number of comparisons carried out. This meant that, in order to maintain a 5% Type I error rate, the differences between the treatment and control groups needed to be greater than those reported in this study. The authors concluded that the differences found at 6 and 12 months were encouraging as this was a once-off brief intervention in a population recruited without regard to their level of interest in change. They recommended use of such a team approach rather than expect GPs to intervene alone for broad-based screening and intervention. However, given that there were no substantial effects of the intervention, regardless of the use of specialist counsellors, this study provided little support for broad-based introduction of such interventions. The nature of the brief intervention, which appears somewhat confrontational, and the fact that no account was taken of motivation to change, may explain this lack of support for the effectiveness of brief interventions.

Other important studies directed at improving quality and delivery of brief interventions.

- Roche & Richard (1994) completed a randomized controlled trial of the effects of sending an unsolicited educational pamphlet to general practitioners (GPs) about the prevalence and treatment of alcohol abuse. The GPs were randomly selected from the phone book and assigned to receive an educational pamphlet or to act as controls. Both groups were followed up 6 weeks later with a questionnaire which sought GPs' views on the alcohol-related matters covered in the pamphlet. This consisted of a single-page survey covering knowledge of early detection and intervention, perceived role of GP, and how effective they believed brief advice might be in reducing drinking.

There were 270 valid responses (65.2%) and no differences were found between groups for age, sex or response rates. There was also no significant effect of receiving the pamphlet on any major variable: knowledge of the percentage of hazardous (non-dependent) drinkers in the community; the number of listed signs and symptoms considered useful indicators of alcohol problems; their rating of the statement that GPs have no role to play in the treatment of alcohol problems; the level of alcohol consumption within sexes and overall; their estimate of the percentage of patients who would reduce alcohol consumption after 10 minutes advice

and counselling from a GP; and the number of listed strategies considered useful for early intervention. The authors concluded that although GPs demonstrated reasonably good alcohol-related knowledge and had positive views about detection and intervention (especially younger doctors), there was considerable scope to improve these variables, especially with regard to female patients. They also concluded that an unsolicited educational pamphlet had no effect on GPs' alcohol-related knowledge or attitudes; so there was a need for more intensive and comprehensive strategies to improve GP understanding of the prevalence of alcohol-related problems, and their treatment in general practice.

- In a study by Strecher et al (1994), 2716 adult patients attending 12 family practices in North Carolina self-administered a questionnaire which assessed their potential for alcohol problems, as well as 7 other health-related behaviours. The questionnaire also assessed interest in changing behaviour and reasons for change as well as perceived barriers. Completion of the various sections of the questionnaire was dependent on response to the interest rating. 125 patients (4.6% of sample screened) were identified as potentially hazardous drinkers (2 or more on CAGE), and of these, 103 (3.8%) said they were seriously considering cutting down in the next 6 months, and 84 (3.1%) planned to cut down in the next month. Those with higher CAGE scores were more interested in cutting back. Most frequently cited reasons to cut back were to improve health (43%); to feel better about oneself (15%); to take more control of own life (10%) and to set a good example for family (10%). Perceived barriers included alcohol helps reduce stress (30%); nothing (26%); pleasure in drinking (24%) and having friends who drink (19%). This approach, which identifies hazardous and harmful drinkers at the same time as assessing their motivation to change, appears less confronting for both GPs and patients and thus has considerable potential for tackling alcohol abuse at primary care centres.

- Carnegie et al (1996) looked at the effects of training and support on the attitudes of medical receptionists towards preventive medicine (in this case a brief intervention for hazardous alcohol use). 150 receptionists were allocated to 4 groups: control, training regarding brief interventions but no support, minimal support and maximal support. They were given a questionnaire at the beginning and at the conclusion of a 3-month trial of the brief intervention at their surgery. The study found that receptionists' attitudes became very negative without training and some support, whereas they remained unchanged with training followed by support over the period of the program. It had been argued from other qualitative research that receptionists' attitudes and beliefs have an immediate effect on the implementation of such programs. It was therefore concluded that their cooperation should be enlisted by use of such supportive training strategies.

- Richmond et al (1998) also investigated alternatives to broad-based implementation of brief intervention strategies (see Strecher et al above) and addressed the issue of the motivation of primary care workers. Theirs was a naturalistic, non-randomized study comparing three methods for training GPs to implement brief interventions. 96 of 149 eligible GPs (64%) agreed to participate in the study, where they chose their training method from (1) a 2-hour

organised training workshop (n=35); (2) a 1-to-1 academic detailing conducted by another GP (n=39); and (3) being mailed a brief intervention kit (n=22).

General practitioners were encouraged to identify hazardous drinkers and maintain an audit of consecutive attenders, as well as recording recruitment rates and usage of the brief intervention. Only patients who were considered ready to change were approached. This assessment was based on response to the question: "How do you feel about your drinking?" If patients were not ready to change they were advised to consider the consequences of continued heavy drinking and invited to return. If they were unsure, they were given a brief motivational interview to enhance readiness to change. Patients considered ready to change were advised to set goals for cutting down, to monitor alcohol consumption, identify and manage high-risk situations, cut down and develop alternatives to drinking.

The mean number of patients recruited was 5 per GP (range 1 to 18) and between 20-25% agreed to participate when approached. Approximately one third of those treated claimed that they had reduced their consumption to achieve their drinking goal when followed up. At 6 months, 54% of GPs reported currently using the program, with those receiving it by mail being significantly less likely to be using it. Three-quarters stated that they preferred the client-centred approach of the program to prescriptive or confrontational approaches. This study was encouraging as it showed a positive approach by the GPs who became involved and positive outcomes for patients due to the brief intervention.

- The third phase of the WHO-sponsored studies on screening and brief interventions ((Gomel, Wutzke, Hardcastle, Lapsley, & Reznik, 1998) - see also section 2.3.2 above) was designed to assist the uptake and implementation of brief interventions by general practitioners. 161 physicians of the 628 randomly selected to be approached regarding the availability of training, requested the brief intervention package (Drink-less) and agreed to participate in the training and support phase of the study. They were matched into one of four training and support conditions: training and no support, training with minimal support, training and maximal support, and a control condition where the package was delivered to the surgery but no training was given. There were 34 physicians in the control condition and the remaining 127 selected their preferred training strategy from 3 conditions: direct mail, telemarketing, and academic detailing. The brief intervention to be implemented involved the physicians or receptionists screening patients with AUDIT prior to the consultation where hazardous drinkers were advised how to reduce or cease alcohol consumption and then given a self-help booklet. The purpose of this study was to ascertain the cost-effectiveness of each of the 3X3 training conditions relative to the control condition. Physicians were followed up over 3 months. The purpose of training and support was to maximize physicians' screening and intervention rates.

  Telemarketing was found to be most cost-effective of the three promotional strategies. Cost was found to increase with increased support, with the exception that minimal support was both more expensive and less effective than no support, in terms of intervention rates, so it

was not a cost-effective option. The authors concluded that it thus became a value judgement as to whether the gains from extra support such as that given in the maximal support condition are considered sufficiently reflected in outcomes to warrant implementation.

Summary of Effectiveness and Expert Commentaries

The reported research on brief interventions has found that they are more effective than no treatment, and often it has been concluded that they are as effective as more intensive interventions. However, as discussed below, this research was often compromised, and experts in the field have emphasized that it is most important for the future development of new and more effective treatment approaches, that the value of intensive interventions in particular contexts is not dismissed out of hand. Similarly, they stress that it is important that inconsistent research findings do not cause policy-makers to ignore the potential usefulness and cost-effectiveness of brief interventions. Ultimately, more research is needed which takes adequate account of the factors confounding the research to date.

Below is a brief outline of the criticisms of the research raised in expert commentaries:

- Results are not generalisable to the broad drinking population (Drummond, 1997; Heather, 1995). Subjects treated with brief interventions in studies of their effectiveness have tended to have good prognoses; that is, they are older and more moderate drinkers with no comorbid conditions. Furthermore, findings of effectiveness have tended not to be replicated in female populations.

- Even though liberal criteria for change have been used, and with the likelihood of inflated effects being reported due to demand, the degree of effectiveness of brief interventions compared with no treatment has tended to be modest. Furthermore, in some studies, no relative advantage of brief intervention had been reported at all (Rollnick et al., 1997).

- There is little evidence of a translation of improvements in drinking practices found in these studies, to improvements in health.

- Research on brief interventions has largely been carried out by motivated practitioners (`motivated converts' as Drummond described them), whereas, if they are to be adopted on a broad basis, they will be implemented by generalists (`world-weary sceptics') (Drummond, 1997), whose attitudes may be reflected in poorer outcomes.

- Studies which compare brief interventions with more intensive interventions are generally compromised because brief interventions have generally been used with less dependent drinkers, while those in intensive inpatient programs have been more dependent as well as being different in treatment history and other demographics.

Apart from these specific criticisms of the research on brief interventions, more general issues have also been raised by expert reviewers. Throughout the literature, brief interventions are referred to as one intervention, when in fact they represent a range of treatments varying in length and content. According to Heather (1995), it was not known which brief interventions are effective for which types of patients and in which circumstances. Hence it was misleading to refer to the effectiveness of brief interventions as such, unless these variables are more clearly specified.

There is research data to suggest that general practitioners need strong evidence of the effectiveness of an intervention if they are to change their consulting behaviour (Rollnick et al., 1997). Rollnick et al suggested that it may be found that a broad-based introduction of brief interventions is not the best approach, because many people who drink hazardously suffer no alcohol-related problems and are likely to outgrow their excessive consumption. GPs may feel they are placing a burden of guilt on patients for what is a pleasurable social activity. In recent years there has been an increase in research on compliance of staff at primary care centres and solutions to some of these problems are starting to emerge (Carnegie et al., 1996; Gomel et al., 1998; Roche, Stubbs, Sanson-Fisher, & Saunders, 1997, Strecher, 1994 #299).

Despite these criticisms of the research to date, the experts were optimistic that further research is likely to lead to more appropriate and cost-effective applications of brief interventions in treating alcohol abuse problems in the community. In particular, Rollnick et al (1997) offered some more optimistic comments regarding research on brief interventions:

(1) Enthusiasm for use of brief interventions will be increased once it is clarified what can honestly and meaningfully be conveyed to a patient in terms of risks associated with their drinking practices. Problem-free drinkers may need no intervention and dependent drinkers may prove to be a legitimate focus for primary care-based brief interventions. Alcohol use should not be screened for in isolation but in the context of the totality of health behaviours, as they are very often inter-linked (Hall & Farrell, 1997)

(2) The effectiveness of brief interventions is likely to improve if a non-confrontational, adult-adult model is adopted where the patient is encouraged to take the lead in re-evaluating an entrenched and damaging lifestyle. Advice-giving should be augmented or replaced with more patient-empowering procedures, which incorporate the principles of stages of change and motivational interviewing.

SUMMARY POINTS

1. Brief interventions are effective in reducing alcohol consumption in those with mild to moderate problems with alcohol.

2. Brief interventions of a motivational, non-confronting style appear most effective.

3. A positive attitude towards change by both those who abuse alcohol and those who implement interventions at primary care centres is essential for their success. General practitioners need to be convinced of the efficacy of brief interventions, trained in their implementation, and able to identify when to implement them. Patients need to be ready to change, or at least amenable to consider change.

4. More research is required to clarify which are the most effective brief interventions and in which circumstances they are most effective. In particular, outcomes for women and those with concomitant physical and psychological problems need to be better researched.

5. Brief interventions have the potential to provide a low cost approach to the problems of alcohol abuse in the general population especially where patients are self-referred. However, this does not deny the importance of greater research efforts to assist those who are unable or unwilling to change their alcohol use which causes harm for the individual or other significant social costs. More intensive and costly approaches may prove more appropriate for this group.

2.5.3. Social Skills Training

An underlying assumption of social skills training is that alcohol consumption has become a preferred way of coping with unpleasant situations and feelings (Chaney, 1989). Social skills training aims to provide alternative behavioural strategies that compensate for social skills deficits. Social skills training generally includes communication skills, effective listening techniques, problem solving, and assertiveness training.

Given the complexity of alcohol problems, social skills training is usually applied in conjunction with other interventions such as pharmacotherapy (Volpicelli et al., 1997) and other broad spectrum treatment programs. Reports of social skills training alone are much less common

In their 1993 review Mattick and Jarvis (1993) found that social skills approaches were appropriate interventions for individuals with varying severity of alcohol problems. They concluded from their review of the nine randomised controlled trials in the area, that there was consistent evidence that social skills training reduced alcohol consumption in both the short-term and long-term among those dependent on alcohol.

The strategy appears to be most useful as a component in relapse prevention with research indicating that social skills training is associated with lower rates of relapse. The interventions included under the term social skills approaches were: drink refusal skills training; assertive skills

training; social skills training; relaxation training; stress management skills training; problem solving and relationship enhancement training.

Monti et al (1994) in reviewing the efficacy of social skills training was consistent with Mattick and Jarvis (Mattick & Jarvis, 1993) in concluding that social skills training is effective in reducing alcohol consumption and relapse. Miller et al (1995) found social skills training to be one of the better therapies based on their methodological analysis of the research to that time. Since these reviews, there have been a number of studies reporting the implementation of skill based training in school populations. The research highlights from these studies are reported below.

Recent Research

- Botvin and colleagues (1995) reported on a long term follow-up of a large study teaching "life skills" and skills for resisting influences to use drugs. Fifty-six schools with 3597 12th grade students were randomly assigned to intervention with formal training workshop, intervention with no formal workshop and control. Follow-up data was collected six years after baseline using school, telephone and mailed surveys. The intervention consisted of 15 class periods focussing on the teaching of information and skills for resisting social influences to use drugs and generic personal and social skills for increasing overall competence. A cognitive behavioural model was followed to teach skills for building self-esteem, managing anxiety, communicating effectively, developing personal relationships and asserting rights. Significant reductions in alcohol and other drug use were found for the intervention group relative to controls. These results are remarkable, given the long follow-up period of the study.
- In contrast to the Botvin et al (1995) study, Clayton and colleagues (1996) reported limited effects from a five year prospective trial of drug resistance education in 7th grade students. Clayton randomly assigned 23 elementary schools to either drug resistance education or general health education. Significant effects were observed at one year for the intervention group with reduced level of drug use including alcohol, however these effects disappeared at five year follow-up.

SUMMARY POINTS

1. There is consistent evidence that social skills training is an important and effective component of alcohol treatment.

2. Given the complexity of alcoholism, social skills training is not expected to be effective on its own, but rather seen as a component of broad spectrum treatment programs. Additional investigation is warranted to explore the unique contribution of social skills training to treatment outcome.

3. There is inconsistent evidence as to the effectiveness of social skills based programs in the prevention and reduction of alcohol use in school based populations.

2.5.4. Behaviourally-Oriented Marital/Family/Community Interventions

The purpose of family and marital therapy is to engage significant others in the rehabilitation of individuals who abuse alcohol. There are various types of family therapy which have been trialled: systems, interactional, behavioural and spouse-directed (Mattick & Jarvis, 1993). The contingency-based community reinforcement approach (CRA) developed by Azrin et al (1996) also aims to engage those close to the affected person in a behaviorally-oriented approach to treatment. CRA was developed as a more intensive and broad-ranging approach which addresses community reinforcers both within and outside the family in an effort to encourage interests and activities which lead to abstinence. CRA tends to involve close family members and was thus incorporated with behavioural family and marital approaches for the purposes of this review.

In their 1993 monograph, Mattick and Jarvis reviewed marital/family therapy and CRA separately. At that stage, non-behavioural approaches to family/marital therapy were being trialled, but only behavioural approaches were found to show promise in the review. Mattick and Jarvis also found that behavioural marital therapy (BMT) was more effective than no treatment at all, but was no more effective than individual alcohol counselling or brief advice and follow-up. In their section on CRA, they found good support for its use in the short-term, but that more research is required to ascertain long-term effects as well as the interaction effects of supervised disulfiram on CRA outcomes. Similarly, Miller et al (1995) found that both CRA and BMT were among the more effective of interventions reviewed.

A further meta-analysis of family therapies for alcohol abuse was completed in 1995 by Edwards and Steinglass (1995). In this meta-analysis, studies of family therapy treatment outcomes were divided into three phases: treatment initiation; primary treatment/rehabilitation; and aftercare. Their criteria for inclusion of studies were that they addressed family therapy outcomes, they used objective outcome criteria and compared the family treatment group with a control group. Random allocation to control and treatment was not required. They considered both clinical and statistical significance in their evaluation and combined results from quite different family treatment modalities to obtain effect sizes.

For Phase I (treatment initiation), the clinical goal was primarily that the individual entered treatment. In the absence of relevant data, a rate of 50% of treated subjects was arbitrarily set as the cut-off for clinical significance for this phase. In phases II and III, they used 50% abstinence to indicate clinical significance, based on expected abstinence with no treatment (2-5%) and outcomes found with other treatment modalities. These criteria for clinical significance

appear somewhat arbitrary, so that only size of effect will be considered for this present review. Due to the wide range of follow-up periods in the 21 studies they identified, no time period to achieve abstinence was specified. This, again, could be considered a weakness in the meta-analysis as treatments which are shown to be effective immediately on completion are given equal status to those which may be effective for at least a year following treatment. Because data in alcoholism treatment studies tends to be presented in the form of comparisons of frequencies of abstinence in the treatment and control groups, they used a probit transformation to calculate effect size over all studies in the meta-analysis. Mean effect sizes were then calculated for each phase based on a simple mean of the contributing effect sizes. Given the large variation in the sample sizes used, it may have been more valid to pool results from the relevant studies and use this larger sample to gain a measure of overall effect.

In phase I, the authors considered there was strong support for family therapy interventions to motivate alcoholics to enter treatment. However, the four studies on which this conclusion is drawn employed three quite different interventions and were limited in size. In the one study using the confrontation method (Betty Ford, "intervention" method), all 24 families that were trained to confront the alcoholic member were allowed to choose whether they would ultimately do so. Those 7 that did, may well have chosen to do so on the basis of perceived likely success in getting the individual to enter treatment – and 6 (87%) of these were right. This result was contrasted with the 17 families who chose not to confront, of whom only 3 (17%) proceeded to treatment. So this result could simply reflect the family's ability to judge whether confrontation would be successful with their particular alcoholic member.

The only large size study used 69 spouses of alcoholics, but allocated only 14 to the control group and this nonrandomly. The other three studies had 25 or less total subject pool, one being the "intervention" study described above. One was considered a pilot study (N=25) for the largest study and the third was a CRA program (N=12) which was also considered only a pilot study. Combining the results from these poorly designed and heterogeneous studies to yield a mean effect size is thus of dubious validity. Hence, contrary to the authors' conclusions, this meta-analysis has provided insufficient evidence in support of the use of family interventions to deliver subjects into treatment programs.

For phase II, two broad types of treatment models were identified: *family systems-oriented approaches* which focus on interactions within the family and in the broader social environment, and *behaviourally oriented approaches* which address specific behaviours within a social learning framework. Four studies that fit the family systems approach were identified, but only one had both random assignment to a plausible control and sufficient numbers to obtain statistically significant findings. This study found no statistically or clinically significant differences between the family therapy group and a control which was given one session of advice only. Hence, contrary to the conclusions of the authors, this meta-analysis provided no support for the family systems approach.

There were six groups of studies on behaviorally oriented family therapy reviewed in this meta-analysis. These found that marital/family therapy led to improvements in drinking behavior, but that these improvements were no better than individual therapy. These studies were somewhat diverse and generally tended to compare one form of therapy with another, with no real control groups - most comparisons were made with "standard treatments" - and family therapy appeared no better than such treatments.

An exception was the group of studies using the CRA approach, which were reviewed by Mattick and Jarvis (1993) above. These CRA studies tended to have significant effect sizes compared with traditional approaches, but used very small numbers. CRA employs other interventions along with marital/family therapy. These include vocational counselling, advice on social and recreational activities, social skills training, and behavioural self-control skills. Hence the presence of other effective treatments along with the family therapy may have led to these more positive outcomes.

For phase III, only two studies, involving family members' participation in post-treatment relapse prevention, were included. However the first of these was not a genuine measure of the effectiveness of family participation because this variable was only one of several variables which differentiated the control and treatment groups. In particular, it could be argued that the behavioural component of the treatment might have caused the significant treatment effect found. The second study quoted also did not directly measure the effects of family participation, so that little could be gleaned from the phase III meta-analysis. There is a problem differentiating aftercare from continuing treatment and this may have led to the paucity of good studies in this section.

Recent Research

Research is continuing in both CRA (Meyers & Smith, 1997; Smith, Meyers, & Delaney, 1998) and BMT (O'Farrell, 1996; O'Farrell, Choquette, & Cutter, 1998; O'Farrell, Choquette, Cutter, Brown, & et al., 1996; O'Farrell & Rotunda, 1997). However, little replication of findings from these two research groups has been carried out elsewhere.

- O'Farrell and co-workers (1998) have recently reported a long-term trial of the efficacy of a relapse prevention program for couples following a 6-month BMT program. They randomly assigned 59 couples to 12-month relapse prevention (RP) or to no RP, and assessed them before the 6 months BMT treatment, immediately after treatment, and at 3, 6, 12, 18, 24 and 36 months post treatment. So this study did not directly assess the efficacy of BMT relative to placebo. However it does provide insight into the long-term retention of treatment outcomes and evidence on the efficacy of the relapse prevention program. It could be argued that the couples RP program is an extension of the BMT

program and provides a higher "dose" of treatment. They found that couples receiving the couples-oriented RP program had improved drinking and marital outcomes for the first 6 months of follow-up, and that, for a sub-sample – those with more severe marital and drinking problems – these outcomes persisted for the full 30 months of the study. However, such research would need to be replicated using a control group for the RP phase as well as for the treatment phase. As the authors suggested, it could be that individual therapy directed at relapse prevention may have similar effects.

- A recent study (Smith et al., 1998) considered the relative advantages of the CRA approach compared with standard treatment (STD) given at a large day shelter for homeless alcohol-dependent individuals. They found that both groups improved significantly following treatment and that those engaged in CRA treatment had significantly superior outcomes to the STD group. However, there were problems in the design of the study in that those engaged in CRA were required to show greater discipline in participation than the STD group, in order to retain the significant benefits of being on the programs (including housing). There were also greater checks and punishments for the CRA group for lapses in drinking whilst participating. Thus, as the authors point out, the study did not adequately compare the two specified treatments, and so does not provide conclusive evidence of the superiority of the CRA approach compared with usual care.

Summary of Effectiveness and Expert Commentaries

Evidence for the efficacy of the CRA approach is still dependent on the research quoted in the Quality Assurance Project by Mattick and Jarvis (1993), which, although showing promise, were based on very small numbers.

As summarised by Baucom et al, (1998) most recent research on BMT includes the use of partner-assistance in maintaining disulfiram contracts as well as motivational presessions as part of the therapy which may confound the effects of the behavioural therapy alone. Similarly, CRA can be considered as a bundle of treatments of varying effectiveness. More evidence on the total package as well as the components, and more replication by other research groups is required, before the effectiveness of BMT alone, or CRA, can be clarified.

Given the lack of good clinical trials with sufficient power, which directly assess the effectiveness of BMT, this review can only conclude, similarly to Mattick and Jarvis (1993), that there is little evidence that inclusion of the spouse or significant others in treatment is any more effective than individual treatment.

SUMMARY POINTS

1. Research has shown that family/marital behavioural interventions are effective but no more effective than individual therapy. The community reinforcement approach has shown greater promise but requires further research.

2. The effectiveness of the community reinforcement approach package needs further assessment and clarification as to which parts are effective and which are not.

3. The possible interaction of family/community reinforcement with degree of dependence and social dysfunction needs to be more thoroughly explored.

4. The influence of supervised disulfiram on outcomes in trials of behavioural marital therapy and community reinforcement approach needs to be assessed. Given the suggestions made by experts in pharmacotherapies (see Section 2.5.1 above) that the use of disulfiram should be curtailed, the effect of its removal or replacement in behavioural marital therapy and community reinforcement approach treatment programs needs clarification.

2.5.5. Cue Exposure

Cue exposure involves exposing clients to alcohol-related cues such as the sight, smell and taste of alcohol, or to the setting where they would usually drink, and, in the case of abstinence-training, not permitting them to drink. Where controlled drinking is the aim, then they would be permitted a restricted amount to drink in the presence of alcohol-related cues. Cue exposure is not considered a purely behavioural activity as it is assumed that cognitions such as self-confidence to resist will also be reinforced through exposure associated with abstinence or controlled drinking (Bradizza, Stasiewicz, & Maisto, 1994).

In their review, Mattick and Jarvis (1993) concluded that use of cue exposure (CE) could not be recommended on the basis of available research, but stated that it had potential as an effective treatment and should be further studied.

Recent Research

- Drummond and Glautier (1994) compared the effects of CE with an equivalent treatment time in relaxation therapy using 35 recently-detoxified alcoholic males who were severely-dependent. The time to relapse and total alcohol consumption up to 6 months post-treatment, as well as alcohol-related problems at 6 months follow-up were used as outcome measures. Significantly superior outcomes were found for CE compared with the relaxation treatment for most of the outcome measures used, although the groups did not differ in alcohol-related problems, nor in time to relapse to lowest-level drinking. This latter result points to the possibility that cue exposure may be of greater use in controlling, rather than

stopping drinking in heavy drinkers. They also found that social stability and level of alcohol-related problems predicted outcome, while level of dependence did not.

As the authors argued, the results of this study support CE as a therapy to assist delay in relapse to heavy drinking, and represented a clinically-significant harm-reduction outcome. However, variables apart from treatment assignment predicted outcome, which indicates that a more complex or multi-modal approach which takes into account such factors as family history and social stability is needed to maximise outcomes.

- Sitharthan et al (1997), compared the effects of CE (n=22) with standard cognitive behavioural therapy (n=20) on a sample of volunteer nondependent problem drinkers using a controlled drinking goal. Treatments were administered in six 90-minute weekly group sessions. Significant improvements in drinking behaviour were found in both groups at 6 months post-treatment, but the CE group had significantly greater decrease in self-reported frequency of drinking and consumption per occasion. The CE group also had significantly decreased problems associated with alcohol in the areas of work, relationships, law and health, while the cognitive behavioural therapy group only had a significant decrease in relationship problems. The authors concluded that, given the accepted effectiveness of cognitive behavioural therapy, these results give strong support for CE as an effective treatment for nondependent problem drinkers, as well as for its use in promoting controlled drinking outcomes. Although an intention-to-treat model was not used in the analysis and adjustments were not made for the number of statistical tests carried out, the sheer number of significant outcomes in this study, which favour CE over standard cognitive behavioural therapy, certainly encourage optimism regarding the use of CE in treating nondependent problem drinkers who are clearly ready to change their drinking habits.

Summary of effectiveness

Cue exposure has demonstrated considerable promise as an intervention for the treatment of alcohol abuse. In particular, it may prove an effective adjunct to standard cognitive behavioural therapy interventions in the achievement of a controlled drinking goal. This therapy has the potential to prevent relapse, which is most likely to occur during exposure to alcohol cues. Its use could thus remove the need for further post-treatment relapse prevention interventions, which would bear directly on the overall costs of treatment.

SUMMARY POINTS

1. Cue exposure is an effective treatment which may be most effective as one facet of controlled drinking programs.

2. Because it directly addresses cues for drinking it may prove a cost-effective addition to programs which would normally require additional relapse prevention training.

2.5.6. Cognitive-Behavioural Interventions

Cognitive behavioural therapy (cognitive behavioural therapy) aims to teach the individuals how to control their responses to their environment through improving social, coping and problem-solving skills. In relation to alcohol problems, it forms the basis of some of the more effective therapies which are discussed above e.g. brief interventions (including motivational interviewing), social skills training and community reinforcement. Stress management is another term which is subsumed under the broad heading of cognitive behavioural therapy because cognitive behavioural therapy in its various forms empowers the individual to control environmental stressors.

Recent Research

It is widely agreed by experts in the field that cognitive behavioural therapy is an important and effective treatment for abuse of alcohol (Hester, 1995). It appears to be most effective for individuals with less severe alcohol-related problems and who have had a shorter duration of drinking problems (Hester & Delaney, 1997). Cognitive, cognitive-behavioural and behavioural therapies were found to be among the more effective interventions in the review by Miller et al (1995). There are few recent controlled studies which specifically address the efficacy of cognitive behavioural therapy in the treatment of alcohol abuse.

