Economic Evaluation of Interventions for Illicit Opioid Dependence: a review of evidence

Dr Chris Doran
University of Queensland
Australia

BACKGROUND DOCUMENT PREPARED FOR THIRD MEETING OF TECHNICAL DEVELOPMENT GROUP (TDG) FOR THE WHO "GUIDELINES FOR PSYCHOSOCIALLY ASSISTED PHARMACOTHERAPY OF OPIOID DEPENDENCE"

17-21 SEPTEMBER 2007
GENEVA, SWITZERLAND

ECONOMIC EVALUATION OF INTERVENTIONS FOR ILLICIT OPIOID DEPENDENCE: A REVIEW OF EVIDENCE

SECTION 1: UNDERSTANDING THE NATURE, IMPACT AND TREATMENT OF OPIOID DEPENDENCE

What is substance dependence?

Substance dependence is a disorder of altered brain function brought on by the use of psychoactive substances. These substances affect normal perceptual, emotional and motivational processes in the brain. The most common psychoactive substances can be divided into depressants (e.g. alcohol, sedatives/hypnotics, volatile solvents), stimulants (e.g. nicotine, cocaine, amphetamines, ecstasy), opioids (e.g. morphine and heroin), and hallucinogens (e.g. PCP, LSD, cannabis)(World Health Organisation, 2005).

A person is diagnosed as being substance dependent if at least three of the following criteria have been experienced or exhibited at some time during the previous year:

i. A strong desire or sense of compulsion to take the substance;
ii. Difficulties in controlling substance-taking behaviour in terms of its onset, termination, or levels of use;
iii. A physiological withdrawal state when substance use has ceased or been reduced, as evidenced by: the characteristic withdrawal syndrome for the substance; or use of the same (or a closely related) substance with the intention of relieving or avoiding withdrawal symptoms;
iv. Evidence of tolerance, such that increased doses of the psychoactive substance are required in order to achieve effects originally produced by lower doses;
v. Progressive neglect of alternative pleasures or interests because of psychoactive substance use, increased amount of time necessary to obtain or take the substance or to recover from its effects;
vi. Persisting with substance use despite clear evidence of overtly harmful consequences, such as harm to the liver through excessive drinking, depressive mood states consequent to heavy substance use, or substance-related impairment of cognitive functioning. Efforts should be made to determine that the user was actually, or could

be expected to be, aware of the nature and extent of the harm. (ref 9 from WHO report)

Why is opioid dependence a problem?

The United Nations International Drug Control program conservatively estimates that 80 million people worldwide currently abuse heroin and other opiate-type substances(United Nations Office on Drugs and Crime, 2004). Estimates from the World Health Organisation place the burden of harm from opiate use at 11.2 million disability adjusted life years (DALYs)(World Health Organization, 2004). Opiate dependence imposes a significant economic burden on society in terms of costs related to treatment and prevention services, other health care costs, work absenteeism of subjects, productivity loss arising from premature death of subjects, costs associated with crime, and social welfare expenditure(Hall, Doran, Degenhardt, & Shepard, 2006).

The association between crime and drug misuse has been reported by many studies(Ball JC, Shaffer JW, & Nurco DN, 1983; Bennett & Wright, 1986; Gossop, Trakada, Stewart, & Witton, 2005; Hall, Ward, & Mattick, 1998; Rothbard, Alterman, Rutherford, Liu, Zelinski, & McKay, 1999). Once individuals become dependent on heroin, the cost of maintaining a heroin habit contributes to an escalating involvement in income-generating crime, reinforcing the relationship between heroin use and criminal activity(Bell, Hall, & Byth, 1992; Bell, Mattick, Hay, Chan, & Hall, 1997; Bennett & Wright, 1986; Hammersley, Forsyth, & Lavelle, 1990). The average heroin user is likely to engage in criminal behavior for 40-60% of the time when they are not incarcerated or in treatment(Ball JC, Shaffer JW, & Nurco DN, 1983). Treatment, however, been linked to a lower involvement in crime by heroin addicts(Bell, Hall, & Byth, 1992; Gossop, Marsden, Stewart, & Rolfe, 2000; Gossop, Trakada, Stewart et al., 2005; Hubbard, Marsden, Rachal, Harwood, Cavanaugh, & Ginzburg, 1989; Rothbard, Alterman, Rutherford et al., 1999).

Treating opiate dependence

Two main types of treatment exist for opiate dependence: pharmacological and behavioural interventions(World Health Organisation, 2005). Pharmacological approaches are designed to interfere in one way or another with the action of the substance in the body, taking away the

positive rewards from using the substance or making its use aversive. For example, the opioid receptor blockers naloxone and naltrexone reduce the rewarding effects of opioids. Other medications such as methadone and buprenorphine, referred to as substitution treatment, mimic the effects of the psychoactive substance without some of the more harmful effects of that substance, or maintenance treatment(World Health Organisation, 2005).

A range of behavioural interventions, commonly known as psychosocial therapies, are also employed in used to treat opiate dependence. These techniques can be grouped into a range of categories including: motivational and cognitive therapies; cognitive behavioural therapies and relapse prevention; contingency management; and, motivational enhancement therapy. Motivational and cognitive therapies are designed to work on the same motivational processes in the brain that are affected by psychoactive substances. These therapies try to replace the motivation to use substances with the motivation to engage in other behaviours. Cognitive behavioural therapies and relapse prevention help the person develop new stimulus-response associations that do not involve substance use or craving. Relapse prevention is an approach to treatment in which cognitive behavioural techniques are used in an attempt to help patients develop greater self-control in order to avoid relapse. Specific relapse prevention strategies include discussing ambivalence, identifying emotional and environmental triggers of craving and substance use, and developing and reviewing specific coping strategies to deal with internal or external stressors. Contingency management is a treatment based on the use of predetermined positive or negative consequences to reward abstinence or to punish (and thus deter) substance-related behaviours. Rewards have included vouchers awarded for producing substance-free urine samples that can be exchanged for mutually agreed upon items (e.g. cinema tickets) and community reinforcement in which family members or peers reinforce behaviours that demonstrate or facilitate abstinence (e.g. participation in positive activities). Motivational enhancement therapy is a brief treatment modality characterized by an empathetic approach in which the therapist helps to motivate the patient by asking about the pros and cons of specific behaviours; by exploring the patient's goals and associated ambivalence about reaching these goals; and by listening reflectively.

Understanding the economic evaluation of opioid dependent treatment

There is an abundance of good quality evidence regarding the efficacy of pharmacological and, to a lesser extent, behavioural, interventions for opioid dependence(Amato, Minozzi, Davoli, Vecchi, Ferri, & Mayet, 2004a, 2004b; Clark, Lintzeris, Gijsbers, Whelan, Dunlop, Ritter et al., 2002; Farrell M, Ward J, Mattick R, Hall W, Stimson GV, des Jarlais D et al., 1994; Gowing L, Ali R, & J., 2002; Gowing L, Ali R, & White J, 2002; Mattick, Kimber, Breen, & Davoli, 2003; National Institute on Drug Abuse, 2004; Tucker T & Ritter A, 2000). However, in comparison to the clinical evidence, there appears to be a dearth of solid evidence pertaining to the economic evaluation of treatment for opioid dependence(Fals-Stewart, O'Farrell, & Birchler, 1997; French MT & Drummond MF, 2005). Economic evaluation is widely recognized as being a relevant and powerful aid to decision making in the health-care sector and its impact in determining the allocation of society's scarce resources is increasing(Drummond, Sculpher, Torrance, O'Brien, & Stoddart, 2005; Gold, Siegel, Russell, & Weinstein, 1996). The objective of economic evaluation is to identify, measure and value what society gives up when it funds an intervention (the opportunity cost) and what it gains (the benefit). A range of economic evaluations are available including: cost-analysis; cost-effectiveness or cost-utility analysis, and cost-benefit analysis.

Although not a formal type of evaluation, a cost analysis is considered to be the foundation of a full economic evaluation. Its primary purpose is to determine the opportunity cost of a project from a societal perspective, which requires information on the full value of all resources employed in a program. Cost-effectiveness analysis (CEA) is an economic evaluation where a single consequence is quantified in a natural unit. The incremental cost-effectiveness ratio is calculated as the difference in costs between alternatives divided by the difference in the consequence. A variety of consequence measures have been used in cost effectiveness analyses including abstinence from or reduction in illicit opiate use, number of life years gained, changes in psychological health status, employment status and crime rates. Cost-utility analysis (CUA) is similar to cost-effectiveness where the consequences is expressed as a utility measure such as the quality adjusted life year (QALY) or disability adjusted life year (DALY). Cost–benefit analysis (CBA) values consequences in monetary terms. A monetary value can be assigned to health benefits by means of, for instance, the willingness-to-pay technique. Other benefits include resource savings from a fall in future medical care costs, reduced crime rates, and social housing demands as a result of maintenance treatment. The result is either presented as a benefit–cost

ratio (i.e., benefit divided by cost) or simply as net benefit (i.e., cost subtracted from benefit). An intervention is considered cost-beneficial if the benefit–cost ratio exceeds unity or if net benefit is positive(Drummond, Sculpher, Torrance et al., 2005; Gold, Siegel, Russell et al., 1996).

In reality, undertaking an economic evaluation to opioid dependent interventions is complex. One issue is the multitude of post treatment outcomes, some of which affect the drug abuser while others affect society at large. Second, imputing a dollar value to certain outcomes may be difficult, especially when dealing with intangibles, such as the number of days experiencing medical problems. However, the role of these techniques in informing choices between interventions competing for society's scarce resources is now well established.

Purpose of this review

The purpose of this review is threefold. The first objective is to conduct a review of the literature on economic evaluation of treatment of opioid dependence (including detoxification, agonist and antagonist maintenance therapy and to the extent psychosocial interventions). Second, to consider areas where further research in the area of economic evaluation of treatment of opioid dependence is warranted with a particular reference to less resourced countries. Third, to consider recommendations for inclusion in the guidelines on psychosocially assisted pharmacotherapy of opioid dependence relevant to minimum requirements for treatment and service provision for psychosocially assisted pharmacotherapy of opioid dependence

This structure of this review is consistent with these objectives. Section 2 provides an overview of the methodology underpinning the review. Section 3 considers the results of the review while section 4 contemplates a research agenda to progress the field. Section 5 postulates a number of recommendations for treatment guidelines and section 6 documents the references.

SECTION 2: METHODS

The following searches were performed on several electronic databases to identify articles used in this report. A sensitive approach was used in order to maximize the number of articles retrieved; no language or publication year limitations were applied to the searches. A combination of subject heading term searches and natural word searches were used. The search terms used can

be divided into two categories: (1) opiates, opiate use and the treatment of opioid dependence, and (2) cost analysis and economic evaluation. The results of these strategies were then combined. As a result, the searches picked up a number of irrelevant articles, such as the economics of the use of opiates in the treatment of pain relief or cancer. All articles were imported into Endnote7, using the discard duplicates function, and were reviewed independently by two researchers to eliminate irrelevant articles. Further, key journals were hand searched to increase coverage of those research articles recently published. The details of the searches are outlined below.

