From The Chief Medical Officer:
Dr Henrietta Campbell CB

Castle Buildings
Upper Newtownards Road
Belfast BT4 3SJ

Telephone: 028 90 520563
Fax: 028 90 520574

E-Mail: henrietta.campbell@dhsspsni.gov.uk

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Publication of "Review of Research on Substitute Prescribing for Opiate Dependence and Implications for Northern Ireland" by Dr Karen McElrath

The number of problem heroin users in Northern Ireland has grown over recent years, and with this growth the subject of substitute therapy as an option for those presenting for treatment has become a significant issue. Decisions about arrangements for Northern Ireland must be evidence-based, and the Department commissioned Dr Karen McElrath of Queen's University, Belfast, to carry out the present review.

The Department has considered the review carefully and agrees with the central thrust of Dr McElrath's recommendations. Given the potential risks attached to substitute prescribing discussed in the review – for example the consequences of diversion and subsequent unauthorised or accidental use – the Department has qualified its response in a number of areas. The views of the Department are set out in the Appendix to the review.

The Department will shortly establish an Implementation Group to oversee the development of structures to support those practitioners dealing with clients for whom substitute therapy is appropriate. These structures will support practitioners to deliver services based on relevant clinical guidelines. The Implementation Group will also consider how services should be configured to take account of logistical and resource issues.

Substitute therapy as a treatment for heroin dependence has not been hitherto used on any significant scale in Northern Ireland. The Department is committed to a thorough process of monitoring and evaluation to ensure that services are delivered appropriately; to maintain public confidence; and to update guidelines and advice to professionals in an effective and timely way.

Yours sincerely

HENRIETTA CAMPBELL (Dr)

Review of Research on Substitute Prescribing for Opiate Dependence and Implications for Northern Ireland

Karen McElrath
School of Sociology and Social Policy
Queen's University, Belfast

with a Response to the recommendations contained in the Review from the Department of Health, Social Services and Public Safety

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This Review was commissioned by the Drug and Alcohol Information and Research Unit, Department of Health, Social Services and Public Safety on behalf of the Northern Ireland Drugs and Alcohol Campaign

Points of view in the Review are those of the author. Points of view in the Departmental Response are those of the DHSSPS.

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Note:

The second draft of this review of research was received by the Department in October 2002. Although discussions between the author and the Department on the review continued after that date, the review does not take cognisance of any research published after September 2002.

Executive Summary

This report draws from extensive literature on subscribing prescribing for opiate dependence, and focuses largely on heroin use. The report includes an international review of both clinical and observational studies. Most research has focused on methadone, largely because of its longer history for treating heroin dependence. The review includes findings from studies that have compared methadone, buprenorphine (Subutex), and to a lesser extent, Levo-Alpha-Acetyl Methadol and heroin maintenance. The effects of these drugs on persons dependent on heroin and other opiates are examined in relation to outcomes, e.g., treatment retention and subsequent opiate use.

The review identified dozens of controlled and observational studies from various countries that have reported favourable outcomes with respect to the effects of methadone treatment for heroin dependence. This literature strongly suggested that methadone maintenance be implemented as a treatment option for persons dependent on heroin in N. Ireland. Several factors (e.g., maintenance rather than reduction or abstinence programmes, dosage levels and flexible dosing policies, treatment in conjunction with counselling), however, were shown to increase or decrease the degree of successful treatment outcomes and programmes should be organised accordingly. Additionally, it was recommended that reduction programmes be an option for heroin users as well, however, this decision should be an informed one, following *balanced* advice from drug treatment specialists or physicians.

Diverted methadone that results in improper use of the drug is a primary concern, however, the review found that programme regulations such as supervised consumption of methadone appears to reduce methadone-related deaths. This literature led to the recommendation that methadone clients undergo supervised consumption of methadone for the first six months of treatment and that drug treatment specialists and physicians consider the possibility of take-home doses after that time. Alternatively, the research suggested that supervised consumption of methadone might reduce the number of clients who otherwise might be interested in methadone treatment, and might also affect treatment retention. The research also identified limitations associated with programmatic urinalysis during treatment and called into question its effectiveness.

The review found that in some instances (e.g., proper dosage), buprenorphine was found to be as effective as methadone. However, little is known about the long-terms of buprenorphine. Additionally, Levo-Alpha-Acetyl Methadol is no longer available in several European countries because of serious adverse effects. The review also noted that although heroin maintenance appears to have some effect on drug-related criminal activity, the effects on other outcomes (e.g., relapse) are considerably less clear. Based on this information, it was recommended that the DHSSPS implement buprenorphine treatment for maintenance purposes, when research has documented favourable results with respect to long-term effects of the drug. However, three of five of Consultant Psychiatrists who would likely be involved if substitute prescribing were introduced in N. Ireland favour buprenorphine over methadone, citing the safety record of buprenorphine.

This report described models for implementing methadone maintenance and the shared care model of treatment delivery appears to offer promising results. It is necessary, however, to provide detailed and regular training of general practitioners (GPs), pharmacists, and drug treatment specialists and the report describes ways to involve GPs and pharmacists. It was noted also that the DHSSPS should provide alternatives to treatment access.

The literature review identified research conducted elsewhere that suggested that problems with childcare may represent a significant barrier to treatment entry, among women in particular. Although three of the Consultant Psychiatrists had not observed this problem among patients to date, they also noted that most patients have been male. It was suggested that obtaining this information about persons already in treatment, may represent a biased sample. It was therefore recommended that childcare be provided by treatment specialist agencies in N. Ireland.

1 *Introduction*

The medical implications of heroin use are noteworthy (O'Connor and Fiellin, 2000). Heroin injection can result in skin abscesses, considerable vein damage, and contribute to various bacterial infections resulting from injection practices (Centers for Disease Control, 2001). The risk of acquiring blood-borne infections also is associated with injection behaviours. Heroin injectors are at risk for HIV, Hepatitis B and C viruses (Crofts, Aitken, and Kaldor, 1999; Hope et al., 2001; Long et al., 2001). Inhaling the vapours from heated heroin (i.e., "chasing") has been linked with leucoencephalopathy (Wolters et al., 1982), a rare disease but one associated with high mortality (Hill, Cooper, and Perry, 2000). Mortality rates among heroin users are high. In a 33-year follow-up study of 581 male heroin "addicts" who were required to undergo drug treatment between 1962 and 1964 in California, the mortality rate among male heroin addicts was estimated to be 50 to 100 times the rate of the general male population of the same age group (Hser et al., 2001).

Recent estimates, generated through capture-recapture methodology, suggested that there were between 695 and 1,018 problem heroin users in Northern Ireland during the 12-month time period, 1 November 2000 and 31 October 2001 (McElrath, 2002). During the same 12-month period, 361 individuals who were using heroin sought treatment or attended a drug service for at least one day. These figures suggest that between 36% and 52% of problem heroin users sought treatment for heroin use during the 12-month period. Treatment outcomes (e.g., retention, reduction in or abstinence from heroin use) are not known for these individuals, however, an earlier qualitative study that focused largely on Belfast heroin injectors suggested that most of the 43 respondents either had never sought treatment or had failed to complete treatment for heroin dependence. Among those persons who had entered drug treatment for heroin dependence, lengths of stay in treatment were very brief and more accurately measured in terms of days rather than weeks or months (McElrath, 2001).

Drawing in part from the definition proposed by Matheson, Bond and Hickey (1999), substitute prescribing for heroin dependence can be described as "the deliberate prescribing of drugs in a controlled manner" in order to

"reduce the use of illicit drugs" or to reduce the harm associated with illicit drug use. This definition suggests that substitute prescribing can occur in maintenance or reduction programmes. Marsden et al. (1998: 244) distinguished between these two types of programmes. They noted that treatment retention is the critical component of maintenance programmes whereby "the substitute [drug] is administered at a stable level for a period of several months and sometimes years." Maintenance treatment through substitute prescribing allows heroin users "to get on with their lives" although complete abstinence might never be achieved (Drucker, 2000: 33). In reduction programmes, patients are prescribed a substitute drug for heroin dependence and subsequently stabilized. A gradual reduction of methadone dosage levels occurs thereafter. The entire process is often short-term but can last for several months (Marsden et al., 1998).

This report addresses the potential treatment use of substitute prescribing for heroin dependence in Northern Ireland. In the United Kingdom, methadone and buprenorphine are licensed drugs that are available for the *treatment* of opiate dependence. Diamorphine is also permitted under special license from the Home Office. Other drugs, e.g., lofexidine, are available in the United Kingdom for detoxification or "drug reduction" only (Department of Health, 1999), however, the effectiveness of substitute drugs used for detoxification is a topic that is not addressed in this report.[1]

Internationally, there exist a number of drugs that are utilised for the treatment of heroin dependence and this report begins with a description of the more common substances that are used for this purpose. Within this section and where possible, the descriptions of each substance include research findings that pertain to the *effectiveness* of the substitute as a treatment for heroin dependence. However, the vast majority of this research, including clinical trials and observational studies, has focused on the effectiveness of methadone treatment as opposed to other drug substitute interventions. This report describes research findings that identify *aspects of programmes, joint interventions, characteristics of individuals, and other factors that have been found to contribute to*

[1] Detoxification is generally not considered to be drug treatment. Rather, detoxification is viewed as one of the initial stages in which opiate dependent persons must engage in order to subsequently reduce their intake of opiates. Gabbay, Jeffrey, and Carnwath (2000) noted the confusion in the literature regarding the terms "reduction" and "detoxification."

treatment outcomes, e.g., treatment retention, subsequent use of opiates or other drugs, and other lifestyle changes. More recent studies have compared treatment outcomes for two or more substitute drugs and these studies are highlighted herein. The report identifies a number of methodological problems that have been associated with studies that examine the effectiveness of substitute prescribing.

This report includes a discussion of various programmes that offer substitute prescribing. Most of this information is drawn from programmes located in Dublin, Glasgow, and Edinburgh. In particular, the role of general practitioners and pharmacists are described in the context of a "shared care" delivery of drug treatment. The review of various literature has identified several problems and issues that must be addressed before substitute prescribing is implemented and these factors are described. The final sections of this report include a summary of major findings and a list of evidence-based recommendations.

2 *Substitute drugs used in the treatment of opiate dependence*

2.1 *Methadone*

Methadone is a synthetic opiate that was developed in Germany in 1941. In the 1960s, the drug was identified as a possible treatment for opiate dependence.[2] Initial clinical trials conducted by Dole and Nyswander (1965) showed positive results and those scientists received the Lasker prize for their discovery (Drucker, 2000).

Used orally, a single dose of methadone can last for 24-36 hours (Lindesmith Center-Drug Policy Foundation, 2000). Initial doses (e.g., the first three days) must be within a "safe range" and increases in dosage levels can occur thereafter. However, methadone clients must be monitored frequently, particularly when dosage levels are modified. The correct dose diminishes withdrawal associated with heroin use as well as cravings for that drug. Withdrawal symptoms associated with heroin use can be minimised with low doses of methadone, however, high doses are required to block the effects of heroin (Lindesmith Center-Drug Policy Foundation, 2000). The effects of sedation and euphoria do not occur if the correct dose of methadone is used. The goal of methadone treatment is to "establish a stable blood level of methadone such that the patient is neither too high (intoxicated) nor too low (in withdrawal)" (Drucker, 2000: 37).

2.1.1 *Outcomes associated with methadone treatment*

Both methadone maintenance and methadone-treated opioid reduction programmes are available in the United Kingdom. Most outcome-based research into the effectiveness of methadone has focused on methadone maintenance so that little is known about the effectiveness of methadone reduction programmes (Gabbay, Jeffrey, and Carnwath, 2000; Seivewright and Iqbal, 2002). In one comparative study, however, Sees et al. (2000) found methadone maintenance to be significantly more effective than methadone reduction. Those authors randomly assigned 179 adults to either 1) methadone maintenance (MMT) combined with one hour of group therapy

[2] Methadone is used primarily to treat heroin dependence but can be used to treat other forms of opiate addiction as well. Most research into the effectiveness of methadone treatment has focused on samples of heroin users.

per week and one hour of individual therapy per month, or 2) a methadone reduction program coupled with enhanced psychosocial services and aftercare (M180). The reduction program included methadone provision for 180 days with continued involvement in other services for the remaining six months. Methadone dosage levels in both groups were comparable. The researchers found no significant differences in opiate-negative urines until the fifth month of the study after which the M180 group showed a significantly higher rate of opiate-positive urines. That pattern continued until month 12. These findings suggested that maintenance programmes are more effective than reduction programmes, even when the latter are combined with enhanced support services.

Methadone maintenance interventions have been widely researched – much more so than other substitute prescribing methods for heroin addiction (Farrell et al., 1994). Scholars have noted that the majority of studies into the effectiveness of methadone treatment have been conducted in the United States (Marsden et al., 1999) and the degree to which US research findings are generalisable to Northern Ireland is unknown. Clearly there are differences in the way that methadone is administered in the United States compared to certain European countries, including England, Scotland, and the south of Ireland. In the US, methadone treatment slots are quite limited, the drug is only available through specialised clinics, and recommended dosage levels are low in comparison.

Substitute prescribing has been available in Scotland, England and Wales for several years, however, clinical studies from those regions are limited. Moran et al. (2001) observed that although a growing body of research has investigated injecting drug use in the Dublin area, very little is known about the impact of methadone prescribing in the region.

Research has demonstrated that the risk of premature death through either overdose or natural causes is lowered among heroin users who have been maintained on methadone compared with heroin users who have left methadone programmes prematurely (Caplehorn et al. 1994; Fugelstad et al., 1995; Langendam et al., 2001).

Marsch (1998) used meta-analysis[3] to examine the effectiveness of methadone maintenance on various behavioural outcomes, i.e., risk behaviours for HIV, criminal activity, and illicit opiate use. In comparison to other outcome measures, she found that methadone maintenance had its largest impact on reducing drug-related crime (but not criminal activity in general). Moderate effects were noted for the reduction of opiate use and small to moderate but significant effects were observed for decreased risk behaviours for HIV infection (see below). The author acknowledged the limitation that her study included only those samples in which all individuals completed methadone treatment.