- Sitharthan et al (1996) used cognitive behavioural therapy for both the treatment and minimal intervention groups in their study of treatment by correspondence, with significant improvements in self-efficacy and drinking behaviour post-treatment and some evidence of greater decline in alcohol consumption for the full cognitive behavioural therapy treatment group. Again, lack of an untreated control group means that the effectiveness of either cognitive behavioural therapy program was not directly assessed.

- Hester & Delaney (1997) recently completed a controlled study of the effectiveness of cognitive behavioural therapy for controlled drinking, using a computer program to teach behavioural self-control. The study included 40 volunteers who scored at least 8 on AUDIT (Saunders et al., 1993) but who scored below 20 on the MAST (Selzer, 1971). Those who scored 20 or more were considered more suitable for a program with an abstinence goal. In order to be included in the outcome analysis, subjects had to complete at least 3 of the 8 therapy program sessions which were administered over 10 weeks. Twenty subjects were randomly assigned to immediate treatment and 20 to 10 weeks delayed treatment. Follow-ups were scheduled at 10 weeks, 20 weeks and 12 months. There were no significant pre-treatment differences between the two groups. At

the 10 week mark, the immediately-treated group showed significant improvement in drinking outcomes on baseline, and compared with the (then untreated) delayed group. The delayed group then received the cognitive behavioural therapy and improved significantly over the next 10 weeks at which time the two groups no longer differed. Gains were maintained at 12 months for the whole sample. This supports the expert opinions that cognitive behavioural therapy is an effective therapy and, as with the study using written correspondence (Sitharthan et al., 1996), provides evidence that non-direct cognitive behavioural therapy may have an important role to play in treating alcohol abuse.

- One important area where cognitive behavioural therapy has been found to have potential to indirectly influence alcohol intake is in the treatment of alcoholics with comorbid depression. Brown et al (1997) quote prior research evidence which suggests that as many as 65-85% of patients entering alcohol treatment have clinically significant levels of depressive symptoms, that depression has been associated with poorer outcomes from alcohol treatment, that depressed mood can trigger alcohol relapse, and that cognitive behavioural therapy for depression (CBT-D) has been shown to be effective in treating unipolar depression. Hence, they hypothesized that CBT-D is likely to improve the achievement and maintenance of alcohol treatment goals.

  This study compared the effect of CBT-D (n=19) plus standard alcohol treatment, with relaxation therapy plus standard alcohol treatment (RTC, n=16) on alcoholics with comorbid depression. They found that the CBT-D group had significantly greater reductions in somatic depressive symptoms post treatment compared with the RCT group. There were few differences between the two groups on drinking outcomes at 3 month follow-up, but significant improvement of the cognitive behavioural therapy group on the 3 outcome measures (percent days abstinent, overall abstinence, and drinks per day) compared with the RCT group at 6 months follow-up. The CBT-D group thus maintained gains made from treatment through to 6 months, while the RCT group did not. The authors argue that this fits with prior research on treatment outcomes for CBT-D which found that treatment gains tend to be maintained among patients receiving CBT-D.

Summary of effectiveness

Cognitive behavioural therapy is an effective treatment procedure which appears to work best with nondependent problem drinkers. Just as in the treatment of other psychiatric illnesses, cognitive behavioural therapy tends to have lasting effects in the treatment of alcohol use problems. Cognitive behavioural therapy is integral to many of the effective treatments discussed in previous sections. Because it is particularly adaptable to programmed learning and manual formats it has considerable potential as computer training and distance education programs. It

has been found to be effective with other psychiatric conditions such as depression, and shows potential to treat alcoholics with such comorbid conditions.

SUMMARY POINTS

1. Current research and expert opinion agree that behavioural self-control as taught through cognitive behavioural therapy is an effective treatment for alcohol abuse.

2. It appears that cognitive behavioural therapy may be most effective with problem drinkers who are nondependent.

3. Cognitive behavioural therapy is particularly adaptable for non-direct interventions such as correspondence and computer training.

4. Cognitive behavioural therapy for depression has the potential to improve drinking outcomes, which reflects the interdependence of these two psychiatric conditions.

2.5.7. Other Interventions

Mattick and Jarvis (1993) reviewed several further categories of interventions for alcohol. Some were considered to have little potential and further research was not recommended. These included alcohol education (used alone), aversive therapy, relaxation training and systematic desensitization, interpretive psychotherapy and hypnosis. Other interventions were found to have potential, but insufficient evidence to recommend them at that time. Examples in this category were covert sensitisation, AA and possibly acupuncture. Unfortunately, since QAP, there have been no further randomised trials on covert sensitisation, despite being recommended by experts (Miller et al., 1995). There have also been no further randomised trials of acupuncture treatment for abuse of alcohol.

Mattick and Jarvis (1993) concluded that AA provides an accessible avenue for self-help and on-going social support for those who choose abstinence as their goal, but that there is no convincing evidence that AA alone is effective. Tonigan et al (1996) attempted a meta-analysis of a broad variety of studies which incorporated AA as part of the treatment. This meta-analysis was intended to determine which variables moderate research findings and concluded that the best potential lies in well-designed studies using larger outpatient sample sizes than used to date. They rated the study quality of the 74 studies from which they drew their conclusions on 5 variables: method of subject selection, assignment to treatment/control, instrument reliability, and use of collateral measures or use of biomedical measures to corroborate self-report. They found that, on average, these studies usually met only one of their 5 criteria for a good quality study and this one was most typically instrument reliability. Hence the quality of research in this area has not been of a sufficient standard to give further insights into the effectiveness of AA.

No further randomised controlled trials were found in the most recent literature. Hence, the status of research in AA has not changed since the review by Mattick and Jarvis (1993).

SUMMARY POINT

The Quality Assurance Project (QAP, Mattick & Jarvis, 1993) concluded that some other interventions had potential but insufficient evidence to recommend them at that time. Examples in this category are covert sensitisation, AA and acupuncture. The status of these other interventions has not changed since the completion of the QAP.

2.5.8. General Commentary

Both the the QAP (Mattick & Jarvis, 1993) and the review by Miller et al (1995) came to similar conclusions regarding the best treatments for alcohol abuse. This is not surprising as both were based on a similar body of research and used rigorous evaluation methods. Two important general observations were made by Miller et al which deserve to be reiterated here:

1. Their study found a large gap between evidence and practice which they considered should be addressed by both scientists and clinicians. They commented that one had to go nearly halfway down Table A1 (see Appendix A1.4) - to disulfiram - before reaching the treatments most commonly used in the United States. They argued that there is often a perception that treatment for alcohol problems does not work and this is unsurprising if the least effective interventions are being used. The data in this study certainly suggests that there are effective treatments for alcohol abuse. One clear way to improve outcomes of alcohol treatment in practice is to promulgate and implement those treatments which have been shown to work.

   Although QAP did not specifically rank interventions in order of effectiveness, it did provide recommendations regarding effective interventions as well as a summary of most-used interventions in Australia. Again there were clear inconsistencies between recommended and most frequently used interventions.

2. In their examination of correlates of quality and effectiveness ratings, Miller et al found no significant correlations between these two variables, nor between quality and cost, severity of problem, sample size, age and gender profile. With effectiveness they reported a similar result with the exception that there was a trend ($r=-0.26$) for more expensive treatment to be less effective which was also found in a previous meta-analysis which costed treatments (Holder, Longabaugh, Butler, & Rubonis, 1991). However, they also reported a trend towards higher quality studies in more recent times.

One further issue which has arisen from the large body of research on treatments for alcohol abuse, is that of patient-treatment matching. This issue was tested in a large study recently (Project MATCH Research Group, 1997) and results with regard to hypotheses about matching were not very encouraging. This study is described in Appendix A2.2. Three treatments were compared (cognitive behavioural therapy, motivational enhancement and 12-step facilitation) to ascertain whether they had differential effects dependent on particular client factors. These client factors were selected because experts in the area and research had suggested they may be relevant to the effectiveness of the different treatments. Few differences were found, but the study did exclude perhaps the more dependent individuals eg those with dual diagnosis and the homeless. This notion warrants further investigation.

SUMMARY POINTS

1. It is important that those treatments which have evidence of effectiveness are implemented. To date little heed has been paid to evidence of effectiveness.

2. It is likely that implementing most effective treatments will cost no more than those currently favoured, and, being more effective will prove to be more cost-effective.

3. The notion of matching patients to treatments requires further investigation.

3.0 OPIATES

3.1 GENERAL INTRODUCTION

The most effective available treatments for heroin addiction involve drug replacement therapy usually supported by specialised psychotherapeutic or counselling programs. The use of opiate replacement therapy is controversial because it involves the delivery of a drug to treat a drug problem. However, as Hall et al (1998b) argue, it can be supported from a utilitarian perspective, in that it can be shown to benefit both society and the individual by significantly reducing illegal injecting heroin use and associated crime, and thereby improving the health and well-being of a significant proportion of patients.

The first drug replacement therapy to be trialled, and now the most widely established, uses the synthetic opioid methadone. Methadone maintenance treatment was introduced by Dole and Nyswander in 1965 (1965); based on the notion that heroin dependence results from 'a permanent metabolic deficiency'. Methadone administration was proposed as a replacement drug which would stabilise this deficiency. Methadone has the properties of suppressing withdrawal and craving for heroin in the addicted individual

The identification of opioid receptors in the brain in the 1970's allowed more specific definition of the neuropsychological effects of heroin and other opiates. Drugs used in opioid replacement therapy are described in terms of their agonistic and/or antagonistic properties in relation to the endogenous opioid receptors. Both methadone and LAAM (levo-alpha-acetylmethadol) are heroin *agonists* because they excite the same (μ) receptors that heroin does, and so can be used for pain relief as well as reducing withdrawal from and craving for heroin, but with lesser narcotic effects.

Naloxone and naltrexone are heroin *antagonists* which have been trialled to replace heroin in dependent individuals. The antagonists function by blocking without stimulating the neural receptors which respond to heroin. Thus they block the euphoric, sedative and analgesic effects of opioids and, as such, do not help reduce withdrawal symptoms. Buprenorphine, another drug that has shown potential as a replacement drug for heroin, is characterised as a mixed agonist-antagonist. It shows an inverted U-type dose-response curve, with maximal opioid effects at medium doses.

These opioid replacement drugs are suitable for oral administration which removes the risks of infections such as HIV/AIDS and Hepatitis B and C arising from syringe use. They also have the advantage of requiring at most a single daily dose which means that normal life activities are less disrupted for individuals in treatment than when using heroin. Such treatments are preferred by the heroin-addicted individuals as an alternative to abstinence. This is evidenced by the fact that most heroin addicts who are given no further treatment return to regular use soon after

detoxification, whereas there is a significant number who have been shown will remain on opioid replacement therapy indefinitely given the right conditions (Ward, Mattick, & Hall, 1998e).

One further form of opioid replacement therapy is heroin maintenance, where dependent individuals are given legal and controlled injections of heroin at treatment centres. It has been suggested that ultimately this may be the most effective treatment for that small hard core of addicts who are resistant to any other form of treatment (Farrell, 1998), and who are most vulnerable to death by overdose as well as being responsible for much of the continued social damage caused by illegal heroin use.

Although the basis of the most effective available treatments for opioid addiction is pharmacotherapy, there are many factors which have a bearing on individual outcomes. Variables such as those the patient brings to the treatment setting and qualities of the treatment setting itself have critical impact on the effectiveness of treatment. Furthermore, non-drug programs such as those practiced in therapeutic communities have a role to play in treatment, as do community-based relapse prevention programs such as Narcotics Anonymous.

3.2 ASSESSMENT

Assessment typically involves a review of the quantity of substance being used or consumed and the consequences of such use. Assessment is used to determine the appropriate treatment and to assess an individual's need for other medical attention. Assessment for treatment is regarded as the lead-in to treatment and how it is conducted can itself have ramifications for treatment outcome (Ward, Mattick, & Hall, 1998a). Furthermore, use of valid and reliable assessment procedures at intake and following treatment is important in order to evaluate treatment effectiveness.

Individuals with drug use problems are often reluctant to commence treatment (see Section 2.3, Assessment and Treatment Planning). Therefore the assessment of motivation to change is of particular importance in individuals with drug use disorders. Further, the manner in which the assessment is conducted, particularly addressing expectations of the patient is an essential consideration in the assessment of illicit drug use and the development of rapport. In a similar way to the approach recommended for assessment of alcohol problems (Section 2.3), it may be more constructive to briefly screen for substance use at initial interview, as lengthy interviews may act to discourage further attendance in the treatment program (Mattick & Hall, 1993). Further information on drug use and associated problems can be gleaned in later sessions and at a pace that will not jeopardise the therapeutic relationship.

Mattick et al in the report on the Quality Assurance Project (Mattick & Hall, 1993) described six major problem areas which it would be expected that effective treatment would impact upon and which should be assessed before recommendation for treatment can be made. These were:

(1) Motivation to change: It is clear that treatment will be more effective where the patient is motivated to change. Motivation can be assessed by a simple questionnaire and, where warranted, motivational interviewing may be used as part of the individual's treatment program. Such procedures have been found to be a useful adjunct to treatment.
(2) Drug use and dependence: Knowledge of the patient's level of dependence can assist with decisions regarding appropriate treatment type and intensity and expectations of withdrawal problems. Less severely dependent clients may be better suited to an abstinence-based treatment than drug replacement, and would expect lesser withdrawal symptoms.
(3) HIV risk and physical health: This assessment should cover both injecting and sexual practices which impinge on HIV/AIDS risk. The QAP recommends that physical assessment should be medical and carried out by primary health care physicians, with additional self-report data on perceived health problems. Apart from HIV sero-toxicity, medical examination should measure Hepatitis B and C and liver function.
(4) Psychological and psychiatric adjustment: Because psychological problems are high amongst opiate dependent patients, and have a negative impact on outcomes, it is essential that these are assessed at entry and that the program ensures a high priority is given to treatment of comorbid psychological conditions.
(5) Social adjustment and functioning and (6) Criminality: It is also important to take into account such factors as level of employment, relationships with family and friends, living conditions and degree of criminal involvement when assessing client needs on entry to treatment as these can impact on treatment and expected outcomes.

Apart from a medical examination and history-taking to assess physical health and HIV/hepatitis risk, various interview protocols have been designed to assist in the assessment process. The Severity of Dependence Questionnaire (SODQ, (Sutherland et al., 1986)) was developed to assess level of dependence in the recent past, and was recommended by Mattick and Hall (1993) to be used as an aid to assess severity of dependence in patients presenting for treatment. Instruments which directly assess the DSM-IV and ICD-10 criteria for dependence would also be suitable to assess level of dependence (Ward et al., 1998a).

Ward et al, in their broad-ranging review of the literature regarding assessment, emphasised that it is important to assess both the level of opioid dependence and problems and risks associated with the health and lifestyle of the patient which may impact on treatment suitability and outcomes. The Addiction Severity Index (ASI (McLellan et al., 1985)) and the Opiate Treatment Index (OTI (Darke, Hall, Wodak, Heather, & Ward, 1992)) are both psychometrically sound instruments which have been designed to assess drug-related problems for both research and clinical purposes, although most use is in research. Both of these instruments assess current drug use as well as health, criminal activity and psychological and social functioning. The OTI also assesses HIV risk-taking behaviour. Mattick and Hall (1993) recommended the OTI for assessing problems and risks associated with alcohol and other drug use, but advised that level of dependence and motivation for change should also be measured at intake assessment.

Most recently, a new assessment instrument has been developed in the United Kingdom arising from the NTORS study (see Appendix A2). The instrument is called the Maudsley Addiction Profile (MAP) and, like OTI and ASI, is a multidimensional measure of substance dependence and problems. However the authors argued that it may be preferable to these other measures because it takes around 12 minutes to administer, compared with 45 minutes for the OTI and the ASI (Marsden et al., 1998). Many of the items and scales were developed and adapted from pre-existing instruments such as the OTI and ASI. Although further research is needed on the clinical utility and predictive validity of this instrument, psychometric information gained to date indicates it is a valid, reliable and brief measure of the variables of interest in assessment for drug and alcohol treatment.

Another recently developed scale is the Injecting Risk Questionnaire (IRQ, (Stimson, Jones, Chalmers, & Sullivan, 1998)) which has been developed in order to obtain standard information regarding HIV risk-taking behaviour in the form of needle-sharing. The IRQ has been shown to be a reliable measure of the risk of sharing of injecting equipment across various settings and with a variety of injecting drug users. Stimson et al found that the multiple question format was more effective in identifying needle-sharing behaviour than a single question on the matter.

Because drug use behaviours are not observed directly by the therapist, it is necessary to use self-report questionnaires such as those described above. This raises the question of the reliability of such measures. Sobell et al (1994) reviewed the scientific literature and concluded that self-reports are reliable if carried out in a clinic or research setting, when the patient is drug-free at the time of completion and where the patient can be reassured that the information will be kept confidential.

SUMMARY POINTS

1. Patients presenting for treatment for opiate dependence should be assessed for: motivation to change; drug use and dependence; HIV/Hepatitis risk behaviour; mental health status; social functioning and criminality.

2. Such an assessment process may be lengthy and this may discourage patients who are often ambivalent about treatment for their dependence. Hence it is recommended that a brief screen for drug use is used at first interview, and that other information is obtained in later sessions as rapport is established with the patient.

3. Standard protocols such as the Severity of Dependence Questionnaire (SODQ), the Opiate Treatment Index (OTI) and the Addiction Severity Index (ASI) have been developed and validated and should be used to assist in the assessment process.

3.3 DETOXIFICATION

A general summary by Mattick and Hall (1996) regarding the place of detoxification in treatment, as well as realistic expectations of detoxification, has been discussed above in the relevant section under Alcohol (Section 2.4). Unlike the experience of alcohol detoxification, the abrupt cessation of opiate use leads to the onset of a withdrawal syndrome which is not life threatening. There appear to be two stages in opiate withdrawal. The first or acute phase which includes such symptoms as irritability, anxiety, nausea, sweating, sniffing, etc begins 8 to 10 hours after last administration and continues for 7 to 10 days with a peak around the third day. This is followed by a period of around 6 months of secondary withdrawal when the patient feels generally unwell and may suffer strong cravings for opiates.

Whereas there appears to be no advantage of inpatient over outpatient setting for alcohol detoxification, research has suggested that inpatient detoxification for opiates is more effective than outpatient, although this may be due to intensity rather than setting of treatment (Mattick & Hall, 1993). Because opioid withdrawal is not life-threatening, detoxification can be viewed as a form of palliative care whilst the individual abstains from drug use.

Detoxification provides an opportunity to consider seeking drug-free interventions which require abstinence prior to entry. However, as discussed in Section 2.4 above, detoxification should not be regarded solely as preparation for treatment for the individual. It has the intrinsic benefit of providing respite from the problems and risks associated with daily use whether followed up with further interventions or not. In addition, detoxification is not necessary for the most widely used method of treatment for heroin dependence - maintenance using the cross-tolerant drug methadone. Dependent persons can transfer from heroin to oral methadone with no withdrawal effects. The issue then becomes one of detoxification from methadone if the patient chooses to become abstinent. Withdrawal from methadone is accompanied by similar symptoms to withdrawal from heroin and morphine, although it is more protracted and less intense.

In contrast to alcohol, level of opioid dependence - as indicated by length of dependence and methadone dose required for stabilisation at the beginning of detoxification – is not predictive of severity of withdrawal from opiates. Instead symptom severity has been shown to be more strongly associated with neuroticism (as assessed by the Eysenck Personality Questionnaire) and expectations about withdrawal distress (Ward, Mattick, & Hall, 1998d). Research has shown that patients with higher levels of fear of detoxification stay on longer in methadone maintenance treatment and make fewer attempts to withdraw. Ward et al report some evidence that giving accurate information regarding what a patient should experience during detoxification can lead to a higher rate of completion.

The review conducted for the Quality Assurance Project (Mattick & Hall, 1993) found that the main non-medicated detoxification procedure for which there was evidence from outcome studies was **electrostimulation** of various parts of the body. The evidence suggested that results were equivocal and that further research was warranted. No further research in the area was located for this review.

Because of the high levels of anxiety and apprehension associated with withdrawal it has been proposed that **counselling and psychotherapy** may be useful as an adjunct to the medicated withdrawal program. Because pharmacological interventions have been so successful with opiate detoxification, psychosocial interventions have received little attention in the research literature. As with electrostimulation, further research is required to demonstrate how much and under what conditions counselling may assist in easing the process of detoxification. Bickel et al (1997) conducted a 26-week trial using buprenorphine for outpatient detoxification. The design was such that it did not directly assess the effectiveness of buprenorphine, but it compared two groups randomly assigned to behavioural (N=19) and standard (N=20) treatment support services. The standard treatment was equivalent to the usual ancillary service provided in methadone clinics and addressed compliance and rehabilitation issues. The behavioural program comprised community reinforcement and contingency management approaches. They found that the behavioural treatment resulted in improved outcomes on virtually all measures compared with standard treatment, although few of the differences were significant. In particular, they found that behavioural treatment improved retention in that 50% of this group were retained to the end of the study compared with 20% of the standard treatment group. They also found a strong association between completion of behavioural activities and both retention and opioid abstinence. The numbers are clearly very low in this study, so that further research using larger numbers and refined and individualised behavioural activities may improve the rather poor retention rate which is currently occurring with pharmacologically assisted detoxification.

Mattick and Hall (1993) concluded that tapering doses of **methadone** is the most effective approach to opiate detoxification. In their review of detoxification from methadone, Ward et al (Ward et al., 1998d) reviewed related evidence which suggests that the process of withdrawal of methadone should be gradual and should be even further tapered when dose reaches around 20 mg where patients may begin to experience an increase in withdrawal symptoms. Whether patients benefitted from being informed of dose levels throughout detoxification appeared to be a matter of individual inclination. Some patients preferred to be blind to dose in order to allay anxiety as dose approaches zero. Others benefitted by being informed and acting as an active participant in the procedure.

Because methadone-assisted withdrawal has been in use for a long time it tends to be used in research as the standard against which to measure other approaches. The alpha adrenergic blocking agent, **clonidine** has been evaluated and, in some studies, has been found to have approximately equivalent efficacy in reducing the symptoms of detoxification. It has the advantage over methadone in shortening the detoxification period and, when combined with **naltrexone**, can reduce it to 2 or 3 days. However, clonidine has significant side effects which include hypotension, sedation, insomnia and possible psychiatric symptoms in those with a history of these disorders. According to Ward et al, comparative studies using clonidine in outpatient settings have tended to find that methadone tapering is overall more effective and that it induces less distress in patients. As with methadone detoxification, clonidine patients relapse rapidly to heroin use, once they leave the detoxification program.

Following the initial promise of clonidine, the effectiveness of other alpha adrenergic agents, particularly **guanfacine** and **lofexidine** have been compared with clonidine and methadone in various studies. Kahn et al (1997) compared lofexidine and clonidine in a randomised trial using an inpatient population, and found lofexidine to be as effective as clonidine with fewer side-effects. Similarly, Carnwath and Hardman (1998) compared these two drugs in a randomised double-blind trial in an outpatient setting, and found that both drugs can be used successfully in outpatient detoxification, but clonidine required more home visits due to hypotensive side effects. San et al (1990) compared guanfacine, clonidine and methadone in an inpatient setting and concluded that methadone was superior to the alpha adrenergic agents in reducing symptoms of withdrawal, and had fewer side effects. They also found that guanfacine appears to be a more manageable drug than clonidine for the purposes of detoxification. Further research is required on the effectiveness of these drugs in assisting detoxification, especially on outpatient samples. It may be that the particular profile of action of the alpha adrenergic agonists will suit sub-groups of patients undergoing detoxification, who are not vulnerable to the side effects of these drugs.

The mixed agonist-antagonist, **buprenorphine**, which is also showing promise in maintenance treatment for opioid addiction, has been found to be equivalent in efficacy to methadone and acceptable to heroin users for detoxification in outpatient settings (Mattick & Jarvis, 1993). Buprenorphine also has the advantage of having lesser abuse potential than methadone. It has similar positive subjective effects, with minimal sedation. O'Connor et al (1997) conducted a randomised double blind clinical trial comparing detoxification outcomes for clonidine (N=55), combined clonidine/naltrexone (N=54) and buprenorphine (N=53) in an outpatient setting. They found that buprenorphine was as effective as clonidine and clonidine/naltrexone for successful completion of outpatient detoxification and resulted in fewer withdrawal symptoms. Because of the partial agonist/antagonist properties of buprenorphine, the authors argued that it is less toxic, less prone to diversion and is easier to withdraw from which make it more suitable than other available medications for outpatient detoxification in primary care settings.

Diamant and co-workers (1998) pointed to research which has found buprenorphine to be more effective than clonidine in attenuating the signs and symptoms of opiate withdrawal. They conducted an exploratory study of the effectiveness of using buprenorphine on a flexible decreasing dosage regime over a period of 10 days, using an outpatient sample. They found that patients tolerated their withdrawal symptoms well during the procedure, with no reported side effects of the buprenorphine. Patients maintained well-balanced mood throughout, and reported minimal or no withdrawal symptoms by day 10. The researchers concluded that buprenorphine is efficient for opiate detoxification and the gradual reduction in dose produced superior outcomes to those found in studies which used rapid dose reduction. Further controlled research is needed to clarify the relative benefits of buprenorphine and its various dosage regimes in opiate detoxification.

The opioid antagonists **naloxone** and **naltrexone** have been used to speed up the process of detoxification in the belief that some individuals may prefer shorter (1 to 2 days) detoxification

with more acute symptoms than lesser symptoms over a longer period (usually 7 to 10 days). It is usually required that they are used in conjunction with another drug (e.g. clonidine) to reduce the intensity of the acute onset of withdrawal symptoms (Mattick & Hall, 1993). Naloxone is the drug most frequently used to reverse the effects of opiate overdose. Naltrexone and naloxone are used in ultra rapid detoxification which has received strong promotion in recent years as a miracle cure for heroin addiction.

Ultrarapid detoxification involves successive administrations of the opioid antagonist under heavy sedation or anesthesia so that heroin-addicted patients are detoxified in 24 hours without suffering the acute withdrawal symptoms that would occur in aware patients. In an editorial in Addiction, Kleber (1998) provided a summary of the issues surrounding utrarapid detoxification. Basic to the discussion was the fact that detoxification is not synonymous with treatment and, as mentioned above, there is a high probability that patients who have undergone detoxification will relapse to opiate use if no further treatment is pursued. Another significant issue that arises is that there is a greater risk of death or harm associated with the procedure, compared to opiate detoxification without anaesthesia. The effectiveness of this procedure needs to be compared with other detoxification procedures using the gold standard of randomised controlled trials. A recent review by O'Connor and Kosten (1998) found that there was a deplorable lack of good research on ultrarapid detoxification and associated risks. Various clinical trials are being conducted throughout the world and the results from these are eagerly anticipated.

SUMMARY POINTS

1. Detoxification is not of itself a treatment for opiate dependence. However reviewers agree that the process of detoxification does have intrinsic benefits for the individual, whether followed by treatment or not, because it provides a respite from the risks associated with daily drug use.

2. Counselling and psychotherapy may be useful in allaying the apprehension associated with withdrawal from opiates but are not effective alone. More research is needed on non-drug adjuncts to assist detoxification.

3. Treating patients with individualised tapering doses of methadone has tended to be the standard effective detoxification procedure, although other drugs are currently being assessed which may prove as effective, or better, for certain sub-groups of dependent individuals.

4. Alpha adrenergic agents such as clonidine, guanfacine and lofexidine have been compared with methadone and, although effective, they have been found to have more side-effects and lesser effects on withdrawal symptoms.

5. The opioid antagonists naloxone and naltrexone (unassisted or with clonidine) may be useful for those individuals who are willing to tolerate a shorter but more intense withdrawal period.

6. Buprenorphine has been found to effectively assist in the process of opiate detoxification. Patients show few symptoms and signs of withdrawal from this medication and its usefulness is enhanced by the fact that it is less vulnerable to abuse than methadone. Further research is recommended to specify appropriate dosing regimes for opiate detoxification.