Medline (Ovid) – 1966 to 2006

1. (cost effectiveness OR cost analysis OR cost benefit OR cost minimization OR cost utility OR economic evaluation).ti,ab.
2. (opiate? OR opioid? OR opium OR heroin OR morphin$ OR morfin$ OR diacetylmorphine OR methadone OR narcotic? OR buprenorphine OR clonidine OR lofexidine OR methadyl acetate OR laam OR naltrexone OR noloxone OR narcotic antagonist? OR opioid antagonist? OR opioid agonist? OR opioid abuse OR opioid dependence OR opioid addiction OR heroin dependence OR heroin addiction OR heroin abuse OR opioid dependence OR opioid addiction OR opioid abuse OR opiate dependence OR opiate addiction OR opiate abuse).ti,ab.
3. 1 AND 2
4. exp Opium/ec
5. exp Methadone/ec
6. exp Narcotics/ec
7. exp Buprenorphine/ec
8. exp Heroin/ec
9. exp Methadyl acetate/ec
10. exp Morphine/ec
11. exp Narcotic antagonists/ec
12. exp Opioid-related disorders/ec
13. exp Substance abuse, Intravenous/ec
14. 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13

15. exp Economics
16. heroin dependence OR heroin addiction OR heroin abuse OR opioid dependence OR opioid addiction OR opioid abuse OR opiate dependence OR opiate addiction OR opiate abuse
17. 15 AND 16
18. 3 OR 14 OR 17

The Cochrane Database of Systematic Reviews (Issue 2, 2006)

1. cost effectiveness OR cost analysis OR cost benefit OR cost minimi#ation OR cost utility OR economic evaluation
2. opium OR opioid OR opiate OR heroin OR diacetylmorphine OR morphine OR morfine OR narcotic OR methadone OR buprenorphine OR clonidine OR lofexidine OR naltrexone OR naloxone OR laam OR methadyl acetate OR heroin dependence OR opioid dependence OR morphine dependence OR heroin abuse OR opioid abuse OR morphine abuse
3. 1 AND 2
4. exp Opioid-related disorders/
5. 1 AND 4
6. exp Costs and cost analysis/
7. 2 AND 6
8. 3 OR 5 OR 7

NHS Economic Evaluation Library Database (via Cochrane Library)

1. opium OR opioid OR opiate OR heroin OR diacetylmorphine OR morphine OR morfine OR narcotic OR methadone OR buprenorphine OR clonidine OR lofexidine OR naltrexone OR naloxone OR laam OR methadyl acetate OR heroin dependence OR opioid dependence OR morphine dependence OR heroin abuse OR opioid abuse OR morphine abuse
2. exp Narcotics/
3. exp Opioid-related disorders/
4. exp Narcotic antagonists/

The Cochrane Central Register of Controlled Clinical Trials (Issue 2, 2006)

1. cost effectiveness OR cost analysis OR cost benefit OR cost minimi#ation OR cost utility OR economic evaluation
2. opium OR opioid OR opiate OR heroin OR diacetylmorphine OR morphine OR morfine OR narcotic OR methadone OR buprenorphine OR clonidine OR lofexidine OR naltrexone OR naloxone OR laam OR methadyl acetate OR heroin dependence OR opioid dependence OR morphine dependence OR heroin abuse OR opioid abuse OR morphine abuse
3. 1 AND 2
4. exp Opioid-related disorders/
5. 1 AND 4
6. exp Costs and cost analysis/
7. 2 AND 6
8. 3 OR 5 OR 7

Web of Science (SCI-EXPANDED 1900 – present; SSCI 1956 – present; (A&HCI 1975 – present)

1. TS=(heroin dependence OR heroin addiction OR heroin abuse OR opiate dependence OR opiate addiction OR opiate abuse OR opioid dependence OR opioid addiction OR opioid abuse OR methadone maintenance OR heroin withdrawal OR opiate withdrawal OR buprenorphine OR opioid detoxification OR heroin detoxification OR methadone OR naltrexone OR naloxone OR clonidine OR opiate* OR opioid* OR opium OR diacetylmorphine OR morphine OR morfine OR laam OR lofexidine OR methadyl acetate OR narcotic*)
2. TS=(cost analysis OR cost utility OR cost benefit OR cost effectiveness OR cost minimi*ation OR economic evaluation)
3. 1 AND 2

EMBASE (WEBSPIRS 1990 - present)

1. exp Opiate addiction/
2. exp Diamorphine/
3. exp Heroin dependence/

4. exp Methadone/
5. exp Methadone maintenance/
6. exp Morphine/
7. exp Buprenorphine/
8. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7
9. exp Economic evaluation/
10. 8 AND 9

PsychINFO (CSA Illumina 1840 – present)

1. exp heroin addiction/
2. exp heroin/
3. exp methadone maintenance/
4. exp narcotic antagonists/
5. exp morphine/
6. exp methadone/
7. exp clonidine/
8. exp opiates/
9. exp detoxification/
10. exp maintenance therapy/
11. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10
12. exp costs and cost analysis/
13. exp economics/
14. 12 OR 13
15. 11 AND 14
16. (heroin addiction OR heroin abuse OR heroin dependence OR opioid addiction OR opioid abuse OR heroin dependence OR opiate* OR opioid* OR opium OR heroin OR morphine OR morfine OR diacetylmorphine OR buprenorphine OR clonidine OR lofexidine OR methadone OR naltrexone OR naloxone OR laam OR methadyl acetate).kw.
17. (cost effectiveness OR cost analysis OR cost benefit OR cost minimi*ation OR cost utility OR economic evaluation).kw.
18. 16 AND 17

19. 14 AND 16
20. 11 AND 17
21. 15 OR 18 OR 19 OR 20

SECTION 3: RESULTS

The literature search generated a total of 1,289 articles. The lead author reviewed each abstract and excluded 1,030 articles for the following reasons: alcohol and/or cocaine dependence rather than opiate dependence; letter to the editor or commentary. A total of 259 articles were considered relevant with 8 review studies identified. The treatment spectrum ranged from detoxification treatments to maintenance treatments involving the use of agonist and/or antagonist treatments. A paucity of research examined psychosocial or behavioural interventions, the majority in conjunction with a pharmacological approach. The following review provides a summary of key findings without being exhaustive.

Economic reviews

Eight review articles were identified(Cartwright, 2000; Choi, Robson, & Single, 1997; French & Martin, 1996a; French MT & Drummond MF, 2005; Hall, Doran, Degenhardt et al., 2006; McCollister KE & French MT, 2003; Simoens S, Ludbrook A, Matheson C, & Bond C, 2006; Simoens S, Matheson C, Inkster K, Ludbrook A, & Bond C, 2002). French and Martin (1996) conducted a review of completed and ongoing studies to provide researchers, clinicians, and policymakers with a common source of published cost estimates for drug abuse consequences(French & Martin, 1996a). Choi et al 1997 provides a list of studies of substance abuse, compares the cost categories considered by various methodologies and describes an inventory of data sources for obtaining relevant information for cost studies(Choi, Robson, & Single, 1997). Cartwright (2000) conducted a comprehensive review of cost–benefit analysis of drug treatment services(Cartwright, 2000). Simoens et al., (2002) reviewed the effectiveness of treatment for opiate dependent drug users with a focus on economic evaluation evidence(Simoens S, Matheson C, Inkster K et al., 2002). McCollister and French (2003) provide a summary of the relative contribution of addiction intervention outcomes to total economic benefit based upon a compilation of 11 published economic studies from the United States(McCollister KE & French MT, 2003). The selected addiction interventions address both alcohol use/abuse and illicit drug

use/abuse and represent various treatment modalities, including a brief physician intervention and long-term residential programs(McCollister KE & French MT, 2003). Hall et al (2006) provided a brief summary of the published economic evaluation literature around treatment interventions for illicit opioid dependence(Hall, Doran, Degenhardt et al., 2006). French and Drummond (2005) reviewed empirical and methodological contributions of economics to the field of substance abuse as well as providing a research agenda for future work(French MT & Drummond MF, 2005). Simoens et al (2006) conducted a literature review on evidence pertaining to the pharmacoeconomic value of community maintenance for opiate dependence(Simoens S, Ludbrook A, Matheson C et al., 2006). The detail of these reviews will be discussed in the forthcoming sections according to the scope of the research.

Quantifying the costs of opioid dependence

Very few researchers have attempted to estimate the cost of opioid dependence. Most efforts to date have considered costs associated with the use of alcohol, tobacco and illicit drugs without specifically focussing on opioid dependence. Single et al. (1998) used international guidelines to quantify the economic costs of alcohol, tobacco and illicit drugs to Canadian society in 1992(Single, Robson, Xie, & Rehm, 1998). An epidemiological approach was adopted with resulting estimates of attributable deaths and hospitalizations used to calculate associated health care, law enforcement, productivity and other costs. Single et al (1998) estimated that the misuse of alcohol, tobacco and illicit drugs cost more than $18.4 billion in Canada, representing $649 per capita. The economic costs of illicit drugs were estimated at $1.4 billion(Single, Robson, Xie et al., 1998). In Australia, Collins and Lapsley used a demographic approach to estimate the total social costs of alcohol, tobacco and illicit drugs in 1998-89 Australian dollars at $34,440 million, of which illicit drugs accounted for $6,076 million(Collins & Lapsley, 2002).

Mark et al (2001) estimated the costs of heroin addiction in the United States, both to the addict and society at large(Mark, Woody, Juday, & Kleber, 2001). Using a cost-of-illness approach, costs were estimated in four broad areas: medical care, lost productivity, crime, and social welfare. An array of data sources were used including secondary analyses of existing databases and literature reviews. The authors estimated the total cost of heroin addiction at US$21.9 billion in 1996 dollars (ranging from US$19.6 to US$33.4 billion). Of these costs, productivity losses

accounted for 52.6%, criminal activities 23.9%, medical care 23.0%, and social welfare 0.5%(Mark, Woody, Juday et al., 2001). García-Altés (2002) estimated the social cost of the consumption of illegal drugs in Spain(Garcia-Altes, Olle, AntoÃ±anzas, & Colom, 2002). A cost-of-illness study was undertaken using a prevalence approximation and a societal perspective for the year 1997. Direct costs included health-care costs, prevention, continuing education, research, administrative costs, nongovernmental organizations and crime-related costs. Indirect costs included lost productivity associated with mortality and the hospitalization of patients. The minimum cost of illegal drug consumption in Spain was estimated at 88 800 million pesetas (PTA) (467 million dollars)(Garcia-Altes, Olle, AntoÃ±anzas et al., 2002).

Costing opioid dependence treatment

A growing body of literature has emerged, predominantly from the US, on the costs associated with opioid dependence treatment. French et al (1997) comments that in spite of the development of guidelines to aid the costing of opiate treatment interventions, standard economic principles are rarely used when conducting cost estimation research(French & McGeary, 1997). The exception to this appears to be studies using the Drug Abuse Treatment Cost Analysis Program (DATCAP). The DATCAP is a data collection instrument and interview guide designed to estimate the costs of a substance abuse treatment program(French, Dunlap, Zarkin, McCeary, & McLellan, 1997).