A large body of research has suggested that methadone can reduce at least some risk behaviours associated with HIV infection (Hoffman et al., 1998, Peters et al., 1998, Sorensen and Copeland, 2000; Wells et al., 1996).[4] Although considerable literature suggests that methadone treatment reduces the use of opiates (Ball and Ross, 1991; Hubbard et al., 1997) and risky injection practices (Ward, Hall, and Mattick, 1999), the evidence appears to be inconclusive regarding the link between methadone treatment and sexual risk behaviours. Some research has found that participation in methadone treatment is followed by a decrease in the number of sexual partners and an increase in condom use. For example, in a Miami, Florida study, Lollis et al. (2000) compared methadone clients with injecting drug users not-in-treatment (N=123). Higher frequency of condom use, fewer sexual partners and fewer "high risk" sex partners were reported among methadone clients at six-month follow-up, compared to IDUs not in treatment. Still though, other research has found that methadone treatment has had little impact on sexual risk behaviours (Magura et al., 1998; Stark et al., 1996). Research on injection drug users in general

[3] Meta-analysis is a useful tool for examining a number of studies that focus on, for example, the effectiveness of drug treatment. The strategy incorporates findings from various studies (with specified criteria for inclusion), and identifies those factors that are significantly related to outcomes, e.g., successful treatment completion. The methodology has other benefits as well, including the potential for resolving discrepant findings from a number of studies (Farré et al., 2002).

[4] Sorensen and Copeland (2000) reviewed 33 studies that focused on drug treatment and HIV prevention. The studies were published between 1988 and 1998. The authors concluded that evidence was inconclusive with respect to the impact of drug treatment on selected HIV risk behaviours, namely, the loaning and borrowing of injection equipment as well as unsafe sex behaviours.

(without specific reference to methadone treatment) has documented that changes in injection and drug use risk behaviours have been more pronounced than changes in sexual risk behaviours.

Zaric, Barnett, and Brandeau (2000) concluded that although some risk behaviours appear to be largely unaffected by methadone treatment, the risk reductions that are associated with such treatment are sufficiently large enough to have a significant effect on reducing HIV infection. Those authors found that costs associated with HIV health care are increased with expansion of methadone maintenance in the United States. However, these costs are offset by a reduction in expenditures associated with the prevention of new infections, decreases in injecting drug use, decreases in disease and ailments that are associated with injecting drug use, as well as lowered mortality. Metzger et al. (1993) found that out-of-treatment IDUs had rates of HIV seroconversion that were *six times* as great as regular methadone clients. The impact of methadone on the prevalence of Hepatitis C Virus has been considerably less.

Many methadone clients return to heroin use after they have dropped out or completed treatment. However, some studies that have focused on long-term follow-up of methadone clients have shown promising results. For example, Byrne (2000) followed 86 methadone clients who had participated in methadone treatment in Sydney between 1987 and 1988. Follow-up data were collected in 1996, about nine years later. The author noted that 41% of clients had remained in treatment during that time period. By follow-up, eight persons had died and seven persons could not be located. Examining data on subjects' progress, the author estimated that between 56% (conservative estimate) and 81% (optimistic estimate) were doing well nine years later. One limitation of this study was that there was no control group. However, longer follow-up periods with good outcomes have reported elsewhere in Australia (Reinart, 2000).

Schwartz et al. (1999) examined follow-up data for 21 methadone maintenance clients in Baltimore, Maryland (US). Clients were monitored by a general practitioner and provided urine samples on a monthly basis. Twelve years after enrolment, treatment retention was observed to be low (i.e., 28.6%), however, self-reported quality of life was enhanced, and methadone-related overdoses were non-existent even with monthly take-home doses.

Moreover, the authors found little evidence of diverted methadone being used for illicit purposes.

Most studies of the effectiveness of methadone have focused on oral methadone. Considerably less is known about injectable methadone, which has been available for prescription in the UK since 1968, although a randomised UK clinical trial of injectable versus oral methadone is in the pilot stages (Beaumont, 2001).

Until early 2002, injectable methadone (unlike prescribed diamorphine) required no special licence in the United Kingdom. However, new licensing arrangements were implemented in 2002 whereby physicians in the United Kingdom must now be licensed if they intend to prescribe injectable methadone. This form of methadone has been used in some clinics and prescribed by some GPs when clients have responded poorly or have been resistant to oral methadone. Some have claimed that injectable methadone also addresses the needle fixation that some clients exhibit. Farrell et al. (1994) noted that clients who are offered injectable methadone might actually increase their frequency of injecting other drugs. However, those authors noted the paucity of research comparing injectable and oral forms of methadone treatment and called for additional research into this issue.
Ford and Ryrie (1999) found that GPs in England who have provided injectable methadone have based those decisions on various factors, e.g., previous poor outcomes with oral methadone, the length of injection history, extent of community support. That study also focused on 34 patients who had been prescribed injectable methadone. The authors observed that methadone dosage was reduced on 23 occasions over time and increased on two occasions only. Beaumont (2001) surveyed GPs in England and Wales about injectable methadone prescribing. Dose levels ranged from 20 to 300 mg per day. When given the choice between prescribed heroin and injectable methadone, some clients have chosen the latter (Metrebian et al., 2001).

2.1.2 *Factors that contribute to methadone treatment outcomes*

Research has suggested that certain factors affect either continued opiate use during methadone treatment, relapse following treatment, or treatment retention. In their extensive review of the literature, Farrell et al. (1994)

concluded that effective methadone treatment outcomes are associated with 1) good quality counselling, 2) good relationships between staff and patients, 3) effective management, 4) low staff turnover, 5) methadone doses in excess of 50 mg per day, 6) maintenance rather than abstinence as a treatment goal, and 7) no withdrawal of privileges. Of importance to Northern Ireland treatment providers, higher rates of opiate use during methadone treatment have been linked with post-traumatic stress disorder (PTSD), notably exposure to violence during adulthood and physical and sexual abuse during childhood (Hien et al., 2000). However, PTSD was not associated with treatment retention.

Retention in methadone maintenance has been identified as a critical factor and length of stay in methadone treatment has been linked with reductions in illicit opiate use and criminal activity (National Evaluation Data Sources, 2000). Further, considerable evidence has suggested that methadone dosage is one of the most important factors for retaining clients in treatment. Robles et al. (2001) suggested that methadone dosage levels appear to be both the most important and most researched factor relating to the effectiveness of methadone treatment. Citing research, they noted that dosage levels are related to treatment retention and to diminished use of opiates among methadone clients.

In maintenance programmes, methadone dosage levels are slowly increased to achieve stabilised levels and because individuals will respond differently to changes in dosage levels, dosages should be adjusted accordingly. Individual metabolism can affect ho w individuals respond to methadone dosage levels. Tolerance to opiates as well as body weight have been identified as other factors that can affect an individual's response to the drug (Lindesmith Center-Drug Policy Foundation, 2000). A growing body of research has suggested that methadone doses might need to be increased in areas characterised by unusually high purity heroin (Bach and Lantos, 1999; Leavitt et al., 2000).

Flexible methadone dosing policies is a critical factor that has been linked to treatment retention. Earlier research found that approximately 50% of methadone clients in the US had been given doses at levels that were unable to prevent subsequent opiate use (D'Aunno and Vaughn, 1992). Further, many programmes have maintained a fixed methadone dosing policy whereby

a 100 mg daily dose has been determined to represent the maximum allowable daily dose (Leavitt et al., 2000). In reviewing the study by Ezard et al (1999), Ling, Huber, and Rawson (2001) noted that as many of 85% of patients in that study were "receiving inadequate doses" of methadone. Such policies fail to consider the individual needs of the patient. The choice of the correct dosage level for a particular patient should be guided by information provided by the patient,[5] the amount of time between methadone consumption and the patient's symptoms, and consideration of changes in symptoms after dosage levels have been increased (Leavitt et al., 2000). Some methadone clients can be comfortable with 50 mg per day, whereas others will require more than 100 mg per day (Payte and Khuri, 1993). Dosage levels that fail to block the effects of opiates, fail to minimise withdrawal symptoms, and fail to reduce cravings offer little in the form of treatment to the patient and are not cost-effective.

Some researchers have recommended that 60 mg of methadone per day is needed for stabilisation. Such dosage would be required for high rates of treatment retention, to decrease the frequency of injecting drug use, and to prevent withdrawal symptoms (van Ameijden et al., 1995). Some research has suggested that the provision of higher doses during detoxification reduces the likelihood of subsequent criminal activity.[6] For instance, Bellin et al. (1999) examined reoffending (measured by the time period between release from jail and subsequent incarceration or end of study period) among prisoners in New York. The authors compared inmates from four groups: 1) those who had received at least 60 mg of methadone while in jail, 2) those who had received 30 mg of methadone or less, 3) those who had been detoxed with methadone but who had not received methadone beyond the detoxification stage, and 4) those who had not received methadone at all. Recidivism was significantly lower in the high-dose group compared with the low-dose group; however, the difference was small between the two groups. The authors noted that their study relied on a fixed dose and that they were not permitted to examine the plasma levels of methadone. They argued that the monitoring of plasma levels is important to determine whether the amount of methadone was able to achieve "adequate blocking

[5] Leavitt et al. (2000: 410) reminded readers that Vincent Dole advised that clinicians should "listen to the patient" before deciding on dosage levels and adjustments.

[6] Or perhaps reduce the likelihood of being apprehended and convicted.

doses" for all clients. They recommended that methadone plasma levels be examined routinely to determine "effective heroin blockade."

Weinrich and Stuart (2000) compared early studies from Glasgow and Edinburgh and observed that the average methadone dose prescribed in Edinburgh was 40 mg, a factor that may have been linked to the lower treatment retention rates (i.e., 39% at 12 months) in that city. Average methadone doses in Glasgow were higher (i.e., 54 mg) as was the treatment retention rate in that city (i.e., 60%). In an observational study, Caplehorn et al. (1993) estimated that a 1 mg daily increase in methadone resulted in a 2% reduction in using heroin during methadone treatment. Further, clinical trials have indicated that methadone doses of 80 to 100 mg per day are more effective than doses of 40 to 50 mg per day (Strain et al., 1999). The higher doses contributed significantly to decreases in opiate use and increases in treatment retention.[7] After 30 weeks of treatment, the percentage of opiate-positive urine samples was 53% for the high-dose group and 61.9% for the 40 to 50 mg group. Reviewing the findings of the Strain et al. study, Leavitt et al. (2000: 408) suggested that despite the significant difference between the two groups, the substantive difference between 53% and 61.9% was "modest." Leavitt et al. (2000: 408) concluded that dosage levels in the Strain et al. study "were clearly subtherapeutic for many patients." In a review of various literature on methadone treatment, Barnett and Hui (2000) recommended that methadone is cost-effective if dosage levels are adjusted to meet individual needs (i.e., flexible dosing) and when high doses of methadone are permitted. It is important to note, however, that methadone maintenance has shown to have little effect on the use of other illicit drugs (Gabbay, Jeffrey, and Carnwath, 2000). Rather, methadone is intended to treat opiate dependence only.

Clients who are made aware of the dosage level that they are consuming and clients who participate in decisions about dosage levels are more likely to refrain from using opiates (Havassy, Hargreaves, and De Barros, 1979; Robles et al., 2001) and to stay in treatment for longer periods (Caplehorn and Bell, 1991). Condelli and Dunteman (1993) found that methadone clients who were informed of the dosage that they were consuming were approximately *three times* as likely to remain in treatment compared to

[7] All methadone clients in that study received substance use counselling as part of treatment.

clients who were not told about their dosage levels. Dosage also appears to "interact" with clinic attendance. Rhoades et al. (1998) randomly assigned 150 opiate users to one of four groups, modified by the daily dose of methadone (50 or 80 mg) and frequency of clinic attendance (two or five days per week). Study retention was lower among clients who visited the clinic five days per week as opposed to two, thus treatment retention was higher among clients who received more take-home doses of methadone. Additionally, higher rates of opiate positive urines were reported for clients who had received low doses of methadone.

Other factors that have contributed to successful treatment outcomes (e.g., retention, drug-free urine samples, injection drug use) among methadone clients have included gender, i.e., female (Gogineni, Stein, and Friedmann, 2001; Staedt, 1996), not living with a substance-using partner (Gogineni, Stein, and Friedmann, 2001), and fewer social connections with drug using networks (Gogineni, Stein, and Friedmann, 2001). A multivariate analysis conducted by Morral et al. (1999) showed that attendance at counselling sessions as well urinalysis results for opiates during the first two weeks of methadone treatment were factors that successfully predicted treatment outcomes at six- and nine-month follow-ups.

2.2 *Buprenorphine*

In 1978, buprenorphine (i.e., in this instance, Temgesic®) was introduced as a painkiller in the United Kingdom (Agar et al., 2001), however, Temgesic®, never proved to be an effective treatment for heroin dependence. Buprenorphine (in the form of Subutex®) is a partial opioid agonist that has been introduced as a treatment for opiate dependence in several European countries (namely France) as well as Australia. Unlike methadone, buprenorphine is not orally active; rather, buprenorphine tablets are consumed sublingually, i.e., under or beneath the tongue. Although buprenorphine is an opioid agonist, its antagonist properties mean that it "reacts against opiates and precipitates withdrawal" (Agar et al., 2001: 69).

Advocates of the drug have argued that there are several benefits for using buprenorphine rather than methadone to treat heroin dependence. First, buprenorphine is a partial opioid agonist so that *with proper dosage*, withdrawal from the drug is thought to be milder than withdrawal from

methadone or levo-alpha-acetyl methadol (Eissenberg et al., 1996; Lenné, Lintzeris, and Ritter, 1999; Schottenfeld et al., 2000). Second, the effects of buprenorphine last longer than methadone so that dosing is less frequent than the daily dosing required with methadone. Research has shown that buprenorphine, administered three times per week, is an effective dose for treating heroin dependence (Schottenfeld et al., 2000). Third, the three-day dosing schedule reduces the need for take-home doses, thus there is a reduced threat to the drug being sold or obtained through illicit purposes. Fourth, it has been suggested that buprenorphine is less likely than methadone to cause respiratory depression (Krook et al., 2002; Walsh et al., 1994), a factor that could lower the rate of overdose. However, Agar et al. (2001) have voiced concern about the effect of combining buprenorphine with "street" drugs. Moreover, some authors have reported that high doses of buprenorphine can actually enhance the effects of certain drugs, i.e., cocaine (Rosen et al., 1993).

Some researchers have found that high doses of buprenorphine (e.g., 12 mg) are more effective than low doses (Pani et al., 2000) whereas others have reported that buprenorphine doses that exceed 12 mg per day might be required for some patients (Schottenfeld et al., 1997). Still others have suggested that because buprenorphine is a partial agonist, the drug may be less effective at higher doses (Barnett, Rodgers, and Bloch, 2001). Chadderton (2000) reported that the opiate agonist effects of buprenorphine reach a ceiling effect estimated at 10 to 12 mg per day.