7. Use of ultrarapid detoxification using naltrexone aided by heavy sedation or anaesthesia has received much publicity but has yet to be properly evaluated. There is also a slightly increased risk of harm associated with the use of general anaesthesia.

3.4 SPECIFIC INTERVENTIONS

3.4.1 Methadone replacement therapy

Methadone maintenance is the most widely applied and researched treatment regime for opiate dependence. It was implemented as a therapy before RCTs were considered the standard method of assessment of efficacy. This means that there have been few opportunities for investigation of outcomes through RCTs because, as soon as methadone maintenance became an accepted treatment, there arose ethical and methodological problems with excluding some patients from treatment in order to have a control condition.

Recent Research

Evidence from Randomised Controlled Trials (RCTs)

In their recent review of the research literature, Hall et al (1998a) summarised evidence from randomised controlled trials as well as observational studies (see Appendix A1). From the three RCTs reviewed by Hall et al, which provided methadone maintenance over an extended period (1 to 20 years), there was strong support for the effectiveness of methadone maintenance over no treatment/placebo despite the use of relatively small samples. Outcome criteria for these studies included rates of imprisonment, daily heroin use, retention in treatment, employment status, and return to further education.

There were three further RCTs reviewed by Hall et al which compared methadone maintenance with an alternative treatment over much shorter periods of time (1 month to 15 weeks). These studies found individuals in methadone maintenance had superior outcomes to comparison groups, using such criteria as retention rates, illicit heroin use and enrolment in a comprehensive methadone maintenance program. However, the studies quoted in this section suffered from methodological problems, such as the difficulty of retaining subjects in a placebo or low-dose condition for any length of time because of the availability of methadone maintenance as a treatment elsewhere. In introducing methadone maintenance, Dole and Nyswander (1965) argued that methadone needed to be in sufficiently high doses to remove the craving for heroin and to block its euphoric effects. They also stated that its effectiveness could only be evaluated over several years. The studies quoted in this section suffered from such drawbacks as using low or unspecified doses of methadone and all were carried out over quite short periods of time.

Evidence from observational studies

Observational studies of the effectiveness of methadone maintenance reviewed by Hall et al (1998a) are divided into two categories: controlled comparative studies and pre-post studies. *Controlled comparative studies* compare outcomes for individuals who self-select for

methadone maintenance and those who enroll for alternative treatments. In these studies conclusions can be drawn about relative treatment effectiveness after statistically correcting for patient characteristics which have been shown to affect preference for particular treatment modalities. Pre-post studies compare relevant outcomes at intake and then at some point following treatment. There is no comparison condition in these studies so outcome changes need to be interpreted cautiously. In such studies time in treatment is compared with outcome to provide evidence of treatment effectiveness. However, again, those with the best prognosis may be more inclined to stay in treatment. Such selection biases can be corrected by comparing relevant prognostic indicators of those retained in treatment with those who drop out, and applying appropriate statistical adjustments.

The summary of observational studies of treatment outcome with methadone maintenance (Hall et al., 1998a) included an evaluation of how rigorously the researchers controlled for the biases discussed above. They found that methadone maintenance produced better outcomes than detoxification alone, voluntary no methadone maintenance treatment, and involuntary no methadone maintenance. In particular they found that evidence from the Treatment Outcome Prospective Study (TOPS) provided clear support for the effectiveness of methadone maintenance in reducing heroin use and crime. The TOPS study is a precursor to the DATOS study which has been summarised in Appendix A. As outlined in that summary, results from DATOS accorded with those from TOPS. DATOS found that methadone maintenance impacted positively on heroin use, marijuana use, criminal behaviour, and risky sexual behaviour.

Several other large US-based pre-post studies were reviewed by Hall et al (1998a) and all showed support, albeit less convincing, for the findings from the RCTs. Heroin use and criminal activity were found to decrease while the addicted individual remains in treatment. However, they also revealed that there were large differences in policies and treatment variables between programs and these significantly influenced outcome. Many programs were rendered ineffective because of these factors. In particular, most programs used lower doses of methadone than defined by the National Institute of Drug Abuse, and there is some evidence from this data that mean dose of methadone predicted retention and continued illicit heroin use. There was also variation on such factors as frequency of urinalysis and consequences of continued drug use. The issue of the influence of treatment variables on outcome will be discussed later in this section.

Hall et al (1998a) argued that the less impressive findings in the more recent observational studies compared with the earlier RCTs, may reflect a shift in policy in the US to use minimal doses of methadone and to strongly urge abstinence rather than maintenance in methadone treatment. This not only arises from ethical concerns of service providers and the government but from reduced financial support for methadone maintenance in the US since the mid 1970s. Other reasons for these less impressive results for naturalistic studies are that RCTs tend to be over-optimistic by being able to control who is treated and to ensure optimal treatment implementation. Also, at the time the RCTs were carried out there were few alternative

treatments, whereas more recently those leaving or refusing methadone maintenance may well obtain treatment elsewhere. It is also suggested that one further factor impacting on treatment outcomes in more recent years is the increased incidence of polydrug use amongst those presenting for treatment.

Hall et al concluded that, from the data reviewed, "on average" there is good support for methadone maintenance as a treatment for heroin abuse. It is better than all available alternatives as it attracts and retains the larger proportion of individuals into treatment and thereby significantly impacts mortality and morbidity of users and social costs for the community. They specified four caveats to this conclusion:
(1) Methadone maintenance did not rid all participating individuals of their heroin abuse or addiction. Approximately half left treatment within 12 months due to continued illicit heroin use and a substantial number continued to use heroin, at a lower rate, whilst still in treatment.
(2) There was significant variability between policies and practices and effectiveness amongst treatment programs. Factors that influenced this will be discussed below.
(3) The most effective programs followed the model proposed by Dole and Nyswander (1965) which required high or blockade doses of heroin and a maintenance rather than an abstinence objective.
(4) Benefits of methadone maintenance only lasts whilst the patient is in treatment. There is a high rate of relapse to regular heroin use on discontinuation of treatment.

Evidence from studies directly assessing the effect of methadone maintenance on HIV/AIDS and infectious Hepatitis

Ward et al (1998b) reviewed the literature which specifically addressed impacts of methadone maintenance on these infectious illnesses, which have high rates of occurrence amongst injecting drug users. They concluded that there was insufficient evidence regarding hepatitis and what was available was contradictory. One factor affecting the possible impact on infectious hepatitis is that it is highly infectious and thus spread widely amongst injecting drug users (50-80% for hepatitis B and C) and from early in their injecting careers. Hence they are likely to have the disease before entering treatment.

On the other hand there was considerable evidence that methadone maintenance programs significantly reduce the risks of HIV/AIDS. In early studies where heroin addicts were virtually randomly placed in methadone maintenance, and thus could be compared with the general population of untreated drug users, there was found strong evidence of the protection of the methadone group from HIV/AIDS infection. This was despite the evidence that there was no equivalent protection from Hepatitis B, which testified to shared needle use prior to methadone maintenance treatment. Ward et al (1998b) reviewed several recent studies which confirmed that methadone maintenance protects its recipients from HIV/AIDS.

Factors impacting treatment outcome

(i) Program factors

Dose: In their summary of the Quality Assurance Project for opioids, Mattick and Hall (1993) conclude that evidence to that time suggested that methadone maintenance is an effective treatment for opioid addiction when delivered in sufficient doses to block withdrawal from heroin, as proposed by Dole and Nyswander (1965). Doses greater than 60 mg per day were recommended. Similarly, following a review of the relevant literature, Ward et al (1998f) found that methadone dose showed a positive linear dose-response relationship with retention in treatment and a negative linear relationship with heroin use, with no plateau being reached in the dose ranges being studied. They therefore assumed that a plateau would only be reached at very high doses. They conclude that doses should be individualised depending on methadone metabolism and psychological factors and that generally, a dose between 50 and 100mg will be adequate to suit the needs of most patients. This does not preclude the options of using higher or lower doses where the need arises.

Rhoades et al recently completed a study which assessed the effects of dose and **dose frequency** on the effectiveness of methadone maintenance (Rhoades, Creson, Elk, Schmitz, & Grabowski, 1998) using survival analysis. This study used 123 subjects in a 2X2 design where visits were 2 or 5 days a week and dose levels were either 50g or 80 mg. Subjects were followed up over 24 weeks of treatment. Using an intention-to-treat analysis, they found that there was significantly poorer retention for those subjects who were required to visit the centre 5 days a week and who were also on the lower (50mg) dose of methadone. The other three groups were retained equally irrespective of visit frequency. Although a subjective measure of AIDS risk found no differences, results from urine screens for opiates found that significantly more on the low dose were using heroin whilst in treatment. The mean per cent testing positive in the 80mg/day group was 20%, compared with 45% for the 50mg/day group. So, overall the higher dose groups were retained in treatment and used less heroin than the lower dose groups. A methodological problem with this study is that the analysis excluded those patients who provided insufficient screens (less than 4, maximum possible screens 16) each month. A conservative, intention-to-treat model would have rated these as positive screens. Despite this drawback, this study can be viewed as providing further support for the notion that methadone maintenance patients fare better on a higher dose regime.

Maintenance or abstinence policies: Programs which promote short-term methadone treatment leading to detoxification and abstinence have been found to be relatively ineffective except for a small number of patients who have been using for a short period and are less severely dependent (Ward, Mattick, & Hall, 1998c). Ward et al reviewed the literature on treatment duration and found that evidence suggests that the longer the time in treatment, the greater the gains made and the likelihood that significant lifestyle improvements will be achieved

and consolidated. They conclude that the research supports a long-term maintenance treatment policy with detoxification from methadone not a necessary (or realistic) goal for many patients.

Take-home dosing/diversion of methadone: The results from the Rhoades et al (1998) study regarding dose frequency are of particular relevance to the issue of take-home dosing and diversion of methadone. They found that allowing patients to take home doses from twice-weekly treatment centre visits, improved retention compared with requiring more frequent (five times per week) visits. Also the group on twice-weekly visits did not have increased heroin use as evidenced by urinalysis, so that they appeared to be able to manage at-home dosing adequately. In their summary of the effects of treatment factors on retention, Ward et al (1998c) also found better retention with take home dosing and less frequent treatment centre visits. Darke (1998) points out that methadone dose diversion appears quite common, although little controlled research has been carried out in the area. Much of this diversion of methadone appears to come from take home doses. Diverted methadone, apart from depriving the individual of the required dose, is used by those heroin users not in treatment. Oral methadone can be diverted for use in injections, thus increasing health risks to the individual. However, Darke does not recommend that take home doses are curtailed, but that clinicians are made aware of the possibility and of the harms that arise from diversion, and should carefully monitor those who are permitted to take home methadone. Rhoades et al conclude from their study that risks such as overdose and dose diversion are outweighed by the clear benefits of providing adequate and accessible doses of methadone.

Style of treatment: In his chapter on treatment delivery, Bell (1998) points to evidence that when similar programs are considered, quite different outcomes can result from differences in the style of treatment. He argues that as with treatment for other medical and psychological problems, methadone maintenance should treat each patient on an individualised basis. Difficulties associated with opioid use and obtaining treatment should be tackled and not dismissed as irritants for clinicians. The outcome for each client will depend on how well they are assisted with their problems. Included within the notion of style is the attitude of staff which Bell rates as probably the most important determinant of outcome after methadone dose. In a well-structured environment, rules and expectations of both staff and clients need to be clearly set out and maintained in order that the treatment environment is regarded as safe and fair for all. Bell argues, therefore, that methadone maintenance treatment is best carried out through primary care centres where individual problems would be more easily addressed than in large methadone clinics. Treatment programs should have clear rationales and objectives with adequate structure and record-keeping. Roles of attending staff should be clear, and regular team meetings are essential for support and maintenance of these roles. However the structure should not be such that it acts as a barrier to entry for patients.

In their study which compared patient and in-treatment variables as predictors of outcome for methadone maintenance treatment, Magura et al (1998) performed a retrospective longitudinal analysis of 1206 admissions to 15 methadone clinics in New York city in 1989-90. They used survival analysis with time in treatment as the outcome and found that variables classed as in-

treatment were better predictors of retention on methadone maintenance. In particular, in the context of style or quality of treatment, they found that constructive response to patient problems positively predicted retention. This study had some methodological problems in that it was retrospective and selective in the clinics it used. However it is an important study to replicate prospectively in order to further clarify the role of style and other treatment variables in treatment outcome.

Counselling and psychotherapy: The role of counselling and psychotherapy in opiate dependence treatment has not been clearly established. In their review of the area, Mattick et al (1998b) concluded that counselling cannot be considered a stand-alone treatment for opiate dependence, but there was reasonable evidence that it adds to the overall effectiveness of methadone maintenance programs. There is a concern that in order to reduce costs, such ancillary services as counselling will be reduced, because their contribution to outcome has not been clearly determined. Methadone maintenance programs with few support services have been shown to be effective, but the cost-benefit added by counselling is less clear. It is likely that not all methadone maintenance patients will benefit from counselling services and that those most likely to benefit are those who need assistance to get some order back into their lives. Such issues would be clarified in methadone maintenance programs where individualisation of treatment is taken seriously.

The review by Mattick et al makes several important summary points:

- where methadone maintenance has been shown to be effective, it has employed counselling as part of the treatment;
- counselling is important for those who need it, but can be counter-productive if mandated;
- there is limited evidence that better quality counselling services work better;
- there is no evidence that ex-addicts are more effective than others;
- there is no evidence that externally qualified counsellors are more effective than those internally-trained;
- there is no evidence that specific techniques such as relaxation training impact on outcomes, although there is some suggestion that motivational interviewing style may be useful in promoting a good working relationship between client and therapist;
- psychotherapy may be useful for treatment of heroin addicts on methadone maintenance who have comorbid psychiatric disorders, but otherwise cannot be justified on present evidence;
- family therapy may be of value in treatment where the clients are willing to participate;
- research has shown that therapist effects may be more important in influencing outcome than the treatment they are using . This needs to be taken into account when amalgamating research findings from different therapists and treatment settings; and
- effective therapists do not necessarily come from a particular theoretical tradition (i.e. psychodynamic or cognitive behavioural therapy), but do employ "sound general counselling principles (reflective listening, establishing an empathic alliance, etc.) rather than confrontation" (Mattick et al., 1998b p298).

In their review of factors affecting duration of treatment, Ward et al (1998c) also pointed to the following further treatment factors which have a bearing on outcome:

- **rapid assessment** prior to induction to treatment leads to better retention,
- the use of **negative consequences** such as reducing dose because of positive opioid screens is counter-productive,
- the improvements in outcome as a consequence of the provision of **ancillary services** such as medical treatment and job training;
- the need for **clinic accessibility** in terms of location and hours, to maintain patient attendance; and
- the negative impact of introducing **fees for treatment** in terms of patient retention.

(ii) Patient factors

Polydrug use: In his summary of the influence of moderator variables in methadone maintenance treatment, Darke (1998) reviewed the research on drug use other than heroin, which has been shown to lead to riskier behaviour and poorer prognosis for patients placed in methadone maintenance. Both benzodiazapines and cocaine are widely used by heroin users and use of benzodiazapines has been shown to be a particular hazard to successful methadone maintenance treatment. Use of benzodiazapines is associated with the incidence of overdose and users who are also heroin addicts tend to be those with the greatest physical, psychological and social dysfunction. As pointed out by Darke, there is some evidence that benzodiazapines may enhance the subjective effects of methadone, so that retention on methadone maintenance may not encourage reduced use of benzodiazapines. Supervising physicians need to be made aware of the risks of continuing to prescribe benzodiazapines to individuals whilst they are in methadone maintenance treatment.

Cocaine users who also abuse heroin tend to engage in riskier sexual and injecting behaviour and have greater HIV seroprevalence. However, Darke concluded from reviewing several studies that there is some evidence that retention on methadone maintenance reduces cocaine use, possibly due to reduced overall injecting behaviour. Thus, although cocaine users are at increased risk whilst still using heroin, retention in methadone maintenance treatment may reduce this risk. Rhoades et al (1998) found in their study that those patients receiving the higher dose of methadone (80mg) were more likely to have higher cocaine use than those on the lower dose (50mg). This runs contrary to prior research findings and the suggestion that decreased injecting opiate use leads to decreased cocaine use. However, such findings would need to be replicated. As Rhoades et al concluded, if cocaine use does indeed increase with methadone dose, this should not be used as a reason to decrease heroin dose as this will result in high drop out rates for the opiate treatment program. The cocaine use must be addressed giving due regard to the need to retain patients in methadone maintenance treatment.

In another study specifically designed to look at patterns of cocaine use in methadone maintenance, Grella et al (1997) found that the percentage of cocaine users did not change from intake to 18-24 months after admission. They found some cross-over between users and non-

users with 17% of those not using at admission becoming users later in treatment and 17% of users at admission stopping using. Use of cocaine powder either alone or combined with heroin in "speedballs" decreased during treatment while use of "crack" cocaine increased.

Psychopathology: Heroin users with antisocial personality disorder (ASPD) tend to be those most severely affected by their addiction. However, as pointed out by Darke, the diagnosis of ASPD for a heroin abuser may be influenced by the fact that it has many behaviours in common with heroin abuse behaviours. He concluded that, although a diagnosis of ASPD may be a marker for riskier behaviour and not true psychopathology, evidence suggests that such individuals can benefit as well as other patients from methadone maintenance treatment. Similarly, heroin users tend to report higher than normal levels of depression and anxiety which may interfere with treatment success. However, Darke pointed to research which has found that participation in methadone maintenance treatment may be associated with declines in such psychological distress.

Other patient variables: Several other patient variables have been found in the research literature to be consistently associated with methadone maintenance treatment outcome. As summarised by Ward et al (1998c), patients who are younger, who have more pre-treatment criminal involvement, who are more dependent, and who have high levels of alcohol use tend to be retained in treatment for shorter periods. Patients who are employed pre-treatment, who are living with a spouse or family, who are motivated and have realistic expectations of treatment are more likely to be retained longer. As a corollary to the last variable, some studies have also found that previous attempts at methadone maintenance predict better outcomes.

For example the study by Rhoades et al (1998) found that younger subjects and those with opiate-positive urine screens at intake were most likely to leave methadone maintenance earlier. They also found that prior attempts at methadone maintenance was positively related to outcome. They concluded that special attention needs to be directed towards retaining the younger and more severely dependent heroin users, as well as ensuring that methadone maintenance continues to be available for those with prior experience with methadone. Similarly, Magura et al (1998) found age and criminal justice involvement predictive of outcome as discussed above. However, unlike Rhoades et al, these researchers found no predictive association with prior attempts at methadone treatment, nor with variables related to severity of addiction. However, as mentioned above, the study by Magura et al was retrospective and more likely to be less accurate, which may have caused it to have less significant findings.

SUMMARY POINTS

1. There is strong support, from the few randomised controlled trials that have been carried out, for the superior effectiveness of methadone maintenance over placebo/no treatment.

2. Observational studies have also shown positive relationships between time in treatment and such outcome variables as opiate and other drug use, criminal behaviour and sexual risk-taking.

3. Dose of methadone is of crucial importance to outcome. Methadone dose is positively related to retention and negatively related to illicit opioid use. It is recommended that dose is individualised to suit the patients' psychological and physiological needs.

4. Methadone is only effective whilst the patient remains in treatment. Once a patient leaves treatment he/she will return to pre-treatment drug taking.

5. Methadone maintenance reduces the risk of the spread of HIV/AIDS due to the decrease in injecting activity. No effects on rates of hepatitis infection have been found, probably due to the fact that most patients have these highly infectious diseases on admission to treatment.

6. Clinic policies have a significant influence on the outcomes of methadone maintenance treatment. Clinics should: be maintenance-oriented; pay special attention to patients' individual needs and problems as they arise; be more accessible by providing take-home dosing; and willing to provide psychological counselling as required.

7. The evidence regarding the effectiveness of methadone maintenance on cocaine use in heroin users remains equivocal.

8. There are particular sub-groups of heroin users who may have better outcomes on methadone maintenance. These include older users, those who have attempted methadone maintenance before and those who have lower dependence. Those who do not do as well on methadone maintenance include patients with a high level of pre-treatment criminal activity and alcohol abuse.

9. Patients with comorbid psychiatric conditions such as antisocial personality disorder or mood disorders, although often the most severely addicted, can benefit from methadone maintenance treatment and cessation of illicit opiate use.

3.4.2. LAAM (levo-alpha-acetylmethadol)

LAAM, like methadone, is a synthetic opioid agonist which is effective when ingested orally. It blocks the effects of other opiates and prevents withdrawal but does not produce a subjective high. It was subjected to extensive trials as a treatment for heroin dependence in the 1970's, but little research has been carried out on it since the early 1980's (Mattick, Oliphant, Ward, & Hall, 1998a).

The Quality Assurance Project (Mattick & Hall, 1993) reviewed the literature on LAAM and concluded that research has found no significant difference in outcomes for patients on high-dose LAAM and high-dose methadone but that LAAM may have a number of advantages over methadone as a maintenance drug. These advantages stem largely from the fact that LAAM has a half-life of 92 hours compared with 24 to 36 hours for methadone. In a recent article, Rawson and co-workers (1998) summarised the findings from 27 double-blind or open trials of thrice-weekly dosing using oral LAAM and involving more than 4000 patients. They concluded that long-term treatment with LAAM is comparable to methadone maintenance in reducing illicit opioid use and associated crime.

The following advantages of LAAM over methadone are listed in reviews of the literature (Mattick & Hall, 1993; Mattick et al., 1998a; Rawson et al., 1998):

- LAAM has a milder, more consistent drug effect due to its slow onset and more sustained action which allows some patients to feel more "normal" than they do on methadone. However, due to the slower onset, induction onto LAAM may require administration of other medications to alleviate transient withdrawal symptoms.
- LAAM would be expected to provide better suppression of withdrawal symptoms and craving for those patients who may experience such symptoms if they miss a scheduled dose of methadone. This would reduce the need to inject heroin to alleviate withdrawal symptoms and thus provide greater protection against HIV infection.
- Patients need only visit the clinic every 3 days to obtain their medication which allows greater flexibility in terms of allowing them to pursue normal life activities without the impediment of daily clinic visits.
- Reduced need for clinic visits would provide a cost benefit in terms of time savings for both patients and clinic staff.
- Because of the reduced dosing frequency there is less need for take-home doses and thus less opportunity for dose diversion. However, as Mattick et al (1993) warn , disallowing take-home privileges has the negative impact of reducing patient acceptance of the regime and can adversely affect retention in maintenance programs. Even allowing take-home dosing, Rawson et al (1998) point out that the slower onset of LAAM means that it less likely to be diverted than methadone.
- Reduced clinic visits would mean fewer people congregating at treatment centres, which may lead to less loitering and other illegal activities in the vicinity which, in turn, may encourage greater community acceptance of such treatment centres.
- Apart from the advantage of greater flexibility, research has found that LAAM is preferred to methadone by patients who have experience with both, because it provides a better blockade and reduces craving.

One risk associated with the use of medications with long half-lives such as LAAM is the increased risk of toxicity which can occur if LAAM is rapidly metabolised when liver function is enhanced. This risk is highest during the stabilisation phase and it is recommended that a minimum 48 hours dosing period is enforced throughout treatment (Mattick, 1998).

Recent Research

Recent research on LAAM has concentrated on establishing the most effective dosing regimes for both induction and maintenance as well as investigating barriers to the wider implementation of the drug.

- Houtsmuller et al (1998) randomly assigned 8 subjects to each of a high dose (75mg) and low dose (25mg) alternate day dosing of LAAM with placebo on intervening days, in a double-blind design. Following stabilisation, subjects were challenged with hydromorphone following 1, 2, 3, or 4 days of placebo (non-LAAM) dosing to ascertain the level of opiate blockade following such non-dosage periods which represent typical gaps in dosing occurring in a thrice-weekly dosing regime and where a dose is missed. Whilst withdrawal symptoms remained mild even 4 days after the last dose of LAAM, they found no dose effect on withdrawal symptoms. However, positive agonist effects were found at all intervals for those subjects who had been stabilised on the low-dose regime, while those on the high dose showed minimal response to the opiate challenge. The authors conclude that 25 mg doses of LAAM do not effectively blockade the opiate receptors, whereas the 75mg doses effectively block the subjective effects of other opiates. Thus the use of high doses of LAAM is likely to attenuate illicit drug use during treatment while 25mg doses will not.

- In a much larger study (N=180), Eissenberg et al (1997) compared the effectiveness of 3 LAAM dosing regimes (Monday/Wednesday/Friday: 25/25/35mg; 50/50/70mg; 100/100/140mg) in a randomised double-blind study. LAAM reduced illicit opiate use and a significant association was found between dose level and both self-reported opiate use and urinalysis opiate levels during the 17-week study period. Dose level did not affect program retention. They concluded that LAAM treatment substantially reduces illicit opiate use and that the effectiveness of LAAM is positively related to dose. Thus subjects can be maintained satisfactorily on LAAM, but higher doses are needed to provide a sufficient blockade to prevent illicit drug use.

- Rawson et al (1998) surveyed all treatment agencies approved for use of LAAM since its implementation in 1993. They found a disappointingly slow uptake of the new pharmacotherapy, especially in light of the extensive research and development that occurred prior to its approval as an alternative to methadone and naltrexone for treatment of heroin addiction. The research literature on LAAM suggests that it is safe and effective and that adequate dosing levels and flexible dosing policies are related to better outcomes. However, it appears that of greater relevance to effective implementation is the attitude of

staff and management to the introduction of the new treatment agent. Services are conservative and slow to accept an alternative to a successful agent such as methadone. The authors suggest the experience with the introduction of LAAM should serve as a lesson for the future when other effective treatments may be approved. As with the introduction of any new technology new treatments should be introduced in a way that takes account of the needs of all stakeholders in the process and an implementation strategy should be developed in advance of implementation. Similar problems to do with attitudes of clinicians, management and consumers were noted in the summary of treatments in the alcohol field (see Section 2.5.2 above).

SUMMARY POINTS

1. LAAM is an effective alternative to methadone for opioid maintenance treatment.

2. The longer half-life of LAAM yields advantages of less frequent clinic visits which have both social and cost benefits. It has the disadvantage of increased risk of toxicity.

3. Higher doses of LAAM effectively block opiate receptors and lead to reduced illicit opiate use, whilst lower doses are ineffective in this regard.

4. As with new treatments for alcohol dependence, greater enthusiasm and belief in its treatment effectiveness need to be encouraged through improved communication of relevant evidence on LAAM to consumers and other stakeholders.

3.4.3. Buprenorphine

Buprenorphine is a partial opioid agonist with very strong analgesic effects which is currently undergoing clinical trials as a pharmacotherapy for opioid dependence. It shows an inverted U shaped dose-response curve where opioid response increases with dose to a plateau, after which antagonistic action comes into play and decreasing opioid effects can be observed. It has poor bioavailability orally but is well absorbed sublingually and is potent when injected. It thus has potential for diversion which has prompted research on a combined buprenorphine-naloxone preparation which would have increased antagonistic properties (and thus reduce diversion potential) but remain an effective replacement therapy. Although it has a relatively short half-life, it binds very tightly to receptors causing slow opioid release and a prolonged duration of action, allowing for the possibility of alternate-day dosing.

Most of the research on buprenorphine to date has been carried out in the US. Mattick et al (1998a) summarised the relevant research which generally compared the effectiveness of buprenorphine to that of methadone. They concluded that:

- buprenorphine appears at least as effective as methadone as a maintenance therapy by reducing craving and illicit opioid use and by retaining patients in treatment;
- buprenorphine appears safer in overdose - overdose has not been observed in doses many times the therapeutic dose. It has been found to induce mild respiratory depression compared with pure opioid agonists, which suggests its use could significantly impact on opioid deaths of patients in treatment. It has been found to be very well tolerated in non-dependent humans. Furthermore, its poor oral absorption reduces the risk of overdose where accidentally swallowed;
- due to its mixed agonist-antagonist action, withdrawal from buprenorphine has been found to be less severe than from pure opioid agonists. Thus, withdrawal from buprenorphine maintenance therapy should prove easier than from methadone maintenance;
- the issue of compliance or patient acceptance needs to be further studied, especially outside the US where opioid replacement therapies are more readily available and thus may compete more effectively with buprenorphine to attract patients because they have no antagonistic properties. Uehlinger et al (1998), discussed below) found that they had difficulty attracting subjects to their study in large Swiss cities where there were more treatment options available; and
- issues of dosing and dose-equivalence to methadone need to be clarified. In particular the research reviewed tended to use fixed and low doses, which may be sub-optimal for effective treatment. More recent studies discussed below have not directly addressed the use of individualised compared with fixed dosing.