Treatment cost estimates using the DATCAP procedure were first published in the early 1990s. Bradley et al (1994) examined the financing and costs of the methadone treatment programs that participated in the methadone enhanced treatment demonstration project(Bradley, French, & Rachal, 1994). French et al. (1994) used the DATCAP methodology to explore the financing and costs of treatment delivered at the four methadone clinics involved in the training and employment program intervention(French, Bradley, Calingaert, Dennis, & et al., 1994). Roebuck et al (2003) conducted a summary of the results from 85 DATCAPs completed over the past 10 years(Roebuck, French, & McLellan, 2003). The authors grouped the DATCAPs into 9 treatment modalities and normalized costs to 2001 dollars. The average weekly economic cost per client ranged from $82 per week for outpatient drug court interventions to $1,138 per week for adolescent residential treatment. Labour was overwhelmingly the most utilized resource across

all modalities, ranging from 48% to 88% of total economic cost. The authors conclude that these findings provide credible cost estimates and resource distribution information for various treatment modalities serving diverse populations(Roebuck, French, & McLellan, 2003).

To date, the DATCAP is the only cost instrument that has undergone extensive testing, regular updates, and peer review(Alexandre, Roebuck, French, & Barry, 2003; Bradley, French, & Rachal, 1994; French & McGeary, 1997; French, Bradley, Calingaert et al., 1994; French & Martin, 1996b; French, Salome, & Carney, 2002; French, Salome, Krupski, McKay, Donovan, McLellan et al., 2000; McCollister KE & French MT, 2003; Roebuck, French, & McLellan, 2003; Salome, French, Miller, & McLellan, 2003). Salome et al. (2003) introduced the Client DATCAP, a standardized, self-administered instrument, to measure the costs incurred by individuals receiving treatment(Salome, French, Miller et al., 2003). The DATCAP family of instruments (Program, Brief, and Client) enables researchers and treatment providers to estimate the costs of treatment more accurately and to compare different programs(French & McGeary, 1997).

Detoxification

The National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD) Project in Australia considered the safety, efficacy and cost-effectiveness of five withdrawal interventions: naltrexone-induced rapid opioid detoxification under anaesthesia (RODA); naltrexone-induced rapid opioid detoxification under sedation (RODS); conventional inpatient (CI) detoxification; conventional outpatient (CO) detoxification; and buprenorphine outpatient detoxification. Details of the actual trials and methods of NEPOD are reported elsewhere(Mattick RP, Digiusto E, Doran CM, O'Brien S, Shanahan M, Kimber J et al., 2001).

Shanahan et al (2005) reports the results of the NEPOD cost-effectiveness analysis(Shanahan, Doran, Digiusto, Bell, Lintzerisa, White et al., 2006). Data from four NEPOD trials involving 365 participants were pooled to compare the cost-effectiveness of the five detoxification methods. The treatment provider perspective was adopted and costs reported in Australian dollars for the year 1998/99. Two short-term outcome measures were used: achievement of an initial 7-day period of abstinence; and, entry into ongoing post-detoxification treatment. The mean costs

of the various detoxification methods ranged widely, from $491 (buprenorphine-based outpatient); to $605 for conventional outpatient; $1,404 for conventional inpatient; $1,990 for rapid detoxification under sedation; and to AUD $2689 for anesthesia per episode. The incremental cost-effectiveness ratios (ICERs) and their confidence intervals demonstrate that for outcome 1 (abstinence), buprenorphine was more cost-effective than CO (at $114 less expensive and 8% more effective). The ICER for CI and RODA were statistically equivalent; RODS was found to be more cost-effective than either RODA or CI when compared to CO. All methods were significantly different from CO. The data for ICER2 (using outcome 2, entry to post-detoxification treatment) showed that CI was significantly less cost-effective than CO. All methods were significantly different from CO, and again RODS was more cost-effective than RODA(Shanahan, Doran, Digiusto et al., 2006).

Community detoxification in different settings

Provision of detoxification services in different settings in the U.K. was considered by Gossop and Strang (2000) who re-analysed earlier clinical studies to incorporate cost information(Gossop & Strang, 2000). The authors reported on a comparison between a dedicated inpatient setting and a specialist drug dependence outpatient clinic. Clients were allocated between programmes either randomly or by expressed preference in a 2 x 2 factorial design. Only health care costs of the interventions were included. The inpatient setting was costed for a 21-day programme and a ten-day programme. Both were more expensive per case than the six-week outpatient programme (£2,782 vs. £1,325 vs. £313). When outcomes were taken into account, the results for the inpatient setting were more favourable. The cost per abstinent case (defined as a minimum of 24 hours at completion) was £3,435 for the 21-day inpatient programme, £1,636 for the ten day programme, and £1,840 for the outpatient programme. The authors concluded that length of stay was an important factor(Gossop & Strang, 2000).

Rapid detoxification

De Jong et al. (2005) reported hospital cost from a prospective, randomized controlled trial conducted across four addiction treatment centres in the Netherlands(De Jong, Laheij, & Krabbe, 2005). Patients received rapid detoxification with general anesthesia (RDGA) or without general anesthesia (RD). The primary end-point was opioid abstinence assessed clinically by analyzing

urine samples. One month after the intervention 62.8% of the patients in the RDGA group and 60.0% in the RD group were abstinent for opioids (P=0.71). The average 1-month cost for RD was €2517 versus €4439 for RD-GA. The higher cost for RD-GA was due largely to hospitalization and general anesthesia, which amounted to €2254. The authors concluded because both treatments showed an equivalence efficacy in this study, RD was the most cost-effective treatment(De Jong, Laheij, & Krabbe, 2005).

Buprenorphine assisted detoxification

Doran et al. (2004) reported the results of an economic evaluation conducted alongside a clinical trial(Doran, Shanahan, Bell, & Gibson, 2004). One hundred and fifteen heroin-dependent patients were randomized to a five-day treatment regime of buprenorphine at a specialist clinic or shared care based treatment agency care involving treatment by a general practitioner, supplemented by weekend dispensing and some counselling at the specialist clinic. The treatment provider perspective was adopted and costs reported in Australian dollars for the year 1998/99. The primary outcome measure was the proportion of each group that completed detoxification and achieved an initial 7-day period of abstinence. Buprenorphine detoxification in the shared care setting was estimated to be $24 more expensive per patient than treatment at the clinic, which had an average treatment cost of $332 per patient. Twenty-three per cent of the shared care patients and 22% of the clinic patients reported no opiate use during the withdrawal period. The incremental cost-effectiveness ratio suggests that it costs $20 to achieve a 1% improvement in outcome in the shared care setting. The authors conclude that the use of a shared care arrangement is a treatment option but more attention needs to be devoted to understanding the reluctance of GPs to become involved in the treatment of opioid dependence(Doran, Shanahan, Bell et al., 2004).

Self-help

Shepard et al (1999) use these data to estimate the cost-effectiveness of involvement in mutual self-help groups, such as Alcoholics Anonymous and Narcotics Anonymous, in sustaining abstinence for up to 24 months after treatment(Shepard, Larson, & Hoffmann, 1999). They find a positive association between self-help involvement and abstinence 12 and 24 months after treatment. Applying statistical methods to correct for the effects of self-selection into self-help,

they find that in a Veterans Administration hospital, the effects of self-help on abstinence persisted after the statistical correction, but at the other site, the results depended on the method of analysis that was used. They estimate the cost of achieving an abstinent year by means of self-help in the year following treatment at US$13,000, all of that due to the costs that participants incurred in attending a group(Shepard, Larson, & Hoffmann, 1999).

Detoxification plus ancillary services

Hartz (1999) examined treatment costs in a study involving 102 opioid-addicted patients randomly assigned to either 180-day methadone detoxification with or without contingency contracting(Hartz, Meek, Piotrowski, Tusel, Henke, Delucchi et al., 1999). Contingency contracting provided financial rewards based on length of continuous abstinence up to a maximum of $755 at four months. Both conditions involved psychosocial treatment, and all participants were stabilized during the first 4 months. A health system perspective was adopted and the primary outcome was continuous substance free status at four months. The marginal cost of enhancing the standard treatment with contingency contracting was approximately 8%. An incremental cost of $17.27 produced an additional 1% increase in the number of participants providing continuously substance-free urine and breath samples during month 4 of the study. For every additional dollar spent on treatment, a $4.87 health care cost offset was realized; however, this difference was statistically insignificant due to extreme variances and small sample size. The authors conclude that contingency contracting may be a cost-effective enhancement to methadone detoxification treatment but more reliable and robust evidence is required to derive a fuller and more accurate picture of health care cost savings(Hartz, Meek, Piotrowski et al., 1999).

Masson et al (2004) compared the cost and cost-effectiveness of methadone maintenance treatment (MMT) and 180-day methadone detoxification enriched with psychosocial services(Masson, Barnett, Sees, Delucchi, Rosen, Wong et al., 2004). One hundred and seventy-nine adults with diagnosed opioid dependence were randomized to MMT (n=91), which required monthly 1 hour/week of psychosocial therapy during the first 6 months or 180-day detoxification (n=88), which required 3 hours/week of psychosocial therapy and 14 education sessions during the first 6 months. A societal perspective was adopted and the QALY was used as outcome measure. The results suggest that MMT produced significantly greater reductions in illicit opioid

use but higher health-care costs ($7,564 versus $6,687) than 180-day detoxification during the last 6 months of treatment. The cost per life-year gained was estimated at $16 967. The authors suggest that the results provide additional support for the use of sustained methadone therapy as opposed to detoxification for treating opioid addiction(Masson, Barnett, Sees et al., 2004).

Cost-effectiveness analysis of maintenance treatments

Agonist maintenance treatments

The National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD) Project in Australia considered the safety, efficacy and cost-effectiveness of four maintenance treatments: methadone maintenance treatment (MMT); buprenorphine maintenance treatment (BMT); levo-alpha-acetylmethadol (LAAM), and naltrexone post-detoxification. Details of the actual trials and methods of NEPOD are reported elsewhere(Mattick RP, Digiusto E, Doran CM et al., 2001).

Doran et al (2005) reports the results of the NEPOD cost-effectiveness analysis for the agonist treatments, MMT, BMT and LAAM(Doran, Shanahan, Digiusto, O'Brien, Mattick, & NEPOD Research group, IN PRESS). Data from four NEPOD trials involving 551 participants were pooled to compare the cost-effectiveness of the three maintenance treatments over a three month period. The treatment provider perspective was adopted and costs reported in Australian dollars for the year 1998/99. Two hundred and seventy two patients (49%) received methadone maintenance (MMT), 238 (43%) received buprenorphine maintenance (BMT) and 41 (7%) of participants received levo-alpha-acetylmethadol. Sixty-three percent of participants in the MMT group were in treatment in the third month, with an average treatment episode lasting 69 days. This compares with 51% of participants in the BMT group with an average treatment episode of 60 days and 71% of participants in the LAAM group with an average treatment episode of 75 days. The results of the cost-effectiveness analysis suggested that, for the primary outcome measure of imputed change in heroin free days, compared with MMT, LAAM was the most cost-effective treatment followed by BMT. No statistically significant differences were found in cost-effectiveness of MMT, BMT and LAAM(Doran, Shanahan, Digiusto et al., IN PRESS).