As a method for treating heroin addiction, buprenorphine was approved in 2000 in Australia, and the drug (i.e., Subutex®) has been available in that country since 2001. Given its recent introduction in Australia, the literature describing the experience of buprenorphine there is quite scant. Considerably more research on buprenorphine as a treatment for opiate dependence has emerged from France where the drug (i.e., Subutex®) was approved as a treatment for heroin dependence in France in 1995 and has been available in pharmacies since 1996 (Reynaud-Maurupt et al., 2000). In that country, the drug is available in .4, 2, and 8 mg tablets. The recommended daily dose is between 8 and 10 mg. For maintenance purposes, clients collect doses from pharmacies and take-home doses (28-day maximum) are permitted (Ling, Huber, and Rawson, 2001). About 60,000 patients were receiving buprenorphine in France in the late 1990s,

approximately seven times the number who were in receipt of methadone (Thirion et al., 2002). Ling, Huber, and Rawson (2001: 82) reported that heroin-related overdose deaths decreased by about 50% since buprenorphine and methadone were made available in the country. Those authors also noted that "general health status and quality of life" have improved among heroin users who have exposed to the intervention.

In France, any physician can prescribe buprenorphine, however, methadone (made available during the same year as buprenorphine) must be prescribed initially through specialised care centres. Following stabilisation, GPs can prescribe but will also "liaise" with the care centres. There is very limited space for methadone treatment and this limitation, coupled with fewer prescribing restrictions for buprenorphine as opposed to methadone probably contributed to the huge disparity in the numbers of clients in receipt of buprenorphine and methadone in the country. Although methadone and buprenorphine have both been available in France since 1996, physicians have been issued very few guidelines as to which drug should be prescribed for particular patients (Thirion et al., 2002).

Illegal street sales of buprenorphine have been reported in a host of countries, including England, Scotland, Bangladesh, and Australia (Agar et al., 2001). Prescribed buprenorphine has been sold on the illicit market in France, where Kempfer (2000) noted the potential for extreme damage to veins and skin when sublingual preparations of the drug are injected.

To prevent buprenorphine from being diverted (i.e., sold or obtained illegally) onto the illicit drug market, efforts have focused on the combined preparation of buprenorphine and naloxone.[8] For instance, Rosenheck and Kosten (2001: 254) have argued:

> "While harmless, if taken sublingually as prescribed,
> when the combined buprenorphine/naloxone preparation
> is injected into as opiate dependent person, it precipitates
> immediate and painful withdrawal and thus is not likely to
> be diverted for abuse."

[8] The combined preparation is of particular interest in the United States.

Those authors argued that a primary benefit of buprenorphine/naloxone is in regards to it "acceptability to society" (Rosenheck and Kosten, 2001: 254).

However, controversy over this combined drug preparation is mounting. Some opponents have argued, for example, that such a policy assumes that drug users are "dishonest" and might impinge upon staff-client relationships in treatment settings. Moreover, Byrne (2001) observed:

> "There are no parallels in other therapeutics as far as I can see that one would add a second drug to make the original drug more palatable to the community or regulatory authorities, but of no added benefit to the patient."

Any maintenance drug can be diverted for illicit purposes. If the buprenorphine/naloxone preparation is diverted and then injected, the naloxone is absorbed which would produce withdrawal in opiate-dependent individuals. The preparation is intended to be consumed sublingually, so that only the buprenorphine is absorbed (Barnett, Zaric, and Brandeau, 2001: 1268). Other authors have suggested that although buprenorphine/naloxone preparations might lower the likelihood of diversion, clients might also exhibit little interest in the combination drug within treatment settings (Agar et al., 2001).

To date, studies of buprenorphine have focused on the short-term effects of the drug such that the effectiveness of the treatment in the long-term is unknown (Barnett, Zaric, and Brandeau, 2001). Moreover, in reviewing the literature on buprenorphine, Gabbay, Jeffrey, and Carnwath (2000) failed to find any study that had examined the effect of buprenorphine treatment on employment and criminal behaviour among clients.

2.3 *Levo-Alpha-Acetyl Methadol*

Similar to buprenorphine, Levo-Alpha-Acetyl Methadol (LAAM) is a long-acting opiate agonist that can be administered three times per week, in comparison to the daily dosing required with methadone. The drug diminishes cravings for opiates and is said to block withdrawal symptoms associated with opiates (Lindesmith Center-Drug Policy Foundation, 2000).

LAAM is more expensive than methadone but since it can be dispensed every 72 hours rather than daily, treatment costs are said to be lower for LAAM than for methadone (National Evaluation Data Services, 2000).

Levo-alpha-acetyl methadol is currently available in clinic settings in the United States, but since April 2001 the use of LAAM in the European Union has been abolished, following the recommendation by the European Medicinal Evaluation Agency (European Centre for Drugs and Drug Addiction, 2002). Concerns over LAAM focused on its link with "unpredictable cardiotoxicity" (European Agency for the Evaluation of Medicinal Products, 2001: 1). Although the drug is not currently licensed as a treatment for opiate dependence in the United Kingdom, it is described herein because recent studies have compared its effectiveness to both methadone and buprenorphine.

Risk of overdose from take-home doses of LAAM is a concern. Effects of the drug are exhibited more quickly with injection rather than from other routes, yet even when the drug is injected, the effects do not appear until three to six hours after administration (Marsden et al., 1999). Because the effects of LAAM take longer than methadone, some clients in the United States are prescribed both LAAM and methadone during the initial stages of treatment, after which the methadone is eliminated (Lindesmith Center-Drug Policy Foundation, 2000).

Valdivia and Khattak (2000: 401-402) suggested that LAAM should be utilised rather than methadone 1) when patients have difficulty collecting daily prescriptions, 2) for patients who have a history of poor treatment outcomes with somewhat high doses of methadone, e.g., more than 60 mg per day, 3) for clients who are suspected of diverting methadone onto the illegal drug market, 4) for patients who are concerned about drug testing in the workplace (the authors noted that urinalysis does not often screen for LAAM), 5) for patients who report extreme sedation while taking methadone, 6) for patients who are "rapid metabolizers." However, as mentioned previously, the negative effects of the drug have created considerable concern.

2.4 *Heroin maintenance*

Prescriptions for diamorphine in the UK can only be written by a medical practitioner who has been granted a special license by the Home Office. In England and Wales, Sell, Farrell, and Robson (1997) estimated that there were approximately 42 physicians who maintained special licenses to prescribe diamorphine in the mid-1990s. Heroin prescriptions, however, represent only a very small minority of prescribed opiates in England and Wales. With its thrice daily dosage, the treatment is considered to be expensive in comparison to methadone (Gabbay, Jeffrey, and Carnwath, 2000). Elsewhere, a randomised clinical trial showed that prescribed injectable diamorphine produced similar outcomes to injectable methadone (Strang et al., 2000). A non-randomised study by Metrebian et al. (1998) confirmed these findings. McCusker and Davies (1996) found that persons who were prescribed diamorphine had higher rates of treatment retention, and lower rates of psychopathology and hopelessness compared to persons who had been prescribed methadone. However, cocaine use was significantly higher among persons who had been prescribed heroin.

Heroin maintenance programmes were implemented in Switzerland in 1992 and randomised trials have been conducted in Geneva (Perneger et al., 1998).[9] In the latter study, subjects were randomly assigned to either heroin maintenance or an alternative treatment programme of their choice (most often, methadone) and re-assessed six months after baseline. Treatment retention in the control group was not examined and all outcome data were measured through self-reports. At six-month follow-up, the experimental group had reduced levels of risky injection practices, lower rates of anxiety, reduced number of suicide attempts, reduced aggression, and better control over aggression violent behaviours. No significant differences were found in self-reported depression, social functioning, income levels, or condom use.

In their review of the literature, Gabbay, Jeffrey, and Carnwath (2000) concluded that heroin (diamorphine) maintenance has shown to reduce criminal activity but with little effect on subsequent use of illegal substances or social functioning. In commenting on the findings from the

[9] Trials are planned in Germany beginning in 2002.

Swiss trials, Farrell and Hall (1998) noted that heroin maintenance may represent a treatment option for persons who respond poorly to methadone. Randomised trials of heroin maintenance commenced in the Netherlands in 1997. The effectiveness of the intervention within that country might provide evidence of the benefits of such treatment. However, Hartnoll (1999) argued that large numbers of out-of-treatment heroin users within a given region would need to participate in heroin maintenance treatment for the intervention to impact substantially on the prevalence of problem heroin use.

2.5 *Substitute treatment in the European Union and Norway*

Table 1 provides a summary of the type of substitute treatment that is available for opiate users in the European Union and Norway. The data were drawn from a report issued by the European Monitoring Centre for Drugs and Drug Addiction (2002). There are a number of limitations to this information. First, in some instances the tabular data from the original report differed from the text. Second, some countries reported an annual count by calendar year whereas other countries reported data for an alternative 12-month period. Still others reported information from a one-day census of persons in receipt of substitute treatment. Third, it would have been helpful to know the percentage of opiate users who were in receipt of substitute treatment. The authors of the original report attempted to do so, but information on the number of problem opiate users from various countries was limited. However, Hartnoll (1999) estimated that substitute prescribing rarely is able to reach more than 50% of problem opiate users, even when a range of these interventions are available. Fourth, in some instances it was unclear whether the substitute drug was used for detoxification only or for short- or long-term maintenance. Despite these limitations, Table 1 shows that at least some regions within all countries of the European Union (and Norway) offered some type of substitute prescribing for problem opiate users, and methadone was available in all countries.

The report by the European Monitoring Centre for Drugs and Drug Addiction (2002) indicated that some countries (e.g., Denmark) implemented methadone treatment over 30 years ago, whereas others (e.g., Greece) did not offer methadone maintenance until the early 1990s. Additionally, some

countries offered substitute treatment as a last resort. In Greece, for instance, there were more than 4,000 persons on the waiting list for substitute treatment in 1999. Waiting lists tended to be higher in those countries that used very strict criteria for admission (European Monitoring Centre for Drugs and Drug Addiction, 2002) and the admission criteria for substitute programmes differed greatly. For instance, in Greece, criteria included injecting drug use, a minimum age of 22, a minimum of two years "drug addiction" and a history of one or more failed treatment attempts. In contrast, Sweden required substitute treatment clients to be "have at least four years of documented intravenous opiate addiction," to have at least made one attempt to engage in drug-free interventions, to be a minimum of 20 years of age, and "to have medical records showing that there is no advanced multiple substance addiction involved" (European Monitoring Centre for Drugs and Drug Addiction, 2002: 25, 77).

Table 1. *Substitute Treatment in the European Union and Norway*

Country	Drug Utilised (Number in Treatment)	Year[a]
Austria	Methadone (3,229) Buprenorphine and Morphine (1,664)	2001
Belgium	Methadone (7,000)	1996
Denmark	Methadone (4,298) Buprenorphine (100) LAAM (200)	1999
Germany	Methadone (32,100) Levomethadone (10,000)[b] Buprenorphine (500) Dihydrocodeine (3,700)	2000
Greece	Methadone (966)	2000
Finland	Methadone (70) Buprenorphine (170)	--[c]
France	Methadone (10,000) Buprenorphine (74,000)	2001
Ireland	Methadone (5,032)	2000
Italy	Methadone (66,550)	1999
Luxembourg	Methadone (170) Mephenon (70)	2001
Netherlands	(11,676)[d]	1997

---- continued ----

Table 1, continued

Country	Drug Utilised (Number in Treatment)	Year[a]
Norway	Methadone (1,100)	2001
Portugal	Methadone (5,400) LAAM (600)	2001
Spain	Methadone (72,236) LAAM (206)	1999
Sweden	(621)[d]	2000
United Kingdom	(19,630)[d]	--[c]

[a] From the text and tabular data in the original report, it is unclear as to whether the time period represents a calendar year, another 12-month period, or a one-day census.

[b] Verthein, Kalke, and Raschke (1998: 75) reported that "Levomethadone is about twice as efficient as methadone."

[c] Year was not reported.

[d] Numbers are not categorised separately for drug type.

Source: *Classifications of Drug Treatment and Social Integration and their Availability in EU Member States plus Norway* (European Monitoring Centre for Drugs and Drug Addiction, 2002).

2.6 *Comparisons between two or more substitute drugs for the treatment of opiate dependence: Treatment outcomes*

2.6.1 *Methadone and buprenorphine*

Studies that have compared buprenorphine with methadone generally have found higher rates of treatment retention among persons who have been administered methadone (e.g., Barnett, Rodgers, and Bloch, 2001; Eder et al., 1998; Fischer et al., 1999; Petitjean et al., 2001). However, methadone dose levels in these studies most often exceeded 50 mg per day. In several studies, a low dosage level of either methadone or buprenorphine has been linked with lower study retention rates (Maddux, Prihoda, and Vogtsberger, 1997),[10] and low doses of methadone (e.g., 20 mg per day or less) in particular are said to be roughly equivalent to placebo-like conditions (Leavitt, 2002). For example (Johnson, Jaffe, and Fudala, 1992) assigned subjects to either 8 mg per day of buprenorphine or 20 mg per day of methadone. Retention was higher and opiate-positive urines were lower among subjects who were administered buprenorphine in comparison to methadone. In their review of several studies that compared buprenorphine and methadone, Ling, Huber, and Rawson (2001: 81) concluded that subjects from both groups "perform comparably once a maintenance dose is reached, although it appears somewhat more difficult to begin treatment with buprenorphine than with methadone in highly opiate dependent patients." In general, buprenorphine dosage levels between 8 and 16 mg are needed to produce similar treatment outcomes as achieved by high-dose methadone (Gabbay, Jeffrey, and Carnwath, 2000).

A few studies have shown no significant differences in treatment outcomes when comparing the two drugs. For instance, Pani et al. (2000) randomly assigned 72 opioid dependent subjects to one of two groups: 1) 8 mg of buprenorphine per day or 2) 60 mg of methadone per day. The rate of drug positive urine samples and study retention did not differ significantly between the two groups. The authors noted that their study was one of the first to use buprenorphine in tablet form, reflecting its availability in treatment settings.

[10] Eight mg of buprenorphine is approximately equivalent to 30 mg of methadone.

Some fairly good recent reviews have used meta-analysis to compare the effectiveness of the two drugs, although authors have noted the difficulties in including studies that have relied on different methodological designs. Barnett, Rodgers, and Bloch (2001) conducted a meta-analysis of five clinical trials that used random assignment to examine the effects of methadone (50 to 80 mg per day) in comparison with buprenorphine (6 to 12 mg per day) among clients treated in methadone clinics. Those authors observed that the extent of drug positive urine samples was significantly higher among clients in receipt of buprenorphine compared with methadone. Moreover, retention rates in treatment were significantly lower among buprenorphine clients compared with methadone clients. The authors concluded that although statistically significant differences between the two groups were observed, the magnitude of the differences was relatively small.