Johnson (1997) has recently reviewed results of US-based clinical trials of buprenorphine and concluded that:

- buprenorphine over a range of doses is more efficacious than placebo and equivalent to methadone at doses between 20 and 60mg;
- the dose-response effect may not be as pronounced as methadone with some evidence of ceiling effects around doses of 12-16mg due to its partial agonist profile. However, some patients may benefit from higher doses; and
- that the treatment plan first proposed by Ling et al (1996) is adopted which begins with rapid induction from heroin onto buprenorphine before further decisions are made regarding continued treatment (see discussion below).

Recent Research

(i) Effectiveness

- Strain et al (1996) compared outcomes for those who completed a 16-week maintenance phase of a double-blind trial comparing buprenorphine (N=43) with methadone (N=43). A flexible-dosing approach was adopted and the mean maintenance dose of buprenorphine was 9.0mg/day and for methadone was 54mg/day. A previous report on this study had found no differences in retention for either group using an intention-to-treat model. The effects on secondary outcome measures such as self-reports on illicit drug use, adequacy of

dosing and withdrawal symptoms and drug-related behaviours for those retained were of primary interest in this report. They found that there were few differences between the two treatments on these outcome measures. Both groups showed large and sustained improvements in all areas of psychosocial functioning as well as decreased illicit opioid and cocaine use. The buprenorphine group showed a trend towards decreasing illicit opioid use over time, while the methadone group stabilised after about 4 weeks of treatment.

- Ling and co-workers (1998) randomly assigned 736 opioid addicts to four fixed doses of buprenorphine (1mg, 4mg, 8mg and 16 mg) for a 16-week treatment period. There were no baseline differences between the groups on demographics and socioeconomic variables and 375 (51%) subjects completed treatment. The main comparison of interest was between 1 and 8 mg for this study and secondary comparisons included the 4 and 16-mg groups. This distinction was made for statistical reasons to make it possible to obtain significant results given the restraints of the sample size and number of comparisons to be carried out. They found outcomes for the 8 mg group were significantly better than for the 1mg group for all outcome measures used: retention in treatment, opioids in urine, self-reported opioid craving and global ratings by both patients and staff.

  Because of its high safety profile, they proposed a sequential pharmacological treatment strategy beginning with rapid induction onto effective doses of buprenorphine. As Johnson (Johnson, 1997) pointed out, it is preferable that patients are inducted directly from heroin use as this is less problematic than transferring from high dose methadone maintenance. Patients who respond well could then choose to be maintained on this medication or proceed to detoxification and abstinence with or without the help of naltrexone. Those patients who do not respond well to buprenorphine can be readily transferred to maintenance on a full agonist, LAAM or methadone.

- This suggestion is echoed by Uehlinger et al (1998) in the conclusion to their recent study which compared the safety and efficacy of buprenorphine (N=27) and methadone (N=31) in a randomised, double-blind study using 58 Swiss patients. Doses of 4, 8, 12 or 16mg/day of buprenorphine were compared with 30, 60, 80 or 120mg/day of methadone. All patients started on the lowest dose of the drug they were assigned and then could choose to increase the dosage following days 3, 7 and 14. They were then maintained on their day 21 dose to the end of week 6 (day 42). Outcome measures were presence of opioids in urine, retention, craving and withdrawal symptoms.

  Preliminary results from this study found that significantly more patients in the buprenorphine than in the methadone group dropped out of the study during the induction phase (days 1 to 21), but were equally well retained in the maintenance phase. Overall 55% of the buprenorphine group and 90% of the methadone group were retained to day 42. The typical dose of buprenorphine during maintenance was 12mg/day whilst for methadone it ranged equally across 30, 60 and 80mg/day. There were no differences between the two

groups in urinalysis results although there was a trend for buprenorphine subjects to produce fewer cocaine-positive samples.

The authors suggested that better results for buprenorphine may have been obtained if it had been induced more rapidly and with higher doses and other research supports this (Ling et al., 1998). They also described findings from a buprenorphine substitution program which has been running in the city of Fribourg for two years and concluded that buprenorphine is a suitable maintenance treatment which should be one of several agents available in a heroin substitution program. They referred to the value of a scheme such as that suggested by Ling et al where patients are vigorously inducted onto buprenorphine and then channelled to other therapies, as appropriate, to improve outcomes. Studies which have shown that buprenorphine and pure agonists are cross-tolerant (Law et al., 1997) support the feasibility of such schemes.

(ii) Buprenorphine-Naloxone Combination

Buprenorphine tablets can be crushed and injected with positive opioid effects so that it has potential for abuse. Naloxone has a low bioavailability sublingually and is being trialled as a combination tablet with buprenorphine where it will have minimal effect sublingually but its antagonistic properties should discourage diversion to parenteral administration.

- Fudala et al (1998) recently completed a small study using 10 morphine-stabilized subjects to assess the effects of various combinations of naloxone and buprenorphine compared with placebo. They concluded that a 1:4 ratio of naloxone to buprenorphine would be expected to produce a sufficient antagonistic effect to discourage diversion.

(iii). Treatment Setting

Some studies have been completed recently which investigated the feasibility of administering buprenorphine in primary care settings rather than in specialised clinics.

- O'Connor et al (1998) compared urinalysis and retention outcomes for 46 patients randomly assigned to thrice-weekly buprenorphine maintenance in a primary care setting or to a methadone clinic setting (23 in each). They found higher rates of retention in primary care settings (78%) compared with methadone clinic setting (52%). The mean rates of opioid-positive urine samples were significantly lower in the primary care setting, where there was a decrease over time, while rates for subjects in the clinic setting tended to remain steady over time. They concluded that thrice-weekly doses administered in a primary care setting, under the supervision of properly trained physicians, provide an effective alternative to treatment in a clinic setting.

- A further study, comparing the effectiveness of primary care with clinic (addiction centre) settings has been reported from France, where buprenorphine is administered in both settings (Vignau & Brunelle, 1998). The researchers followed up two cohorts of patients for

180 days, 32 who had enrolled with general practitioners and 37 treated in addiction centres. They found little difference in effectiveness between the two settings, despite the baseline difference that there were more severely dependent patients in the addiction centre group. Retention in both groups was 65% and significant improvements on psychosocial and health variables were found for those who remained in treatment. The general practitioners in this study used a stricter regimen than that used in the addiction centres, which may account for the disparity with findings in the O'Connor et al study above. However, as the authors concluded, the study does demonstrate that patients with different social and health profiles can be effectively maintained on buprenorphine in the therapeutic settings that were available.

(iv). Effective Dose Levels

- Schottenfeld et al (1997) compared dose levels of methadone (65mg and 20mg/day) and buprenorphine (12mg or 4mg/day) in a randomised double-blind study using 116 subjects. They found that higher daily maintenance doses of both methadone and buprenorphine were significantly better than the lower doses for reducing illicit opioid use, but no differences were found for retention. They used daily clinic visits only.

- Compton et al (1996b) followed up 100 consecutively admitted patients to a buprenorphine maintenance program. They were randomly assigned to 4mg/day to 32mg/day doses and assessed at the end of 16 weeks when they were given a composite score for therapeutic response, which included urinalysis, withdrawal symptoms and toxicity symptoms. They found that 34 patients met their response criteria at an average daily dose of 14.6 ±6.5mg which is higher than levels used in recent efficacy studies.

- At the conclusion of their study which compared treatment settings, O'Connor et al (1998) reviewed the literature on dose levels of buprenorphine and concluded that lower doses (4-8mg/day) are less effective in general than "standard" doses of methadone or higher doses of buprenorphine (12-16mg/day). Their study found that thrice-weekly dosing was feasible and they suggested it may be even more effective if higher doses (averaging 16mg/day) were used.

- Ling et al (1998) also found that there was a trend towards a linear relationship between dosage and outcomes in the dose range used, although differences between the 8mg and 16mg group tended to not be statistically significant. In their discussion, Ling et al reviewed the research comparing methadone and buprenorphine dose and suggested there was a growing consensus that 8mg of buprenorphine is equivalent to a "relatively modest" dose of methadone. They concluded that there appear few barriers to using doses up to 32mg and buprenorphine may prove a useful therapeutic choice for particular patients.

(v) Buprenorphine and cocaine abuse

- Schottenfeld et al (1993) looked at the dose-effect of buprenorphine on both cocaine and illicit opioid use. They maintained 30 cocaine-abusing opiate addicts on a regimen of ascending, then tapering doses of 4, 8, 12 and 16mg/day buprenorphine over a 21-day period. At the same time they measured levels of illicit opioid and cocaine use. Only 15 completed the study, which is an acceptable outcome for polydrug users. They found a highly significant (negative) relationship between buprenorphine dose and illicit opioid use, and a similar, though not as strong, significant effect with cocaine use.

- Uehlinger et al (1998) reported fewer cocaine positive samples for the group treated on buprenorphine compared with their methadone-treated group although differences were not significant.

- Strain, et al (1996) compared the effectiveness of buprenorphine with methadone and found no significant variation from baseline rates of cocaine use by urinalysis for the two groups throughout the 16 weeks of their study. However, self-reported cocaine use, which they argued is a more sensitive measure, declined significantly over time for both treatment groups.

- In their research on dosing levels described above, Schottenfeld et al (1997) found that buprenorphine was no more effective than methadone in reducing cocaine use as measured by urinalysis. As the authors discussed, cocaine challenge studies have tended to find that maintenance on opiates does not attenuate the subjective effects of cocaine and it has been suggested that higher doses of methadone may augment cocaine effects. However, this study did not find that higher doses of methadone were related to higher rates of cocaine use. It did find that patients maintained on 4mg of buprenorphine increased their usage of cocaine over time in treatment, whilst those in the other three treatment groups did not.

SUMMARY POINTS

1. Buprenorphine is a partial opioid agonist that has shown considerable potential for treating heroin dependence. It has the advantages of being safer in overdose than pure opiates, amenability to thrice-weekly dosing and reduced withdrawal symptoms on cessation. It warrants inclusion as an alternative maintenance pharmacotherapy for patients presenting for treatment for opioid dependence.

2. Research has shown buprenorphine to be as effective as methadone in retaining patients in treatment and reducing illegal opioid use. It may also prove more effective in assisting patients to become abstinent because of its cross-tolerance to pure opioids and less severe withdrawal symptoms.

3. At least three groups of researchers have proposed that a sequential pharmacological treatment strategy, which commences with rapid induction directly onto buprenorphine from heroin may prove most effective in ascertaining the best treatment program for patients presenting for treatment for their opioid dependence.

4. The use of a buprenorphine-naloxone mix may help improve patient compliance in allowing take-home doses without increasing the risk of diversion.

5. Studies which have compared addiction clinic settings with primary care settings have indicated that both are amenable to buprenorphine maintenance programs and a suitable mix in the availability of both settings is likely to cater best for the range of clients who present for treatment.

6. Much recent research has tended to use quite low doses of buprenorphine, given its safety profile and its advantages both clinically and pharmacologically. Many studies have been initiated on the premise that 8mg is an effective mean dose but it appears that it is in effect a low to average effective dose. Individualised dosing may prove most effective in ensuring best treatment response and doses up to 32mg may be well tolerated and lead to optimal outcomes for some individuals.

7. There has been some suggestion from research that buprenorphine maintenance may lead to reduced usage of cocaine. The issue of the relative accuracy and validity of self-report drug use and urinalysis requires further investigation.

3.4.4. Naltrexone

Naltrexone is a long-acting opioid antagonist which blocks the subjective and physical responses to opiates. It can be administered on a daily basis at around 50mg/day or in 100 to 150mg doses two or three times a week. It has good bioavailability when taken orally and even large doses of opiates are blocked by this medication. If taken following opiate use it will induce withdrawal. It has been shown to be safe and well tolerated as a treatment with few side effects, although in high doses it is associated with a rise in transaminases and it may induce depressed mood for some months after the last opiate use (Foy, Sadler, & Taylor, 1998). Post-treatment effects on morbidity and mortality are just beginning to be investigated.

In a review carried out on the use of naltrexone, Farren (1997) indicated that naltrexone has several potential advantages which are listed as follows:

- It has the advantage of being non-addictive and thus suitable for use in a variety of settings.
- It can be administered on a less-than-daily-basis which may improve patient compliance as well as delivering cost benefits for both patient and the provider.
- Once a patient is stabilised on naltrexone, the chances of long-term opiate abstinence may be increased as, unlike with methadone, there is no protracted withdrawal from naltrexone.
- Patients are less likely to continue on intravenous illicit drug use because such additional drug taking is not reinforcing, which is not the case with methadone.

A further advantage of naltrexone is that it provides a chemical blockade to opiate injection which permits the decay of associations between drug effects and environmental cues. Thus contact with that environment will gradually cease to stimulate an urge to relapse.

Despite its advantages, naltrexone has not been well accepted by patients as evidenced by the very high drop out rates from clinical trials assessing its effectiveness (Farren, 1997; Mattick & Hall, 1993). However, it has been found to be successful with those patients who are highly motivated to cease their opiate use such as health professionals, businessmen and legal detainees. However, as Farren quoted, it is possible that highly motivated and co-operative patients will do well in any kind of rehabilitative program.

Recent research

(i) General Effectiveness

- Foy et al (1998) reported an open trial of naltrexone which was carried out as a pilot for a planned randomised controlled study on naltrexone treatment for opiate dependence. The aim of this pilot was to determine the applicability of naltrexone treatment in an Australian setting and to ascertain sample size in order to detect an effect, as well as to identify any confounders which may arise. The pilot attracted 44 suitable patients, 3 of whom dropped out early, apparently due to side effects of the naltrexone. Patients were detoxified using clonidine over 5 to 10 days and started on naltrexone 2 days before clonidine was stopped. They were prescribed 50mg/day naltrexone which was presumably taken unsupervised and

were not discharged from the study if they had positive opiate urinalysis results. They were seen weekly for the first 6 months and monthly for another 6 months. They were given supportive counselling throughout.

The study found that patients tolerate the naltrexone well and tend to be free of side effects after the first 3 days. Overall 10 of the original 44 sample were abstinent at 12 months (22%); 8 of whom had been abstinent from the beginning of the pharmacotherapy. They also found that being employed at the time of study entry and impending legal charges were associated with better outcomes, although the latter result may not be significant using Bonferroni adjustments for number of statistical tests carried out on the sample. They found no significant effects for inpatient versus outpatient detoxification and for having undergone a residential rehabilitation program. Numbers were low in this pilot and the completion of the randomised controlled trial using appropriate numbers will be of considerable clinical and research interest. It should be noted that most completers ceased using naltrexone before the intended 6 months as they considered it unhelpful/unnecessary for that length of time.

- D'Ippoliti et al (1998) have recently reported the results of a prospective observational study which compared the effectiveness of methadone with naltrexone and drug-free treatments in a sample of 1503 heroin users attending public treatment centres in Italy. All those attending these centres in the first 6 months of 1995 were followed up until the end of 1995. There were 721 patients who entered methadone maintenance, 216 in naltrexone and 566 in drug-free treatment programs in that time. Data on sociodemographic characteristics, patterns of drug use, type of treatment and methadone dose are routinely kept, so that the method involved accessing this information. There were no fixed guidelines for admission to the different programs but the tendency was that: methadone (individualised dose) was offered to patients with a history of heavy drug use and/or health crises; naltrexone (50mg/day) was offered to those who were more highly motivated; and a drug-free program was generally available which involved outpatient counselling groups and behaviour therapy.

  The outcome variable for this study was retention in treatment. Probably the most compelling outcomes from this study relate to methadone maintenance, where it was found that higher dose meant longer retention in treatment, which fits with conclusions drawn in 3.4.1 above. They found that the retention rate for naltrexone (18%) was no different from the drug-free group (15%) but these were significantly less than for the methadone group (40%). Unfortunately the study does not make it clear whether dropout from naltrexone reflected success or failure in preventing relapse. As the study above (Foy et al., 1998) suggests, long-term maintenance on naltrexone is not necessary, and non-relapsing patients may find that more than 6 months treatment is excessive.

(ii) Studies on highly-motivated subjects

- Roth et al (1997) report a study which followed a group of opiate abusing health professionals (N=20) who had been referred for naltrexone treatment over a 5-year period. Treatment also involved weekly attendance at psychotherapy group. They were treated with naltrexone for an average of 8 months and were required to continue with psychotherapy until an agreed graduation time. Mean program duration was 1.9 years, and long-term abstinence rate was 94% (17/18) for those referred to the program. Two other self-referred patients left the program abruptly, but had much longer duration of addiction, and were omitted from the abstinence statistics. Twelve out of the 20 had also returned to work. The results were clearly very good for this group of highly motivated health professionals and the authors emphasised the importance of the group therapy sessions and the constant monitoring of patients that the program involved. Hence it is clear that naltrexone accompanied by appropriate psychosocial interventions can be most effective for opiate-abusing health professionals.

- Another recent study which attempted to demonstrate the efficacy of naltrexone treatment with specialised populations was reported by Cornish et al (1997). Fifty-one parolees from the US prison system voluntarily participated in a randomised controlled trial assessing the effectiveness of naltrexone as a treatment for their opiate addiction. The control group subjects (N=17) were required to attend three orientation and drug counselling sessions per week for the first two weeks of the study and then saw their parole officer twice weekly for the remaining 22 weeks of the study. The treatment group was administered naltrexone in a dose of 25mg/day for the first 2 days, then 50mg/day for 3 days, then stabilized onto 100mg on Tuesdays and 150mg on Fridays. All naltrexone administration was closely supervised.

  Outcome measures were weeks retained in the study, opiate and other drug use and revocation of probationary status. They found a trend to lower retention in the control group (mean weeks retained = 14.2) than the naltrexone group (mean weeks retained = 16.6). The percent positive urinalysis for the naltrexone group was 8% while for the controls it was 30% which is significant at the 5% level. There were no significant differences for the other drug groups compared (cocaine, amphetamine, benzodiazepine, marijuana and alcohol). There was also a significantly greater proportion of parole violators in the control group with 56% being reincarcerated, whilst for the treatment group, this figure was 26%. Unfortunately there is no mention of Bonferroni corrections for the number of statistical tests carried out, and, although the authors highlight the good retention outcome compared with naltrexone patients in other studies with less legal pressure to cooperate, the lack of difference from the control throws assumptions of the effectiveness of naltrexone in doubt. The particular conditions of the study, for example, the increased parole officer attention may have led to better outcomes for the whole study sample.

- Rabinowitz et al (1997) have recently reported results of a study which followed up a group of patients who underwent naltrexone treatment following ultra-rapid detoxification in a specialised clinic. The authors reviewed the literature on naltrexone and noted the tendency

for naltrexone to be effective for highly motivated groups such as health care workers and legal detainees, but commented that studies that compared naltrexone to placebo tend to find no difference in relapse rates. Their study was a retrospective investigation of naltrexone compliance over 9 months of post-detoxification treatment. Patients received 25-50mg/day unsupervised naltrexone as well as 15 intensive counselling sessions during the study period. This included psycho-education on the use and role of naltrexone as well as relapse prevention and assistance with job search and family stabilisation. Patients paid $4500 for the detoxification and treatment package.

A random sample of 120 graduates from this program was selected and ultimately 83 comprised the usable sample. Interviews were conducted by telephone and included questions about opiate and other drug use, compliance with naltrexone treatment and attendance at counselling. A significant other was also interviewed independently. Some of this information would be expected to be available at time of treatment and may have been more accurate if obtained at that time. However there was high agreement between patients and significant others regarding use of opiates and time on naltrexone. They found that 57% (47/83) of respondents did not relapse to opiate use and survival analysis showed a significant difference between relapsers and non-relapsers in naltrexone use over the 9 months of the study. The major loss to relapse occurred in the first two months of treatment after which differences between the two groups stabilised. The high motivational status of the sample would account for the good retention rates for this study and the correlation between compliance on naltrexone maintenance and abstinence from opiates reflects the ability of naltrexone to block opiate use. However, it is yet to be demonstrated that the therapy without special motivation can be of any lasting value in combating heroin abuse.

(iii) Effect of adding anti-depressants to naltrexone therapy

Because of the dysphoria associated with naltrexone use, research has been carried out on the effects of adding antidepressants to the treatment for opiate dependence. Research outcomes using the selective serotonin reuptake inhibitor, fluoxetine, have been equivocal.

- Researchers in Spain (Landabaso et al., 1998) found significant improvements in retention rates for a group randomly allocated to receive 20mg/day fluoxetine compared with a control (naltrexone only) group. Both groups also received individual and family counselling. They found that the use of fluoxetine significantly improved retention rates with a retention of 53% compared with 32% for controls at 12 months. This study did not use a placebo, but the authors argued that the differences observed were sufficiently large to not be explained solely by a placebo effect. Because earlier research has been equivocal, it is necessary for more research, in other settings, to further assess the usefulness of fluoxetine as an adjunct to naltrexone treatment.

(iv) The safety of naltrexone post-treatment

While methadone has been shown to lead to a four-fold decline in mortality and morbidity, naltrexone has not been found to be associated with a decrease in these figures (Miotto, McCann, Rawson, Frosch, & et al., 1997). There is a concern that patients treated with naltrexone may be more likely to overdose when they return to high doses of heroin to which they are no longer tolerant. Associated depression may also impact on suicide rates.

- These concerns were reflected in a paper by Miotto et al which looked at the high death rate from one particular study in the US comparing adjunctive psychosocial treatments for a sample of naltrexone-treated opioid addicts. Four of the 81 subjects (4.9%) died by overdose during the 12 months of the study - three by accidental and one by deliberate overdose. A further 9 subjects overdosed but survived during the period of the study. Of these, 4 were suicide attempts. As pointed out by the authors, these figures are comparable to rates found amongst untreated heroin addicts. There was no association of overdose with treatment condition and those who overdosed tended to have been on naltrexone for a short period and there tended to be a long time gap since last taking naltrexone. Although no causation can be assumed, the authors believed it was important to note these high mortality and morbidity rates for the samples studied. Furthermore, there is little data on such rates for patients being treated with naltrexone. Considering the long gaps between last dose of naltrexone and overdose, it would appear that those discharged from naltrexone programs should also be followed up to ascertain morbidity figures following discharge.

SUMMARY POINTS

1. Naltrexone is an opioid antagonist that effectively blocks opiate receptors so that opiates are unable to have their usual analgesic and euphoric effects.

2. Naltrexone maintenance programs tend to have high dropout rates compared with opiate maintenance programs, but naltrexone has been found to be particularly effective for those patients who are highly motivated to cease their opiate abuse. These include health care workers and those who pay large amounts of money for their treatment. Legally mandated naltrexone treatment may also be effective, but the evidence is equivocal. It has not been established whether these sub-samples are responding specifically to naltrexone or whether they would do well with any plausible intervention.

3. Comparisons of naltrexone with methadone need to be clear about achievable outcomes, as expected outcomes for these groups may turn out to be different. Whereas retention in treatment is a primary goal of methadone maintenance, it appears that an abstinence goal after relatively brief (less than 6 months) treatment with naltrexone may be appropriate. Illicit opioid use at any particular time post treatment initiation may be a more appropriate comparison measure.

4. Good long-term follow-up studies of those who become abstinent following naltrexone treatment have not been completed to date. It is most important that post-treatment mortality and morbidity is closely monitored for patients who have undertaken naltrexone treatment. More research is needed on this matter.

5. The evidence regarding adding antidepressants to naltrexone treatment remains equivocal.

3.4.4. Prescribed Heroin

There remains an entrenched group of heroin users for whom oral medication appears unhelpful, it has been proposed that prescribed injectable heroin may assist these patients to improve their health and general quality of life by encouraging a movement away from the illicit drug-taking community and towards a more mainstream existence. It has been suggested that provision of heroin in this way would also impact on criminal activity and associated costs to society. However, it has also been argued that heroin maintenance is difficult to manage because of the need for frequent clinic attendance, which is costly for patients and service providers and also causes congregation at clinic sites. The alternative of providing take-home doses is considered likely to lead to diversion or inappropriate self-administration. Another argument against heroin maintenance is that continued injection leads to greater risk of viral infection. Opponents also point to earlier studies which found difficulties in stabilising patients on short-acting opioids.

Mattick et al (1998a) reviewed the limited literature regarding provision of prescribed heroin and commented that the lack of empirical data appears to be obscured by the ideological debate going on around provision of such a therapy. As this review pointed out, and despite predictions to the contrary, evidence suggests that it is possible to stabilise illicit heroin users on prescribed heroin. However, the single randomised controlled trial which compared injectable heroin maintenance with methadone maintenance (Hartnoll et al., 1980) found mixed results, in that although retained at a higher rate in treatment, the heroin-prescribed group did not differ significantly from the methadone-maintained group on physical health, employment or criminal activities at 12 months, and these variables did not improve significantly over this period for either group. Furthermore, the heroin-maintained group continued to inject illicit heroin regularly to supplement their prescription. However, overall illicit opiate use decreased significantly for both treatment groups - reducing from a whole group average of 74mg/day at baseline to 21mg/day for the heroin group and 37mg/day for the methadone group in the 12th month.

Although some patients may prefer treatment with prescribed heroin, researchers in the area warn that there is a risk that prescribing merely encourages the continuation of high-risk behaviour in the name of harm minimisation. The aim of eventually transferring all patients onto orally-prescribed medications appears illusory. A further issue related to the prescription of injectable heroin is that its availability may make it more difficult to attract patients seeking treatment for the first time into demonstrably effective oral opiate maintenance programs.

It is important in a humane society that individualised treatment programs are developed for those with heroin addiction. Much of the hyperbole surrounding heroin maintenance may then be ameliorated once this research has been done. As Mattick et al (1998a) concluded, there is a paucity of good research in the area, so that the efficacy of this therapy has not been properly evaluated. They point to the research being carried out in Europe at the time of their review, with the expectation that this may add significant objective information to clarify the issue (see below).

Recent Research

The trial in Switzerland of an experimental heroin maintenance program was reported in July 1998 (Perneger, Giner, Rio, & Mino, 1998). Patients were randomised to immediate placement on heroin maintenance (experimental group, N=27) or to a 6-month waiting period during which time they received conventional treatment, usually methadone maintenance (control group, N=24). Following the 6 months wait, the control group was offered the heroin maintenance program. The subjects were socially distressed and/or in poor health and had made at least 2 prior attempts at methadone maintenance. Apart from receiving prescribed heroin, the experimental group was also provided with enhanced health and psychosocial services, which were not generally provided to control subjects.

This study found that subjects were able to be stabilised on heroin and there were no medical problems associated with drug injection. The heroin maintained group used significantly less street heroin and diazepines than the control group at 6 months follow-up. There was a significant decline in overdoses in the experimental group while only a small improvement was found for the control group, but low numbers meant that differences between the two groups were not at significant levels. There were generally greater improvements in health status for the experimental group as well as decreased involvement in crime.

The study has been criticised for inequities in the ancillary services provided to the two groups. It may well be that improvements in the experimental group could be ascribed to the greater attention and care that group received. This may also account for the discrepancies found between the outcomes for this study and the one previous randomised study comparing heroin and methadone maintenance (Hartnoll et al., 1980), reviewed by Mattick et al (see above). The authors acknowledged this limitation of the study and have not claimed definitive outcomes. Their study does not specifically relate to use of heroin maintenance as a first-line treatment for heroin addiction. Instead they suggested that heroin maintenance is feasible and may be the most appropriate treatment for those individuals for whom other treatments have repeatedly failed. They recommended that further research is undertaken with larger samples, in which treatment ancillary services are controlled.

SUMMARY POINT

The issue of provision of prescribed heroin for those individuals for whom conventional treatments have repeatedly failed should be subjected to further investigation. The area has not been adequately researched and definitive conclusions cannot be drawn regarding the efficacy of this particular therapy.