Methadone maintenance treatment

Simoens et al., (2006) conducted a review of the international literature on the pharmacoeconomics of community methadone maintenance for opiate dependence(Simoens S, Ludbrook A, Matheson C et al., 2006). This article adds to a previous literature review by Barnett and Hui (2000)(Barnett & Hui, 2000). Simoens et al (2006) identified twelve studies that investigated different aspects of maintenance of opiate-dependent subjects with methadone(Avants, Margolin, Sindelar, Rounsaville, Schottenfeld, Stine et al., 1999; Barnett, 1999; Barnett & Hui, 2000; Dijkgraaf, van der Zanden, de Borgie, Blanken, van Ree, & van den Brink, 2005; Doran CM, 2005; Harris, Gospodarevskaya, & Ritter, 2005; Masson, Barnett, Sees et al., 2004; Miller, Schechter, Wood, Spittal, Li, LalibertÃ© et al., 2004; Rosenheck & Kosten, 2001; Strang, Marsden, Cummins, Farrell, Finch, Gossop et al., 2000; Zaric, Barnett, & Brandeau, 2000). Evidence from these studies is reported below according to study context.

The cost-effectiveness of methadone maintenance as compared with usual treatment, generally drug-free, was modelled in a study by Barnett (1999)(Barnett PG, 1999). Secondary data was used to model the costs and life years gained of a cohort of 25-year-old heroin users. Costs were restricted to the costs of methadone treatment and were estimated at $437 per month at 1996 prices. The results suggest that providing opiate addicts with access to methadone maintenance have an incremental cost-effectiveness ratio of $5,915 per life-year gained, varying in the sensitivity analysis from $3,451 to $9,103 per life year gained. In spite of several limitations pertaining to quality and relevance of secondary data, the author concluded that the ratio is lower than that of many common medical therapies(Barnett PG, 1999).

Zaric et al., (2000) estimated the cost-effectiveness of expanding methadone maintenance treatment for heroin addiction, particularly its effect on the HIV epidemic(Zaric, Barnett, & Brandeau, 2000). The authors developed a dynamic epidemic model to study the effects of increased methadone maintenance capacity on health care costs and survival, measured as QALYs. We considered communities with HIV prevalence among injection drug users of 5% and 40%. The authors report that additional methadone maintenance capacity costs $8,200 and $10,900 per QALY gained in the high and low prevalence communities, respectively. More than half of the benefits are gained by individuals who do not inject drugs. The authors conclude that expansion of methadone maintenance is a cost-effective strategy and barriers to treatment deny

injection drug users access to an intervention that generates significant health benefits for the general population(Zaric, Barnett, & Brandeau, 2000).

Strang et al., (2000) conducted a randomized clinical trial of supervised injectable versus supervised oral methadone maintenance treatment (MMT)(Strang, Marsden, Cummins et al., 2000). The authors do not do a formal economic evaluation but did calculate the direct costs of the supervised methadone administration within each treatment for comparison purposes based on the costs of medication, the costs of any directly involved equipment and the staffing costs of supervising the methadone administration. These costs were used to compute a crude cost-effectiveness ratio based on changes in heroin use from intake to 6-month follow-up. The authors report costs of the supervised methadone administration for each patient over the 6-month trial at £402 for oral MMT and £1,973 for injectable MMT. Crude economic calculations of effectiveness were performed based on chosen target outcomes of increased heroin abstinence (by 45% for the injectable MMT treatment and by 34% for oral MMT) and for abstinence from illicit injecting (by 27% for the injectable MMT treatment and by 26% for oral MMT). These indicate that the average cost-effectiveness ratios are 3.7 and 5.8 times greater for the oral MMT treatment on these heroin and injecting outcomes. The authors concluded that it is feasible to implement supervised injectable methadone maintenance treatment in the context of (although separate from) a specialist oral methadone maintenance service(Strang, Marsden, Cummins et al., 2000).

Methadone maintenance treatment plus psychosocial services

McLellan et al., (1993) compared methadone maintenance treatment alone with two levels of additional psychosocial support: one provided regular counseling and the other provided regular counseling plus the other elements of an integrated program. The most intensive treatment was the most effective, and the intermediate program was the most cost-effective(McLellan, Arndt, Metzger, Woody, & O'Brien, 1993).

Kraft et al. (1997) examined the cost-effectiveness of supplementary services provided with methadone maintenance therapy(Kraft, Rothbard, Hadley, McLellan, & Asch, 1997). Clients were randomly allocated to different support packages for 24 weeks. The minimum service was

the FDA standard of one counselling session per month. No ancillary services were provided except in emergencies. The counselling group received three sessions per week including behavioural interventions and the enhanced group received counselling plus on-site medical, psychiatric, employment, and family therapy services. All clients then received counselling plus methadone and were followed up to one year. All services used were expressed in 1993 prices. At 12 months the annual cost per abstinent client was estimated at $16,485 for minimum methadone services, $9,804 for counselling plus methadone services, and $11,818 for enhanced methadone services. A similar trend was found at 6 months. The authors concluded that the results suggest a nonmonotonic relation between the level of treatment services and the decrease in drug use. The minimum service level provides too little treatment, and the maximum service level provides more than is needed, to achieve a similar result(Kraft, Rothbard, Hadley et al., 1997).

Avants et al. (1999) examined the differential efficacy and relative costs of two intensities of adjunctive psychosocial services(Avants, Margolin, Sindelar et al., 1999). Clients were randomised to weekly counselling (two hours) with intensive day therapy (five hours per day five days per week) within a community-based methadone maintenance program. Clients were randomly allocated to either a day treatment program or enhanced methadone care. The day treatment program was an intensive, 25 hour per week program while the enhanced standard care was standard methadone maintenance plus a weekly skills training group and referral to on and off site services. The intensive day therapy was three times as expensive as weekly counselling with only small cost offsets in the use of other services. No significant difference in effectiveness was detected overall. Analysis of client sub-groups produced only one significant result: clients with no previous history of methadone maintenance treatment were more likely to be retained in treatment with the lower intensity intervention and had better outcomes at six months. The authors conclude that providing an intensive day treatment program to unemployed, inner city methadone patients was not cost-effective relative to a program of enhanced MMT, which produced comparable results at less than half the cost(Avants, Margolin, Sindelar et al., 1999).

Sigmon and Stitzer (2005) evaluated the use of a low-cost incentive intervention to improve counselling attendance among methadone-maintained patients(Sigmon & Stitzer, 2005). Upon attending each counselling session, patients could draw for prizes under an escalating draw

system with a 50% probability that draws would result in a prize. Incentives included small ($1), moderate ($5), and large ($20) prizes, with chances of winning inversely related to prize costs, and a maximum possible total of $160 per patient. The results suggest that the incentive policy significantly increased the percent of counselling sessions attended (52% vs. 76%) and promoted periods of continuous attendance. The authors conclude that these data further support the effectiveness of low-cost incentive programs in enhancing counselling attendance among methadone patients(Sigmon & Stitzer, 2005).

Buprenorphine versus methadone maintenance

There was mixed evidence about the pharmacoeconomic profile of community maintenance with methadone versus buprenorphine. Barnett et al., (2001) using a similar approach to Zaric et al. (2000), examined the potential economic impact of providing buprenorphine to expand treatment and/or to substitute for methadone maintenance in the U.S.A(Barnett PG, Zaric GS, & Brandeau ML, 2001). The results suggest that buprenorphine had an incremental cost-utility ranging from US$ 10,800 to $84,700 per QALY gained at 1998 prices under different assumptions about pricing and treatment effectiveness. The authors reported that buprenorphine maintenance treatment (BMT) was much less effective and more costly than MMT, hence methadone the dominant treatment. The authors suggested that, unless longer-term studies reverse the current evidence on relative effectiveness, buprenorphine does not appear to be a cost-effective alternative to methadone for general use(Barnett PG, Zaric GS, & Brandeau ML, 2001). Rosenheck and Kosten (2001) evaluated the potential economic impact of the buprenorphine/naloxone combination in the context of practice in U.S.A. under the assumption that the effectiveness of buprenorphine/naloxone and methadone was equal. The authors argued that BMT could be less costly due to savings in travel costs and reductions in mandatory counselling(Rosenheck & Kosten, 2001). The authors conclude that the ultimate economic impact of buprenorphine/naloxone will be determined by whether it fosters expanded use of opiate agonist stabilization among high cost recidivists (in whom the savings potential is large) or among lower cost, higher functioning opiate users with lower potential for savings(Rosenheck & Kosten, 2001).

Doran et al., (2003) compared the cost-effectiveness of BMT versus MMT for opioid dependence(Doran, Shanahan, Mattick, Ali, White, & Bell, 2003). In a randomized controlled trial, 405 subjects were assigned to each treatment at one of three specialist outpatient drug treatment centres in Adelaide and Sydney, Australia. The perspective of analysis was that of the service provider and included costs relevant to the provision of treatment. The primary outcome measure was change in heroin-free days from baseline to the sixth month of treatment. Treatment with methadone was found to be both less expensive and more effective than treatment with buprenorphine, which suggests methadone dominates buprenorphine. However, statistical testing found that the observed difference between the cost-effectiveness of methadone and buprenorphine treatments was not statistically significant. The authors suggest that buprenorphine provides a viable alternative to methadone in the treatment of opioid dependence(Doran, Shanahan, Mattick et al., 2003).

Harris et al., (2005) conducted a randomised trial of the cost effectiveness of buprenorphine as an alternative to MMT for heroin dependence in a primary care setting(Harris, Gospodarevskaya, & Ritter, 2005). The study was a randomised, open-label, 12-month trial of 139 heroin-dependent patients in a community setting receiving individualised treatment regimens of buprenorphine or methadone. Those who were currently on a methadone program were analysed separately from new treatment recipients. The study took a broad societal perspective, used clinical records and self report data, and included the cost of health, crime and personal costs in 1999 Australian dollars. The main outcomes were incremental cost per additional day free of heroin use and per QALY. The estimated mean number of heroin-free days did not differ significantly between those randomised to methadone or buprenorphine over the year of the trial. BMT was associated with an average 0.03 greater QALYs over 52 weeks (not significant). The total cost was $17,736 with MMT and $11, 916 with BMT; costs excluding crime were $4,513 and $5,651. With additional heroin-free days as the outcome, and crime costs included BMT has a lower cost but less heroin-free days. If crime costs are excluded BMT has a higher cost and worse outcome than methadone. With additional QALYs as the outcome, the cost effectiveness of BMT is $39,404 if crime is excluded, but BMT is dominant if crime is included. The authors conclude that the trial found no significant differences in costs or outcomes between MT and BMT in this particular setting(Harris, Gospodarevskaya, & Ritter, 2005).

Heroin prescribing versus methadone maintenance treatment

Bammer et al (2003) summarised the results from the Swiss and Dutch heroin trials. In the Netherlands, the costs of co-prescribed heroin treatment were found to be strongly dependent upon the type of treatment implementation(Bammer, Van Den Brink, Gschwend, Hendriks, & Rehm, 2003). The total direct medical cost of treatment, embedded in the special treatment centres for the scientific trials, ranged from €15,307 per patient per treatment year for a unit with capacity of 75 participants and up to €27,000 for a 25-patient unit. Most of the costs arose from the supervision of heroin use and the security required to prevent the diversion of heroin to the black market. Injectable heroin maintenance needs to produce substantially greater benefits for each participant than MMT to make it as cost-effective as MMT(Bammer, Van Den Brink, Gschwend et al., 2003).