A second meta-analysis that compared the effectiveness of methadone and buprenorphine was conducted by West, O'Neal and Graham (2000). The authors identified nine studies that compared these two substitute drugs. The authors observed the difficulties in comparing across studies because of the different dosage levels that were utilised in the studies. Equally important, the authors were limited to one outcome measure only, i.e., urinalysis results. Based on this outcome, the authors concluded that the two drugs produced approximately equal rates of drug positive urines. Also important, the researchers found that persons who had a prior history with methadone tended to do better with buprenorphine than persons who had no experience with methadone. The authors noted, however, that more research is needed to investigate this issue.

2.6.2. *Methadone and LAAM*

Glanz et al. (1997) used meta-analysis to compare the effectiveness of methadone and LAAM. Those authors found that methadone produced higher retention rates than LAAM. No significant difference was observed with respect to illicit drug use.

2.6.3 *Methadone, buprenorphine, and LAAM*

Farré et al. (2002) utilised meta-analysis to explore the effectiveness of low- and high-dose methadone, LAAM, and buprenorphine from 13

randomised, controlled studies. High-dose methadone (i.e., 50 mg per day or more) was significantly more likely to result in decreases in illicit opiate use compared to low-dose methadone (less than 50 mg per day). Retention rates did not differ significantly between the low- and high-dose groups.

High-dose methadone was superior to low-dose buprenorphine (less than 7 mg per day) but approximately equal to high-dose buprenorphine, in terms of reductions in opiate-positive urines. Results for retention data showed similar results, that is, high-dose methadone was about equal to high-dose buprenorphine but produced significantly better results than low-dose buprenorphine.

Comparisons between high-dose methadone and LAAM showed that the two interventions had approximately the same impact on reducing opiate-positive urines. Retention, however, was higher for high-dose methadone. Fewer opiate-positive urines were associated with low-dose methadone when compared with LAAM, but retention did not differ significantly between low-dose methadone and LAAM.

Based on the results from their meta-analysis, Farré et al. (2002: 289) concluded that:

> "The new drugs, buprenorphine or LAAM, do not seem superior to methadone in terms of efficacy. In our opinion, the most important advantage of LAAM and buprenorphine is the '3-days a week schedule…"

The authors also noted that unlike methadone, studies that have examined buprenorphine or LAAM as they relate to criminal behaviour, HIV risk behaviours and other outcomes have yet to be examined.

A 17-week study by Johnson et al. (2000) also compared methadone, buprenorphine, and LAAM. A total of 220 heroin "addicts" were randomly assigned to one of four conditions: 1) thrice weekly buprenorphine dosing (16-32 mg per dose),[11] 2) thrice weekly LAAM dosing (75-115 mg per dose), 3) daily methadone dosing (20 mg per dose), and 4) daily methadone dosing

[11] Friday doses were higher for subjects in the LAAM and buprenorphine groups in order to allow for the additional days before the next dose was administered.

(60-100 mg per dose). Doses were increased if attendance was satisfactory and subjects were not absent on a Friday. Outcome measures included self-reported heroin use, urinalysis results, and study retention. Self-reported heroin use was approximately equal across groups. The LAAM group had the highest percentage of 12 or more consecutive opiate-free urine samples (36%) and the high-dose methadone and the buprenorphine groups were approximately the same (28%, 26%, respectively). Only 8% of the low dose methadone group had 12 or more consecutive "drug-free" urine samples. Moreover, persons in the low-dose methadone group had higher rates of cocaine use than subjects assigned to the other groups. Subjects were asked to report the severity of problems associated with drug use. Subjects assigned to the buprenorphine group reported the lowest severity rating whereas persons in the low-dose methadone group reported the highest severity rating. One problem with this 17-week study was the retention rate of 51%. Moreover, retention varied across groups: High-dose methadone (73%), buprenorphine (58%), LAAM (53%) and low-dose methadone (20%). It is not known whether subjects in this study were exposed to counseling or related interventions.

Shortly after the Johnson et al. (2000) was published, the lead author was interviewed by the (US) National Institute on Drug Abuse. Despite the comparison study that involved three substitute drugs and varying dosage levels, the lead author noted that information about the most effective match between patient and type of substitute drug still was lacking (National Institute on Drug Abuse, 2001). In other words, research has yet to identify which patients will benefit most from a particular drug and which will benefit most from an alternative. One report, however, indicated that buprenorphine might be more suitable than other drugs for people who exhibit high levels of psychosocial functioning (Resnick, Resnick, and Galanter, 1991).

Leavitt (2002) examined reports of adverse effects associated with methadone, LAAM, and buprenorphine for a three-year period.[12] The data were reported initially to the US Food and Drug Administration (FDA) and

[12] Leavitt's review appeared to be extremely thorough and he has published quite extensively on substitute prescribing. However, a potential conflict of interest is worth mentioning here. Leavitt is editor of the Addiction Treatment Forum On-line and that Forum is funded at least in part by a company that manufactures methadone and naltrexone.

re-analysed by the author. A substantially higher number of adverse effects were associated with buprenorphine and LAAM, in comparison to methadone. Moreover, buprenorphine (57%) was more likely than methadone (26%) and LAAM (45%) to be listed as the "sole agent" that contributed to the adverse effects. A similar conclusion was reached for morbidity and these prescribed drugs. The author of the report acknowledged that the study was limited in that FDA data were not validated against external criteria.

2.7 *Substitute prescribing in conjunction with other interventions*

2.7.1 *Treatment goals*

The programme philosophy often varies across substitute treatment programmes. Some programmes are characterised by the treatment goal of abstinence whereby rules and regulations are designed to meet this objective. Other programmes reflect a harm reduction philosophy, and recognise that some clients will need to be maintained on substitute drugs for years. The goal of abstinence from all drugs may be inappropriate for several methadone clients. Research has demonstrated that clients have tended to do better in methadone clinics that are characterised by treatment goals that incorporate continued maintenance rather than abstinence (Ball and Ross, 1991; Caplehorn, Lumley, and Irwig, 1998). Indeed, a study by Sees et al. (2000) suggested that programmes characterised by "abstinence only" ideologies - might negatively affect treatment outcomes. Abstinence may be a goal suited for some clients but when this goal is not feasible, reducing harm to self and others should be the goal. Treatment programmes that pose limits on the length of time in which a person can receive methadone generally have less successful treatment outcomes than programmes that pose no such restrictions (Caplehorn et al., 1993; McGlothlin and Anglin, 1981).

2.7.2 *Counselling*

In their review of the literature, Gabbay, Jeffrey, and Carnwath (2000) concluded that methadone maintenance was more effective when used in conjunction with counselling, however, those authors suggested that

counselling for opiate-dependent persons in the absence of substitute prescribing had not been shown to be effective.

In many regions, methadone clients generally are not *required* to undergo counseling. For example, in the south of Ireland, counselling is available for clients in methadone maintenance, but is provided on a voluntary basis. Moran et al. (2001) reported that research has yet to be undertaken on the extent or impact of counseling on methadone clients in the south of Ireland. In Edinburgh, use of counselling services among methadone clients varied considerably in the early 1990s (Peters and Reid, 1994). Similar claims have been reported in Glasgow (Gruer et al., 1997). Mandatory counselling might lower treatment retention rates, and hence might prove to be counter-productive. Such a policy, for example, could undermine the goals of individual treatment plans. Because of the possibility that some clients are not in need of regular counselling, requiring client participation in regular counselling might not be cost-effective.

Although few studies have examined the joint effects of substitute prescribing and counselling, research that has been conducted shows promising results. For example, McLellan et al. (1993), first stabilised 79 males with 60-80 mg of methadone per day and then randomly assigned them to one of three groups: 1) minimum methadone maintenance, i.e., blocking doses of methadone coupled with emergency counselling and referral only, 2) standard methadone maintenance, i.e., blocking doses of methadone combined with regular counselling and contingency management involving take-home doses for attendance, employment, and negative urine samples, and 3) enhanced methadone maintenance, i.e., incorporating the factors from the other groups but including employment and family counselling, social work intervention, and medical and psychiatric care. The authors found a significantly higher rate of drug positive urines were observed among clients assigned to the methadone only group. By the end of the first three months of the study, 69% of the subjects in the methadone only group were either "protectively terminated" from the study or were transferred to the standard methadone group. Similarly, within the first six months of the study, approximately 41% of the standard methadone group began to display the same behaviours (e.g., drug use) as many subjects in the methadone only group. In contrast, only 19% of the enhanced methadone group fell within the protection termination category.

Weekly counselling held in conjunction with methadone prescribing has been shown to be more effective than methadone treatment without counselling (Ling, Huber, and Rawson, 2001, citing Rounsaville and Kosten, 2000). However, Ling, Huber, and Rawson (2001: 87) concluded that "extensive day program treatment within a methadone program has not produced better outcomes."

Barnett and Hui (2000) suggested that additional support services, e.g., counselling, may be of greater importance in the early stages of methadone treatment, however, the authors argued that more research is needed as to the cost-effectiveness of support services during the final stages of methadone treatment.

2.7.3 *Contingency management*

The philosophy of contingency management assumes that behaviours can change for the better when individuals are either provided with incentives or sanctioned with disincentives. With respect to substitute prescribing, most research on contingency management has focused on short-term detoxification programmes. Griffith et al. (2000) used meta-analysis to examine the effect of contingency management on illicit drug use (measured by urinalysis) during methadone treatment. The authors found that incentives such as take-home doses and dosage increases and decentives such as thrice weekly urinalysis significantly contributed to reduced drug use during treatment. Other researchers have focused on the role of contingency management as well as dosage on treatment outcome. For example, Preston, Umbricht, and Epstein (2000) provided subjects with 50 mg of methadone per day, and then randomly assigned them to one of four conditions 1) contingent vouchers for goods and services when urines were opiate-negative, 2) dosage increase to 70 mg per day, 3) contingent vouchers for negative urines coupled with dosage increase to 70 mg per day, and 4) maintain at 50 mg per day. The authors found independent effects of methadone dosage and voucher rewards. That is, both factors contributed independently to opiate-negative urine samples and lowered self-reported craving for heroin. More research is needed with respect to the role of contingency management in conjunction with substitute prescribing in maintenance programmes.

2.7.4 *Other programme aspects*

Many programmes exclude or terminate clients who fail to abide by programme rules and regulations. More intensified care (in the form of behavioural reinforcement) in response to client instability in treatment shows promise (King et al., 2002), although more research is needed in the area of "stepped care" treatment. Others have suggested that intensified care for clients who exhibit major adjustment problems takes into the consideration the concept of patient-treatment matching and is cost-effective (Davison, 2000).

2.8 *Problems associated with studies that address the effectiveness of substitute drugs*

Studies, including clinical trials that have compared the effectiveness of one or more substitute drugs often are plagued by various methodological problems. These problems are highlighted in the paragraphs that follow.

2.8.1 *Stringent study criteria, insufficient detail, and experimental conditions*

Study exclusion criteria often fail to reflect realistic profiles of heroin users, so that external validity is questionable. For example, some studies exclude polydrug users whereas other research excludes drug users with psychiatric or mental health problems. Research has suggested that in some regions - more than 60% of injecting drug users have contracted Hepatitis C Virus (Coppola et al., 1994), yet some studies exclude individuals who have been diagnosed with medical illnesses relating to the liver (e.g., Amass, Kamien, and Mikulich, 2001). Such a criterion would thus exclude a disproportionate number of injectors and other drug users who have developed Hepatitis C Virus. The effectiveness of substitute prescribing for persons who have been infected with Hepatitis C Virus requires further attention by researchers. In a similar vein, other studies have included only those clients who were in full-time employment, excluding persons who were unemployed or who worked part-time (e.g., King et al., 2002). Further, the vast majority of studies on treatment effectiveness exclude adolescents and very young adults, i.e., younger than 18 years, thus we know very little about the efficacy of methadone treatment among young heroin users.

Although some research includes joint interventions, e.g., methadone combined with counselling, too often these other interventions are not described with adequate detail. The nature and quality of these other interventions, and how the quality might vary across clients often is not reported. White, Alcorn, and Feinmann (2001) suggested that double-blind conditions as part of an experimental condition can be problematic because this condition generally prohibits flexible dosing of the substitute drug. Similar criticisms have been voiced about other studies (Leavitt, 2002). Prohibiting flexible dosing runs counter to good quality treatment.

Finally, in several studies of the effectiveness of buprenorphine, researchers have utilised a liquid form of the drug, when in several countries, the drug is used in tablet form and administered sublingually. Nath et al. (1999) suggested that the bioavailability of buprenorphine from the tablets is considerably less than the bioavailability from the liquid form. Experimental conditions should reflect the form in which substitute drugs are available in treatment settings, so that external validity might be improved.

2.8.2 *Study retention rates*

In some studies (e.g., Amass, Kamien, and Mikulich, 2001; Metrebian et al., 2001), approximately one-half of the subjects or more dropped out of treatment prior to the end of the study period. Low retention rates can impact upon behavioural outcomes such as opiate use. It is often unclear whether the drop-outs would have yielded higher rates of opiate use (because they failed to respond adequately to treatment) or lower rates (because they were no longer using opiates and hence were no longer in need of treatment). Jain (1992: 178) noted that:

> "high and differential dropout rates for different reasons in different treatment groups can compromise estimation of treatment effects. For example, the drugs may "cure" certain patients, and as such, they do not need treatment anymore (and they drop out). In other cases, the drug may be a failure, and as such, the patients do not come back."

Further, differential retention rates are often reported for two or more different substitute drugs that are being compared, and little is known about efforts that were used in attempts to improve retention.

2.8.3 *Reliance on self-reports and urinalysis*

Many studies rely heavily on self-reported drug use and similar measures. Although self-reports can yield valid measures of drug use, particularly among those in treatment, verification of these data would strengthen the results. Urinalysis results as measures of illicit drug use are problematic for several reasons. First, urinalysis is only able to determine whether an individual used a particular drug very recently, e.g., the 24-48 hour period prior to the collection of the urine sample. Second, urinalysis cannot determine the route of administration. Third, the amount of drug consumed generally cannot be identified (c.f. McLachlan-Troup, Taylor, and Trathen, 2001). Fourth, urinalysis cannot detect the number of times that a person used a particular substance in the 24-48 hour period before the urine sample was collected. Johnson et al. (2000) noted that "opioid use can decline by 75% (for example, from four times to once daily) and still yield 100 percent opioid-positive urine specimens." Those authors also cautioned that when urinalysis is conducted too frequently, drug use can be overestimated because the same drug use episode can be identified on two or more occasions. Fifth, instances of both false positives and false negatives have been identified in the literature. Neale (1999) cited research by Mackie (1996) who reported that cloxacillan can produce a false positive for benzodiazepine in the urine and diphenhydramine can show a false positive for methadone. Finally, rates of metabolism and excretion can influence urinalysis results of persons who consumed drugs recently (Cone and Dickerson, 1992).