3.4.5. Drug-Free Treatment

There is no research evidence on the effectiveness of self-help approaches such as that provided by Narcotics Anonymous (NA). There have been no randomised controlled trials of therapeutic communities or outpatient drug-counselling services. Most of the evidence for effectiveness of such programs comes from observational studies such as DATOS (Hubbard, Craddock, Flynn, Anderson, & Etheridge, 1997), NTORS (Gossop et al., 1997) and CALDATA (Gerstein et al., 1994). In general, therapeutic communities and drug counselling are more demanding of drug users, and hence are less successful than methadone maintenance in attracting and retaining dependent heroin users in treatment. Observational studies have found that they do nonetheless substantially reduce heroin use and crime in the minority of entrants who remain in treatment for long enough to benefit (at least three months). There is some evidence that therapeutic communities may be more effective if they are used in combination

with legal coercion or during imprisonment to ensure that heroin users are retained in treatment long enough to benefit from it (Hubbard et al., 1997).

SUMMARY POINT

No randomised controlled trials have been conducted to ascertain the effectiveness of Narcotics Anonymous, therapeutic communities and outpatient drug counselling. Observational studies have found that reduced heroin usage can result for those who remain within non-drug treatment programs.

4.0 CANNABIS

4.1 GENERAL INTRODUCTION

Description and Neurobiology

The term cannabis refers to the psychoactive substances obtained from the plant Cannabis Sativa. In fact the plant contains over 60 cannabinoids, but the most potent active ingredient is Delta-9-tetrahydrocannabinol, or THC (World Health Organization, 1997). The THC content of cannabis plants is variable and depends on the variety of the plant and growing conditions. Marijuana, the weakest of the cannabis preparations, is a dried preparation of the leaves and stem of the plant and is usually ingested by smoking, in hand-rolled cigarettes (joints, sometimes mixed with tobacco) or specially designed pipes (bongs). Hashish is a resin prepared from the flowering tops of the plant, while hashish oil is a concentrate of cannabinoids extracted by solvent from the plant. These also tend to be mixed with tobacco and smoked. An alternative form of ingestion is through eating which has a much slower onset of acute effects.

Cannabinoid receptors have been located in large numbers and differentially distributed in various regions of the brain, in a pattern common across a variety of mammalian species. They are concentrated in the basal ganglia, cerebellum, cerebral cortex and hippocampus which appears to roughly account for the short-term and chronic effects of cannabis use. An endogenous cannabinoid ligand has also been identified (anandamide) but so far no primary function has been identified for a cannabinoid neurochemical system and it may be that its function is neuromodulatory (World Health Organization, 1997). Stimulation of the THC receptors starts a series of cellular reactions leading to the experience of the high that is associated with cannabis use (National Institute on Drug Abuse, 1999b).

Effects and Risks

The acute or short-term effects of cannabis include a mild euphoria with increased sociability, as well as feelings of heightened sensory perception and increased appetite. This is followed by a sense of relaxation and drowsiness. There are also associated impairments in motor skills and reaction time, memory retention and retrieval and the loss of time sense. Anxiety, tension and confusion are also frequently reported. Higher doses have been reported to cause perceptual changes, depersonalization and panic.

Long-term chronic use can lead to tolerance and dependence, lung damage and changes in respiratory function as well as triggering first onset psychosis in vulnerable individuals. Cannabis use also increases heart rate and there is a potential danger of using it in combination with cocaine as it increases the cardiovascular effects of either drug alone (National Institute on Drug Abuse, 1999b). Concerns have been raised that there is an increased risk of motor and other accidents when a person is affected by marijuana as it impairs psychomotor performance. However, evidence based on actual road statistics is equivocal possibly due to the increased awareness of intoxication which is not found with, for example, alcohol users (Hall & Solowij,

1998). Hall and Solowij (1998) also report that chronic use may lead to subtle impairments in attention and memory which may not be reversible on cessation of use. There is also some evidence that smoking cannabis increases the risks of cancers of the mouth, pharynx and oesophagus. Exposure to cannabis in utero may induce lower birth weight in the new-born as well as childhood cancer, but further evidence is required to clarify these risks.

Epidemiology

Cannabis is the most commonly used illicit drug in Australia with 39% of adults having used it at some time in their lives and 18% used in the past year (Hall & McKetin, 1999). This compares with 65% and 26% respectively for tobacco usage and 90% and 81% for alcohol. Data from the U.S. indicates that although cannabis use amongst adolescents is lower now (with 49.6% of 12th graders having ever used) than in 1979 (60.4%), it has been increasing steadily for this group since 1992 (32.6%) (National Institute on Drug Abuse, 1999b). This trend is also occurring in Australia where 55.4% of 17 year-olds had ever used cannabis in 1996 compared with 32.6% in 1989 (Lynskey & Hall, 1998).

4.2. SPECIFIC INTERVENTIONS

Research on treatments for marijuana is scarce, due partly to the fact that, in the past, few people have presented for treatment and there has been equivocal acceptance of a marijuana dependence syndrome. In her summary of treatments for drug dependence, Carroll (1998) pointed out that there are no effective pharmacotherapies, so that only psychosocial interventions are being used in the clinical setting and this is the area where the small amount of research on interventions for this drug has been carried out.

4.2.1 Evidence from large-scale studies

The Drug Abuse treatment Outcome Study (DATOS) reviewed in Appendix A2.5, found significant reductions in marijuana use in long-term residential and outpatient drug free modalities with greater improvements generally associated with greater length of stay in treatment (see Table A3). Similarly CALDATA reported significant reductions in marijuana usage in long-term residential and outpatient nonmethadone as well as improvements in psychosocial functioning. The National Treatment Improvement Evaluation Study (SAMHSA, 1999) found that the combined results for all marijuana use, whether clients were treated for marijuana-only or for poly-drug use, showed large reductions in cannabis use following treatment.

As reported in relation to alcohol and social skills training (Section 2.5.3 above), Botvin and co-workers (1995) presented the outcomes of long-term follow-up of adolescents randomly assigned to a comprehensive, age-relevant social and resistance skills training program at school. This study found that for the group that attended at least 60% of sessions during years 7, 8 and 9, there were significant decreases in cannabis use compared with the control group at

6-year follow-up. The authors emphasised the importance of dosage, proper implementation, comprehensiveness as well as the use of booster sessions to consolidate improvements.

4.2.2 Evidence from controlled trials

- Azrin and co-workers (1996) compared a comprehensive outpatient behavioural program with supportive treatment for all illegal drug use. Of the 82 individuals in the program, 18 were primary marijuana users and 42 were secondary marijuana users. Subjects were assigned randomly to the behavioural and nonbehavioural programs. The behavioural treatment consisted of training in stimulus and urge control, contracting/family support and competing responses training. These skills were taught on an individual basis with at least one 1-hour session scheduled per week over the 12 months of the program. Supportive therapy was delivered largely through weekly 2-hour group sessions. These sessions were carried out in a manner considered typical of supportive therapy programs. Counsellors encouraged expressing feelings, recounting experiences and relating to others, with praise for expression of abstinence desires. Mean treatment sessions attended were 1.6 times per month for the behavioural program and 1.9 per month for the nonbehavioural group which were not significantly different. Outcome measures included self-reported drug use, urinalysis and other-reported drug use, as well as school/job attendance, institutionalizations and police contacts, family realtionships and depression.

  They found that individuals in the behavioural program showed significant improvements over the 12-months of the program compared with those in the nonbehavioural program and that this applied irrespective of sex, age, educational level, marital status and type of drug. These differences were also found with all the psychosocial variables assessed. They did not use an intention-to-treat analysis, as they included only those individuals who attended a minimum of 4 sessions and who provided 12 months of drug use data. However, there were no differences between the two treatment groups on drop-out rate or between those who stayed and those who dropped out on relevant pretreatment variables. No follow-up data was presented. The authors conclude that behavioural programs are superior to nonbehavioural in the outpatient setting. On average only 19 sessions were attended and after 9 months there was typically 6 weeks between program attendances. They argued from this that behavioural treatment programs with intensive initial sessions and booster sessions as needed would be less costly than the typical 30-day inpatient programs provided for drug treatment. This is especially true considering that no controlled studies had been carried out to demonstrate the effectiveness of inpatient programs.

- Stephens , et al (1994) compared a nonbehavioural social support group discussion program with a relapse prevention group program based on improving cognitive and behavioural coping skills to help avoid further marijuana use. Subjects (N=382) were recruited by advertising and exclusion criteria were evidence of recent dependence on alcohol or other drugs, too infrequent use of marijuana or evidence of psychoticism. In total 212 entered treatment, 161 men and 51 women. Subjects were randomised to treatment and required to

place a $50 deposit at entry which was returned in $10 lots on completion of 1-, 3-, 6-, 9- and 12-month posttreatment assessments. Each group met for 10 two-hourly sessions carried out over 12 weeks – once per week in the first 8 weeks and fortnightly for the last 2 sessions. Booster sessions were offered at 3 and 6 months posttreatment. Both treatments were manualised and training in use of the manualised procedure was provided for the therapists.

Outcome measures included self-reported marijuana use, alcohol and other drug use, drug-related problems and collateral verification of these measures. The intention-to-treat data analysis found substantial reductions in marijuana use and related problems for both groups for the 12-month follow-up period. Although nearly two-thirds initially achieved abstinence, round 30% of both groups were abstinent or improved compared with pretreatment assessments at 12-month follow-up. There were no significant differences between the two treatment groups.

Although there was no nontreatment control condition, the authors regarded the nonbehavioural intervention as the treatment-as-usual condition and had hypothesised that relapse prevention would have superior outcomes. The absence of the nontreatment control and no significant group differences means that definite conclusions cannot be drawn regarding the efficacy of these treatments. The authors acknowledge this but argue that the high pretreatment usage rates and evidence of many previous atempts to quit indicate that the outcomes were likely due to the effects of the treatments. They also point out that what the study does clearly indicate is that there is a considerable number of marijuana users who regard their use as a problem and would like assistance to quit. It also demonstrates the resistance to change of this drug abuse behaviour, which has also been demonstrated for the other drugs of addiction including alcohol.

- Budney et al (1997) reported the results of a further study completed by Stephens and Roffman which randomly assigned subjects to either a comprehensive group relapse prevention plus social support (RPSG) program, a brief individual intervention or to a delayed treatment control group. The RPSG received 14 sessions over 4 months accompanied by a 4-session supporters group which encouraged significant others to attend to learn how to assist relapse prevention. Formation of ongoing support networks was also facilitated. Thus they combined the two procedures investigated in their 1993 study and which appeared to have positive impacts on marijuana use. The brief intervention was adapted from one used to treat alcohol abuse and involved 2 sessions one month apart which deliverd feedback on assessment and aimed to promote discussion and self-motivational statements and incorporated the principles of motivational interviewing. Participants in th control group waited four months before entry to treatment.

  Outcome criteria were self-and collateral-reported drug use. They found similar outcomes to those from their 1993 study for both the RPSG and the brief intervention groups in that there were significant improvements on pre-treatment assessment. The delayed treatment

group showed significant improvements whilst waiting but these were smaller than for the treatment groups. Unfortunately this study has not yet been reported in full in the research literature which makes it difficult to evaluate. More research is required in this area, as from evidence to date, it is clear that marijuana use is a problem for many users and marijuana dependence appears as difficult to treat and intractable as other addictive behaviours.

SUMMARY POINTS

1. Although results from pre-post studies do not adequately demonstrate specific treatment effects, outcomes for marijuana from these types of studies have been positive, and of a similar magnitude to those for other drugs. In particular, the demonstration of treatment dosage effects in the DATOS study lends credence to the conclusion that current treatment programs are reducing marijuana use and abuse.

2. Comprehensive prevention programs delivered in early adolescence may have potential to reduce initiation to marijuana use. Further research is needed to specify the best model and intervention implementation procedures.

3. Insufficient recognition has been given to the need for treatment for marijuana abuse and dependence. This is evidenced in the paucity of research on specific interventions and the high response rates when volunteers are sought for marijuana treatment research programs.

4. There is some evidence that the community reinforcement approach, relapse prevention, marijuana-focussed supportive social interaction groups and brief motivational interventions, or combinations of these, are likely to be effective in clinical treatment for marijuana abuse and dependence.

5. The few controlled studies completed to date have not demonstrated conclusively the superiority of any one of these interventions and further research is required.

5.0 COCAINE

5.1 GENERAL INTRODUCTION

Description and Neurobiology

Cocaine is a powerful stimulant affecting the cells of the central nervous system and the cardiovascular and sympathetic nervous systems. It has potent energizing and euphoric effects (Addiction Research Foundation, 1998). It is derived from the leaves of the South American coca bush and is most commonly seen as a white powder called cocaine hydrochloride. This powder is usually taken nasally ("snorted") or injected. More recently a freebase form of cocaine ("crack") has been developed which can be smoked leading to almost immediate euphoric effects. Cocaine differs from other drugs of abuse in that it tends to be used in heavy binges rather than on a more continuous basis. Cocaine abusers tend to also abuse other drugs (especially alcohol and sedatives) as well as having a high prevalence of other psychiatric disorders (Withers, Pulvirenti, Koob, & Gillin, 1995).

Cocaine is a highly reinforcing and addictive drug and it is widely accepted that its reinforcing properties are largely due to its action of blocking the reuptake of dopamine (Compton, Anglin, Khalsa-Denison, & Paredes, 1996a; Klein, 1998; Kuhar, Ritz, & Boja, 1991). This action leads to potentiation of dopaminergic neurotransmission in the mesolimbic pathways which activate natural reward centres in the brain. Cocaine acts upon other neurotransmitter systems including serotonin and norepinephrine which also impact on the same reward system as dopamine. Its effects can last for minutes or hours and can include euphoria, increased heart rate, agitation, sexual arousal, increased alertness and energy, inability to assess risks, unpredictable and aggressive behaviour, reduced appetite, increased body temperature and enlarged pupils. Cocaine also acts as a local anaesthetic used for legitimate medical purposes such as eye, ear and throat surgery (National Institute on Drug Abuse, 1999a).

Epidemiology

The advent of the more affordable crack cocaine in the US in the 1980s is considered to have led to a marked increase in usage of this drug and in the number of individuals who are dependent (approx. 1.5 million, or 0.7% of those aged 12 and over in 1997 in the US) (National Institute on Drug Abuse, 1999a). As Withers et al pointed out in their 1995 review (Withers et al., 1995), cocaine abuse was being described as the most serious psychiatric problem of that time in the United States. It now appears that cocaine abuse in the US has stabilized and may be declining (National Institute on Drug Abuse, 1999a) but in Australia there has been growing evidence of an increase in cocaine usage (McKetin, Darke, & Godycka-Cwirko, 1998).

Cocaine use is also high amongst pregnant women. The estimated prevalence from the US National Pregnancy and Health Survey, carried out in 1992 (National Institute on Drug Abuse, 1996) was 1.1% (0.4% of whites, 4.5% of blacks and 0.7% hispanics).

Risks

The acute risks associated with cocaine use include death through overdose or from accidents whilst under the influence of the drug. Regular use can also cause nasal congestion (if snorted), inflammation and perforation of the septum of the nose as well as malnutrition. Injecting cocaine also carries with it the risk of HIV and Hepatitis infections. Smoking crack cocaine can cause chronic inflammation and soreness of the throat and lung complications. Heavy (binge) use of cocaine can also result in increased anxiety, restlessness and paranoia which may lead to full-blown psychosis (National Institute on Drug Abuse, 1999a).

Death from overdose can generally be ascribed to its effects on the cardiovascular system which is likely to be due to its inhibition of norepenephrine uptake at nerve receptors. As summarised by Platt (1997), cocaine use can induce tachycardia, vasoconstriction, and increased systolic blood pressure, all or combinations of which can lead to cardiovascular crises which in turn may lead to death or irreversible cardiovascular damage. Another common cause of death or illness through cocaine abuse is convulsions or seizures which occur as a consequence of its effect on the central nervous system. Seizures do not necessarily result from binge use and can occur on first use and with small amounts of the drug. There is also evidence of an association between cocaine use and strokes with the incidence of strokes temporally related to cocaine use increasing markedly since the early 1980s with the increase in cocaine use in the US. At the same time, the overall incidence of strokes in the US has decreased by 50% for the same period (Platt, 1997).

Sensitization tends to occur to cocaine's anaesthetic and convulsive effects so that even low doses may increase the risks of these reactions. On the other hand, tolerance to its stimulant effects is observed for both chronic and acute administration. Research has found that repeated administration of cocaine can lead to neuroadaptations in the dopaminergic system which it is assumed underlie both sensitization to the drug and withdrawal symptoms on cessation of use (Izenwasser, 1998).

Because of the high prevalence of use by pregnant and nursing mothers, researchers have been examining the risks to the new-born. Cocaine use can have direct effects on the unborn child because it can cross the placenta, as well as the indirect effects associated with the health of the mother during pregnancy. It is difficult to assess the extent of damage by cocaine use *per se* because of the generally poor health care received by women within this sociodemographic group as well as comorbidity factors (eg polysubstance use, depression) influencing the health of cocaine using mothers and their children.

Thus there are considerable social and personal costs associated with addiction to cocaine and this has stimulated a concerted search for effective treatments. The positive effects of cocaine are strongly reinforcing, which means that the drug is highly addictive. However, vulnerability to

the physical action of the drug is moderated by a complex set of social and environmental factors with which use of the drug has been associated. The search for effective treatments for cocaine abuse has thus involved investigations of combinations of both pharmacological and psychosocial variables.

5.2 TREATMENT SETTING

The American Psychiatric Association (American Psychiatric Association, 1995) has specified that patients of drug and alcohol treatment programs should be treated in settings which are as unrestrictive as possible, whilst remaining safe and effective. Thy reported that there appeared to be no RCTs in the literature where inpatient treatment for cocaine dependence has been found to be more effective than placebo. Any studies demonstrating treatment effectiveness had been carried out in outpatient settings with intensive programs (American Psychiatric Association, 1995; Higgins & Wong, 1998). However, there was no support for low intensity outpatient treatments in the literature (Platt, 1997).

In the one randomised trial specifically comparing the effectiveness of inpatient and day hospital treatment programs (both intensive), Alterman and co-workers found that inpatients were more likely to complete treatment, but there were no significant differences between the two groups on outcomes at 7 months post-treatment assessment (Alterman et al., 1994). This study also reviewed the relative costs of inpatient and outpatient (day hospital) treatment and found that inpatient treatment was approximately twice the cost per patient of outpatient treatment. The authors conclude that inpatient programs would be best directed towards those whose physical, psychiatric and motivational problems indicate that they would be at high risk of dropping out from an outpatient program. In their review of treatment settings, Higgins and Wong (1998) also concluded that outpatient care should be first choice treatment for cocaine addicts.

SUMMARY POINT

Intensive outpatient treatment is less expensive and generally more effective than inpatient treatment. However, inpatient treatment should be available for more intractable patients for whom outpatient programs are unlikely to succeed.

5.3 ASSESSMENT

As with assessment for abuse of other substances, it is important that the process of assessment does not alienate the patient. The assessment phase should be regarded as the time when a positive therapeutic relationship can evolve and where patients are encouraged to explain their reasons for attending and describe their symptoms in a non-stressful, non-threatening environment. As Platt concluded in his review of cocaine abuse, a non-confrontational, empathic

and mutually respectful therapeutic relationship is more likely to engage those more entrenched patients who are unwilling to accept that they have a problem (Platt, 1997).

The assessment should obtain a history of drug use including where, how and why cocaine has been used. It should also obtain a psychiatric history and any information that relates psychiatric ill-health to cocaine use. Finally it should include a thorough physical examination, including urinalysis.

There are standard self-report questionnaires available which have been designed specifically for the assessment of cocaine abuse. The Voris Cocaine Craving Scale (Smelson, McGee Caulfield, Bergstein, & Engelhart, 1999) and the Halikas-Crosby Drug Impairment Rating Scale (Halikas, Crosby, & Nugent, 1992; Halikas, Nugent, Crosby, & Carlson, 1993) have both been shown to have good reliablity and validity for assessing self-reported impairment both for assessment and treatment outcome measurement purposes. Kampman and co-workers recently developed the Cocaine Selective Severity Assessment (CSSA), a scale to measure the symptoms of early cocaine withdrawal (Kampman et al., 1998). They have found the instrument clinically useful especially in predicting early treatment failure and presented evidence of good reliability and validity in their 1998 report.

There are also general addiction measures which have been found to be useful for assessment of cocaine dependence prior to treatment. For example, standard measures of readiness to change (Barnes & Samet, 1997; Prochaska & DiClemente, 1986) may assist the clinician to establish the patient's presenting attitudes towards their drug problem as well as provide a basis for motivating change behaviour. Broad instruments such as the OTI and the ASI which have been discussed in the related section under opiates (Section 3.2 above) are adaptable to assessment for other drugs of abuse and have good psychometric properties. Similarly the SODQ and IRQ reviewed in that same section are adaptable measures of current dependence and injecting risk behaviour.

SUMMARY POINTS

1. The aims of assessment are to reveal the level of dependence and psychosocial impairment of the patient, as well as establishing a rapport to serve as a basis for positive treatment interaction.

2. Standard measures of dependence, motivation and psychosocial impairment are available and should be used.

5.4. DETOXIFICATION & WITHDRAWAL

DSM-IV (American Psychiatric Association, 1994) characterised cocaine withdrawal after several days heavy use, as consisting of dysphoric mood (anhedonia or sadness, rather than depression); and at least two of the following symptoms: fatigue, insomnia or hypersomnia, psychomotor agitation or retardation, drug craving, increased appetite and vivid, unpleasant dreams. Withdrawal has been reported to reach its peak in 2 to 4 days with dysphoric symptoms persisting for several weeks (Lago & Kosten, 1994).

Gawin and Kleber (1986) described withdrawal from cocaine as consisting of three stages, the first of which is commonly termed the "crash". The crash was described as developing rapidly after ceasing heavy cocaine use, and initially consisted of very intense withdrawal symptoms, which gradually dissipate over the next 9 hours to 4 days, during which time the patient's craving for sleep and feelings of exhaustion replace cravings for cocaine. Phase 2 is called the withdrawal phase and is initially characterised by euthymia and little craving for cocaine and normal sleep patterns (1-4 days), but dysphoria and craving start to increase again, reaching moderate symptom levels, lasting up to 10 weeks. The third phase is the extinction phase which has no dysphoria but cocaine craving is intermittently experienced due to exposure to contextual cues associated with prior cocaine use.

Gawin & Kleber (1986) drew up this model from observation of 30 subjects in an outpatient setting. However, Lago and Kosten (1994) reviewed the literature on stimulant withdrawal and concluded that evidence from inpatient studies did not support the notion of the "crash". These studies found a persistent gradual decline in symptomatology throughout the observed withdrawal period. However, as pointed out by the authors, the crash may have occurred prior to hospitalisation of these patients. Alternatively, it could be a consequence of exposure to contextual drug cues from which hospitalised patients are protected.

As Lago and Kosten concluded, the absence of clear-cut withdrawal symptoms with cocaine abstinence, along with the limited numbers of relevant studies, meant that the existence of a withdrawal syndrome was at best equivocal (Lago & Kosten, 1994). Because of the low intensity of symptoms, recommended interventions for detoxification (initiation of withdrawal) were of a supportive rather than medical nature (American Psychiatric Association, 1995; Klein, 1998). No specific recommendations were found regarding psychosocial support for detoxification. In a sense withdrawal from cocaine can be viewed as occurring over an extended period, so that interventions which are used to treat withdrawal are also those used in treatment. The following section on treatments for cocaine abuse reviews these interventions and their efficacy in dealing with this withdrawal over time.

SUMMARY POINTS

1. There is some disagreement in the literature regarding the course of withdrawal from cocaine, with some theorists arguing that there are three stages beginning with the highly aversive "crash". Others claim that there is a gradual decline of withdrawal symptom severity which is not initially excessive.

2. Due to the relatively low intensity of withdrawal symptoms, medicated assistance is not recommended.

5.5. SPECIFIC INTERVENTIONS

5.5.1. Pharmacotherapies

Expert reviews (eg (Bigelow & Walsh, 1998; Platt, 1997; Tutton & Crayton, 1993)) have classified pharmacotherapies for cocaine abuse into four broad categories: (1) drugs which treat pre-morbid co-existing psychiatric disorders; (2) drugs which treat cocaine withdrawal and craving; (3) cocaine antagonists which block the action of cocaine; and (4) drugs which cause an aversive reaction to cocaine. As is clear from the following discussion there are drugs and drug groups (largely the antidepressants) which fall into more than one of these categories. One further category, raised by Kaminiencki et al in their review of interventions and care for psychostimulant users, is that of stimulant replacement therapy.

1. Drugs treating comorbid psychiatric disorders

Individuals presenting for treatment for cocaine dependence are likely to have pre-existing psychiatric disorders. Studies have found some 30% of this group suffers from depressive disorders, 20% have bipolar disorders and 5%, attention deficit disorders (ADD, (Tutton & Crayton, 1993)). Tutton and Crayton emphasised the importance of matching treatment to psychiatric condition because misapplication may prove counter-productive in treatment. These authors concluded that, although accurate diagnosis is difficult with cocaine-abusing patients, the large number who are likely to have comorbid conditions justifies concerted efforts to diagnose and treat pre-existing psychiatric conditions.

Because chronic cocaine use leads to a compensatory reduction of natural dopamine production with associated neuronal changes, withdrawal from cocaine is believed to be associated with a deficit of dopamine. This is believed to be the basis of the anhedonia and craving associated with cocaine withdrawal symptoms. Thus depression in patients being treated for cocaine abuse may be pre-existing or withdrawal-induced.

Desipramine and other tricyclic antidepressants:

Research findings regarding the therapeutic effectiveness for cocaine use of the tricyclic antidepressant desipramine are equivocal (Platt, 1997). However, some studies conclude that desipramine may have differential effectiveness dependent upon underlying pre-existing psychiatric conditions. For example, research suggests that desipramine is ineffective with patients with antisocial personality disorder. There has also been a tendency for desipramine and other tricyclics to be more effective with patients with pre-existing depression than with non-depressed patients. Some more recent studies, which have involved a more seriously damaged population of users - crack smokers - have found desipramine more generally effective in reducing cocaine use as well as reducing craving and depression during withdrawal. However, other studies have not been able to replicate these findings in similar populations. Similarly, some human laboratory studies have reported reductions in craving but no effect on use with desipramine therapy, yet other studies have found the converse.

There is evidence that the dose-response curve for desipramine may not be linear and, like buprenorphine with methadone, there may be a ceiling effect on dose response -which could explain the variations in findings for this drug (Platt, 1997). Furthermore, as Halikas et al concluded from their research on carbamazepine (Halikas, Crosby, Pearson, & Graves, 1997), the use of fixed dosages may be counter-productive. It may be more efficacious to individually manage serum levels of the drug being evaluated. Of concern are findings which suggest that tricyclic antidepressants may interact with cocaine to increase its toxicity, although some studies have failed to support this finding as well. Overall, Platt concluded that clinical effectiveness of tricyclic antidepressants was yet to be demonstrated and that there are possible negative cardiovascular side effects of desipramine which adds a note of caution to use of this drug with cocaine addicts.

This conclusion has been supported by other reviewers in the field (Bigelow & Walsh, 1998; Fischman & Foltin, 1998; Higgins & Wong, 1998; Schuckit, 1994). Withers et al (1995) pointed out that desipramine therapy also suffers from the disadvantage of a 2 to 3 week delay before the drug becomes effective. As drop-out rates in this early period tend to be very high, this medication may not have an opportunity to demonstrate its efficacy. Although desipramine may not be effective alone, some research suggests that it does reduce subjective craving (Fischman & Foltin, 1998). Fischman and Foltin proposed that use of desipramine in combination with a behavioral intervention aimed at teaching alternative reinforcers to cocaine may be an effective treatment. They also concluded from their review that desipramine may be more effective with patients with less severe cocaine dependence and no other psychopathology. This has also been highlighted by Higgins & Wong (1998).