In Canada, a model of the potential impact of heroin prescription pointed to increased life expectancy, reduced costs of hospital and emergency room use, diminished costs of criminal activity, and an increased employment level(Miller, Schechter, Wood et al., 2004). However, cost and consequence estimates were not combined into cost-effectiveness ratios(Miller, Schechter, Wood et al., 2004).

Dijkgraaf et al., (2005) conducted a cost utility analysis of medical co-prescription of heroin compared with MMT for chronic, treatment resistant heroin addicts, psychosocial treatment was offered throughout(Dijkgraaf, van der Zanden, de Borgie et al., 2005). The author's pooled data from two open label randomized controlled trials conducted in the Netherlands. One year costs estimated from a societal perspective. Quality adjusted life years (QALYs) based on responses to the EuroQol EQ-5D at baseline and during the treatment period. The authors report that co-prescription of heroin was associated with 0.058 more QALYs per patient per year and a mean saving of €12,793 per patient per year. The authors conclude that co-prescription of heroin is cost effective compared with treatment with methadone alone for chronic, treatment resistant heroin addicts(Dijkgraaf, van der Zanden, de Borgie et al., 2005).

Prison based substance abuse programs

Research has shown that prison methadone treatment reduces heroin use and drug injecting and increases post-release treatment uptake (Bellin, 1999; Magura, Rosenblum, Lewis, & Joseph, 1993). Although knowledge of costs and outcomes of community methadone programs is improving, the cost-effectiveness of prison methadone programs has not been assessed previously. Previous evaluations of prison-based substance abuse programs have focused on the outcomes related to reincarceration or relapse without considering cost–effectiveness(Warren, Viney, Shearer, Shanahan, Wodak, & Dolan, IN PRESS).

A series of economic analyses suggested that providing treatment to individuals in prison followed by aftercare services post release can be a cost–effective combination(French, Zarkin, Hubbard, & Rachal, 1993; McCollister, French, Prendergast, Hall, & Sacks, 2004; McCollister, French, Prendergast, Wexler, Sacks, & Hall, 2003). For example, Griffith et al. (1999) determined that treatment was most cost– effective for those at high risk who completed the entire program(Griffith, Hiller, Knight, & Simpson, 1999).

In the United States, the cost of in-prison substance abuse treatment programs in the state of Connecticut ranged from $189 to $5,699 per attendee in 1996/97(Daley, Love, Shepard, Petersen, White, & Hall, 2004). The more intensive and therefore more expensive programs were associated with lower rates of re-arrest and delivered benefits to the corrections service which were 1.8 to 5.7 times greater than the costs of the programs. However, a recent review concluded that the incremental costs of providing treatment in prison settings can be quite modest(Belenko, Patapis, & French, 2005).

Warren et al (2006) conducted an economic evaluation of the New South Wales (NSW) prison methadone program(Warren, Viney, Shearer et al., IN PRESS). Information from the NSW prison methadone program was used to construct a model of the costs of the program. The information was combined with data from a randomised controlled trial of provision of prison methadone in NSW. The total program cost was estimated from the perspective of the treatment provider/funder. The cost per heroin free day, compared with no prison methadone, was estimated. The results suggest that the annual cost of providing prison methadone in NSW was estimated to be AUD$2.9 million (or $3,234 per inmate per year). The incremental cost

effectiveness ratio is AUD $38 per additional heroin free day. The authors concluded that from a treatment perspective, prison methadone is no more costly than community methadone, and provides benefits in terms of reduced heroin use in prisons, with associated reduction in morbidity and mortality(Warren, Viney, Shearer et al., IN PRESS).

Antagonist maintenance treatment

Only one economic evaluation involving naltrexone was found. The National Evaluation of Pharmacotherapies for Opioid Dependence Project involved a cost-effectiveness analysis of methadone, buprenorphine, LAAM (levo-alpha-acetylmethadol), and naltrexone maintenance treatments(Mattick RP, Digiusto E, Doran CM et al., 2001). The NEPOD study did report that naltrexone was the least cost-effective maintenance treatment. A study by Doran et al (2006) conducted a cost-effectiveness analysis of NEPOD agonist treatments(Doran, Shanahan, Digiusto et al., IN PRESS). These results were reported earlier. Naltrexone was not included in this evaluation for two reasons. First, it is an antagonist treatment and second, only a few patients that entered naltrexone treatment actually finished. The high patient drop out rate limited the usefulness of data.

Treatment settings

Mojtabai and Zirvin (2003) conducted a cost-effectiveness analysis of four treatment modalities for substance abuse, inpatient, residential, outpatient methadone detoxification and outpatient drug-free(Mojtabai & Zivin, 2003). Data from the Services Research Outcomes Study was used. The SROS, a survey of 3,047 clients in a random sample of 99 drug treatment facilities across the U.S.A. Treatment success was defined in two ways: as abstinence and as any reduction in substance use. Clients were stratified based on propensity scores and analyses were conducted within these strata. The costs were $15,600 in the inpatient modality, $14,900 in the residential modality, $12,400 in the detox/methadone modality, and $6,300 in the outpatient drug-free modality. Cost of successful treatment in the outpatient drug-free modality was lower than both inpatient and residential modalities at a statistically significant level but not lower than the detox/methadone modality. Average cost incurred across all modalities was $12,400 per abstinent case. There were also considerable differences across modalities in cost per case of reduced use. The costs were $6,100 in the inpatient modality, $6,700 in the residential modality, $4,600 in the

detox/methadone modality, and $2,400 in the outpatient drug-free modality. In this case, the cost of successful treatment in the outpatient drug-free modality was lower than all other modalities, including detox/methadone, at a statistically significant level. The authors conclude that substance disorders can be treated most cost-effectively in outpatient drug-free settings(Mojtabai & Zivin, 2003).

Cost-benefit analysis of maintenance treatments

A number of reviews have collated evidence pertaining to the cost-benefit of substance abuse treatments. Cartwright (2000) conducted a comprehensive review of cost–benefit analysis of drug treatment services. In 18 cost–benefit studies, a persistent finding is that benefits exceed costs, even when not all benefits are accounted for in the analysis(Cartwright, 2000). Simoens et al., (2002) reviewed the effectiveness of treatment for opiate dependent drug users with a focus on economic evaluation evidence(Simoens S, Matheson C, Inkster K et al., 2002). The authors commented that most of the limited number of studies including a cost-benefit analysis pointed towards positive net benefits from intervention(Simoens S, Matheson C, Inkster K et al., 2002). A review of 11 studies conducted in the U.S.A by McCollister and French (2003) found that the benefit–cost ratios associated with substance abuse treatment ranged from 1.33 to 23.33 and that benefits were overwhelmingly because of reductions in criminal activity, with smaller contributions of earnings, and averted health care(McCollister KE & French MT, 2003). Simoens et al (2006) conducted a literature review on evidence pertaining to the pharmacoeconomic value of community maintenance for opiate dependence(Simoens S, Ludbrook A, Matheson C et al., 2006). French and Drummond (2005) reviewed empirical and methodological contributions of economics to the field of substance abuse as well as providing a research agenda for future work(French MT & Drummond MF, 2005).

The vast majority of research undertaking cost-benefit analysis of opioid dependence treatment has taken place in the context of one of the following: the Treatment Outcome Program Study (TOPS); the Treatment Alternatives Program (TAP), California Drug and Alcohol Treatment Assessment Program (CALDATA); the California Treatment Outcome Project (CalTOP); and the National Treatment Outcome Research Study (NTORS). These key data studies will be briefly

discussed followed by a consideration of additional research efforts by treatment setting and/or population target.

Treatment Outcome Program Study (TOPS)

Harwood et al., (1988) and Hubbard et al. (1989) used data from the TOPS to estimate the relative economic benefits of outpatient methadone, residential, and outpatient drug-free drug treatment units in terms of reduction of drug users' criminal activity(Harwood, Hubbard, Collins, & Rachal, 1988; Hubbard, Marsden, Rachal et al., 1989). Regression analyses examined correlates between the average cost per treatment day and the reduction in crime-related costs during the year following discharge from treatment. Other variables included in the model include economic benefit from increased length of stay, the effects of previous treatment episodes, pre-treatment involvement in crime, and criminal justice system involvement at entry into treatment. The focus of the analysis is on outcomes related to decreased crime costs that were measured in counts of specific criminal acts and then valued by cost per act. A pre–post design was used to evaluate treatment programs using short-term benefits. The methadone maintenance benefit–cost ratio was 0.92, the lowest in all completed studies, and was due to the statistical insignificance found in total benefit after treatment. Inclusion of this benefit would raise the benefit–cost ratio to 1.66, which is consistent with other positive findings. Residential treatment benefits were $5,910, and outpatient benefits were lower at $2,595 (in 1981 dollars)(Harwood, Hubbard, Collins et al., 1988; Hubbard, Marsden, Rachal et al., 1989).

Rajkumar & French (1997) also used data from TOPS to illustrate a benefit-cost analysis using the valuation techniques outlined in their paper(Rajkumar & French, 1997). Baseline data for TOPS were collected from 1979 to 1981, and clients were followed for up to 5 years after treatment initiation. The authors compared self-reported criminal activity in a sample of 2,420 treatment clients at baseline and 12-month follow-up. To estimate the economic benefits of treatment, the authors applied their crime cost estimates to the reported frequency of criminal acts and compared the resulting crime costs at baseline and follow up. Economic benefits were expressed as reduced crime costs resulting from treatment. The total annual economic benefit per client for the TOPS sample was $17,823(Rajkumar & French, 1997).

Treatment Alternatives Program (TAP)

Mauser et al (1994) conduct a study of the Treatment Alternatives Program (TAP) that is modelled on the Treatment Alternatives to Street Crime (TASC)(Mauser, Van Stelle, & Moberg, 1994). The study was conducted in three Wisconsin counties in 1990–91. The intervention is based on a case management model that includes assessments and referrals, treatment and monitoring of offender compliance. Services delivery organization varies in the three counties with one site providing intensive day treatment and the others outpatient treatment. Costs are measured for treatment, drug testing, overhead costs, case management, medical care expenses, screening and assessment. Treatment is from a variety of programs: outpatient; inpatient; residential; halfway houses; day treatment and mental health outpatient. Two benefit-cost ratios are reported. In the first, only criminal justice benefits are included, and in the second, medical costs, and client income change are added to the criminal justice cost. The benefit-cost ratio is lower for the more inclusive measure because of the increase in medical costs and the decrease in client income after treatment. Medical costs are biased upward since future averted cases of HIV/AIDS, or other medical costs are not counted as a benefit in such a short-term study(Mauser, Van Stelle, & Moberg, 1994).

California Drug and Alcohol Treatment Assessment Program (CALDATA)

Gerstein, Harwood, and Suter's (1994) California Drug and Alcohol Treatment Assessment Program (CALDAT) is the most comprehensive cost-benefit analysis carried out to date(Gerstein DR, Johnson RA, Harwood HJ, Fountain D, Suter N, & Malloy K, 1994). CalDATA was a large-scale study of the effects of alcohol and drug treatment on participant behavior, treatment costs, and economic benefits to society. The authors examine the effects of treatment - residential programs, outpatient programs, and methadone programs - on alcohol and drug use, criminal activity, health and health care utilization, and source of income. For each treatment modality, they found that the benefits during the first year of treatment significantly exceeded the cost of delivering the care. The benefit-cost ratio was 4.8 for residential treatment and 11.0 and 12.6 for outpatients and discharged methadone participants, respectively(Gerstein DR, Johnson RA, Harwood HJ et al., 1994).