Urinalysis might be useful as a method for guiding treatment but otherwise the measure has little value (Barnett and Hui, 2000). One estimate suggested that urinalysis in methadone programmes might reduce the number of drug positive urine results by a factor of 5% to 11% but those authors were less clear about whether urinalysis was a cost-effective measure in methadone treatment (Havassy and Hall, 1981). Baker, Rounds, and Carson (1995) found that the percentage of opiate-positive urines was

approximately the same for clients who knew that urine samples would be collected versus those who did not know.

3 *Possible negative implications of substitute prescribing*

3.1 *Non-fatal overdoses, morbidity and mortality associated with substitute prescribing*

Some estimates have suggested that approximately 30 mg of methadone is considered to be a lethal dose for individuals with low tolerance to the drug (Daniels, 1997 citing information from the Edinburgh Poisons Information Service). Determining the correct dosage level is critical in the initial stages of methadone treatment, particularly among persons who have used opiates infrequently (van Ameijden, Langendam, and Coutinho, 1999), e.g., persons recently released from jail, are using other substances, or smoke heroin rather than inject the drug. Ling, Huber, and Rawson (2001: 88) noted that the initial seven days of methadone treatment has been described as a high risk period for death and emphasised the need for a careful "clinical review of subjects' tolerance to methadone."

Several studies have attempted to estimate the number of methadone-related fatalities. In Scotland, methadone was a leading factor or was used in combination with other drugs in the majority of drug-related deaths (Cooper et al., 1999). However, the method by which deaths are recorded by researchers can have implications for the research findings. Karch and Stevens (2000) noted that a total of 38 methadone-related deaths occurred in San Francisco in 1997-1998, however, methadone toxicity was listed as a cause of death in only half of those deaths.

Auriacombe, Franques, and Tignol (2001) compared buprenorphine- and methadone-related death rates in France between 1994 and 1998. The authors concluded that methadone-related fatalities were at least three times as great as buprenorphine-related fatalities. The authors did not report how they categorised deaths for which two or more drugs were implicated. The study has been critically reviewed by Leavitt (2002) who reported that laboratory results from coroners were not used to verify the original data that were analysed by Auriacombe and colleagues. The original authors also acknowledged that they did not have access to information on other drugs, pre-existing conditions among the deceased, dosage, and other factors.

Some writers have voiced concern that take-home methadone doses or methadone consumed without professional supervision can lead to the diversion of methadone that subsequently will be consumed inappropriately or by persons not in methadone treatment. Although mortality data have shown that the number of fatal overdoses relating to opiates is higher in Australia compared to the United Kingdom, the number of these deaths in which methadone is implicated is higher in the United Kingdom (Hall, Lynskey, and Degenhardt, 2000). In their review, Ling, Huber, and Rawson (2001) observed that this differential was perhaps due to the easier accessibility of methadone in the United Kingdom compared to Australia. Scholars have attempted to link diverted methadone with methadone mortalities. For example, Valmana et al. (2000) found that methadone was implicated in 40 of 154 reported drug-related deaths reported in England and the authors observed that methadone had not been prescribed for the majority of these 40 persons.

As noted previously, illicit use of buprenorphine has been reported in several countries, including England, Scotland, Bangladesh, and Australia (Agar et al., 2001). Buprenorphine "abuse" has had several negative implications in for patients in France, e.g., extreme damage to veins and skin when sublingual preparations of the drug are injected (Kempfer, 2000). Further, some scholars have suggested that physicians in France appear to have contributed to overdoses resulting from polydrug use, e.g., buprenorphine and benzodiazepine (e.g., Reynaud et al., 1998; Tracqui, Kintz, and Ludes, 1998). Barrau et al. (2001) found that 25% of methadone and buprenorphine clients in their study (France) had consumed benzodiazepines. Among benzodiazepine users, 75% of the methadone group and 80% of the buprenorphine group consumed benzodiazepine daily.[13] Some physicians in France have prescribed both buprenorphine and benzodiazepines to patients (Seyer et al., 1998). In a study of one region in France, researchers found that 43% of patients in receipt of buprenorphine had also received a prescription for benzodiazepine and "the daily does were often far above the maximum recommended dose…" (Thirion et al., 2002: 200).

[13] Benzodiazepine use has been high among methadone clients in Germany (Verthein, Kalke, and Raschke, 1998).

It has since been reported that buprenorphine clients were able to obtain multiple prescriptions from various doctors during the same time period (Thirion et al., 2002). In Germany, the government has recently introduced a federal register of methadone recipients in order to reduce the number of multiple prescriptions for the drug (Tuffs, 2001). The south of Ireland implemented its register in 1993, but GPs were not required to submit patient details to the central register until 1999 (Keenan and Barry, 1999).

3.2 *Supervised consumption to prevent the diversion of substitute drugs*

Several authors have speculated that the supervision of methadone consumption might assist with preventing the diversion of methadone onto the illicit market, however, there is no legal requirement in England and Wales for doses to be consumed under supervision by a general practitioner, pharmacist, or other health care worker. The Department of Health (2001) recently recommended that daily supervised consumption occur during the first three months, and possibly the first six months of treatment. Such supervision works to maintain a power imbalance between patient and doctor or patient and pharmacist. A policy of supervised consumption assumes that clients may use methadone for other means, e.g., sell or give the drug to others. Moreover, methadone remains one of the few drugs for which supervised consumption occurs. Vanderkloot (2001, no page listed) critiqued methadone maintenance polices for being "over-regulated," characterised by control and power over the patient:

> "No other medication is so restricted that most patients must ingest it daily under the scrutiny of suspicious staff. No other substance can be prescribed only under the condition that the patient submit to "counseling" and screens for illicit drug use—in perpetuity."

Robinson et al. (2000) observed that there have been very few studies that have focused on the extent to which drug users consume illegal methadone, thus we know little about diversion and how and why it occurs.[14] In their own

[14] These authors referred to three studies only, all of which were conducted in either the United States or Canada, e.g., Inciardi (1977), Spunt et al. (1986), and Lauzon et al. (1994). Two of those studies are now quite dated.

study of 19 attendees who frequented a needle exchange programme in New Zealand, nine respondents reported that "needle fixation" represented one factor that contributed to their use of diverted methadone.[15]

Neale (2000) interviewed 33 drug users who had recently overdosed (non-fatal) and had been identified by hospital accident and emergency departments in Glasgow and Dundee. Methadone was implicated in substantially more overdoses in Dundee than in Glasgow. Moreover, heroin had been consumed just prior to overdose in 16 cases (67%) from Glasgow but was not implicated in any of the overdoses in Dundee. Neale (2000) concluded that the pattern of drugs involved in non-fatal overdoses in her study mirrored the mortality data from the two cities. That is, methadone was far more likely to be involved in overdoses in Dundee than in Glasgow, and the author suggested that this difference resulted from a policy of supervised methadone consumption in Glasgow but not in Dundee. Similar explanations have been provided with regards to differential causes of fatal overdoses in Glasgow and Edinburgh (Weinrich and Stuart, 2000).

In reducing the extent of methadone diversion, the Department of Health (1999) has placed the burden on prescribers by suggesting that they develop methods to decrease the possibility of diversion.

[15] Locally, one study found that some heroin injectors pretended to inject during detoxification, and one reported that he would "nod off" after doing so (McElrath, 2001). Other research has suggested that needle fixation can be a powerful incentive to inject (McBride et al., 2001). Although little research has focused on needle fixation among injecting drug users, these reports indicate that the issue should be addressed in substitute prescribing programmes.

4 *Substitute prescribing and dispensing practices*

Drug treatment agencies, general practitioners, pharmacists and other professionals have important roles in which to engage for substitute prescribing to be effective. Moreover, patients who are prescribed substitute drugs for heroin dependence benefit greatly when treatment providers and other professionals in the management of drug users are involved in mutual support, share common goals, communicate effectively, and interact often.

Seven of 16 European countries examined in a report by the European Monitoring Centre for Drugs and Drug Addiction (2002) allowed for GPs to prescribe substitute drugs to opiate users, either in conjunction with a specialised care centre or autonomously. The Department of Health has recognised that the role of the general practitioner is critical in the provision of drug treatment (Department of Health, 1996; 1999), and the available evidence appears to support this claim. Physicians' offices have been described as effective settings in that they provide little stigma for patients (Gabbay, Jeffrey, and Carnwath, 2000). Office-based settings in primary care also minimise the amount of contact a patient has with other drug users (O'Connor and Fiellin, 2000). Other scholars have noted that methadone treatment offered by primary care physicians can allow for better treatment provision of comorbidity among drug users, as well as better geographic access to treatment (Weinrich and Stuart, 2000).
Although research in the area is quite limited, studies have suggested that general practitioners can provide methadone treatment effectively (Macleod et al., 1998; Weinrich and Stuart, 2000). Moreover, treatment provided in general practice has been found to be the preferred type of intervention among drug users (Hindler et al., 1995).

Although any general practitioner in England and Wales can legally prescribe methadone as a treatment for opiate addiction, many GPs in those regions have been resistant to treat drug users (Deehan, Taylor, and Strang, 1997). GPs who provide care to drug users often spend more time with this category of patient (Gabbay, Jeffrey, and Carnwath, 2000), leaving less time for other patients. Weinrich and Stuart (2000) reviewed literature and noted that US physicians have various concerns about introducing methadone treatment within the context of office-based practice. These concerns

include the risk of mortality through methadone overdose, concern about physician responsibility in treating what is perceived to be a difficult clientele, and doubts about the effectiveness of treatment provided by a physician as opposed to specialised drug treatment clinics.

Research conducted in various countries, including England, has shown that external support from other agencies, such as specialised drug treatment centres is a critical factor that can contribute to a willingness to treat drug users (Abouyanni et al., 2000; Groves and Strang, 2001).

4.1 *Shared care as a model for best practice*

In recent years, "shared care" has emerged as an important concept in the management of drug use and the delivery of drug treatment. Citing its 1995 report, the Department of Health (1999: 10) has defined shared care as:

> "The joint participation of specialists and GPs (and other agencies as appropriate) in the planned delivery of care for patients with a drug misuse problem, informed by an enhanced information exchange beyond routine discharge and referral letters. It may involve the day-to-day management by the GP of the patient's medical needs in relation to his or her drug misuse. Such arrangements would make explicit which clinician was responsible for different aspects of the patient's treatment and care. These may include prescribing substitute drugs in appropriate circumstances."

Shared care arrangements can be organised differently, depending on local needs. Although support extended to GPs from specialist drug services is often viewed as a primary aspect of shared care programmes, Gabbay, Jeffrey, and Carnwath (2000) noted that specialist drug agencies also can benefit from the support extended by physicians.

In some regions, assessment is conducted and initial dosage is provided by specialist agencies whose staff seek to stabilise patients. Once patients are stabilised, they are then "transferred" to a GP. Designated staff that are linked with specialist drug agencies liaise with and provide support to GPs in

primary care. In some areas, specialised drug centres continue to deal with difficult, aggressive, or unstable patients (van Brussel, 1995).

Such a model has operated in Edinburgh since the mid- to late-1980s, whereby specialist agencies offer support to clients and GPs, review progress, and are responsible for treating certain sub-groups of patients (Marsden et al., 1999). Greenwood (n.d.) described the development and the role of the Community Drug Problem Service (CDPS) in Edinburgh, which operates under the principles of shared care. The ideology of the Service has reflected harm reduction rather abstinence (Weinrich and Stuart, 2000).

Established in 1988, the CDPS serves the Lothian region and in 1995 the Service included 530 GPs from 133 practices (Greenwood, n.d.). Referrals are made to and assessment is done initially by a community psychiatric nurse. A multidisciplinary team decides the appropriate treatment and this decision is passed on to the GP. If the treatment plan is acceptable to the GP, the client can be treated with methadone for three days through the CDPS. Following central prescribing, the case is then transferred to the GP. The GP and the client receive support from a staff member, e.g., a nurse. Greenwood (n.d.) noted that that the willingness by GPs to participate in the scheme has been influenced greatly by the fact that the client is first stabilised in the CDPS setting before the case is transferred to the GP. The CDPS engaged in a variety of methods to further increase GP participation in the scheme, e.g., meetings with local GPs were held in their own surgeries, training on various drug-related topics was offered frequently, postal distribution of relevant information occurred regularly. In 1995, a document entitled, "Managing Drug Users in General Practice," (Primary Care Facilitator Team (HIV/AIDS and Drugs), 1996) was distributed to all GPs in the region.[16] Methadone prescribing policy requires urinalysis and requires that self-reported drug use be recorded in client-kept journals.

Drawing from the Lothian training material, the shared care programme in Tayside has assigned a keyworker to each practice. Rome (2001) reported that face-to-face communication with GPs was far more beneficial than written correspondence that discussed a particular case. He noted also that

[16] The document has been revised periodically.

GPs in need of support were offered it as quickly as possible (e.g., within hours) and that liasing with GPs in this manner contributed to the immediate reduction of waiting lists. The support provided by the Tayside facilitator varied depending on the needs of the each practice.

The Glasgow Drug Problem Service was implemented in January 1994 and from its inception, the Glasgow Service adopted a harm-reduction philosophy, similar to the CDPS n Edinburgh. The Glasgow Service reflects a "shared care" philosophy and has been described as a "medically led specialist service" (Gruer et al., 1997).

In the south of Ireland, methadone can be prescribed by clinic staff or by GPs who have completed training. There were 53 methadone clinics in 2000, the vast majority of which are located in the Dublin area (Moran et al., 2001). In August, 2000 there were 158 GPs who were prescribing methadone and 207 pharmacists who were dispensing the drug (Moran et al., 2001). Reflecting the principles of shared care, GPs in the south of Ireland and methadone clients in their care can benefit from support offered by methadone clinic staff.

Since October 1998, GPs in the south of Ireland have been required to submit details of methadone patients to a central register. Staff in methadone clinics supervise the methadone consumption, as do pharmacists. Within clinics, clients whose urines are negative for opiates over time can be allowed to collect take-home doses from the clinic. Satellite clinics operate in some areas characterised by a low prevalence of opiate users. Within these settings, methadone can be prescribed but is dispensed through pharmacies.