Stitzer and Walsh (1997) argued cogently that the benefits of pharmacological treatments for stimulant abuse may be discounted unfairly because there also needs to be complementary psychosocial interventions in place to yield a truly effective package. They reviewed recent research and drew a parallel with effective psychosocial and pharmacological treatments for

nicotine addiction which have demonstrated additive effects. They caution that pharmacotherapies in isolation may not be effective, but that it is important to test pharmacotherapies in combination with a range of psychotherapies. This reasoning again could help to explain the equivocal findings for pharmacotherapies. It should be added that research must be able to demonstrate that the effects of pharmacotherapies augment those of psychotherapies.

Recent Research

- Nunes et al (1995) examined the differential effectiveness of imipramine treatment for cocaine abuse for 113 subjects in a 12-week, double-blind and controlled study. Imipramine is another tricyclic antidepressant which had previously been found to reduce cocaine craving and feelings of euphoria associated with cocaine use. The aim of the study was to replicate these findings and to look at the effectiveness of imipramine with particular sub-groups of cocaine users. The study was randomised and stratified by route of administration as well as by level of depressive disorder. As well as receiving imipramine or placebo, patients also had one medication-oriented visit and one counselling session per week.

  As with most cocaine pharmacotherapy trials, there was a high attrition rate for this study, with 54% of those randomised reaching a minimum adequate trial of 4 weeks, and 15% completing all 12 weeks. This study found overall that imipramine reduced cocaine craving, euphoria and depression, but had no significant effects on cocaine use. There were no interaction effects of level of depression or route of administration on these variables, but results suggest that abstinence may be encouraged by imipramine therapy in nasal users or those with more severe depression. These results are tenuous (do not reach statistical significance) and suffer from the problem of conducting a large number of statistical tests with no adjustment for Type I error rate. As concluded by the authors the study provides little support for this pharmacotherapy for cocaine abuse.

Other antidepressants

Monoamine oxidase inhibitors (MAOIs) have been used to treat cocaine dependence, especially where tricyclics have been contraindicated. However, no controlled trials have been carried out on this group of drugs for this purpose. MAOIs can also cause serious hypertensive reactions in cocaine using patients which makes their use for treating this group of uncertain safety.

The serotonin reuptake inhibitor, fluoxetine hydrochloride (Prozac), was reviewed by Tutton and Crayton (1993) and they concluded that it has potential because of its superior side effect profile and likelihood of good patient compliance. At that time they recommended that controlled studies were needed to test the efficacy of this antidepressant. Platt (1997) reported that positive results have been obtained for this drug in mostly open trials with cocaine-abusing

methadone maintenance patients, with few side effects being reported. Most patients tend to report a decrease in craving as well as a decrease in the "high" obtained from cocaine. Thus, Platt also concluded that fluoxetine has good potential as a treatment for cocaine addiction and also for cocaine-abusing opiate addicts. Clearly more randomised controlled trials should be carried out to test this pharmacotherapy. No further trials of fluoxetine were detected in the literature since the review by Platt.

In their review of the research on pharmacotherapies for stimulant abuse, Stitzer and Walsh (1997) concluded that although fluoxetine may not prove effective for primary cocaine abusers, it has shown potential to effectively treat polydrug users. They also make an important point that choice of outcome measures could significantly influence findings from clinical trials of cocaine pharmacotherapies. In particular qualitative testing ie presence/absence of metabolites in urine may be too insensitive to highlight genuine change in drug-using behaviours. They suggest that quantitative testing ie how much metabolite is in the urine, is a more sensitive outcome measure and should be used when assessing these pharmacotherapies. This conclusion could be applied to the assessment of outcomes for pharmacotherapies as well.

Other antidepressants such as bupropion and trazodone have either too little research data on their efficacy in this area, or have had equivocal findings.

Drugs directed at other comorbid psychiatric disorders

Tutton and Crayton (1993) concluded that lithium treatment affects discontinuation of cocaine use in patients with bipolar or cyclothymic disorders. However, the review by Platt (1997) found that there was little recent research support for the use of lithium for this sub-group of cocaine abusers, except in that it remains an effective treatment for such disorders irrespective of cocaine use.

Tutton and Crayton also concluded that treatment with appropriate stimulants for ADD-disordered patients (methylphenidate and pemoline) influences cessation of cocaine use. However, there is some evidence that methylphenidate may increase cocaine craving. Platt pointed out that, although research to date favoured the hypothesis that these medications were effective with those cocaine users with ADD, studies tended to consist of small numbers of case studies which could not lead to any clear conclusions.

There was no further research identified in the literature on these treatment sub-groups.

2. Drugs treating withdrawal and craving

Drugs which treat withdrawal symptoms and craving include dopamimetic agents which are aimed at increasing dopamine concentrations at receptor sites to counter the depletion due to neural adaptation associated with cocaine abuse. Such drugs as methylphenidate, bromocriptine, amantadine and pergolide mesylate fall into this category. As discussed in the

section above, methylphenidate is not generally effective and may act to increase craving. According to Schuckit (1994), whilst earlier open trials of bromocriptine had some positive findings, controlled research had not supported its usefulness. Tutton and Crayton (1993) found similarly and also referred to the negative side-effects of this drug, which include nausea, headache, orthostatic hypotension and psychotogenic effects. Another dopamimetic drug which has been studied is amantadine, and this drug has again had widely varying results.

Pergolide mesylate, which is used in the treatment of Parkinson's disease, is 10 to 100 times more potent, has a longer duration of action than bromocriptine and appears to have fewer side effects. Results from open trials for this drug were very promising but more recent controlled studies have found that it may increase cocaine craving whilst having no effect on intravenous cocaine-taking behaviour (Fischman & Foltin, 1998). These reviewers conclude that this drug does not warrant further investigation.

The dopamine precursor levodopa, along with carbidopa to counter side effects, has been administered to patients to assist withdrawal. Some positive findings have been reported from open trials with few reported side effects. This treatment clearly needs further research using randomised controlled trials. Dietary precursers to dopamine, tyrosine and tryptophan have not been found to be successful in assisting withdrawal from cocaine.

The anticonvulsant, carbamazepine (tegretol) has been trialled because it has been shown in animal studies to selectively inhibit the "kindling" effects (of increased limbic seizures) resulting from chronic cocaine use. Several open trial studies carried out in the late 1980s and early 1990s led to some optimism that this medication may effectively reduce cocaine use through reduced craving and blocking of euphoria. However subsequent randomised controlled trials (Campbell, Thomas, Gabrielli, Liskow, & Powell, 1994; Cornish et al., 1995; Kranzler, Bauer, Hersh, & Klinghoffer, 1995; Montoya, Levin, Fudala, & Gorelick, 1995) found no evidence of superior efficacy of carbamazepine compared with placebo. Furthermore, Withers et al (1995) have cautioned that at least one study has noted increased cardiovascular effects of cocaine used in combination with carbamazepine. Although not observed in research on treating cocaine dependence, this drug can also cause seizures and tachycardia in overdose, due to reductions in norepinephrine turnover. It appears that the manner and timing of carbamazepine administration are crucial as it can induce seemingly paradoxical effects (Platt, 1997). In animal studies it has been found that chronic administration reduces kindling effects, while intermittent administration increases them. Other minor side effects such as skin irritations and drowsiness have also been reported from human research.

Recent Research

- The most recent study completed on carbamazepine was reported by Halikas and coworkers (1997). This research team has been responsible for much of the recent controlled research on pharmacotherapy for cocaine abuse. In this latest study, 183 subjects were randomised to either placebo, 400mg weekly fixed-dose carbamazepine or

800mg carbamazepine. Of these 150 returned for the first weekly assessment and this formed the "evaluable" sample pool for the study. The study was carried out over 12 weeks and retention averaged 38% of evaluable subjects with no significant differences in retention between groups.

Although there were not notable differences between the three treatment groups (especially if Type 1 error rates are accounted for), the study did find a large number of significant differences in outcome variables based on serum levels of carbamazepine. They conclude that although improvements were positively related to steady state serum levels, it is likely that individual titration of the medication rather than increased fixed doses will lead to improved patient response. They also suggested that an individualized dosing procedure may be more efficacious with other drugs used to treat cocaine dependence.

Another important finding of this study is that increased hours of psychosocial treatment combined with higher serum carbamazepine levels led to a further significant decline in cocaine use as measured by urinalysis.

- Crosby et al (1996) assessed the effects of another anticonvulsant phenytoin and found that this drug was significantly associated with reduction in cocaine use compared with placebo. The study commenced with 44 subjects and ran for 12 weeks, when only 12 subjects (6 in each group) remained. The high drop-out rate and the fact that 85% of the phenytoin group believed they were taking phenytoin, means that these results are inconclusive.

The antianxiety agent buspirone enhances dopaminergic and noredrenergic firing whilst suppressing some serotonergic activity (Platt, 1997). It has been found to be more effective in decreasing withdrawal symptoms than placebo but only after 10 days of administration. Diazepam which has been used to treat withdrawal from other drugs of abuse, has been found to blunt cocaine-induced tachycardia and hypertension and to protect against cocaine intoxication. Animal studies have indicated that it is not entirely effective against cocaine-induced seizures and it may not be protective at higher doses. There is no controlled human research in the literature which assesses diazepam treatment for cocaine abuse.

The final group of drugs used to treat withdrawal and craving is the antidepressants which have been reviewed in section 1 above.

3. Cocaine antagonists

The neuroleptics, haloperidol, chlorpromazine, fluphenazine, flupenthixol decanoate are all dopamine receptor blockers which have been shown to attenuate self-administration of cocaine in animals (Tutton & Crayton, 1993). No controlled studies and few open studies have been carried out on the neuroleptics possibly because of their side-effect profile. Tutton and Crayton concluded that flupenthixol has shown some potential and should be studied further. In particular, Fischman and Foltin (1998) pointed out that it may prove useful for the patient sub-

group of cocaine abusers with schizophrenia. Although flupenthixol acts as a neuroleptic at higher doses, at lower doses it acts as an antidepressant. It is also possible that it may act as an aversive agent when used with cocaine, at least for a sub-group of cocaine users (Gawin, Khalsa-Denison, & Jatlow, 1996). In one study researchers reported that flupenthixol was superior to placebo in reducing crack cocaine use and symptoms of withdrawal (Khalsa, Jatlow, & Gawin, 1994).

In his review of cocaine pharmacotherapies, Platt (1997) concludes that flupenthixol has three properties which make it attractive, namely that it has only modest reinforcing qualities, it has few unpleasant side-effects compared with other anti-depressants, and it may act to attenuate cocaine reinforcement and allow extinction to occur. A further property suggested by Gawin and co-workers (1996) is that it may prove aversive when used with cocaine for at least some cocaine users.

Imipramine, bromocriptine, trazadone, lithium and buprenorphine are also potential cocaine antagonists which have been studied for their effects on recovery from cocaine abuse. Some of these drugs have been discussed in other categories in this review. According to the review by Tutton and Crayton, there is no good evidence of the clinical efficacy of any of these drugs.

Schuckit (1994), however, concluded that the mixed opioid antagonist, buprenorphine, deserves further research because laboratory studies on both humans and animals have suggested that it leads to a decreased response to cocaine. Fischman and Foltin (1998) reported that in recent research it has been demonstrated that buprenorphine does not block cocaine-induced craving or euphoria but appears to facilitate some of these effects. However, and despite this facilitation, choice to take cocaine decreases on increasing dose of buprenorphine. Hence studies on cocaine-using opiate abusers are currently being carried out with some results suggesting that buprenorphine is more effective than methadone in attenuating cocaine use in this sub-group of patients. At this stage Fischman and Foltin regarded buprenorphine as a promising treatment for cocaine abuse for at least some opiate users. As Schuckit concluded in his 1994 review, no randomised controlled trials have been carried out using buprenorphine over extended periods and these are needed.

4. Aversive agents

Phenelzine is an MOAI which in combination with cocaine has unpleasant side effects such as headaches, hypertension, palpitations and chest pain. It has been trialled but it has been found to result in death in a small number of patients and is clearly not a recommended therapy for cocaine abuse (Tutton & Crayton, 1993). Platt reviewed this drug as an alternative to tricyclic antidepressants and also concluded that it should be avoided because of its potentially toxic interaction with cocaine as well as its strong association with relapse.

Mazindol acts in a similar way to cocaine to block both dopamine and norepinephrine uptake. Research has found that this drug has no effects on cocaine use or that it is counterproductive, as well as showing some evidence of increased cardiovascular risk (Platt, 1997).

As mentioned in the preceding section one study has reported increased aversive effects of flupenthixol decanoate for some subjects who also use cocaine (Gawin et al., 1996). However, no controlled research has been completed assessing this particular property of this drug.

5. Stimulant replacement therapy

Kaminiencki et al (1998) suggest that there is some limited evidence that use of prescribed stimulant replacement drugs, in particular oral amphetamines (dexamphetamine) may prove useful to attract injecting cocaine users to treatment as this has been found anecdotally to be effective with some injecting methamphetamine users. There is no controlled research evidence to support this notion, but, given the paucity of effective and attractive treatments for this group of drug abusers, trials of such interventions may be warranted.

SUMMARY POINTS

1. Desipramine, although showing early potential for improving treatment outcomes, has not been found to be generally effective in treating cocaine addicts. Further research is needed into its usefulness particularly as a part of a broader behavioural program and with patients with lower levels of dependence.

2. The specific serotonin reuptake inhibitor fluoxetine has shown some positive outcomes with cocaine abusing subjects, especially for those patients also addicted to opiates. However it needs to be further assessed in randomised controlled trials.

3. Antidepressant medications (other than fluoxetine) have shown little potential to assist with treatment for cocaine abuse.

4. There is little research support for the use of lithium to control cocaine use with individuals with bipolar disorder; nor for the use of stimulant drugs used in general treatment of ADD for cocaine use in ADD.

5. There is little research evidence to support the use of dopamimetic agents, dopamine precursors, anticonvulsants nor diazepam to treat cocaine abuse. However, if these classes of drugs are to be investigated further, it is recommended that individualised rather than fixed dosing is used, along with monitoring of serum levels.

6. Treatment with the blocking agents flupenthixol and buprenorphine may be effective in reducing cocaine use, especially in psychotic and opiate-abusing patients respectively. Further controlled research is warranted on these drugs and for these sub-groups of cocaine abusers.

7. No aversive medication has been identified to treat cocaine abuse, although the neuroleptic flupenthixol decanoate should be further studied for its aversive effects.

8. Consideration should be given to placebo-controlled trials of oral amphetamine replacement therapy to ascertain the safety and efficacy of such interventions.

9. Further research on pharmacotherapies for cocaine (and other stimulants) needs to factor in complementary psychosocial therapies, but also to demonstrate that specific pharmacotherapies add to overall treatment effectiveness.

10. Because the safety of cocaine use is unpredictable and considering the poor retention rates achieved in this area of research, caution should be exercised when trialling new medications because of the possibility of additive negative effects of the trial drug and cocaine.

5.5.2. Nonpharmacological Interventions

Although different types of psychological therapy have been found to be variously effective, the American Psychiatric Association (American Psychiatric Association, 1995) emphasises that different findings may be due more to intensity than type of therapy. In fact outcomes of the recently published Collaborative Cocaine treatment Study (Crits-Cristoph et al., 1999) suggest that differences found between results in this study and previous studies may be due to differences in the quality of treatments provided. This study is discussed below.

It is estimated that about half the patients seeking treatment are lost before initial assessment interview. In their review of the research literature, Higgins and Wong (1998) address this issue and conclude that high attrition rates can be reduced by accelerating the intake process. They also conclude that, on the basis of limited evidence available, best outcomes have been demonstrated where:

- treatment duration is three or more months;
- therapy sessions (either group or individual) occur at least once per week; and
- there is weekly or more frequent monitoring of urine and clinical status.

They found no evidence to support individual over group therapy. However, they emphasised the need for prospective experimental studies to address all these treatment issues.

Psychosocial therapy for cocaine addiction has traditionally been based on the twelve-step approach and much of the controlled research in this area has concentrated on comparing newer therapies with this approach. The APA concluded that attendance at AA-based self-help groups may improve long-term outcomes (American Psychiatric Association, 1994). They also concluded that psychodynamic approaches have little research support to date, but that two psychotherapeutic approaches based on behavioural and cognitive-behavioural theory have both shown promise.

1. Behavioural Reinforcement Approach

As summarised by Higgins (1997), cocaine is abused, in part, because of its reinforcing effects. Basic to this approach is the understanding that the acquisition and maintenance of cocaine abuse is liable to manipulation through the use of other salient reinforcers in the environment.

Both Higgins and Wong (1998) and Carroll (1998) agree that contingency-based behavioural interventions are the most promising psychosocial interventions for treatment of cocaine abuse. Research has found that increasing the magnitude of alternative food reinforcers reduces cocaine self-administration in rhesus monkeys (Higgins, 1997). It has also been demonstrated with rats, that rates of cocaine self-administration are malleable and dependent upon the reinforcement value of competing reinforcers in the environment. Higgins pointed out that such studies have also found that in an environment where both cocaine and palatable alternative reinforcers are freely available, acquisition of cocaine-reinforced responding is more likely to be disrupted than maintenance of established cocaine using behaviour. This data suggests that in order to modify established cocaine-using behaviour, it may be necessary to expose individuals to alternative nondrug reinforcers in the absence of cocaine - making them contingent on forgoing cocaine use. This is the theory underlying the research carried out by Higgins and co-workers on alternative nondrug reinforcers (Higgins, Budney, Bickel, & Badger, 1994a; Higgins et al., 1997; Higgins et al., 1994b). In their research they have used vouchers which were exchangeable for retail items or housing and job opportunities as positive reinforcers for cocaine abstinence in combination with the community reinforcement approach (CRA), and produced substantial reductions in rates of cocaine use. CRA involves individual therapy directed at relationships and other living skills in order to increase non-cocaine reinforcers in the individual's environment. They found that this approach is superior to standard outpatient drug abuse counselling and also that there were significant improvements on outcomes for the voucher plus CRA compared with the non-voucher plus CRA condition (Higgins & Wong, 1998). One study has also found significantly greater abstinence for a group given contingent vouchers compared with another group given non-contingent vouchers (Higgins & Wong, 1998).

These researchers also incorporated monitored disulfiram therapy in their program for those cocaine users who also abuse alcohol, and found promising reductions in cocaine (as well as alcohol) use. Considering that it is estimated that some 60% of cocaine abusers are also alcohol dependent, this finding is important.

In his review of the literature Platt commented that research had indicated that the magnitude of reinforcement and immediacy of reinforcement may be critical in determining efficacy of a voucher system. He also pointed to some research which has not supported the use of vouchers to encourage abstinence from cocaine, especially on a longer-term basis. In attempting to explain the disparities in the literature, he suggests that the study samples were from widely divergent social settings. Those which obtained best results were from a rural environment, whilst those with negative findings were from an inner-city environment where there were few alternative reinforcers to drug use apart from those provided in the study environment.

Recent research

- Kirby et al 1998 (1998), compared treatment effects of adding voucher payments for cocaine-free urine screens to a comprehensive treatment package. The treatment package was 26 sessions of cognitive behavioural therapy plus 10 one-hour sessions of interpersonal problem-solving carried out over the 12 weeks of the study. Half of the sample (total n=90) also received vouchers, while the rest did not. The sample was a severely disadvantaged group of largely (88%) crack cocaine users. The voucher delivery in the first experiment was on a weekly basis with initial values low but increasing with production of consecutive negative results. Values were reset to zero on production of positive screens (schedule 1). No effects were found for use of vouchers on this schedule. As this did not agree with prior findings, the researchers carried out a second experiment to look at the effects of varying the schedule of voucher delivery.

  The second experiment involved lower numbers (total n=23). Half the group received vouchers as for experiment 1, on a weekly basis. The other half received vouchers immediately on producing the cocaine-free urine. The values of the vouchers started high ($30 for the first 9 cocaine free specimens) with no punishment for positive screens. Repayments became more intermittent after this, but overall maximum earnings were greater. There was a trend for this system of voucher delivery (schedule 2) to improve retention and attendance outcomes, but low numbers probably prevented these differences from being significant. There were also significant improvements on measures of abstinence for this voucher delivery system compared with voucher schedule 1. About half the patients on voucher schedule 2 completed treatment and showed continuous abstinence at 1 month following treatment. None of the patients on voucher schedule 1 reached 1-month continuous abstinence. Thus this schedule was effective in assisting initiation of abstinence. As the authors point out whether treatment gains are maintained needs to be further studied. They also commented that significant outcomes were found using the vouchers as part of a cognitive-behavioural intervention, which had not to that time been shown to be effective in promoting abstinence from cocaine.

Cognitive behavioural therapy for cocaine use is aimed at helping individuals to recognize that they have a problem with their cocaine use, to understand their problem and to assist them modify the dysfunctional cognitions underlying this problem behaviour. It typically involves skills training and practice to deal with craving, monitoring thoughts about drugs and monitoring high-risk situations associated with relapse (Carroll, 1998).

As Carroll pointed out cognitive-behavioural interventions had not generally been demonstrated to be superior to other psychotherapies in initiating abstinence, but research suggested that its effects may be more durable and thus protective against relapse. Furthermore, it may be more effective with more severely dependent users. This was also the conclusion of the American Psychiatric Association in their 1995 Guidelines (American Psychiatric Association, 1994).

Recent Research

- Maude-Griffin and coworkers (1998) have recently completed a randomised study comparing cognitive-behavioural therapy with 12-step facilitation on 128 crack smokers. This was a very disadvantaged group with 75% homeless or marginally housed, 84% unemployed, 82% with comorbid psychiatric disorders and almost half with two other psychiatric disorders and a mean length of cocaine use of 19 years. Apart from comparing the two treatments, the researchers tested 5 matching hypotheses:

    1. Cognitive behavioural therapy would be more effective than 12-step facilitation for patients with a history of depression;
    2. Cognitive behavioural therapy would be differentially effective based on abstract reasoning skill with those with higher abstract reasoning doing better, with no such differential effectiveness for 12-step facilitation;
    3. Cognitive behavioural therapy would be more effective than 12-step facilitation for patients with more severe drug use at intake;
    4. Patients who endorsed the disease model would do better in 12-step facilitation than in cognitive behavioural therapy; and
    5. Patients who were more religious would do better in 12-step facilitation than cognitive behavioural therapy.

    Participants attended three group therapy and one individual therapy session per week over 12 weeks. Treatments were manualised and administered by counsellors with extensive experience. The therapists administered both therapies to avoid therapist effects. The 12-step facilitation group was encouraged to attend Cocaine Anonymous, while the cognitive behavioural therapy group was encouraged to attend Rational Recovery, a cognitively-based self-help group. Outcomes were abstinence-based and self reports were validated with random urine sampling. Missing samples were coded as not abstinent.

    One hundred and thirty-four from 159 recruits were deemed eligible for the study and 6 refused to participate, leaving 128 as the treated sample. Although there was good study

follow-up (84% at six month assessment) attendance at treatment groups was low, with only 17 participants (13%) attending at least 75% of both group and individual sessions. Outcome variables were at least 4 weeks of abstinence during treatment, and frequency (point prevalence) of abstinence over all assessments. All self-reported abstinence was verified by urinalysis.

Participants in cognitive behavioural therapy were found to be significantly more abstinent than those in 12SF, using either outcome measure. With regard to the matching hypotheses:

- patients with a diagnosis of major depressive disorder at intake were more likely to achieve four consecutive weeks of abstinence when treated by cognitive behavioural therapy than 12-step facilitation. No equivalent interaction effects were reported for the point prevalence outcome criterion;
- patients with high abstract reasoning had significantly more positive outcomes in the cognitive behavioural therapy group (using either outcome measure) than patients with low abstract reasoning. Using point prevalence alone it was also found, although not hypothesised, that patients in 12-step facilitation treatment with low abstract reasoning fared better than those with high abstract reasoning;
- although overall religiosity did not predict differential outcomes, a post hoc analysis using only African American participants found that those who were more religious had better outcomes in 12-step facilitation than those with low levels of religious belief; and
- no significant interaction effects were found for either outcome criterion or the other matching variables (problem severity and belief in the disease model).

These results contrasted with those found by Crits-Cristoph and co-workers reviewed below and differences may relate to the samples used, treatment intensity and consistency as well as the rigour of assessment of abstinence. These differences are further discussed below.

- Monti et al (1997) have recently completed a study comparing brief coping skills treatment with an attention placebo. Both treatments were additions to a comprehensive treatment package incorporating both 12-step and social learning principles. The skills training was directed towards high-risk situations and the attention placebo involved the same number of hours in manualised meditation and relaxation training which the researchers regarded as a credible but ineffective treatment. All treatment and control procedures were administered on an individual basis in eight 1-hour sessions with 3-5 sessions per week based on length of stay. (Average length of stay for the treatment programs was 16.8 days.) Time Line Follow Back was used to assess self-reported cocaine use at 6 months pre-treatment and 1-month and 3-month follow-up assessments. These were confirmed with urine tests as well as collateral reports. Demographic information and indices of psychosocial well-being were also obtained using the Addiction Severity Index (ASI) at pretreatment and 3-month follow-up.

The intention-to-treat sample for this study was 128, and the authors considered that 108 of these received at least 50% treatment exposure. Seventy-three percent of these were approached for follow-up. They found that there were no differential effects of the two additional interventions in terms of total abstinence during the 3-month follow-up period. However, there were significant reductions in days of use as well as length of bingeing for patients in the coping skills treatment condition compared with placebo. The authors point out that the continuous variables are more sensitive outcome measures than the categorical abstinence measure. There were, however, no differences between conditions for the outcome of longest continuous abstinence. Overall, the authors conclude that the brief skills intervention, teaching how to cope with cocaine-specific high-risk situations, leads to shorter and less severe relapses. These results fit with prior findings that interventions based on cognitive principles may have more impact on longer-term relapse prevention than on more immediate broad measures of usage or abstinence.

- Crits-Cristoph and co-workers have published outcomes for the National Institute on Drug Abuse multicentre collaborative cocaine treatment study (1999). In this study 487 patients were randomised to four treatment conditions:
  (1) individual drug counselling plus group drug counselling;
  (2) cognitive therapy plus group drug counselling;
  (3) supportive-expressive therapy plus group drug counselling; and
  (4) group drug counselling alone.

  All treatments were manualised with a 6-month active phase and a 3-month booster phase. The individual drug counselling and group drug counselling were based on the disease model with strong encouragement to participate in 12-step programs and taught patients how to progress through stages of recovery from addiction. Cognitive therapy followed a cognitive therapy program for substance abuse based on social learning theory. Supportive-expressive therapy was based on the psychoanalytic approach to treatment for substance abuse.

  They used a composite outcome measure of cocaine use which ascribed the rating "abstinent" or "not abstinent" for each month. Any indication of drug use from either urine tests, Addiction Severity Index responses or a weekly cocaine use inventory led to a "not abstinent" rating. Where no measures were available (which occurred on 19% of possible occasions) patients were rated as "not abstinent". However, as only 42.6% of all potential urine specimens were collected, and presumably non-randomly, this global abstinence rating may be unreliable. If patients reported abstinence and did not produce a urine sample, then they would be rated as "abstinent". Whether patients would be truthful about this would depend on the benefits they perceived accruing through appearing to be abstinent.

  The sample was obtained from a total of 2197 persons screened by phone, of whom 1777 met inclusion criteria and 870 were considered to have begun what was termed an orientation phase. During this phase patients were required to attend 3 clinic visits within 14 days to demonstrate their motivation. At this time the patients were encouraged by group

counsellors to attend self-help groups based on 12-step principles. Housing, job and financial needs were also addressed during orientation. Only 487 (56%) proceeded to randomisation and the active therapy stage.

Their main hypothesis was that any of the individual therapies plus group drug counselling would be more efficacious than group drug counselling alone. They also hypothesized that cognitive therapy plus group drug counselling and supportive-expressive therapy plus group drug counselling would be more effective with patients with high psychiatric severity. Furthermore, they hypothesised that patients with antisocial personality traits (external coping style) and treated with cognitive therapy plus group drug counselling would have better outcomes than those treated with supportive-expressive therapy plus group drug counselling.