The California Treatment Outcome Project (CalTOP)

Ettner et al (2006) examined the costs and monetary benefits associated with substance abuse treatment using data from the California Treatment Outcome Project (CalTOP), a large demonstration project that collected outcomes data on clients admitted to 43 substance abuse treatment providers in 13 counties in California(Ettner, Huang, Evans, Ash, Hardy, Jourabchi et al., 2006). Using a social planner perspective, the estimated direct cost of treatment was compared with the associated monetary benefits, including the client's costs of medical care, mental health services, criminal activity, earnings, and (from the government's perspective) transfer program payments. For the main sample of 2,567 clients, information on medical hospitalizations, emergency room visits, earnings, and transfer payments was obtained from baseline and 9-month follow-up interviews, and linked to information on inpatient and outpatient mental health services use and criminal activity from administrative databases. The authors report that on average, substance abuse treatment costs $1,583 and is associated with a monetary benefit to society of $11,487, representing a greater than 7:1 ratio of benefits to costs. These benefits were primarily because of reduced costs of crime and increased employment earnings(Ettner, Huang, Evans et al., 2006).

The National Treatment Outcome Research Study (NTORS)

The National Treatment Outcome Research Study (NTORS) was the first national prospective study of treatment outcome among drug misusers in the United Kingdom. Three studies have carried out an economic evaluation of the British National Treatment Outcome Research Study(Godfrey, Stewart, & Gossop, 2004; Gossop, Marsden, Stewart, & Treacy, 2001; Healey, Knapp, Marsden, Gossop, & Stewart, 2003). Patients were assigned to methadone maintenance, inpatient treatment or residential rehabilitation, with the majority participating in the maintenance programme. At 1 year following intake to methadone maintenance, additional health care costs per crime prevented amounted to £76 (US$ 127) for subjects who did not inject heroin and £121 (US$ 201) for subjects who injected heroin at 1999 prices. At 2 years following intake to opiate dependence treatment, additional health care costs of £1,831,000 (US$ 3,037,996) generated savings in crime costs of £27,347,000 (US$ 45,374,149) at 1999 prices, yielding a benefit–cost ratio of 15:1(Godfrey, Stewart, & Gossop, 2004; Gossop, Marsden, Stewart et al., 2001; Healey, Knapp, Marsden et al., 2003).

Pregnant women

French et al., (2002) estimated the costs and benefits of speciality and standard residential substance abuse treatment for pregnant and/or parenting women in Arkansas(French, McCollister, Cacciola, Durell, & Stephens, 2002). Data were collected as part of the CSAT funded Treatment Outcome Pilot Prospective Study. The average cost of treatment in specialty programs was $8,035 versus $1,467 for standard residential treatment. Average net benefits (benefit–cost ratios) were estimated to be $17,144 (3.1) for specialty and $8,090 (6.5) for standard respectively. The authors concluded that investment in specialty residential treatment for pregnant and parenting substance-abusing women appears to be economically justified, but future evaluations should analyse larger and more comparable samples to improve power and precision in the benefit–cost statistics(French, McCollister, Cacciola et al., 2002).

Daley et al (2000) examined crime costs and benefits of treatment for pregnant women(Daley, Argeriou, McCarty, Callahan, Shepard, & Williams, 2000). Using the Addiction Severity Index, differences in pre- and post treatment criminal involvement were measured for a sample of 439 pregnant women who entered publicly funded treatment programs in Massachusetts between 1992 and 1997. Accepted cost of illness methods was supplemented with information from the Bureau of Justice Statistics to estimate the costs and benefits of five treatment modalities: detoxification only (used as a minimal treatment comparison group), methadone only, residential only, outpatient only, and residential/outpatient combined. Projected to a year, the net benefits (avoided costs of crime net of treatment costs) ranged from US$32,772 for residential only to US$3,072 for detoxification. Although all five modalities paid for themselves by reducing criminal activities, multivariate regressions controlling for baseline differences between the groups showed that reductions in crime and related costs were significantly greater for women in the two residential programs. The authors concluded that their results provide further justification for the continuation and possible expansion of residential substance abuse treatment programs for criminally involved pregnant women(Daley, Argeriou, McCarty et al., 2000).

Residential and outpatient treatment settings

French et al., (2000) performed a benefit–cost analysis of residential and out-patient substance abuse treatment in Washington State(French, Salome, Krupski et al., 2000). For the benefit–cost

evaluation, 103 clients receiving a full continuum (FC) of treatment, which included inpatient, intensive out-patient and aftercare, were compared to 63 clients receiving a partial continuum (PC) of treatment (out-patient treatment only). Outcome data came from an augmented version of the Addiction Severity Index instrument. Economic benefits were originally assessed over 9 months and included reduced criminal activity, health services utilization and expenditures on illicit drugs and alcohol as well as increased earnings from employment. Total 12-month economic benefit for the average FC client was $29 503, comprised of $21 131 in reduced criminal activity (72%), $3900 from increased employment earnings (13%), $1397 from reduced health services utilization (5%) and $3074 from reduced expenditures on illicit drugs and alcohol (10%). Total economic benefit for the average PC client was $17 837 ($11 573 in criminal activity (65%), $3371 in health services utilization (19%), $2399 from employment income (13%) and $493 from reduced illicit drug and alcohol expenditures (3%))(French, Salome, Krupski et al., 2000).

French et al (2002a) performed a second benefit–cost analysis of residential substance abuse treatment programs in Washington(French, Salome, & Carney, 2002). The sample included 178 individuals across nine adult residential treatment programs. An augmented Addiction Severity Index instrument was used to collect the outcome data for the benefit estimation. Three outcome measures were used to estimate economic benefits over a 6-month period: criminal activity, health services utilization and employment earnings. Total 12-month treatment benefit per client was $44 863, comprised of $37 239 in reduced criminal activity (83%), $5014 in employment earnings (11%) and $2610 in reduced health services utilization (6%)(French, Salome, & Carney, 2002).

Cost-benefit analysis of behavioural couples therapy

Pals-Stewart (1997) conducted a cost-outcome study of behavioural couples therapy for male substance-abusing patients(Pals-Stewart, O'Farrell, & Birchler, 1997). The cost outcomes for married or cohabiting substance-abusing male patients who were randomly assigned to receive either behavioural couples therapy (BCT) or individual-based treatment (IBT) were compared. Social costs incurred by patients in several areas (e.g., cost of substance abuse treatment, support from public assistance) during the year before and the year after treatment was estimated. The

benefit-to-cost ratio was nearly four times higher for husbands receiving BCT (5.01) than husbands receiving IBT (1.37). The net benefit (i.e., monetary benefit minus the cost of treatment delivery) of the interventions was nearly nine times higher for husbands receiving BCT ($4,856.01) than for husbands who did not receive BCT ($544.95). BCT was more cost-beneficial than IBT; although the monetary outlays for delivering IBT and BCT were not different, the average reduction in aggregate social costs from baseline to follow-up was greater for patients who received BCT (i.e., $6,628) than for patients who received IBT (i.e., $1,904). BCT was also more cost-effective than IBT; for each $100 spent on treatment, BCT produced greater improvements than IBT on several indicators of treatment outcome (e.g., fewer days of substance use, fewer legal problems)(Pals-Stewart, O'Farrell, & Birchler, 1997).

SECTION 4: FURTHER RESEARCH

The quantity and quality of economic evaluations in the addiction areas are limited(French MT & Drummond MF, 2005). Most economic evaluations of treatment options for opioid dependence are limited in terms of the range of costs and benefits considered. Costs comparisons between treatment alternatives are generally restricted to the health care costs of the interventions and do not consider indirect costs such as travel expenses or costs related to productivity loss. Existing studies, with the exception of studies using the DATCAP and ASI, rarely examine health benefits and benefits related to reduced criminal activity. The DATCAP and ASI instruments provide a solid platform for costing treatment services and the transferability of these instruments to countries outside the United States is warranted.

None of the economic evaluations discussed the transferability of results to other settings or contexts. Translating findings on interventions for opioid dependence in developed countries into priorities for opioid dependence in developing countries presents three major challenges(Hall, Doran, Degenhardt et al., 2006). First, countries differ in the scale of illicit opioid use and in the resulting disease burden. Second, societal wealth and health care infrastructure affect the capacity of developing societies to treat illicit opioid dependence. Third, in societies with a sizable illicit opioid dependence problem, cultural attitudes and beliefs will affect societal responses, especially attitudes toward illicit opioid use and dependence. A more concerted effort is needed to better understand the transferability of economic evaluation finding across countries. In particular, a

priority should be the identification of safe, innovative, and less expensive ways of effectively delivering culturally acceptable forms of opioid maintenance treatments in developing countries.

There is a need for better-designed economic evaluations comparing the cost-effectiveness of drug treatment modalities and by particular sub-groups. For example, there has been an emphasis in UK and Australian policy on development of treatment in the primary care setting, and this needs further evaluation. Limited to no evidence was also found on the cost-effectiveness of treatments options for adolescents or pregnant women. Another previously under-represented area of research that has been expanding is the economic evaluation of treatment in criminal justice settings. All of these issues need attention.

A particular void in the literature is the extent that psychosocial interventions work. A limited number of authors have reported that, in the context of methadone maintenance treatment, mmoderate levels of psychosocial services are more cost-effective than minimum levels of services. However, it is not known which elements work best and in which phase the psychosocial interventions are necessary. Further more research is required to determine minimum level of staff qualifications and how these interventions vary by treatment and treatment setting.

Future research needs to consider outcomes relevant to opioid dependence including: drug use other than heroin, physical health, crime, mortality and psychological functioning. The QALY may be one way forward but researchers need a better understanding of how preferences for different outcomes vary by region, country, or by a decision-maker. Alternatively, health economists may opt to conduct a cost–benefit analysis, although assigning monetary values to health benefits is controversial and requires additional work. Additional effort also needs to be devoted to placing results of economic evaluations in the context of other second filter criteria such as equity, feasibility, acceptability and affordability.

Cartwright (2003) has commented that optimal allocation of resources for drug abuse treatment does not prevail under current financing arrangements. The failure of drug abuse treatment financing to comply with rational budgeting means that net social welfare is not being maximized

for the present level of resources expended for those presently in treatment. Substantial and additional welfare losses are also incurred because of the insufficient funding to provide for those individual drug abusers not in treatment inclusive of those demanding and not receiving services. The extent to which equity is facilitated is difficult to determine, given the complexity of fiscal mechanisms and structures employed to finance treatment as well as the lack of resources for those in need of service. The outcome is an institutionalization of health disparities(Cartwright & Solano, 2003). Hence, it is important that issues of funding are better researched and integrated into results of economic evaluations.

Researchers must continue to improve the quality of economic analyses of addiction treatment(French MT & Drummond MF, 2005). Employing consistent methodology and proper terminology will enhance the standardization and value of future economic evaluation studies.