4.1.1 *Training GPs*

GPs who are involved in substitute prescribing under shared care conditions undergo fairly extensive training, although this review was unable to locate studies that have focused on process evaluations of such training. In the south of Ireland, GPs who wish to prescribe methadone must participate in training sessions provided by the Irish College of General Practitioners (Moran et al., 2001). The completion of basic training allows GPs to prescribe methadone only after patients have been stabilised in a methadone

clinic. Completion of this training allows GPs to prescribe methadone for a maximum of 15 patients. More intensive training is available for GPs who wish to initiate methadone treatment for patients. A requirement of this training is that GPs must have worked for a minimum of one year in a methadone clinic. GPs who complete this training can prescribe methadone for a maximum of 35 patients, although that number can be exceeded if the GP is in practice with two or more physicians.

In Glasgow, GPs must apply to the scheme and if accepted by the physician-led screening board they then are provided with material on methadone prescribing and related information. There are special requirements for GPs who wish to participate in the scheme. On-going training sessions are offered four times annually and occur during evening hours (Gruer et al., 1997). Those authors noted also that the training sessions allowed for GPs to interact with other GPs who were involved in the scheme. Similar to policy in the south of Ireland, GPs in Glasgow can be "assigned" between 5 and 20 methadone clients and additional fees are paid for each methadone patient.[17]

The Department of Health (1999) recommended several issues pertaining to training in the shared care of drug users, and outlined topics to be covered in training sessions. Information on the extent and nature of compliance has yet to emerge. One study examined the Department of Health's earlier recommendations with regards to prescribing and dispensing methadone (Strang and Sheridan, 1998). Specifically, the authors examined the following recommendations: 1) the discontinuance of prescribed methadone tablets, 2) daily as opposed to less frequent dispensing, and 3) dosage levels to range from 50 to 100 mg per day. Using randomly selected samples from 1995 and 1997 surveys, the authors found that prescriptions for methadone tablets decreased from 12.1% to 9.5% and that daily prescriptions increased from 52.1% to 55.8% between 1995 and 1997. With regards to the recommended daily dose of 50 to 100 mg, the authors found no change in this measure. The authors concluded that there was little evidence in substantial compliance with the Department's earlier recommendations.

[17] Earlier reports from Amsterdam indicated that GPs in that city were responsible for approximately 40% of the methadone prescriptions and were limited to ten methadone patients (maximum) per year (van Brussel, 1995).

4.1.2 *Effectiveness of substitute prescribing in shared care programmes and office-based settings*

Penrose-Wall, Copeland, and Harris (2000) reviewed the literature on shared care involving the treatment of drug use and noted the paucity of research on the topic. Moreover, the limited research has been largely descriptive. For example, a study of 89 health authorities in England, Wales and Scotland revealed that 26 had developed protocols regarding shared care for the treatment of drug use (Gerada and Tighe, 1999). Most agencies responding to the survey had developed informal protocols only. Of those agencies which had developed formal protocols, approximately one-third of the agencies had arrangements with general practitioners. The authors noted that the role of the GP in these arrangements most often was limited to prescribing. These findings run counter to the guidelines issued by the Department of Health (1999: 12) which suggested that "the level of specialist support available to the GP and Primary Health Care Team, ease of access to this support, and the willingness and flexibility of all parties involved in shared to work together" are all fundamental in the effectiveness of shared care models. However, it is possible that advances have been made since Gerada and Tighe published their report. More recent reports from Scotland indicated that some aspect of shared care in the treatment of drug users was operating among 20 of 22 Drug Action Teams in that region (Gray, 2001).

Research that has examined the effectiveness of methadone treatment in general practice settings has shown promising results. O'Connor et al. (1998) compared the effectiveness of buprenorphine in two settings: a primary care office and a methadone maintenance clinic. The rate of treatment retention was higher among clients in the office-based setting as was the rate of opiate negative urine samples.

In the United Kingdom, largely England and Wales, Gossop et al. (1999) examined six-month outcome data for 452 opiate "addicts" who had received methadone treatment from either a general practice or a specialist drug clinic. Comparing the two treatment settings, the authors observed similar improvements since baseline in the areas of health, social functioning, and drug-related problems.

The shared scheme in Glasgow, with its supervised daily consumption of methadone, formed the basis of a recent study by Hutchinson et al. (2000). Using baseline data from 204 IDU methadone clients in Glasgow, researchers examined changes in behaviours at six and 12 months. Follow-up rates were 73% (six months) and 58% (12 months). A total of 29% of the sample had received methadone treatment during the entire 12-month period. The authors noted significant reductions in daily opiate injecting (self-reported data), drug expenditures, involvement in acquisitive crimes, and overdoses at both 6- and 12-month follow-up interviews.

In Edinburgh, supervision by the shared care team (in particular, the involvement of nursing staff) was deemed to have contributed to the very low mortality rates among methadone clients (Macleod, Whittaker, and Robertson, 1998).

4.1.3 *The role of the pharmacist in shared care arrangements*

Shared care involving pharmacists has been much more prevalent in various parts of Scotland than in England and Wales and in the south of Ireland.
In Glasgow, a large proportion of prescribed methadone is consumed under the supervision of pharmacists, and this policy was introduced to reduce the likelihood of diverted methadone. Gruer et al. (1997) reported that in the mid-1990s, approximately 91% of methadone patients consumed methadone under pharmacist supervision even though pharmacists are not legally required to do so. Gruer et al. (1997) cited research from England and Wales that reported a much lower figure (i.e., approximately one-third) of pharmacist supervision in those regions. The review by Luger et al. (2000) confirmed that pharmacist supervision of methadone consumption is far more prevalent in some regions (e.g., Glasgow) than in others (e.g., London).

Roberts et al. (1998) noted that guidelines issued by the Greater Glasgow Health Board included the recommendation that patients undergo supervised consumption of methadone during the first year of methadone treatment and that this policy should continue unless the GP strongly believes that the prescribed dose will be taken as intended. In some regions, take-home doses can be arranged for collection for clients who progress well in treatment.

Pharmacist supervision of methadone consumption was endorsed by the local pharmaceutical body in greater Glasgow (Gruer et al., 1997). Additional fees are paid to pharmacists who supervise methadone taking, and who report information on dispensing, maintain records for auditing purposes, and participate in training.

Roberts et al. (1998) estimated that over one million supervised doses of methadone had been administered in Glasgow between 1994 and early 1998. Those authors also reported that as of early 1998, 89% of Glasgow pharmacies were involved in methadone dispensing and that most pharmacies were open six days per week.

In the Lothian region of Scotland, Greenwood (1997) noted that several methadone-related deaths in that area appeared to have occurred in people who were not in receipt of methadone treatment. This information led to a discussion of whether the region should adopt a policy of supervised methadone consumption. Supervised consumption now occurs in Edinburgh but the practice still occurs less frequently than in Glasgow. In the south of Ireland, the prescription must note whether the methadone is to be consumed in the presence of the pharmacist (Moran et al., 2001).

Some research has found that pharmacists have expressed a willingness to supervise the consumption of methadone; however, other pharmacists noted that they lacked training with regards to dealing with "difficult situations," e.g., patients who become aggressive in pharmacy settings (Sheridan et al., 1996).

Research conducted in London (Luger et al. 2000) found that the supervision of methadone consumption took approximately five minutes or less (although the amount of time spent on completing forms was not measured). That study also showed that pharmacists generally were *not* concerned that supervising methadone consumption would negatively affect their business. Pharmacists who participated in the study reported having had fewer problems with patients whose methadone was supervised compared to other drug users who frequented the pharmacy. The study also found that relationships between patients and pharmacists improved over time, that is the daily contact between patient and pharmacist led to "trust and mutual

respect" and daily contact meant that the pharmacist was in a better position to advise about other health issues.

Research has investigated methadone clients' attitudes about collecting methadone prescriptions from pharmacies and supervised consumption in those premises. An Australian study found that many methadone clients voiced concern about the public visibility of collecting prescriptions in pharmacy settings as well as discrimination by pharmacists (Ezard et al., 1999). Luger et al. (2000) found that methadone clients were in general quite satisfied with the pharmacist-based practice, however, the primary areas of concern among clients focused on 1) the lack of privacy during methadone consumption, and 2) pharmacist-led decisions about the timing of dispensing.

Neale's study of drug users in receipt of substitute treatment in Scotland (1999) found that respondents held mixed views of supervised methadone consumption, although most respondents favoured supervision. For instance, some respondents felt that supervised consumption in pharmacy settings provided them with a safe environment. Alternatively, several other respondents preferred to not be supervised and the major reason for this decision was the perceived lack of privacy in pharmacy settings. Supervised consumption produced feelings of embarrassment and degradation among these clients.

To address the issue of privacy, some pharmacists have designated special private places within the pharmacy where supervised consumption occurs (Gruer et al., 1997). The perception of "privacy" can differ between pharmacists and patients. For example, one study found that pharmacists reported that they practiced methods to create a sense of privacy during methadone consumption. However, the majority of client respondents in that study voiced concern about privacy, noting how they consumed the liquid quickly to avoid embarrassment in front of other customers (Luger et al., 2000).

One disadvantage of supervised consumption is that the policy requires methadone clients to travel to a particular pharmacy on a daily basis.
Clients have reported that daily dosing interferes greatly with other life activities (Ling, Rawson, and Compton, 1994). Neale's qualitative study of 96

individuals from Scotland who were in receipt of substitute drugs found that most respondents appeared to be "dissatisfied" with the requirement of daily trips to the pharmacy because of travel costs, or because the daily trips interfered with other lifestyle activities, e.g., work or study, travel, holiday plans. Daily dosage consumed outside the home might be one factor that affects treatment retention, although little research has examined this issue with respect to methadone (c.f. Rhoades et al., 1998).

Take-home doses diminish the need for daily travel to and from pharmacies. Illegal or unsafe use of methadone is alleged to result from legitimate sources, i.e., unsupervised consumption of methadone, take-home doses (Farrell et al., 1998). However, few studies have investigated the source of "street" methadone. Moreover, take-home doses might allow for greater trust and rapport between client and clinician. If take-home doses are allowed, clients need to be instructed on proper storage. In one study from Dublin, approximately one-fourth of opiate users who were permitted take-home doses had used baby bottles to measure methadone (Harkin, Quinn, and Bradley, 1999).

Programmes should recognise the difficulties that clients experience when organising visits to and from pharmacies. A review of the literature has failed to identify methods that strike a balance between meeting client needs with respect to daily dosing and preventing methadone from being leaked to illicit drug markets.

4.1.4 *Training pharmacists*

In shared care arrangements, the training of pharmacists is just as important as the training of GPs. In Glasgow, accredited training for pharmacists focuses on the areas of drug use and related issues. Meetings are organised and attended by both pharmacists and GPs who are involved with the dispensing and prescribing of methadone (Roberts et al., 1998). Information and training topics are also available through distance learning. Matheson, Bond and Hickey (1999) suggested that training should incorporate pharmacists' negative attitudes towards drug users so that the provision of services can be improved and additional pharmacists will be motivated to become involved in the management of drug users.

5 *Further considerations*

5.1 *Costs of substitute prescribing*

In their review of various literature, Rosenheck and Kosten (2001) observed that the introduction of opiate substitution could result in lowered or delayed relapse, lowered medical costs such as HIV, Hepatitis C, and other infectious disease, as well as resulting in reduced expenditures for the criminal justice system. Those authors compared projected costs of buprenorphine/naloxone and methadone maintenance in the United States. Slightly higher costs were associated with methadone although the authors cautioned that their analysis made several assumptions about hypothetical factors that could affect costs, e.g., fewer counselling sessions among buprenorphine clients. Also, in the US, methadone is not prescribed in office settings; rather, methadone maintenance is available through selected clinics. For example, the authors noted that "patient time and travel costs" would be higher for methadone maintenance in part because of travel time to and from those few methadone clinics. In contrast, buprenorphine administered in primary care settings would reduce travel time. Considerably less is known about cost comparisons in the United Kingdom.

5.2 *Substitute prescribing and pregnancy*

A report issued by the Lindesmith Center-Drug Policy Foundation (2000) concluded that detoxification from heroin can produce miscarriage and premature birth. Methadone can be used safely during pregnancy, however, the risk of miscarriage is increased if methadone dosage levels are reduced during the first trimester of pregnancy. The report also indicated that methadone has been shown to be safe for breastfed babies.

A study of methadone treatment coupled with monetary vouchers for treatment attendance and cocaine-negative urine samples found that attendance was significantly higher for subjects who were assigned to the voucher incentive group compared to controls (Jones et al., 2001). Moreover, illicit drug use as measured by urinalysis was lower among participants in the voucher incentive group than in the control group during the first week of outpatient treatment.

Considerably less research has investigated the use of buprenorphine among pregnant opiate-dependent women. The few studies that have been conducted (e.g., Fischer et al., 1998) have been based on small sample sizes and possibly confounded by the effect of other interventions, e.g., participation in comprehensive treatment.

5.3 *Parenting and substitute prescribing*

Dependent heroin users with children have special needs and programmes need to recognise and respond effectively to these needs. With respect to this issue, female dependent users are likely to be affected than males. For example, data from the US have shown that females in methadone treatment have more dependent children than males (Rowan-Szal et al., 2000; Wechsberg et al., 1998). Women methadone clients who seek employment outside the home have reported having experienced problems associated with finding and paying for adequate child care. A qualitative study conducted in Dublin suggested that disproportionately more women than men drug users reported that the lack of adequate childcare was a barrier to effective treatment, as well as a barrier to educational and employment possibilities (Moran, 1999). Only nine of the 45 drug treatment centres in the region provided childcare through crèche facilities (Moran, 1999). In some treatment settings, childcare was provided through "drop in" services whereby children were cared for as parents sought treatment. Although the nature of the study precluded generalisations to the wider population of opiate-dependent parents, the availability of childcare appeared to contribute to more amenable treatment options for women. The study identified the need for two types of childcare for drug users: 1) facilities that offered childcare for the entire day, and 2) "drop in" facilities to be used as needed.

Substitute prescribing programmes that do not permit take-home doses could pose major problems for parents. Clients with very young children will have to either arrange and perhaps pay for childcare while they travel to and from pharmacies or have the children accompany them. Parents with school-age children might find that visits to pharmacies conflict with collection from schools. In-patient treatment, even for short stays involving detoxification may not be an option for primary caregivers. It is unacceptable that some parents must in effect choose between participating

in drug treatment and managing childcare. Programmes must develop "family friendly" methods that encourage parents to participate in drug treatment. If not, substitute prescribing programmes will disproportionately exclude parents of young and school-age children.