They found that their first hypothesis was supported in that the three groups which included individual therapy had significantly better outcomes than the group drug counselling alone group. Results did not support the predicted differential effects for patients with high psychiatric severity and antisocial personality traits. They also compared the effects of the two professional psychotherapies with the individual counselling group and found, contrary to predictions based on previous research, that individual counselling plus group drug counselling was more effective than cognitive therapy plus group drug counselling or supportive-expressive therapy plus group drug counselling in promoting abstinence (lower average drug use in past 12 months), despite the poorer retention in the individual counselling plus group drug counselling group.

As the authors point out the superiority of individual counselling plus group drug counselling in this study may be due to the additive effect of the single focus (on 12-step principles). Further, as Carroll (1999) comments, a focus on the 12-step principles in the orientation phase may have proven selective for those who were more amenable towards this approach. This, along with possible differential attendance at AA-type self-help meetings would also explain the need for less treatment in this group and thus lower retention. These factors are yet to be examined by the study group.

The authors suggested that one reason for the effectiveness of individual counselling, when it had not been found to be effective in previous studies, is the use of high quality manualised counselling with highly selected and experienced counsellors. Thus the greater intensity of treatment provided by individual counselling plus group drug counselling compared with group drug counselling alone may be interpreted as a response to a higher dose of treatment. On the other hand the interaction of two approaches based on different models (as with the psychotherapies plus group drug counselling) may be counterproductive. It could be argued that this study demonstrates that a singular concerted approach may be more effective than the more eclectic approach often found in drug counselling in the community. This point was also raised by Carroll (1999) in relation to the transfer from orientation to active phase. This study demonstrates that manualised individual therapy in

addition to group counselling leads to significant improvements in outcome. However, because of the correlation of selection (orientation), group and individual counselling procedures offered, it is difficult to draw hard conclusions from this study regarding the relative merits of individual counselling versus cognitive therapy and supportive-expressive therapy psychotherapies.

- Another very recent report has analysed information from DATOS (Appendix A2.5) on posttreatment outcomes for the community treatment of cocaine dependence (Simpson, Joe, Fletcher, Hubbard, & Anglin, 1999). This study followed up 1605 cocaine-using patients approximately one year after discharge from long-term residential, short-term inpatient or outpatient drug-free programs. Although this was an uncontrolled study, some outcomes provide valid information about treatment of cocaine abuse. It should be noted that this study involved patients of widely varying dependence and disability. The study by Crits-Cristoph and coworkers discussed above was much more selective and excluded patients with significant psychosocial or medical disability.

  This study found that long-term residential programs attracted patients with greater disability as measured by their Problem Severity Index – a summary measure derived from scores on seven indicators: multiple drug use, alcohol dependent, criminally active, unemployed, low social support, depression or anxiety and no insurance. It also found that longer time in treatment was associated with lower relapse to weekly cocaine use one year following discharge and that the less severe patients had a lower relapse to weekly cocaine use. Second- and third-order interactions revealed that in the long-term residential programs long-term patients were less likely to relapse than patients retained for a short term (<90 days).

  The authors concluded that it requires more than 3 months treatment to obtain change in medium to high severity groups. The study by Crits-Cristoph (1999) described above found the therapy with the shorter retention rate had better outcomes but probably included few patients with high severity as found in the DATOS sample. As Simpson and co-workers conclude, longer-term programs can significantly improve outcomes for more severely-affected cocaine abusers, provided they stay in treatment for more than three months.

SUMMARY POINTS

1. High early dropout rates are related to waiting list time, and therefore experts recommend rapid induction to treatment.

2. There is consensus that more intensive programs (sessions at least once per week) are more likely to be effective. No clear-cut treatment period has been specified, but research suggests that for patients with medium to severe disability, a minimum of 3 months is

recommended. Further research is required on these issues, taking into account both the severity of disability and the nature of the treatment being offered.

3. There is little research evidence to support use of psychodynamic therapy, while the efficacy of the 12 step approach requires further investigation.

4. The use of vouchers to reward abstinence, either alone or within a broader treatment program such as CRA, has been demonstrated to be effective in treating cocaine abuse. Further research is needed to establish appropriate schedules and most fitting contexts for these.

5. Recent research has lent support to the use of cognitive-behavioural techniques for treating cocaine abuse. In particular, manualised interventions which address coping skills and dealing with risky drug-taking situations have shown promise. However, the few RCTs to date have not clearly demonstrated the effectiveness of this intervention.

6. Results from various studies have suggested future directions for research especially in terms of matching patients to treatment on the basis of personal interests, abilities and level of disability.

6.0 AMPHETAMINES

6.1 INTRODUCTION

Description

Amphetamine is the prototype of the family of synthetic stimulant drugs, which includes the widely abused methamphetamine - also called "speed'. This form of amphetamine has been most abused because of its more pronounced effects on the central nervous system. It is powerfully addictive and can be made in a basic laboratory with readily available ingredients. Methamphetamine can be smoked, injected intravenously, snorted or ingested orally. Smoking and injecting lead to more immediate and intense pleasurable effects and in many areas have taken over from snorting as the most common method of use of amphetamines (National Institute on Drug Abuse, 1999c). Amphetamines act in a similar way to cocaine to stimulate the central nervous system, but their duration of action is much longer than that of cocaine. While cocaine has an approximate half-hour duration of action and has a half-life of 1 hour in the body, methamphetamine has acute effects that last from 8-24 hours and a half-life of around 12 hours. The reinforcing effects from amphetamine, as with cocaine, come from the increased availability of dopamine in the brain which gives rise to increased stimulation of the brain's reward systems.

Amphetamines act to cause wakefulness, increased mental alertness and ability to concentrate, reduced appetite and euphoria. They have traditionally been used by people in occupations where prolonged wakefulness is required and by those who wish to lose weight. More recently they have been used recreationally at youth dance parties, along with newer 'designer' drugs such as ecstasy. The 1998 report from the Australian National Drug Strategy (Australian Institute of Health and Welfare, 1999) found that amphetamine was the first drug injected by a majority of those who had ever injected illicit drugs, indicating a major role of amphetamines in initiating injecting behaviour in young users. Undesirable effects of amphetamines include overstimulation with restlessness, insomnia, tremor, stress and irritability. Physical tolerance develops rapidly and letdown after a binge can result in acute depression. Excessive and continued use of amphetamines can induce toxic psychosis characterised by delusions and hallucinations. It can also precipitate out-of-control rages and extremely violent behaviour.

Amphetamines have cardiovascular effects including tachycardia, hypertension and damage to blood vessels in the brain, predisposing to stroke. In overdose it can cause convulsions and hyperthermia which may be fatal. The fact that they are commonly injected means that they expose users to increased risks of HIV/AIDS and hepatitis C infections.

Epidemiology

Use of amphetamines has been increasing in Australia where latest National Drug Strategy figures have indicated a life-time prevalence of 8.7% while 3.6% have used in the past year. In

1995 the equivalent figures were 5.8% and 2.1% respectively (Australian Institute of Health and Welfare, 1999). The National Drug Strategy also found that amongst recent injecting drug users amphetamines were the most commonly injected drug (70%). In the U.S. the abuse of methamphetamine is increasing and spreading geographically as well as to a more diverse cross-section of the population. Consecutive National Health Surveys on Drug Abuse have found progressive increases in numbers of respondents who had ever used over the years 1994, 1995 and 1996, from 1.8 to 2.2 to 2.3 % of the population surveyed (National Institute on Drug Abuse, 1999c).

Treatment Setting, Detoxification & Withdrawal

Amphetamine and cocaine have similar actions, therefore much of the discussion above (Sections 5.2, 5.3 and 5.4) about cocaine withdrawal and detoxification as well as appropriate treatment setting applies to amphetamines (American Psychiatric Association, 1994; Lago & Kosten, 1994).

6.2 SPECIFIC INTERVENTIONS

Despite its high prevalence of use and the harms associated, there are very few specialist services catering for amphetamine abuse. As a corollary, little research has been carried out on appropriate treatments. Individuals with problems with their use of amphetamine rarely present for treatment at specialist drug and alcohol agencies, as users perceive these services to be primarily concerned with opiate abuse (Kamieniecki et al., 1998). However, they do present to primary care facilities and it is important that problem use of amphetamines is identified at this point. In this regard Kamieniecki et al proposed that research was needed in order to ascertain the perceived needs of users, knowledge and resources of generalist health staff and the availability and quality of specialist referral services. Similar to shared care proposals for alcohol use disorders, improved outcomes for methamphetamine users are likely to result if there are clear guidelines in place specifying appropriate brief treatment at the primary care level with referral as needed to specialised treatment agencies. Given the level of personal harm and social costs of abuse of this drug, such research as proposed by this group of researchers is clearly warranted.

6.2.1 Pharmacotherapies

In his review of treatments for stimulant dependence, Schuckit (1994) concluded that no pharmacological intervention had been found to be superior to placebo for the treatment of stimulant-dependent individuals. Kamieniecki et al (1998) provide a thorough review of the treatment needs and provision of treatment services for psychostimulant abuse in Australia. They reviewed the literature worldwide to ascertain the efficacy of possible interventions. They found that, despite concerns expressed in the literature regarding the long-term safety of amphetamine use, replacement of methamphetamine with prescribed oral amphetamine holds considerable potential as an effective treatment. Programs in the UK have found that services which offer prescription amphetamines attract large numbers of illicit amphetamine users. As with

methadone replacement therapy, programs using prescribed amphetamines provide an opportunity for users of 'street drugs' to come into contact with services which can provide advice, counselling and such harm minimisation strategies as needle exchange services, even if they do not take up the prescription offer.

Positive clinical impressions from recent UK observational studies have included reduced illicit amphetamine use, reduced injecting behaviour, improved social functioning and engagement with treatment services (Shearer et al., 1999). These have however been based on small samples and have lacked effective control groups. Contrary to fears expressed in the literature, there has been no evidence that psychotic episodes have been precipitated by the use of prescribed amphetamine (Charnaud & Griffiths, 1998; McBride, Sullivan, Blewett, & Morgan, 1997).

Although some small studies have been reported which assess the effectiveness of anti-depressants for amphetamine abuse, these studies have used small numbers and results have been equivocal (Galloway, Newmeyer, Knapp, Stalcup, & Smith, 1996; Jittiwutikan, Srisurapanont, & Jarusuraisin, 1997).

Thus it is important that suitable pharmacotherapies are sought and tested in order to assist individuals with amphetamine use problems. As with other drugs of abuse (including alcohol) it is important that any pharmacotherapy is supported by relevant and effective psychological intervention. Stitzer and Walsh (1997) provide compelling arguments supporting the importance of assessing pharmacotherapies along with best available complementary psychotherapies. They argue that combined treatments are likely to produce additive effects which are significant, whilst individually such therapies may appear ineffective.

6.2.2 Non-pharmacological interventions

The Treatment Improvement Protocol (TIP) for stimulant use disorders (Rawson, 1999) is a set of guidelines resulting from a series of consultations and consensus-finding with practitioners, researchers, administrators and client advocates. These guidelines list best practice for psychosocial treatment of cocaine and methamphetamine abuse. They recommend that most appropriate treatments for psychostimulant abuse are those based in learning theory and include contingency management, such as the community reinforcement-plus-vouchers approach, and cognitive-behavioural interventions focussing on relapse prevention. Relapse prevention strategies include modification of attitudes, expectancies and behaviour in relation to harmful drug use, and to increase coping skills. TIP recommends that all treatments should be manualised to ensure uniform delivery of best practice.

Kamieniecki et al (1998) point out that other psychosocial interventions such as therapeutic communities and 12-step programs have not been properly evaluated and research is needed to clarify their effectiveness in treating amphetamine abuse. Reviewers have also commented that an additional benefit of providing psychosocial assistance services may be that such services will

attract individuals who are experiencing problems with their drug use and who would not otherwise seek help. Clearly research is needed to measure the effectiveness of such services.

SUMMARY POINTS

1. There is a need for greater recognition of the prevalence and harms associated with amphetamine abuse.

2. It is recommended that the feasibility of a shared care approach to treatments for amphetamine abuse is investigated, with greater intervention by GPs at the primary level and improved specialised referral services.

3. Treatments for amphetamine abuse have been poorly researched. To date no pharmacological interventions have been found to be effective. One possible area of research is the use of replacement medication based on harm minimisation principles. Other pharmacotherapies may emerge once there is appropriate recognition of the extent of the problem.

4. As with cocaine, care is needed in applying pharmacotherapies in a situation where a potentially very harmful drug is being abused. Pharmacotherapies should be supported by effective psychosocial interventions.

5. Manualised contingency management and cognitive-behavioural therapy incorporating relapse prevention have been recommended as the best available therapies for amphetamine abuse. There are no published trials of these interventions and there is a need for more formal controlled research on these approaches. Similarly the efficacy of 12-step and therapeutic community approaches should be assessed.

7.0 APPENDICES: LARGE-SCALE REVIEWS AND STUDIES

A1: LARGE-SCALE REVIEWS

The present review draws on a number of recently conducted reviews of the alcohol and drug treatment literature. These studies are described on the following pages and their results are referred to in the main body of the report as appropriate.

A1.1 An Outline for the Management of Alcohol Problems: Quality Assurance Project.
(Mattick & Jarvis, 1993)

This project provided a thorough review of the evidence for treatment of alcohol dependence. The review was conducted in three parts. The first was a review of the alcohol abuse treatment literature; the second a survey of current practice in Australia; and the third an analysis and integration of the first two stages by an expert committee. This methodology was based on procedures developed by Andrews et al (Andrews et al., 1982) to establish guidelines for the management of a number of psychiatric disorders. Thus, it presents treatment outlines for various levels of alcohol use, which had been shown to be well supported by available research evidence and expert opinion.

The review of the relevant empirical treatment outcome literature for alcohol problems combined a strictly quantitative meta-analysis with a qualitative procedure to integrate findings in the area. The researchers maintained a comprehensive and up-to-date set of references on treatment outcome studies which they obtained from Psychological Abstracts, Index Medicus databases and other broad reviews in the area.

The meta-analytic approach involves calculating a standardised statistical assessment of the size of effect of a given treatment which allows for direct comparison of results from different studies, even if they have used different outcome measures. A positive effect indicates that the treatment under review was superior to a no treatment condition while a negative effect indicates the converse. In order to counter previously-expressed criticisms of the meta-analytic approach, the reviewers included only randomised (or matched) controlled studies using methodologically sound and accepted treatment procedures on clinically relevant samples of clients.

The qualitative component was included in order to incorporate information from studies which were relevant but which did not contribute outcome data directly usable by meta-analysis. This qualitative aspect also included information on the statistical significance of differences between treatment and control conditions, where available. Where the two approaches agreed, this was considered to enhance the robustness of the overall findings; and where they differed, an attempt was made to resolve apparent contradictions. In a similar manner, agreements and

differences between the findings of this review and previous large-scale reviews were incorporated and discussed throughout.

The survey of current practice which was carried out in March 1990, was designed to achieve a better understanding of the types of intervention that workers who deal with alcohol-dependent and alcohol-abusing populations believe to be valuable. 329 treatment centres were surveyed which represented an 82% return rate for all identifiable alcohol treatment agencies in Australia. Areas covered in the survey were:

- assessment/screening procedures;
- use of detoxification;
- treatment goals, length, setting, target group and forms of intervention;
- severity of clients;
- aftercare;
- problems encountered;
- relapse prevention; and
- procedures for dealing with other drug use.

In its final chapter, the report presented a list of **recommendations** regarding alcohol treatment which represented the views of the expert committee after it had considered the results from the treatment-outcome literature, the survey of specialist agencies and the views of each expert. Rather than providing inflexible rules for intervention, or detailed instructions for delivery of these interventions, the report aimed to provide outlines for ideal treatment approaches. The expert committee emphasised that it is intended as a resource to encourage greater flexibility of approach by people working in the field and to ensure awareness of the existence of treatments which have proven to be effective.

A1.2 A Treatment Outline for Approaches to Opioid Dependence: Quality Assurance Project. (Mattick & Hall, 1993)

This was part of the same *Quality Assurance in the Treatment of Drug Dependence* project, for which a review of effective treatments for alcohol problems appears in Section A1.1 above (Mattick & Jarvis, 1993). A similar methodology was used, combining an empirical and narrative review of relevant research, a survey of current practice, and the views of an expert panel.

The review of the treatment-outcome literature covered the more common treatments for opiate dependence. It included:

- detoxification;
- drug maintenance treatments including methadone, levo-alpha form of methadone(LAAM), antagonists such as naloxone and naltrexone and the agonist-antagonist buprenorphine; and

- drug-free approaches including self-help groups, inpatient and outpatient drug-free counselling, therapeutic communities, behavioural treatment approaches such as aversion therapy, self-control training, social skills and contingency management; family therapy, and the impact of after-care services.

Because of the small number of randomised controlled trials in this domain, it was not feasible to carry out a meta-analysis of such trials. Instead a structured approach was used in which the best available evidence for each treatment method was critically analysed. The order of preference for standards of evidence ran from randomised controlled trials to quasi-experimental studies, longitudinal studies and, finally, single group studies. Where no data was available on a procedure, commentaries were used.

The survey of current practice included 229 agencies (Baillie, Webster, & Mattick, 1992) which reflected an 80.6% response rate for the 284 agencies contacted. Variables covered were:

- assessment procedures;
- detoxification methods used - medicated and/or unmedicated;
- treatment goal(s);
- treatment methods; and
- aftercare procedures

Finally, **recommendations regarding intervention** were developed, based on an analysis by the expert committee of the review of the literature, the survey findings, and the individual views of the experts themselves.

Thus, this report provides guidelines for best practice for management of opioid dependence, supported by available evidence and expert opinion. Again it is emphasized that these guidelines should not be regarded as inflexible rules for intervention, and that new and innovative approaches should be encouraged and evaluated scientifically, in the interests of advancing the treatment of opioid dependence.

A1.3 What Works? A Methodological Analysis of the Alcohol Treatment Outcome Literature. (Miller et al., 1995)

This review is a broad-ranging meta-analysis of outcomes for alcohol treatments described in the literature up to 1993. Criteria for inclusion were (1) treatment directed at alcohol problem, (2) treatment compared with a control or another treatment, (3) proper procedure used to equate groups prior to treatment, and (4) included at least one outcome measure of drinking and/or of alcohol-related problems. 219 studies were found to fit these criteria but 8 of these were excluded because outcome criteria were not ratable. The purpose of the meta-analysis was not only to rate effectiveness of treatment modalities, but to consider other factors which

may relate to the broad quality and effectiveness measures i.e. whether quality of study and effectiveness outcomes are correlated, or whether either relates to cost, severity of problem, sample size, age or gender profile.

The 211 studies in the meta-analysis were rated for methodological quality by a rigorous 6-stage process which included attempts to gain consensus with authors regarding the ratings made for their studies. There were 12 scales yielding categorical ratings which were then summated to give the overall Methodological Quality Score (MQS). These categories were:

- group allocation where a score of 4 was given for random allocation, whilst 0 was given for nonequivalent groups and 1,2 or 3 for studies in-between;
- quality control - 1 for using standardised procedures and 0 for no standard procedures;
- follow-up rate;
- length of follow-up, with 0 for less than 6 months, 1 for 6-11 months and 2 for greater than 12 months;
- type of contact which rated personal or telephone contact as 1 and questionnaire or unspecified as 0;
- use of collateral evidence;
- objectivity in record keeping and assessment;
- treatment dropout rate clearly stated;
- loss to follow-up clearly stated;
- use of treatment blind researchers for follow-up;
- use of appropriate statistical analyses; and
- parallel replications at two or more sites with different research teams.

The highest possible MQS was 17 because group allocation, follow-up rate and follow-up length were considered relatively more important and used more than the 0/1 categories of the other scales.

Outcomes were rated using a 4-point scale:

- +2 for strong evidence for a specific positive effect e.g. treatment found to be better than no treatment, or adding the treatment is better than not adding it;
- +1 for evidence for specific positive effect e.g. comparisons between two specified treatments, no control;
- -1 no evidence for specific positive effect e.g. equivalent effects of two levels or doses of the treatment; or
- -2 no evidence for specific positive effects - stronger designs e.g. treatment no better than no treatment control.

In assessing outcomes, this study used the intention to treat model, even if the original study did not. Cumulative evidence scores (CESs) for each treatment modality were obtained from the 211 studies, by summing all relevant cross-products of MQSs by outcome ratings. These are listed, in order of effectiveness for each modality in Table A1, along with number of positive studies (Np), number of negative studies (Nn), a weighted evidence index (WEIn) derived from

Np and Nn, MQS, mean severity of subjects in relevant studies (SEV) and estimated cost for whole treatment (COST). Modalities with two or fewer contributing studies have been listed separately from the rest at the bottom of the table. These results are discussed in the main body of the review on interventions for alcohol.

Overall Evaluation

This is a well-designed and thorough meta-analytic study which adds significantly to the literature in support of effective and cost-effective treatments for problem drinking. However, it can be criticised on some counts:

- It is unclear whether adequate account is made of the wide range in sample sizes of the studies used. For example, the studies on CRA used small numbers yet obtained strong findings which resulted in a moderately positive CES score. With sample sizes lower than 20 (as occurred in these and several other studies), it is difficult to have confidence in a meaningful outcome.

- The CES scores are difficult to interpret, except relative to each other and their relationship to 0. It is not possible to talk about levels of significance with the data as presented. In the QAP (Mattick & Jarvis, 1993), measures of effect size were used to overcome this problem and it is difficult to see why such measures were not used here.

- In assessing outcomes, the CES used the "best" outcome if there were several e.g. at 0, 3, or 6months post-treatment. The authors admitted that usually the shorter-term outcomes were the strongest, so that the resultant CES scores are likely to be based on quite short follow-up periods. Length of follow-up was one of the 12 factors contributing to the QMS, but it could have a low value and be associated with a high QMS. The QAP (Mattick & Jarvis, 1993) overcame this problem by measuring effect sizes for each different period of follow-up found in the research.

- A further problem, pointed out by the authors, is that the effectiveness ratings for two modalities may be equal and mediocre, but for different reasons. It may be that there have been few studies on a particular modality or that there have been several studies with significant positive and negative outcomes which even out overall.

TABLE A1: Summary of cumulative evidence scores (Table 2.4 in Miller et al. 1995).

TREATMENT MODALITY	Np	Nn	WEIn	MQS	SEV	CES	COST
Brief Intervention	17	6	+26	13.0	2.5	+239	46
Social Skills Training	11	5	+15	11.1	3.8	+128	270
Motivational Enhancement	5	2	+6	13.6	3.0	+87	46
Community Reinforcement Approach	4	0	+6	13.3	3.0	+80	492
Behaviour Contracting	4	0	+6	10.8	3.8	+73	164
Aversion Therapy, Nausea	3	3	+1	10.3	3.8	+34	1380
Client-Centred Therapy	3	1	+3	9.8	3.3	+34	738
Relapse Prevention	3	4	0	12.6	3.0	+34	433
Self-Help Manual	2	1	+1	12.7	3.0	+33	20
Cognitive Therapy	3	4	0	10.3	3.6	+22	433
Covert Sensitization	3	5	-1	10.9	3.5	+18	328
Marital/Family, Behavioural	3	2	+2	13.4	3.6	+15	513
Disulfiram	10	11	+7	10.8	3.8	+09	637
Behavioural Self-Control Training	14	16	+10	13.0	2.9	-07	105
Systematic Desensitization	1	2	-1	11.0	3.0	-07	120
Lithium	3	3	+1	11.3	3.8	-08	441
Marital/Family, Nonbehavioural	3	4	0	12.4	3.7	-22	513
Aversion Therapy, Electrical	6	9	+1	11.1	3.8	-25	410
Hypnosis	0	4	-4	10.8	3.8	-41	738
Milieu Therapy	3	7	-3	11.7	3.6	-41	1960
Psychedelic Medication	2	6	-4	9.9	3.6	-45	637
Unspecified “Standard” Treatment	0	3	-3	10.7	3.0	-53	738
Videotape Self-Confrontation	0	6	-6	10.8	3.8	-77	548
Antianxiety Medication	1	7	-6	7.4	3.3	-79	637
Metronidazole	1	10	-9	9.6	3.7	-102	637
Relaxation Training	3	11	-7	11.1	2.8	-109	120
Confrontational Counselling	0	7	-7	12.4	2.9	-125	375
Psychotherapy	1	9	-8	11.3	3.1	-127	4050
General Alcoholism Counselling	1	15	-14	11.3	3.4	-214	738
Educational Lectures/Films	3	18	-14	9.9	2.2	-239	135

MODALITIES WITH TWO OR FEWER STUDIES

TREATMENT MODALITY	Np	Nn	WEIn	MQS	SEV	CES	COST
Sensory Deprivation	2	0	+2	10.0	1.0	+40	92
Developmental Counselling	1	0	+1	9.0	2.0	+28	738
Acupuncture	1	0	+1	10.0	4.0	+20	923
Exercise	1	1	0	10.5	2.5	+9	270
Aversion Therapy, Apneic	1	1	0	10.0	3.5	0	570
Problem-Solving Training	0	1	-1	12.0	4.0	-12	164
Functional Analysis	0	2	-2	11.0	2.5	-22	164
Self-Monitoring	1	1	0	12.5	3.5	-23	20
Antidepressant Medication	0	2	-2	6.0	3.0	-24	457
BAC Discrimination	0	2	-2	12.0	3.5	-24	500
Calcium Carbamide	0	2	-2	10.0	4.0	-32	637
Antipsychotic Medication	0	2	-2	9.0	3.5	-36	637
Alcoholics Anonymous	0	2	-2	13.0	3.5	-52	0

7.0 APPENDICES: LARGE-SCALE REVIEWS AND STUDIES

A1.4 Methadone Maintenance Treatment and Other Opioid Replacement Therapies *(Ward et al., 1998e)*

This edited book is an update of a previous review of the research literature by the same group of authors (Ward, Mattick, & Hall, 1992). The 1992 review covers such areas as the effectiveness of methadone maintenance treatment in preventing illegal opioid use, its effect on HIV/AIDS risk, and treatment variables such as assessment, dose, duration, urinalysis and counselling. Maintenance during pregnancy and the withdrawal strategies were also researched. This original review process involved identifying and critically reading the relevant literature from Psychlit and Medline as well as bibliographies from this literature, from researchers working in the field and from the library of the Australian Council on Alcohol and Other Drug Associations. The draft review was then commented upon by a panel of experts working in the field of methadone maintenance in order to detect omissions, errors in interpretation and how well the review fitted with their clinical experience. The draft was then revised on the basis of these comments.

The new edition is, however, broader than the first edition in that it includes opioid maintenance treatments other than methadone. It has also changed format from a review to an edited book with contributions from practitioners and policy makers in the field. The book provides a clear and cogent summary of the origins and ethical bases of opioid maintenance as well as summarising the results of research on outcomes, process and related issues. This review also covers patient factors which may influence outcome, cost effectiveness, factors affecting delivery, staff training considerations and methadone maintenance in prisons.

Chapter 1 (Hall et al., 1998a) deals specifically with the effects of methadone maintenance on heroin use and crime. Randomised controlled trials (RCTs) were not standard research procedure prior to the introduction of methadone maintenance and as it quickly became widely available, there arose an ethical issue regarding withholding the treatment in order to obtain a control sample for "research purposes". Because of the paucity of randomised controlled trials to provide evidence of the efficiency of methadone maintenance, the summary of the outcome research in this chapter also includes observational studies - both controlled comparative and pre-post studies. Apart from a shortage of good RCT evidence, the authors argued that it is important to include data from quasi-experimental studies in order to justify the inference that individuals included in RCTs are comparable to those receiving treatment in practice. The level of rigour of the various sources of evidence is clearly evaluated throughout.

Chapter 2 (Ward et al., 1998b) reviews the evidence regarding methadone maintenance and HIV and infectious hepatitis. Studies which assess the effects of methadone maintenance on rates of HIV infection and injection-related risk behaviours are evaluated separately. The third chapter (Darke, 1998) reviews the literature regarding factors which moderate MM treatment outcome, which fall into three main areas: drug use other than heroin, psychopathology and

methadone dose diversion. Chapter 5 (Ward & Sutton, 1998) evaluates various issues relating to estimations of cost-effectiveness - in particular the rationale for determining cost effectiveness, and the types of analyses that can be employed – as well as providing an overview of the relevant literature. Chapter 6 (Mattick et al., 1998a), the final chapter on outcome, reviews the literature on alternative opioid replacement treatments for heroin abuse. The alternative treatments reviewed are LAAM, heroin, buprenorphine, naltrexone and injectable (cf. oral) maintenance.