SECTION 5: RECOMMENDATIONS FOR TREATMENT GUIDELINES

Clinical assessment of opioid dependence

- A thorough clinical assessment is required applying DSM-IV criteria to ascertain if patient is opioid dependent. Clinical assessment should consider

Quantifying the costs of opioid dependence- within context of clinical trial

- Utilisation of Drug Abuse Treatment Cost Analysis Program (DATCAP) and

Detoxification treatment

- Buprenorphine and supervised naltrexone accelerated withdrawal delivered on an outpatient basis are the most cost-effective ways to achieve withdrawal from opioids.
- Treatment should be provided in the context of appropriate recommended psychosocial support.
- In the absence of financial hardship the patient should be referred to self help groups. These groups provide the simplest form of post-withdrawal support for enduring abstinence and are also a low-cost intervention, because patients bear most of the costs; however, they have a low rate of uptake, and their effectiveness is only modest.

Cost-effectiveness analysis of maintenance treatments

- Agonist maintenance treatments such as methadone and buprenorphine should be considered first line treatment options for opioid dependent patients.
- Treatment should be provided in the context of appropriate recommended psychosocial support. Moderate levels of services are more cost-effective than minimum levels of services.

SECTION 7: REFERENCES

Alexandre, P.K., Roebuck, M.C., French, M.T., & Barry, M. (2003). The cost of residential addiction treatment in public housing. *Journal of Substance Abuse Treatment*, 24(4), 285-290.

Amato, L., Minozzi, S., Davoli, M., Vecchi, S., Ferri, M., & Mayet, S. (2004a). Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification, *Cochrane Database of Systematic Reviews*.

Amato, L., Minozzi, S., Davoli, M., Vecchi, S., Ferri, M., & Mayet, S. (2004b). Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence, *Cochrane Database of Systematic Reviews*.

Avants, S.K., Margolin, A., Sindelar, J.L., Rounsaville, B.J., Schottenfeld, R., Stine, S., Cooney, N.L., Rosenheck, R.A., Li, S.-H., & Kosten, T.R. (1999). Day treatment versus enhanced standard methadone services for opioid-dependent patients: A comparison of clinical efficacy and cost. *American Journal of Psychiatry*, 156(1), 27-33.

Ball JC, Shaffer JW, & Nurco DN (1983). The day-to-day criminality of heroin addicts in Baltimore--a study in the continuity of offence rates. *Drug and Alcohol Dependence*, 12(2), 119-142.

Bammer, G., Van Den Brink, W., Gschwend, P., Hendriks, V., & Rehm, J. (2003). What can the Swiss and Dutch trials tell us about the potential risks associated with heroin prescribing? *Drug and Alcohol Review*, 22, 363-371.

Barnett, P.G. (1999). The cost-effectiveness of substance abuse treatment. *Current Psychiatry Reports*, 1(2), 166-171.

Barnett, P.G., & Hui, S.S. (2000). The cost-effectiveness of methadone maintenance. *Mount Sinai Journal of Medicine*, 67(5-6), 365-374.

Barnett PG (1999). The cost-effectiveness of methadone maintenance as a health care intervention. *Addiction*, 94(4), 479-488.

Barnett PG, Zaric GS, & Brandeau ML (2001). The cost-effectiveness of buprenorphine maintenance therapy for opiate addiction in the United States. *Addiction*, 96, 1267-1278.

Belenko, S., Patapis, N., & French, M.T. (2005). *Economic benefits of drug treatment: a critical review of the evidence for policy makers.* Philadelphia: Treatment Research Institute, University of Pennsylvania

Bell, J., Hall, W., & Byth, K. (1992). Changes in criminal activity after entering methadone maintenance. *British Journal of Addiction*, 87, 251-258.

Bell, J., Mattick, R., Hay, A., Chan, J., & Hall, W. (1997). Methadone maintenance and drug-related crime. *Journal of Substance Abuse*, 9, 15-25.

Bellin, E. (1999). High dose methadone reduces criminal recidivism in opiate addicts. *Addictive Research*, 7, 19.

Bennett, T., & Wright, R. (1986). The impact of prescribing on the crimes of opioid users. *British Journal of Addiction*, 81, 265-273.

Bradley, C.J., French, M.T., & Rachal, J.V. (1994). Financing and cost of standard and enhanced methadone treatment. *Journal of Substance Abuse Treatment*, 11(5), 433-442.

Cartwright, W.S. (2000). Cost-benefit analysis of drug treatment services: review of the literature. *Journal of Mental Health policy and Economics*, 3, 11-26.

Cartwright, W.S., & Solano, P.L. (2003). The economics of public health: financing drug abuse treatment services. *Health Policy*, 66(3), 247-260.

Choi, B., Robson, L., & Single, E. (1997). Estimating the economic costs of the abuse of tobacco, alcohol and illicit drugs: a review of methodologies and Canadian data sources. *Chronic Diseases in Canada*, 18(4), 149-165.

Clark, N., Lintzeris, N., Gijsbers, A., Whelan, G., Dunlop, A., Ritter, A., & Ling, W. (2002). LAAM maintenance vs methadone maintenance for heroin dependence, *Cochrane Database of Systematic Reviews*.

Collins, D.J., & Lapsley, H.M. (2002). *Counting the cost: estimates of the social costs of drug abuse in Australia in 1998-99. National Drug Strategy Monograph Series No. 49* Canberra: Commonwealth of Australia

Daley, M., Argeriou, M., McCarty, D., Callahan, J.J., Shepard, D.S., & Williams, C.N. (2000). The costs of crime and the benefits of substance abuse treatment for pregnant women. *Journal of Substance Abuse Treatment*, 19(4), 445-458.

Daley, M., Love, C.T., Shepard, D.S., Petersen, C.B., White, K.L., & Hall, F.B. (2004). Cost-effectiveness of Connecticut's in-prison substance abuse treatment. *Journal of Offender Rehabilitation*, 39, 69–92.

De Jong, C., Laheij, R., & Krabbe, P. (2005). General anaesthesia does not improve outcome in opioid antagonist detoxification treatment: a randomized controlled trial. *Addiction*, 100(2), 206-215.

Dijkgraaf, M.G.W., van der Zanden, B.P., de Borgie, C.A.J.M., Blanken, P., van Ree, J.M., & van den Brink, W. (2005). Cost utility analysis of co-prescribed heroin compared with methadone maintenance treatment in heroin addicts in two randomised trials. *BMJ*, 330(7503), 1297.

Doran, C.M., Shanahan, M., Mattick, R.P., Ali, R., White, J., & Bell, J. (2003). Buprenorphine versus methadone maintenance: a cost-effectiveness analysis. *Drug and alcohol dependence.*, 71(3), 295-302.

Doran, C.M., Shanahan, M., Bell, J., & Gibson, A. (2004). A cost-effectiveness analysis of buprenorphine-assisted heroin withdrawal. *Drug Alcohol Rev*, 23(2), 171-175.

Doran, C.M., Shanahan, M., Digiusto, E., O'Brien, S., Mattick, R.P., & NEPOD Research group (IN PRESS). A cost-effectiveness analysis of maintenance agonist treatments in the National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD). *Expert Review of Pharmacoeconomics and Outcomes Research*.

Doran CM (2005). Buprenorphine, buprenorphine/naloxone and methadone maintenance: a cost-effectiveness analysis. *Expert Review of Pharmacoeconomics and Outcomes Research*, 5(5), 583-592.

Drummond, M.F., Sculpher, M.J., Torrance, G.W., O'Brien, B.J., & Stoddart, D.L. (2005). *Methods for the economic evaluation of health care programmes* Oxford: Oxford Medical Publications

Ettner, S.L., Huang, D., Evans, E., Ash, D.R., Hardy, M., Jourabchi, M., & Hser, Y.I. (2006). Benefit-cost in the California treatment outcome project: Does substance abuse treatment "pay for itself"? *Health Services Research*, 41(1), 192-213.

Fals-Stewart, W., O'Farrell, T., & Birchler, G. (1997). Behavioral couples therapy for male substance-abusing patients: A cost outcomes analysis. *Journal of Consulting & Clinical Psychology*, 65(5), 789-802.

Farrell M, Ward J, Mattick R, Hall W, Stimson GV, des Jarlais D, & al, e. (1994). Methadone maintenance treatment in opiate dependence: a review. *British Medical Journal*, 309, 997-1001.

French, M., & Martin, R. (1996a). The Costs of Drug Abuse Consequences: A Summary of Research Findings. *Journal of Substance Abuse Treatment*, 13(6), 453-466.

French, M., Dunlap, L., Zarkin, G., McCeary, K., & McLellan, A. (1997). A Structured Instrument for Estiminating the Economic Cost of Drug Abuse Treatment. *Journal of Substance Abuse Treatment*, 14(5), 445-455.

French, M., & McGeary, K. (1997). Estimating the economic cost of substance abuse treatment. *Health Economics*, 6, 1-6.

French, M., McCollister, K., Cacciola, J., Durell, J., & Stephens, R. (2002). Benefit-cost analysis of addiction treatment in Arkansas: specialty and standard residential programs for pregnant and parenting women. *Substance Abuse*, 23(1), 31-51.

French, M.T., Zarkin, G.A., Hubbard, R.L., & Rachal, J.V. (1993). The effects of time in drug abuse treatment and employment on posttreatment drug use and criminal activity. *American Journal of Drug and Alcohol Abuse*, 19, 19-33.

French, M.T., Bradley, C.J., Calingaert, B., Dennis, M.L., & et al. (1994). Cost analysis of training and employment services in methadone treatment. *Evaluation and Program Planning*, 17(2), 107-120.

French, M.T., & Martin, R.F. (1996b). The costs of drug abuse consequences: a summary of research findings. *Journal of Substance Abuse Treatment*, 13(6), 453-466.

French, M.T., Salome, H.J., Krupski, A., McKay, J.R., Donovan, D.M., McLellan, A.T., & Durell, J. (2000). Benefit-cost analysis of residential and outpatient addiction treatment in the State of Washington. *Evaluation Review*, 24(6), 609-634.

French, M.T., Salome, H.J., & Carney, M. (2002). Using the DATCAP and ASI to estimate the costs and benefits of residential addiction treatment in the State of Washington (Provisional record). *Social Science and Medicine*, 55(12), 2267-2282.

French MT, & Drummond MF (2005). A research agenda for economic evaluation of substance abuse services. *Journal of Substance Abuse Treatment*, 29, 125-137.

Garcia-Altes, A., Olle, J.M., AntoÃ±anzas, F., & Colom, J. (2002). The social cost of illegal drug consumption in Spain. *Addiction*, 97(9), 1145-1153.

Gerstein DR, Johnson RA, Harwood HJ, Fountain D, Suter N, & Malloy K (1994). *Evaluating recovery services: The California drug and alcohol treatment system (CALDATA)* Sacramento: California Department of Alcohol and Drug Programs

Godfrey, C., Stewart, D., & Gossop, M. (2004). Economic analysis of costs and consequences of the treatment of drug misuse: 2-year outcome data from the National Treatment Outcome Research Study (NTORS). *Addiction*, 99(6), 697-707.