5.4 *Methadone maintenance in prison settings*

Methadone clients who are detained by police or incarcerated in prison are of special concern. Of 276 methadone clients imprisoned during a 12-month period in Scotland, only 4% of cases involved subsequent communication between the prison doctor and the client's general practitioner (Gruer and Macleod, 1997). Methadone is available for detoxification or as a treatment intervention in selected countries only. In Australia, researchers have found that methadone maintenance reduces injecting drug use in prison (Dolan, Hall, and Wodak, 1996). According to 1999 government estimates, between 1,200 and 1,500 prisoners in Mountjoy Prison (Dublin) were undergoing methadone detoxification annually (Department of Justice, Equality and Law Reform, 1999). Very few prisoners, however, were afforded methadone maintenance during their incarceration. Recently released prisoners appear to be at higher risk for methadone overdose (Cooper et al., 1999).

6 *Recommendations*

6.1 It is recommended that methadone maintenance be made available as a treatment option to individuals dependent on heroin.

The review of the cumulative evidence suggests that methadone treatment can increase treatment retention, reduce subsequent opiate use, and reduce drug-related criminal activity (pages 7-15). The evidence to date is less conclusive about the effects of methadone treatment on risk behaviours for HIV infection, particularly sexual risk behaviours. However, the evidence from some countries suggests that HIV seroprevalence rates are lower for methadone clients compared to other problem opiate users who have not undergone methadone treatment (pages 9-10).

Regarding subsequent heroin use and drug-related criminal activity, the evidence suggests that methadone treatment is most effective in programmes that are based on the philosophy of *maintenance* rather than *abstinence* or *reduction* (pages 7-8; 12). Higher treatment retention rates have been associated with maintenance programmes compared to reduction programmes.

6.2 It is recommended that a maximum length of time in methadone treatment should *not* be imposed.

The primary goal of such intervention should be to retain individuals in treatment. Reduction programmes should be an option as well, but this decision should rest with the client after *balanced* advice is provided by professionals. Moreover, it is important that methadone reduction does not become a "de facto" intervention, i.e., one that is applied universally within any particular treatment agency or by any physician, without regard to client need.

6.3 It is recommended that the DHSSPS does *not* implement a central register that would collect information on persons in receipt of methadone.

Qualitative research with largely Belfast heroin injectors found that many heroin users were quite suspicious of official drug data that included personal information (McElrath, 2001). In that study, heroin users perceived that they could not be guaranteed complete confidentiality with respect to their drug user identities. In turn, some individuals avoided contact with GPs and other treatment providers.

It is recognised, however, that some type of monitoring is necessary in order to reduce the possibility of double prescribing by two or more physicians. Creative strategies should be developed that would diminish double prescribing while at the same time, would not deter persons coming forward for treatment. The Addicts Index and Drug Misuse Database are already in place and might represent two methods for monitoring persons in receipt of methadone.

6.4 Liquid rather than injectable methadone should be used for methadone maintenance.

Most of the research has examined the effectiveness of oral methadone so that considerably less is known about the effectiveness of injectable methadone (page 11). Although prescribing injectable methadone might address needle fixation, injection risk behaviours might still present problems. Injectable methadone might be an option at a later date, but this decision should be guided by the professional opinions of treatment staff and physicians in N. Ireland, as well as subsequent research findings. For example, a study on injectable versus oral methadone is currently underway in Scotland. Results from that study might be quite useful to drug policy makers in N. Ireland.

6.5 Methadone should be the preferred substitute drug for heroin dependence, however, clinical discretion with regards to the choice of substitute drug should be acknowledged.

The Department of Health permits the use of buprenorphine as a treatment for opiate dependence, thus clinicians who prescribe buprenorphine are acting in accordance with guidelines. However,

clinicians should be aware that in comparison to methadone, considerably less is known about buprenorphine as a treatment for opiate dependence. In particular, long-term studies of buprenorphine in comparison to methadone have yet to be published so that we know little about long-term effects of such treatment (page 18). Studies that investigate the relationship between buprenorphine treatment and subsequent drug-related criminal activity also are lacking (page 18).

The Advisory Board overseeing this report suggested that this researcher contact the five consultant psychiatrists (CPs) in N. Ireland who would likely be involved if substitute prescribing were implemented, in order to ascertain their views on methadone and buprenorphine (Subutex). From those discussions, three of five CPs have used methadone sparingly, whereas two have had more experience with patients in receipt of methadone. Three of five had provided buprenorphine (i.e., Subutex) to patients undergoing either detoxification or for longer-term use.

CP 1 prefers Subutex to methadone for long-term (i.e., reduction or maintenance) use, citing its safety record. CP 1 also notes that Subutex works effectively for patients undergoing detoxification, was in favour of some type of substitute prescribing but did not appear to have a preference for either methadone or Subutex. CP 2 does not oppose methadone but prefers Subutex because of the latter's "greater safety record." CP 2 acknowledges the possibility of diverted Subutex and suggests the combined buprenorphine/naloxone might work well here (but see pages 16-17), if approved by the DOH. Overall, CP 2 states that the choice between Subutex and methadone should be a "clinically driven" decision and that with time, the problems and successes of each substitute drug will emerge locally. CP 2 notes also that Subutex might be more successful than methadone during detoxification. CP 1 and CP 2 suggest that Subutex might be more effective with younger persons who have used heroin for shorter lengths of time than more experienced, older persons.

Although CP 3 has worked with very few persons who are dependent on heroin, s/he prefers Subutex to methadone, citing the safety record of Subutex.

CP 4 has treated patients with methadone and with Subutex. S/he also reports that patients generally have had positive outcomes with either of these substances. CP 4 reports that the goal is to match patients' expectations with what a particular substitute drug can offer, thereby taking into account users' opinions when deciding on which substitute drug to prescribe.

CP 5 reports that methadone maintenance should never be implemented in N. Ireland. CP 5 notes the "negative aspects of methadone maintenance" (e.g., dependence on methadone) and that heroin use in N. Ireland would *increase* with the availability of methadone maintenance. CP 5 has treated some heroin users here, and in the last six months, has noted a small increase in the number of people seeking treatment for heroin dependence. CP 5 states that most patients treated in the site move to or return to N. Ireland from elsewhere, and do so because they wish to abstain completely and do not wish to reside in settings in which heroin and methadone are available. The site in which s/he works operates under an abstinence only policy. S/he prefers to provide inpatient detox with Lofexidine and if needed, prescribes Naltrexone for a period of six months to one year. CP 5 might, however, be in favour of Subutex in the long-term, but in general CP 5 does not advocate maintenance.

These discussions indicate that some consultant psychiatrists have prescribed buprenorphine for persons dependent on heroin in N. Ireland. Some CPs mentioned the safety record of Subutex, however, none indicated that the long-term effects of Subutex have yet to be examined. Nor did they mention the lack of research concerning the relationship between Subutex maintenance and subsequent drug-related criminal activity (nor were they asked about these drawbacks). Written guidance about the possible limitations of buprenorphine should be distributed to CPs and other professionals who will be involved in prescribing substitute drugs to persons dependent on opiates.

6.6 At present, heroin maintenance should not be offered as a treatment option.

Research into the effectiveness of heroin maintenance suggests that the treatment can reduce criminal activity, but the evidence is less clear about the effects of heroin maintenance on other outcomes, e.g., relapse (pages 20-21). Considerably more research is needed in this area before heroin maintenance can be offered as a treatment for persons dependent on heroin. A review of findings from current studies being conducted in the Netherlands, and planned clinical (heroin maintenance) trials in Germany might be relevant for N. Ireland in the future.

6.7 Diagnosis and assessment of drug dependence should be guided by the recommendations issued by the Department of Health as well as experts from Glasgow and Edinburgh.

The Department of Health (1999: 19-21) has outlined those areas that might be covered in the diagnosis of drug dependence and assessment. This information should be reviewed carefully by clinicians and other professionals who will be involved in a programme of substitute prescribing. Moreover, it is important to obtain up-to-date information with respect to diagnosis and assessment. Discussion with experts from Glasgow or Edinburgh should be held with regards to additional issues that might be important for assessing opiate or heroin dependence. Methadone will not be effective for all opiate-dependent persons, and further, some clients will not opt for methadone. Thus, assessment is a critical stage of the treatment process.

6.8 It is important that initial dosage levels be monitored very closely. and that the DHSSPS implement a flexible methadone dosing policy.

Decisions about initial dosage levels are critical. Initial doses should seek to reduce craving for heroin and prevent withdrawal. Sedation effects should be avoided. In the majority of cases, initial doses of

20 to 30 mg per day are considered to be in the safe range (Payte and Khuri, 1993), however, the Department of Health (1999: 46) recommended an initial dose of 25 to 40 mg per day if tolerance is high, and between 10 to 20 mg per day if tolerance is low or unknown. Lower initial doses of methadone might be more suitable for users who smoke or chase the drug, rather than inject (Payte and Khuri, 1993). During induction in particular, tolerance to methadone should be monitored frequently. Some information suggests that patients presenting for methadone treatment might misrepresent their opiate history in order to obtain higher doses of methadone (Payte, 1999). Monitoring methadone plasma levels could assist with dosing decisions (Department of Health, 1999). Women patients should undergo pregnancy testing before methadone is provided. Persons recently released from prison or similar setting and persons who have not used heroin for some time should generally be given lower doses. Following the first dose, an additional dose of approximately 10 mg can be provided 3-4 hours later if cravings continue and withdrawal symptoms persist (Payte and Khuri, 1993). The Department of Health (1999) recommended that second doses can be a maximum of 30 mg, however, subsequent doses in outpatient settings should not exceed 5 to 10 mg per day. Additionally, the total increase during the first week "should not usually exceed 30 mg above the starting day's dose" (Department of Health, 1999: 46). Stabilisation should begin to occur between 4 and 10 days after the initial dose (Payte and Khuri, 1993). *It is recommended that there is an urgent need for regular and consistent follow-up.* Once a patient is stabilised, changes to dosage levels can be made particularly in times of stress, anxiety or depression (Payte and Khuri, 1993). Methadone clients must be provided with educational information about methadone, including methods to avoid overdose and dangers associated with drug interactions. Clients should be made aware of initial dosage levels and dosage changes. For clients who wish to withdraw from methadone, decreases in doses should not exceed 10% of the stabilised dose and subsequent dose reductions should occur between 10 and 14 days later (Payte and Khuri, 1993).

The impact of methadone dosage levels has been well-researched and the cumulative evidence suggests that high-dose methadone

contributes significantly to improved treatment retention as well as reduced risk for relapse (pages 11-15). Further, the research suggests that flexible dosing policies produce more favourable outcomes (pages 12-13). Some clients will feel comfortable on 50 mg of methadone or less per day whereas others will require considerably higher doses. Dosing decisions must consider the extent of dependence, the intensity of cravings and withdrawal symptoms, the frequency of opiate use, recent opiate use, other drug use, and the purity of heroin within a particular region. Monitoring methadone plasma levels can assist with dosing decisions. Based on the evidence, it is recommended that methadone treatment programmes incorporate flexible dosing policies.

6.9 Prescribers must be provided with very detailed information on drug interactions.

The Lindesmith Center-Drug Policy Foundation (2000: 21) reported that methadone dosage may need to be increased if the client is using any one of the following drugs: Carbamazepin (Tegretol), Phenytoin (Dilantin), Neverapine (Virammune), Rifampin, and Ritonavir (Norvir). These drugs reduce the effect of methadone because the drug interactions "cause the liver to metabolise methadone more quickly." The authors also note that use of other drugs may increase the effect of methadone, whereas other interactions can produce withdrawal. Certain antidepressants can increase methadone concentrations in the body whereas benzodiazepines and St. John's Wort can produce adverse side effects when used with methadone (Goodman, Jones, and Glassman, 2001). Alcohol, barbiturates and other sedatives may increase the metabolism of the methadone (Payte and Khuri, 1993). Gourevitch and Friedland (2000) reported that the interaction between methadone and AZT and other medications used to treat HIV infection can produce withdrawal symptoms in patients. The authors recommended that with some medications, methadone doses should be increased in small increments at a time, and health care providers must be knowledgeable about the interactions between methadone and the various substances used to treat HIV infection. Other possible drug interactions are described in the report issued by the Department of Health (1999). It is recommended that

prescribers be fully aware of drugs that can interact with methadone. The Department of Health (1999) provides guidance on this matter, but their list of drug interactions is by no means exhaustive.

6.10 Where possible, it is recommended that shared care protocols for the treatment of heroin dependence be implemented.

Shared care models show great promise, however, research into the effectiveness of shared care is limited. Still though, the few studies that have examined the effectiveness of shared care or practice-based treatment have reported favourable results (pages 42-44). Implementation of such models require considerable planning and a co-ordinated effort involving several professionals. It is important to identify creative methods that will contribute to participation among physicians, pharmacists, and other professionals. Initial and on-going training as well as an organised support network are critical components of successful shared care models.

Following the recommendation by the Department of Health (1999: 12), guidelines should reflect "national" policy [or in this instance, N. Ireland policy), but at the same time "be locally determined." N. Ireland guidelines should allow for flexibility with respect to problems and issues that emerge locally. Shared care operates under the principles of frequent and effective communication between and among professionals. The development of the guidelines should involve all participants, e.g., general practitioners, pharmacists, drug workers, voluntary and statutory agencies. *It might also be useful to solicit the opinions of users themselves*. User input into several areas of drug policy appears to be lacking. Topical areas to be included in local guidelines should be drawn from the Department of Health (1999: 13), although additional topics should be addressed if pertinent to the locality. Roberts et al. (1998: 193) suggested that regions that seek to implement a shared care model of drug treatment involving methadone need the following: 1) good leadership within a team approach, 2) clearly defined roles and excellent communication between professionals, 3) the use of contracts outlining expectations of the team members.

The Department of Health (1999: 14) recommended the establishment of a "shared care monitoring group," comprised of representatives from various sectors. The monitoring group should have responsibility to "approve local agreements and protocols, review training needs, clarify performance indicators and monitor the delivery and effectiveness of shared care service provision in the area." It is recommended that monitoring groups be established within various regions of N. Ireland.

6.11 Persons who are dependent on heroin should be provided with various methods for accessing substitute drugs.

In some instances, specialised drug treatment sites should provide assessment, prescribing as well as the supervision of methadone consumption. In other instances, stabilised clients should be transferred to GPs, with supervised consumption provided by pharmacists. Other individuals might benefit most when assessed and treated solely by the GP (although the monitoring of detoxification might be difficult in physicians' offices). For instance, some individuals might have considerable concerns about confidentiality, given their physical presence in a drug treatment setting. Additionally, other persons who desire treatment might be disadvantaged because of the proximity between their residences and the locations of drug treatment sites. We must assume that there are people dependent on heroin in N. Ireland who will *not* seek assistance from a drug treatment agency but might consult a GP. It is important that heroin-dependent persons are provided with different options for accessing treatment. The general practitioner is often the "first point of contact" for young drug users in particular (Department of Health, 1999: 11). In addition to prescribing methadone, GPs can also treat or refer for psychological and physical morbidity and drug-related illnesses. They can test for HIV antibodies, and test for Hepatitis B and C viruses, and immunise where necessary. GPs can also distribute material with regards to safer injecting, needle exchange, condom use, and make referrals to specialist drug clinics, psychiatrists, social workers, drug services (e.g., Narcotics Anonymous).