A2: LARGE-SCALE STUDIES

There has been a number of large and important treatment outcome studies reported for drug and alcohol. While not randomised controlled trials, the size of these studies warrants detailed consideration of their findings.

A2.1 The California Drug and Alcohol Treatment Assessment (CALDATA) (Gerstein et al., 1994)

CALDATA is a large-scale before-after study of the effectiveness, costs and overall economic value to society of drug and alcohol treatment in California. In the first phase of the study, a random sample of 3055 individuals was selected from the approximately 150,000 individuals discharged from treatment between October 1991 to September 1992. In the case of methadone maintenance, those selected were in treatment for the identified period. Treatment records were accessed in order to provide additional information and to verify self-report data obtained during the follow-up period. This sample was selected such that it represented all participants in the following treatment groups (bracketed is the number of programs accessed):

- residential programs in general (21);
- social model recovery houses (23);
- outpatient nonmethadone (29);
- methadone maintenance outpatient (18); and
- methadone treatment and detoxification which can be both residential and outpatient (19).

While the residential and outpatient nonmethadone programs tended to treat the whole range of addictions, the social model was restricted to alcohol and/or stimulant dependency and methadone treatments to opioid dependency.

The second phase of this program involved interviewing those members of the selected sample who were contactable during the next 9 months (N=1859; 61%). These interviews occurred on average 15 months after treatment, extending to 24 months for those on continuing methadone treatment.

Outcomes

Usage of alcohol and drugs

- A reduction in use in an average of 40% of all those interviewed for all drugs and alcohol was reported for the period of the study.

- Treatment for stimulants was about as effective as for alcohol and both were somewhat more effective than heroin treatment in reducing use.

Personal/social function

- There was a significant (17%) improvement overall in self-reported health which was verified by significant decrease in hospitalization rates (see below).
- There was no overall positive effect for personal economic situation.
- Employment was positively affected by longer length of treatment stay.

Public health & safety

- Treatment resulted in a two-thirds decline in level of criminal activity in the sample. There were significant reductions for all treatment modalities with greatest reductions for the social model recovery participants and least for the discharged methadone group. The longer time spent in treatment, the greater the reductions in criminal activities. Participants whose main drug was alcohol showed greater reductions than those using heroin. Sex, age and ethnicity did not relate to reduction in criminal activity due to treatment. (However see note below re statistical analyses.)
- There was an approximately 1/3 reduction in hospitalizations as well as improvements in other health indicators.
- Paradoxically treatment led to increased public medical insurance rebates, as treatment qualifies individuals for disability coverage in California.

Cost effectiveness

- This was considered from both the taxpayer's and overall society's points-of-view. Costs to society include the criminal justice system, victim losses resulting from predatory crime, health care utilisation by users and lost legitimate earnings of users. Costs to taxpayers includes all the above minus earnings of user but including income transfers i.e. taxpayers money being spent on substance abusers.
- The study found that costs to taxpayers of treating the 150,000 users represented by this study was $US209 million; while benefits during treatment and in the year after were worth approximately $US1.5 billion, due largely to decrease in crime. The benefits of drug and alcohol treatment were shown to outweigh costs by ratios of from 4:1 to more than 12:1 depending on drug and treatment.
- Savings to society were lower with cost-benefit ratios ranging from 2:1 to more than 4:1 for all treatment modalities except discharged methadone recipients.

Overall Evaluation

The study design presents some problems which were addressed to a greater or lesser extent by the authors:

- 39% of the randomised sample could not be interviewed. However, careful comparisons of the responding and non-responding groups led the authors to conclude that loss of selected sample participants to follow-up was due to factors unrelated to type or quality of treatment or to individual risk factors.

- Information was obtained in the one interview which, for pre-treatment information, required retrospective recall of activities carried out up to 3 years prior to interview. Inherent biases in retrospective recall may have influenced outcomes. Considering that the major conclusion of the study is that it is cost-effective to treat addictions and that this is due largely to participants' estimates of their before-and-after-treatment criminal activity, then if there is a tendency to under-report recent criminal activity the results may be spurious. The researchers excluded the last 30 days' criminal activities because of such concerns but this may not have been sufficient to remove this highly relevant confounding factor.

- There appear to be no corrections made for the large number of t-tests carried out in the study. However, virtually all before-after differences are large and significant which means that it is likely that this data reflects considerable improvement over the range of outcome variables.

- The study would have had more strength if multiple regression analysis was used instead of a series of t-tests and ANOVAs. Demographics such as sex, age, ethnic/social background need to be controlled when drawing conclusions about other variables in the study. For example the study found significant differences for sex and ethnic group on types of drug used, which means that the various treatment programs studied would have different compositions of these factors. Furthermore, comparisons between programs which treat mainly heroin users and those which treat alcoholics may be inappropriate if they are quite different demographically. If participants in the social model program tend to be alcohol-dependent then the greater improvement in employment status for this group post-treatment could well be a social class effect. So although they went to great lengths to have a sample representative of the treatments used, they have failed to control for other significant factors.

- Even though the pre-post- design helps control for individual differences, it does not take into account placebo effects. What such a study is able to demonstrate is that some attention leads to significant economic benefit and possibly more attention leads to more economic benefit. Other studies discussed later in this review use controlled designs which enables them to tease out factors which are most likely to influence treatment outcome more effectively.

A2.2 Matching alcoholism treatments to client heterogeneity: Project MATCH posttreatment drinking outcomes (Project MATCH Research Group, 1997).

This study was designed to test the effectiveness of matching three different psychotherapeutic treatments for alcohol dependence to particular client attributes. The basic "matching hypothesis" was that clients who are appropriately matched to treatments will show better outcomes than those who are unmatched or mismatched.

Two parallel but independent randomized clinical trials were undertaken. One trial used clients enrolled for outpatient therapy (N=952), while the other involved clients who had undergone residential treatment for at least 1 month prior to the study and were classified as being in aftercare (N=774).

Treatment strategies, client matching variables and the specific hypotheses for the study were based on theoretical considerations and prior empirical findings.

Three treatment strategies were compared. Cognitive Behavioural Coping Skills Therapy (cognitive behavioural therapy) is based on social learning theory which assumes that alcohol abuse stems from life experiences and poor learning of life skills, and thus treatment addresses skills deficits and coping with situations where relapse is likely to occur. Motivational Enhancement Therapy (MET) focuses on motivational strategies which are aimed at mobilizing the individual's own resources rather than specifying a particular path to recovery. Twelve-Step Facilitation Therapy (TSF) is based on the concept of alcoholism as a spiritual and medical disease and aims to foster participation in traditional fellowship activities of AA Each therapy was individually administered and protocols were specified in detailed therapy manuals.

An extensive review of the literature yielded the following client characteristics to be used as matching variables:

- severity of alcohol involvement,
- cognitive impairment,
- client conceptual level,
- gender,
- meaning seeking,
- motivational readiness to change,
- psychiatric severity
- social support for drinking
- sociopathy, and
- typology.

The primary outcome measures were percent days abstinent (PDA) and average number of drinks per drinking day (DDD); and these were used to test sixteen specific matching hypotheses which were generated from the review of previous research findings.

Subjects were interviewed intensively prior to random assignment to treatment condition. They were then interviewed at the end of treatment (3 months), and at 6, 9, 12 and 15 months after entry to the study. Collateral measures and test-retest interview measures indicated that interviewer assessments were both reliable and valid.

Outcomes

Usage of alcohol and drugs

- Irrespective of treatment strategy, there were substantial positive changes in PDA and DDD for both aftercare and outpatient subjects which were largely sustained over the 12 month follow-up. For example, prior to treatment, after-care patients were abstinent approximately 20% of days per month, while at post-treatment and at 15 months this became 90% days abstinent per month. The relative figures for outpatient subjects were approximately 23% pre- and 80% post-treatment.

- No consistent and clinically meaningful differences were found between the three treatments in either group.

- The study found little support for the matching hypothesis. Only one attribute showed a significant interaction between personal attribute and treatment type. For the outpatient group low psychiatric severity showed more abstinent days with the 12-step (TSP) treatment than with the cognitive behavioural therapy approach.

Overall Evaluation

As the authors noted, the general lack of support for the matching hypothesis from this study does not require outright rejection of the hypothesis. The sample used specifically excluded codependent subjects and the homeless who would be regarded as at greater than average risk on a variety of measures. It is also possible that treatments for illicit drug abuse may fit the matching hypothesis. The use of rigorous manual-guided and individual treatment procedures in this study has possibly ensured a maximal success rate with little room for matching effects to emerge.

For the purposes of evaluating the cost-effectiveness of treatment, this study did not include a no-treatment control group and so there is no direct measure of the efficacy of the three treatments used nor of treatment in general. Hence measures of the cost-effectiveness of the

procedures trialled cannot be obtained. However, as noted in the report, the striking decrease in drinking following treatment suggests that participation in any of these treatments will lead to substantial and sustained changes in drinking which, in turn, would have personal, public health and thus economic benefits.

A2.3 The National Treatment Outcome Research Study in the United Kingdom (NTORS): Six-month follow-up outcomes *(Gossop et al., 1997)*

NTORS is the first broad-based study of treatment outcomes carried out in the United Kingdom (UK). Fifty-four treatment agencies were chosen for the study in order to represent the four main treatment modalities in the UK. Eight inpatient drug dependence units (DDUs), 15 residential rehabilitation units, 16 methadone maintenance clinics, and 15 methadone reduction programs yielded some 1075 problem drug users. Participants were selected from those who met inclusion criteria from consecutive admissions to each agency during the 5 months from March to July 1995. Inclusion criteria were (a) starting a new treatment episode, (b) presenting with a drug-related problem, and (c) able to provide an address in the UK for follow-up. Those with a primary diagnosis of alcohol dependence and those who had been previously enrolled in the study were also excluded.

Inpatient DDUs tend to be unique to the UK and typically focus on illicit drug (usually opiate) problems. They are based within psychiatric hospitals and provide medically supervised detoxification along with some psychosocial rehabilitation. Duration of treatment programs ranges from 2 weeks to 3 months. *Rehabilitation units* are represented in the UK by 12-step abstinence-based programs, therapeutic communities, Christian houses, and general houses. They tend to be residential, often rural-based, and provide intervention and support services aimed at changing the individual's lifestyle. Most require the participants to be drug-free on entry. Treatment length varies from several weeks with after-care to more than a year. In the UK, *Methadone maintenance* programs can be administered through specialist clinics or through independent general practitioners, and can involve nonsupervised or supervised (structured) methadone administration. *Methadone reduction* programs are abstinence-oriented and may vary in duration from a few weeks to many months. Reduction schedules may be fixed by the prescribing agency or may involve some negotiation with the individual.

Data was collected at intake and 6 month follow-up using a manual-guided structured interview, which covered patterns of drug and alcohol use, health risk behavior, readiness for treatment and motivation to change, physical health problems, criminal behavior, and treatment history. Urine samples were also taken from 50% of sites for comparison with self-report data. High rates of concordance were found between these two measures across all drug groups.

A total of 809 patients (75.3%) were contactable for the 6 month's follow-up interview - some 43% still being in their index treatment episode.

The most frequently reported problem drug for all participants was heroin, ranging from 72% of those in residential treatment, 85% in inpatient DDUs, 91% in methadone maintenance to 98% in methadone reduction. Many of the clients reported excessive alcohol use and virtually all were polydrug users. Those not contacted at follow-up tended to have higher numbers of days of heroin usage in the 3 months prior to intake than those contacted.

Outcomes

This paper is the first of several to be written to report the outcomes of NTORS. It covers immediate (6-month) outcomes with regard to usage of drugs only. Measures compared over the 6-month period were use of heroin, cocaine (all types), crack cocaine, amphetamines, illicit methadone, alcohol on a daily basis, injecting behavior and sharing of injecting equipment. Results regarding other relevant outcome measures relating to personal/social functioning, public health and safety, and cost-effectiveness are to be the subject of later reports. The project has also been extended to include follow-up over a 5-year period with a mid-term report at 2-3 years.

Usage of alcohol and drugs

At 6 month follow-up significant reductions were found in:

- the use of illicit opiates (heroin and illicit methadone) with the proportion of clients regularly using, and the frequency and amount of usage, dropping significantly at all four modalities,
- injecting drug use and needle sharing in all modalities.
- amphetamine use in the methadone maintenance group, and
- the use of all categories of stimulants and daily drinking in the rehabilitation group.

As the researchers pointed out, the rehabilitation group for which most improvements were found also comprised those people most likely to be abusing stimulants and alcohol and to have shared injecting equipment prior to intake.

Overall Evaluation

There was a loss to follow-up of 24.7% of the sample which is considered modest with the type of groups being studied. The authors claimed that there was no fundamental differences between contacted and non-contacted group, so there was no need to adjust data for loss to follow-up. However, their data showed that a greater proportion of the more frequent heroin users may have been lost, which may limit the generalisability of their findings.

The authors stressed the importance of avoiding direct comparisons between modalities because of lack of knowledge about self-selection for particular modalities, and order effects of treatments. They found that there was a tendency for clients to have tried community-based programs first, before proceeding to residential programs. They also point out that different

findings between modalities is likely to reflect differences in the types of client attracted (age, previous treatment, severity of dependence, personal/social influences, etc). Also within modalities there is likely to be a diversity of treatment approaches which is not considered in this report.

Effects of treatment on physical and psychological health behaviors, social functioning and criminal behavior and the reporting of further outcomes for usage from NTORS over the next five years will be of considerable practical and research interest. Importantly, as found with the CALDATA study in the US (Gerstein et al., 1994), it is likely that considerable cost benefits will accrue, simply from these more immediate reductions in hazardous drug-taking behavior.

A2.4 The Drug Abuse Treatment Outcome Study (DATOS) in the U.S.: 1-Year Follow-up. (Hubbard et al., 1997).

The Drug Abuse Treatment Outcome Study (DATOS) is the third and most comprehensive in a series of national community-based treatment outcome studies sponsored by the National Institute on Drug Abuse (NIDA) in the U.S (Flynn, Craddock, Hubbard, Anderson, & Etheridge, 1997). The first study in this series was the Drug Abuse Reporting Program (DARP) which collected data on 44,000 clients entering treatment between 1969 and 1973 and set the standard for longitudinal field-based research on drug treatment effectiveness (Fletcher, Tims, & Brown, 1997). The second study in the series was the Treatment Outcome Prospective Study (TOPS) which was an expansion of DARP to obtain more patient and program information for the cohort of clients entering treatment between 1979 and 1981 (n=11,000).

Both of these studies demonstrated reduced usage following treatment, and that length of stay in a program positively influenced outcome. A minimum stay of 3 months was necessary to produce positive changes - beyond those first three months, outcomes improved with time spent in treatment. TOPS also demonstrated the cost-effectiveness of treatment as a consequence of decreased predatory crime, both during and following treatment; and that legally mandated treatment could be effective in interrupting criminal and drug abuse careers. The authors point out that the focus of DATOS has altered to reflect (1) changes in preference for particular drugs, in particular the increased cocaine and crack cocaine use in the U.S.; (2) increased concerns regarding HIV infection; and (3) the reduced availability of treatment services in a system increasingly dominated by managed care strategies.

Description of the Study

DATOS is a multi-site prospective cohort study of adults entering drug and alcohol treatment across the U.S. between 1989 and 1996. Overall, an initial sample of 10,010 individuals was identified from 96 treatment programs in 11 cities. Participants were required to complete two 90-minute, structured interviews approximately one week apart (Intake 1 and Intake 2). The

Intake 1 interview obtained baseline data on sociodemographics, drug use and other behaviours. The Intake 2 interview assessed psychiatric status, health status and social functioning.

In-treatment client-level data was collected by structured interview for those still in treatment at 3, 6 and 12 months, and at 12 months post-treatment. It was planned to further interview this cohort at 36 months post-treatment. Information on treatment programs was obtained through director-counselor questionnaires. This included information on treatment philosophy, services available, program policies and procedures, client characteristics, retention and dropout, staffing, caseload size, treatment planning and aftercare, and practices related to methadone and other medications.

Programs were selected such that they represented clinical treatment in typical community-based programs offering a wide array of services in medium to large cities in the U.S. The four major treatment modalities covered by the study were:

- **outpatient methadone treatment (OMT)**, including private for-profit freestanding methadone programs, non-profit community-based programs, hospital-based community clinics, and county-managed clinics or programs;
- **long-term residential (LTR)**, including traditional and modified therapeutic communities and other long-term programs requiring more than 6 months in-residence treatment;
- **outpatient drug-free (ODF)**, including therapeutic community-managed outpatient programs, non-profit community-based organizations, criminal justice programs, mental health programs for substance abusers, short-term managed programs, and private for-profit programs; and
- **private/public short-term inpatient (STI)** chemical dependency programs, including freestanding for-profit and non-profit short-term chemical dependency programs, public and non-profit hospital settings, and county-managed programs.

The follow-up sample was selected from those 8110 participants who completed both intake interviews and who were from programs with more than 20 clients. The latter restriction was imposed due to the limitations small numbers place on analysis and to simplify follow-up procedures. In all 76 programs were represented (21 OMT, 19 LTR, 24 ODF and 12 STI). The follow-up comprised 4786 clients, stratified and randomly chosen to include at least 1150 for each treatment modality; and weighted toward clients who completed 1- and 3-month in-treatment interviews. Of these 4786 clients, 557 were deemed ineligible due to inaccessibility or incapacity. Of the remaining 4229 clients, 70% (n=2966) were interviewed successfully at 12 month follow-up.

A random sample of 25% (770) of follow-up participants was selected to have urine testing and samples were successfully obtained from 80% (618) of these. Drugs screened for in the urine test were amphetamines, barbiturates, benzodiazapines, cannabinoids, cocaine metabolite, methaqualone, opiates and phencyclidine. These measures will be used to assess the reliability of the self-report data in a later report.

Outcomes

Usage of alcohol & drugs

(a) Changes in Usage from the preadmission year to the follow-up year.

Usage in preadmission and follow-up years for each modality is shown in Table A2. As can be seen, there are major reductions in most types of drug use across all modalities. In **OMT**, the percentage of clients using heroin weekly or daily (89.4%) had reduced to a third of this value in the follow-up year (27.8%). For this same modality, cocaine usage almost halved (41.9 to 21.7%), whilst marijuana and alcohol use did not change markedly. In **LTR**, usage in all drug categories reduced by half to two-thirds between preadmission and follow-up years and in **ODF** and **STI**, marked reductions were found in the use of all drugs.

The authors pointed out that improvement was also seen for those who completed intake and remained in treatment for less than a week, which can be attributed to motivation and other non-treatment factors. Hence, in an attempt to account for these confounding factors, this study next considered effects on usage and length of treatment.

(b) Usage and Treatment Duration

Chi-square comparisons were made between individuals who stayed in treatment from 1 week to less than 3 months, and those who stayed more than 3 months, in OMT, LTR and ODF modalities; and between those who stayed less than 2 weeks, and those who stayed more than two weeks, in STI. However, of greater interest are the results of multivariate logistic regression analyses which compared usage rates for a minimal (baseline) treatment stay with various specific retention and post-treatment periods. Table A3 gives the relevant time periods and odds ratios (ORs). An OR indicates the odds of drug use and other behaviours relative to the base estimate of 1.00 for clients in treatment for less than 3 months, except for STI clients, for whom the base was clients in treatment for less than two weeks. ORs of less than 1.00 indicate decreased odds of usage while ORs of greater than 1.00 indicate an increase in such odds. According to the authors, this analysis strategy enables a clear statement of the likelihood that various lengths of exposure to treatment for this sample were related to important clinical and significant statistical reductions in the odds of drug use and other behaviours in the follow-up year.

This analysis confirmed conclusions drawn from the descriptive data described above, and also findings from the earlier TOPS study. Clients who stayed in **OMT** until the follow-up period had an OR of .24 for weekly or more frequent heroin use at follow-up compared with clients staying less than 3 months ($p<.01$). Furthermore, the odds of weekly or more frequent marijuana use for long-term OMT clients was significantly decreased. However, the odds of

heavy alcohol use significantly increased for those who stayed between 3-6 months, compared with the 0-3 months in OMT. This effect decreased with greater treatment time. With other factors taken into account, OMT had no significant effect on cocaine use, despite the reduction reported in (a) above at 12 months posttreatment.

The numbers in the heroin usage groups were too low to permit meaningful analyses in the other three modalities. Significant improvements in ORs for cocaine usage were found for the **LTR** modality. These ORs improved with time in treatment. Similar progressive improvements in ORs were found for marijuana and alcohol groups. This supports the notion that there is a broad-based effect of time in treatment in such programs. There was also support for a positive effect of length of stay in **ODF** programs across all drug groups. However, there was no evidence of an effect of time in drug treatment for the **STI** group. So, apart from the STI modality, the above findings suggest that treatment of sufficient duration improves the odds of change in drug use.

Other behaviours

For **OMT**, the probability of predatory illegal activity and sexual risk behaviour halved post-treatment (Table A2), while suicidal thoughts/attempts, percent in less than full-time work, and percent with other health limitations did not alter significantly. However, as shown in Table A3, when other influential factors are controlled, there were no significant effects of treatment duration in OMT clients for health, sexual risk and criminal behaviour apart from an increased probability of illegal activity in those leaving treatment after 3-6 months. Overall, there was little change in other non-drug behaviour beyond that associated with improvements in heroin usage for the OMT group.

In **LTR**, large reductions were also found for percent with suicidal thoughts/attempts, illegal activity and sexual risk, but negligible reductions were found in percent in full-time work and with other health problems. From the logistic regression analyses (Table A3), length of stay in LTR was found to be predictive of decreased odds of predatory illegal activity and increases in full-time employment. In the **ODF** group, there were marked reductions in the percent of all other behaviours apart from involvement in less than full-time work. The proportion with health limitations decreased most for this modality, from 28.4 to 16.8%. The multivariate analysis for this modality found improved odds of long-term employment and decreased odds of suicidal ideation. No other improvements in ORs - for post-treatment behaviour compared with behaviour in the first 3 months - were found for either LTR or ODF modalities.

Despite large changes in the percentages of most other (non-drug) behaviours for **STI,** the logistic regression analysis found no significant improvement in ORs of posttreatment behaviour compared with behaviour in the first two weeks of treatment.

Overall Evaluation

This is a very broad-based study, many aspects of which are not covered in this summary. Not covered here are the studies relating to program diversity and retention rates (Simpson et al., 1997a) and in-depth analyses of treatment retention (Simpson, Joe, & Brown, 1997b) and treatment careers amongst clients (Anglin, Hser, & Grella, 1997). There is also further research planned for this cohort of individuals and many concerns regarding treatment are yet to be addressed.

The problem of following a single cohort with no control is addressed in this study by treating behaviour in the first three months (or 2 weeks with STI) as the control in the multiple logistic regression analyses. This appears to be an arbitrary choice of control period and it is not clear that the effect of such a control procedure would be equivalent to a truly controlled study.

Similarly as the authors pointed out, neither the programs involved, nor the clients studied randomly represent all drug programs, and all drug abusers in treatment.

Of the 4786 clients targeted for follow-up interview, 2966 (62%) were interviewed successfully. This attrition rate was accounted for by: 557 (12%) located but deemed either inaccessible or incapable of responding; 64 (1.5%) deceased, 117 (2.7%) refused to be interviewed; and 1082 (23%) were not located. The bias due to attrition is to be assessed in future analyses by the DATOS team, but this large dropout rate makes it even more difficult to generalise about causality from the study.

One final criticism of the study is the use of self-report data, but as the authors point out, despite the presence of bias in such data, self-reports are the only means of assessing the complex cognitive and behavioural issues surrounding drug abuse. The urine analysis sub-study will provide a measure of bias in reporting of usage data, but this has yet to be completed.

TABLE A2 (modified Table 2, Hubbard et al. 1997) Drug Use and Behaviours in the Preadmission and Follow-up Years by Modality

Drug Use/Other Behaviour	Outpatient Methadone Treatment (**OMT**)			Long-Term Residential (**LTR**)			Outpatient Drug Free (**ODF**)			Short-Term Inpatient (**STI**)		
	Preadmission Year (p=% of *N*=1203)	Follow-up Year (f=% of *n*=727)	Relative Risk (f/p)	Preadmission Year (p=% of *N*=2293)	Follow-up Year (f=% of *n*=676)	Relative Risk (f/p)	Preadmission Year (p=% of *N*=2000)	Follow-up Year (f=% of *n*=764)	Relative Risk (f/p)	Preadmission Year (p=% of *N*=2613)	Follow-up Year (f=% of *n*=799)	Relative Risk (f/p)
Heroin[a]	89.4	27.8	.31	17.2	5.8	.28	5.9	3.3	.56	7.0	2.2	.31
Cocaine[a]	41.9	21.7	.52	66.4	22.1	.33	41.7	18.3	.44	66.8	20.8	.31
Marijuana[a]	17.1	13.9	.81	28.3	12.7	.45	25.4	8.5	.33	30.3	10.5	.35
Alcohol[b]	14.8	16.3	1.10	40.2	18.8	.47	31.0	15.1	.49	48.1	19.7	.41
Suicidal Thoughts/Attempts	16.6	12.7	.77	23.6	13.2	.56	19.3	11.4	.59	31.0	16.3	.53
Predatory Illegal Activity	28.6	13.7	.48	40.5	15.9	.39	21.9	14.1	.64	25.9	10.5	.41
Sexual Behaviour Risk	25.2	12.9	.51	47.8	28.4	.59	34.6	22.0	.64	41.3	27.7	.67
Less than full-time work	84.9	81.8	.96	87.6	77.0	.88	81.8	75.7	.93	67.0	63.8	.95
Health limitations	39.7	34.7	.87	29.1	24.9	.86	28.4	16.8	.59	36.5	25.1	.69

Note. Preadmission year data are reported for the follow-up frame (*N*), and follow-up year data are reported for the weighted sample of respondents (*n*).
[a]Weekly or more frequent use of drug during the 1-year period. [b]Weekly or more frequent use with five or more drinks at a sitting.

TABLE A3 (Table 5, Hubbard et al. 1997) Odds Ratios of Likelihood of Drug Use and Behaviours in the Follow-up Year by Modality and Treatment Duration Relative to Stays of Less Than 3 Months (Less Than 2 weeks for Short-Term Inpatient)

Dependent Variable	Outpatient Methadone Treatment **OMT** (*n* = 727)			Long-Term Residential **LTR** (*n* = 676)			Outpatient Drug Free **ODF** (n = 764)		Short-Term Inpatient **STI** (*n* = 799)
	3-6 months	More than 6 months[a]	Still in treatment in follow-up year	3-6 months	6-12 months	More than 1 year	3-6 months	More than 6 months	More than 2 weeks
Heroin[b]	1.10	0.73	0.24**	—[c]	—[c]	—[c]	—[c]	—[c]	—[c]
Cocaine[b]	0.99	1.22	0.70	0.60*	0.23**	0.11***	0.50*	0.29**	1.02
Marijuana[b]	0.41	0.44*	0.49	0.67	0.45*	0.16*	0.95	0.29**	2.42
Alcohol[d]	2.73*	1.67	1.16	0.60	0.21**	0.10***	0.86	0.43**	0.86
Suicidal Thoughts/Attempts	1.63	0.86	0.99	1.38	1.02	0.77	0.80	0.40*	1.51
Predatory Illegal Activity	3.11*	2.16	0.99	0.86	0.37**	0.30*	1.44	0.58	0.71
Sexual Behaviour Risk	1.54	1.59	0.96	0.91	0.95	1.46	0.84	0.68	0.93
Less than full-time work	1.03	1.12	1.10	0.76	0.40***	0.42*	1.15	0.56*	0.90
Health limitations	0.91	0.64	0.96	1.67*	0.83	1.28	1.22	1.39	1.16

[a]More than 6 months but not still in the same treatment program at follow-up. [b]Weekly or more frequent use of drug during the 1-year period.
[c]Number of heroin users in modality too small for meaningful analysis. [d]Weekly or more frequent use with 5 or more drinks at a sitting.
*p<.05; **p<.01; ***p<.001.

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