Gold, M., Siegel, J., Russell, L., & Weinstein, M.C. (1996). *Cost-effectiveness in health and medicine* New York: Oxford University Press

Gossop, M., Marsden, J., Stewart, D., & Rolfe, A. (2000). Reductions in acquisitive crime and drug use after treatment of addiction problems: 1-year follow-up outcomes. *Drug & Alcohol Dependence*, 58(1-2), 165-172.

Gossop, M., & Strang, J. (2000). Price, cost and value of opiate detoxification treatments - Reanalysis of data from two randomised trials. *British Journal of Psychiatry*, 177, 262-266.

Gossop, M., Marsden, J., Stewart, D., & Treacy, S. (2001). Outcomes after methaodne maintenance reduction treatments: two-year follow-up results from the National Treatment Outcome Research Study. *Drug and Alcohol Dependence*, 62, 255-264.

Gossop, M., Trakada, K., Stewart, D., & Witton, J. (2005). Reductions in criminal convictions after addiction treatment: 5-year follow-up. *Drug & Alcohol Dependence*, 79(3), 295-302.

Gowing L, Ali R, & J., W. (2002). *Opioid antagonists with minimal sedation for opioid withdrawal (Cochrane Review)* Chichester, UK: John Wiley & Sons Ltd

Gowing L, Ali R, & White J (2002). *Buprenorphine for the management of opioid withdrawal (Cochrane Review)* Chichester, UK.: John Wiley & Sons Ltd.

Griffith, J.D., Hiller, M.L., Knight, K., & Simpson, D.D. (1999). A cost-effectiveness analysis of in-prison therapeutic community treatment and risk classification. *Prison Journal*, 79, 352–368.

Hall, W., Doran, C., Degenhardt, L., & Shepard, D. (2006). Illicit Opioid Use. In D. Jamison,J. Breman,A. Measham,G. Alleyne,M. GClaeson,D. Evans,P. Jha,A. Mills, & P. Musgrove (Eds.), *Disease control priorities in developing countries* (pp. 907-932). New York: Oxford University Press.

Hall, W.D., Ward, J., & Mattick, R. (1998). The effectiveness of methadone maintenance treatment 1: Heroin use and crime. In J. Ward,R. Mattick, & W. Hall (Eds.), *Methadone Maintenance Treatment and Other Opioid Replacement Therapies.* Amsterdam: Harwood Academic.

Hammersley, R., Forsyth, A., & Lavelle, T. (1990). The criminality of new drug users in Glasgow. *British Journal of Addiction*, 85, 1583–1594.

Harris, A.H., Gospodarevskaya, E., & Ritter, A.J. (2005). A randomised trial of the cost effectiveness of buprenorphine as an alternative to methadone maintenance treatment for heroin dependence in a primary care setting. *PharmacoEconomics.*, 23(1), 77-91.

Hartz, D.T., Meek, P., Piotrowski, N.A., Tusel, D.J., Henke, C.J., Delucchi, K., Sees, K., & Hall, S.M. (1999). A cost-effectiveness and cost-benefit analysis of contingency contracting-enhanced methadone detoxification treatment. *American Journal of Drug and Alcohol Abuse*, 25(2), 207-218.

Harwood, H., Hubbard, R., Collins, J., & Rachal, J. (1988). The costs of crime and the benefits of drug abuse treatment: a cost-benefit analysis using TOPS data, *Compulsory treatment of drug abuse: research and clinical practice.* (pp. 209-235). Rockville, MD: United States Department of Health and Human Services

National Institutes of Health.

Healey, A., Knapp, M., Marsden, J., Gossop, M., & Stewart, D. (2003). Criminal outcomes and costs of treatment services for injecting and non-injecting heroin users: evidence from a national prospective cohort survey (Structured abstract). *Journal of Health Services Research and Policy*, 8(3), 134-141.

Hubbard, R.L., Marsden, M.E., Rachal, J.V., Harwood, H.J., Cavanaugh, E.R., & Ginzburg, H.M. (1989). *Drug Abuse Treatment: A National Study of Effectiveness.* London: Chapel Hill

Kraft, M., Rothbard, A., Hadley, T., McLellan, A., & Asch, D. (1997). Are Supplementary Services Provided During Methadone maintenance Really Cost-Effective? *Amercian Journal of Psychiatry*, 154, 1214-1219.

Magura, S., Rosenblum, A., Lewis, C., & Joseph, H. (1993). The effectiveness of in-jail methadone maintenance. *Journal of Drug Issues*, 23(75-99).

Mark, T., Woody, G., Juday, T., & Kleber, H. (2001). The economic costs of heroin addiction in the United States. *Drug and Alcohol Dependence*, 61, 195-206.

Masson, C., Barnett, P., Sees, K., Delucchi, K., Rosen, A., Wong, W., & Hall, S. (2004). Cost and cost-effectiveness of standard methadone maintenance treatment compared to enriched 180-day methadone detoxification. *Addiction*, 99(6), 718-726.

Mattick, R.P., Kimber, J., Breen, C., & Davoli, M. (2003). *Buprenorphine Maintenance Versus Placebo or Methadone Maintenance for Opioid Dependence* Chichester, UK: John Wiley & Sons

Mattick RP, Digiusto E, Doran CM, O'Brien S, Shanahan M, Kimber J, Henderson N, Breen C, Shearer J, Gates J, Shakeshaft A, & NEPOD Trial Investigators (2001). National evaluation of pharmacotherapies for opioid dependence (NEPOD). Canberra: Commonwealth Department of Health and Ageing.

Mauser, E., Van Stelle, K.R., & Moberg, D.P. (1994). The economic impact of diverting substance-abusing offenders into treatment. *Crime & Delinquency*, 40(4), 568-588.

McCollister, K., French, M.T., Prendergast, M., Wexler, H., Sacks, S., & Hall, E. (2003). Is in-prison treatment enough? A cost-effectiveness analysis of prison-based treatment and aftercare services for substance abusing

offenders. *Law Policy*, 25, 63-82.

McCollister, K., French, M.T., Prendergast, M., Hall, E., & Sacks, S. (2004). Long term cost-effectiveness of addiction treatment for criminal offenders. *Justice Quarterly*, 21, 659–679.

McCollister KE, & French MT (2003). The relative contribution of outcome domains in the total economic benefit of addiction interventions: a

review of first findings. *Addiction*, 98, 1647–1659.

McLellan, A.T., Arndt, I.O., Metzger, D.S., Woody, G.E., & O'Brien, C.P. (1993). The effects of psychosocial services in substance abuse treatment. *Journal of the American Medical Association*, 269, 1953-1959.

Miller, C.L., Schechter, M.T., Wood, E., Spittal, P.M., Li, K., LalibertÃ©, N., Montaner, J.S., & Hogg, R.S. (2004). The potential health and economic impact of implementing a medically prescribed heroin program among Canadian injection drug users. *International Journal of Drug Policy*, 15(4), 259-263.

Mojtabai, R., & Zivin, J.G. (2003). Effectiveness and cost-effectiveness of four treatment modalities for substance disorders: a propensity score analysis (Provisional record). *Health Services Research*, 38(1), 233-259.

National Institute on Drug Abuse (2004). *Report of the Blue Ribbon Task Force on Health Services Research at the National Institute on Drug Abuse* Washington DC: National Institutes of Health, U.S. Department of Health and Human Services.

Pals-Stewart, W., O'Farrell, T.J., & Birchler, G.R. (1997). Behavioral Couples Therapy for Male Substance-Abusing Patients: A Cost Outcomes Analysis. *Journal of Consulting and Clinical Psychology*, 65, 789-802.

Rajkumar, A.S., & French, M.T. (1997). Drug use, crime costs, and the economic benefits of treatment. *Journal of Quantitative Criminology,*, 13, 291–323.

Roebuck, C., French, M.T., & McLellan, T. (2003). DATStats: results from 85 studies using the Drug Abuse Treatment Cost Analysis Program (DATCAP). *Journal of Substance Abuse Treatment*, 25, 51-57.

Rosenheck, R., & Kosten, T. (2001). Buprenorphine for opiate addiction: potential economic impact. *Drug and Alcohol Dependence*, 63(3), 253-262.

Rothbard, A., Alterman, A., Rutherford, M., Liu, F., Zelinski, S., & McKay, J. (1999). Revisiting the effectiveness of methadone treatment on crime reductions in the 1990s. *Journal of Substance Abuse Treatment*, 16(4), 329-335.

Salome, H.J., French, M.T., Miller, M., & McLellan, A.T. (2003). Estimating the client costs of addiction treatment: first findings from the client drug abuse treatment cost analysis program (client DATCAP). *Drug and Alcohol Dependence*, 71(2), 195-206.

Shanahan, M.D., Doran, C.M., Digiusto, E., Bell, J., Lintzerisa, N., White, J., Ali, R., Saunders, J.B., Mattick, R.P., & Gilmour, S. (2006). A cost-effectiveness analysis of heroin

detoxification methods in the Australian National Evaluation of Pharmacotherapies for Opioid Dependence (NEPOD). *Addictive Behaviors*, 31(3), 371-387.

Shepard, D.S., Larson, M.J., & Hoffmann, N.G. (1999). Cost-effectiveness of substance abuse services: Implications for public policy. *Psychiatric Clinics of North America*, 22(2), 385-400.

Sigmon, S.C., & Stitzer, M.L. (2005). Use of low-cost incentive intervention to improve counseling attendance among methadone maintained patients. *Journal of Substance Abuse Treatment*, 29(4), 253-258.

Simoens S, Matheson C, Inkster K, Ludbrook A, & Bond C (2002). *The effectiveness of treatment for drug users: An international systematic review of the evidence* Edinburgh: Scottish Executive Drug Misuse Research Programme

Simoens S, Ludbrook A, Matheson C, & Bond C (2006). Pharmaco-economics of community maintenance for opiate dependence: A review of evidence and methodology. *Drug and Alcohol Dependence*, IN PRESS.

Single, E., Robson, L., Xie, X., & Rehm, J. (1998). The economic costs of alcohol, tobacco and illict drugs in Canada, 1992. *Addiction*, 93(7), 991-1006.

Strang, J., Marsden, J., Cummins, M., Farrell, M., Finch, E., Gossop, M., Stewart, D., & Welch, S. (2000). Randomized trial of supervised injectable versus oral methadone maintenance: report of feasibility and 6-month outcome. *Addiction*, 95, 1631-1645.

Tucker T, & Ritter A (2000). Naltrexone in the treatment of heroin dependence: a literature review. *Drug and Alcohol Reveiw*, 19, 73-82.

United Nations Office on Drugs and Crime (2004). *World Drug Report.* Vienna: UNODC

Warren, E., Viney, R., Shearer, J., Shanahan, M., Wodak, A., & Dolan, K. (IN PRESS). Value for money in drug treatment: economic evaluation of prison methadone. *Drug and Alcohol Dependence*.

World Health Organisation (2005). *WHO Report on Neuroscience of Psychoactive Substance Use and Dependence* Geneva: WHO

World Health Organization (2004). *The World Health Report 2004* Geneva: WHO

Zaric, G.S., Barnett, P.G., & Brandeau, M.L. (2000). HIV transmission and the cost-effectiveness of methadone maintenance. *American Journal of Public Health*, 90(7), 1100-1111.