Shared care options might include facilitator teams that include trained drug workers or public health nurses who can assist physicians with various patients. There should be written agreement with regards to which shared care team member will be responsible for co-ordinating the treatment plan and delivery. "Key workers" are appointed for a number of clients in various parts of Scotland (Effective Interventions Unit, 2001). All professionals involved in the treatment of heroin dependence should be required to undergo initial and subsequent training. Training might be provided through contractual arrangements with professional staff from Scotland who have worked in similar schemes. Staff involved with the programme in Edinburgh have described methods for encouraging physician participation. Weinrich and Stuart (2000) concluded that physician leadership is a critical factor for the establishment of successful shared care programmes to assist drug users. Additional creative strategies might be needed in N. Ireland. GPs and pharmacists should be provided with on-going support from drug service agencies. Support should be provided on demand, depending on the needs of the individual physician. Updated information on methadone treatment should be distributed frequently to GPs, pharmacists and drug workers who are involved in methadone treatment.

6.12 It is recommended that methadone consumption be supervised for the first six months of treatment, and perhaps longer for some clients.

It is critical that we aim to reduce the likelihood of methadone-related deaths. Although some researchers have argued that the risk of fatal overdoses from heroin are reduced among methadone clients (page 8), it is equally important to diminish the risk of methadone-related fatalities. A report issued by the *Advisory Council on the Misuse of Drugs* (2000: 63) states that:

> "It could be argued that there may be an inverse relationship between the number of heroin and methadone-related deaths, with reductions in heroin overdose deaths partially offset by an increase in methadone-related overdose deaths. If this is true

> then the answer should be to find a system which does not lose the benefit of reducing heroin-related deaths by increasing methadone-related deaths, but which has appropriate prescribing controls built in, so as to obviate the downside."

The literature reviewed herein found that other scholars have suggested that a policy of supervised consumption appears to be linked to fewer methadone-related fatalities (page 40). Recommendation 6.12 is consistent with the guidance offered by the *Advisory Council on the Misuse of Drugs* (2000). This recommendation is based on the premise that supervised consumption will reduce the likelihood of methadone mortality. Agar et al. (2001: 76) suggested that "an effective maintenance drug will always be interesting to the streets as well," and supervised consumption is thought to prevent diversion. In fact, diverted methadone has not been well-researched (pages 39-40) and in fact, we may have no way of knowing whether the methadone associated with a drug-related death indeed derived from a legitimate medical source in N. Ireland.

It is important to note that a policy of supervised consumption might lead clients to terminate treatment or avoid it altogether. *This issue should be monitored closely*. Following six months of treatment, take-home doses should be permitted for clients who have shown to be actively engaged in other programme activities and whose urinalyses results have been negative for opiates. Sunday and holiday collections will be problematic when take-home doses are not permitted. Supervised consumption of methadone should occur in pharmacies or in specialised treatment sites. Pharmacists must provide privacy for supervised consumption. However, some clients, e.g., pregnant women, parents with young children, will have difficulty arranging for the collection of daily doses of methadone. In these instances, a member of the shared care team should visit the homes of clients so that methadone treatment can be continued. Two of the CPs and two CAT staff members suggest a flexible policy about supervised consumption, recognising that supervision by pharmacists might be impossible to implement on Sundays, holidays, etc. In these instances, these individuals report that take-home doses should be permitted. One

CAT staff member reports that take-home doses are permitted one day per week (i.e., Sundays).

With regards to a time period of supervised consumption, CP 2 refers to the guidelines developed by the DOH (i.e., 3 months) and by the Advisory Council on the Misuse of Drugs (i.e., 6 months), but notes that flexibility is needed. For example, CP 2 notes that women in the late–stage of pregnancy might have difficulties collecting daily (methadone) and thrice-weekly (Subutex). Take-home doses should be considered for these patients. CP 2 also notes that individuals residing in rural settings also experience problems with daily dosing. A staff member from one Community Addiction Team reports that for at least the past year, nearly all clients have been required to participate in supervised consumption of methadone or Subutex. One exception was made for a client who travelled a great distance to the programme site. However, this client has actively engaged in counselling and other program components, and urine specimens for this client have been consistently "clean." CP 4 reports that take – home doses are permitted on days when pharmacies are closed, e.g., Sundays, bank holidays, or when clients are on holiday.

6.13 Implement a monitoring system for tracking methadone-related deaths.

In order to monitor methadone-related deaths following the implementation of substitute prescribing, it is important to collect baseline mortality data. Recorded deaths where methadone is listed as a primary or secondary cause of death should be noted for the five years prior to the implementation of substitute prescribing. It is important to collect information on how deaths are recorded by coroners and to note any possible sources of error in these mortality data.

6.14 Urinalysis should be used only as a method to monitor treatment progress and as a tool to assist with the prevention of overdose.

Urinalysis can produce both false positives and false negatives and is only able to detect very recent drug use. The cost-effectiveness of

urinalysis has been questioned (pages 34-35), and one study found no differences in urinalysis results between clients who were informed of checks prior to the collection of urine samples and clients who were not informed (pages 34-35). Urinalysis should be conducted on a periodic and random basis, however, urines that are positive for opiates and other drugs should *not* result in treatment termination.

6.15 The number of persons in receipt of methadone and other substitute drugs for maintenance should be monitored closely.

Hartnoll (1999) estimated that substitute prescribing rarely is able to reach more than 50% of problem opiate users, even when a range of these interventions are available. Assuming a point estimate of 828 problem heroin users during 1 November 2000 to 31 October 2001 for N. Ireland (McElrath, 2002), it is estimated that the maximum number of different people taking part in substitute prescribing during a given year would be 414. If that point estimate has increased since that study was conducted, we might expect a similar increase in the estimate. Low numbers of persons in receipt of substitute drugs could indicate that the treatment or programme components are not being implemented correctly.

6.16 Develop outreach teams within various regions in N. Ireland.

A recent study from N. Ireland found that between 48 and 64% of problem heroin users had *not* been in treatment during the 12-month period, 1 November 2000 to 31 October 2001 (McElrath, 2002). It is important that we improve participation rates in various forms of drug treatment in N. Ireland. Moreover, relapse after treatment is a matter of concern. Several studies show that a number of clients continue to use opiates during methadone treatment or do so after treatment has ended. There is a need for the development of creative strategies that would reduce the probability of relapse. In order to improve treatment participation and to prevent relapse, it is recommended that outreach workers be assigned at local levels to deal specifically with problem heroin users. The outreach workers should seek out-of-treatment heroin users, make referrals to specialist agencies, deliver advice about methods to prevent overdose

with methadone and heroin, and distribute material on safer injecting, and needle exchange. Outreach workers should also seek to establish and maintain contact with persons who have discontinued substitute prescribing and determine those factors which have influenced treatment termination. This information could then be fed back to treatment agencies, not for monitoring purposes but to assist agencies in identifying programmatic issues that might assist treatment retention.

6.17 Counselling should be offered to clients in receipt of methadone.

Although counselling in conjunction with methadone treatment produces more favourable outcomes than methadone alone (pages 29-31), a policy of mandatory counselling ignores the importance of matching individual needs with treatment options. Moreover, not all methadone clients are in need of intensive counselling. Some evidence suggests that other support services, e.g., employment skills training, can contribute to more favourable outcomes (page 30), however, few studies have examined this issue. Mandated long-term counselling is not recommended, however, all clients should be required to undergo counselling during the early stages of treatment and some clients should be entitled to long-term counselling if needed and desired. The frequency of counselling should depend on the needs of the individual. If one goal is to reduce the frequency of injection, then the issue of needle fixation should be addressed during counselling

6.18 Counselling should address issues pertaining to post-traumatic stress.

N. Ireland has experienced widespread political conflict and several persons have been exposed to extreme violence. Research has found high rates of posttraumatic stress disorder (PTSD) in post-conflict societies (de Jong et al., 2001; see also page 12). Other research has found linkages between exposure to traumatic events and post-traumatic stress disorder (PTSD) (Breslau et al., 1999) and between PTSD and drug use (Bremmer et al., 1996; Chilcoat and Breslau, 1998). Still other research has found that drug misusers have high rates of PTSD and this co-morbidity has implications for treatment retention

(Back et al., 2000). Some methadone clients will need counselling that focuses on traumatic experiences relating to the wider N. Ireland political conflict.

Additionally, other support services should include a focus on child care, improving parenting skills, improving family relationships, identifying employment and education opportunities, and addressing acute needs such as housing (Effective Interventions Unit, 2001).

6.19 It is recommended that crèche facilities be implemented at specialised drug treatment centres, to enable parents with young children to have greater access to treatment.

Issues relating to child care may reduce the likelihood that some parents will participate in methadone treatment (pages 52-53). The provision of crèche facilities in specialised drug treatment sites might increase treatment participation and retention among parents. A total of four of five of the Consultant Psychiatrists report that child care issues do not appear to be a major treatment barrier to female parents, although all four indicate that the majority of their patients are male. It is important to note that one would need to conduct research with women heroin users who have *not* participated in treatment because of child care problems in order to investigate the matter fully. CP 5 mentions that women can use child care problems as an excuse for not participating in treatment. A CAT staff member reports that issues surrounding child care have surfaced for some women in treatment. A second CAT staff person notes that although the agency in which s/he works has not incorporated substitute prescribing (except for detox), s/he notes that significant numbers of women in treatment for alcoholism have had child care problems, and at least one facility in N. Ireland has implemented crèche facilities for parents receiving treatment or support services for alcohol problems. CP 2 suggests that the "service must be perceived as "beneficial" in order for prospective female patients with children to come forth for treatment. Consistent with the literature, four of five CPs acknowledged that methadone rather than Subutex was appropriate for use among pregnant women.

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APPENDIX: DHSSPS response to the recommendations contained in the report "Review of Research on Substitute Prescribing for Opiate Dependence and Implications for N. Ireland" by Dr Karen McElrath

Recommendation 1: Methadone maintenance be made available as a treatment option to individuals dependent on heroin.

DHSSPS Response: Accept.

The Department is satisfied that the review of the literature and the experience of service deliverers support the availability of maintenance therapy/substitute prescribing in Northern Ireland. The Department will establish an Implementation Group to oversee how this issue should be progressed.

The Department acknowledges that the research evidence base for methadone is stronger than that for other drugs, and that the concerns outlined by Dr McElrath, especially in relation to buprenorphine, are reasonable. However, it is clear from Dr McElrath's report that there is significant support for buprenorphine amongst consultant psychiatrists in Northern Ireland, and there are a number of clients currently in receipt of buprenorphine. If practitioners follow Orange Book[18] guidelines when prescribing buprenorphine, the Department considers that it should support these practitioners in the management of clients in receipt of buprenorphine. To do otherwise in the absence of strong evidence in relation to negative effects of buprenorphine would risk creating a two-tier service. The Department also has to consider the position of those patients for whom

[18] "Drug Misuse and Dependence – Guidelines on Clinical Management", issued in 1999 by the Department of Health; the Scottish Office Department of Health; the Welsh Office; and the Department of Health and Social Services, Northern Ireland. This publication is commonly referred to as the "Orange Book".

methadone has been tried but has not worked. Practitioners may need an alternative therapy and buprenorphine could well provide this.

The Department will continue to monitor the research position with regard to all drugs used for substitute therapy and will review this position if the need arises.

Recommendation 2: A maximum length of time in methadone treatment should not be imposed.

DHSSPS Response: Accept.

The Department accepts the view that where appropriate, maintenance therapy produces better results than reduction strategies. Although regular review of treatment is essential, and accepting that there will be circumstances in which it will be appropriate for patients to move from a maintenance programme to a reduction/detoxification programme, the Department recognises that maintenance is a valid therapy in its own right.

Recommendation 3: DHSSPS does not implement a central register that would collect information on persons in receipt of methadone.

DHSSPS Response: Not accept.

The Department does not accept this recommendation for a number of reasons. First, there is a legal requirement for doctors treating addicts to notify the Addicts Index under Regulation 3 of the Misuse of Drugs Regulations (Northern Ireland) 2002.

Secondly, in relation to individual clients, there will be a need for a mechanism to ensure that multiple scripting from a variety of sources does not take place. The

research evidence strongly suggests that abuse in this way with consequent diversion of substitute drugs to the illegal market is likely to be a significant problem, and most jurisdictions have had to implement mechanisms to prevent this. The precise nature of such controls will be determined by the Implementation Group which will be set up to oversee practice in relation to substitute prescribing, but the Department's view is that this is likely to involve some sort of monitoring system that will be capable of identifying the prescription and dispensing of substitute drugs to individual users.

Finally, it is clear that the establishment of substitute prescribing services will come under close scrutiny and monitoring data will be required to assess the efficacy of the intervention; to provide data for evaluation; and to provide public confidence in the policy.

Recommendation 4: Liquid rather than injectable methadone should be used for methadone maintenance.

DHSSPS Response: Accept.

The Department does not see any strong case for the availability of injectable methadone at this time.

Recommendation 5: Methadone should be the preferred substitute drug for heroin dependence, however, clinical discretion with regards to the choice of substitute drug should be acknowledged.

DHSSPS Response: Accept with qualification.

The Department acknowledges that, in individual circumstances, the choice of substitute drug used should be based on clinicians' assessment of the patient including taking into account the patient's views. See response to Recommendation 1.

Recommendation 6: At present, heroin maintenance should not be offered as a treatment option.

DHSSPS Response: Accept.

The Department agrees that it is not appropriate to introduce heroin maintenance in Northern Ireland at this time. The relatively low numbers of problem heroin users in Northern Ireland; lack of familiarity of practitioners and dispensers with substitute programmes; the high (thrice-daily) dosing requirement and associated logistical and resource costs militate against the introduction of heroin maintenance, especially given the equivocal nature of the research evidence.

Recommendation 7: Diagnosis and assessment of drug dependence should be guided by the recommendations issued by the Department of Health as well as experts from Glasgow and Edinburgh.

DHSSPS Response: Accept with qualification.

The Department endorses the view that diagnosis and assessment should be guided by the Orange Book[19]. However the Department also considers that treatment should be guided by best practice from a wide variety of locations and

[19] Although the Orange Book was published by the Department of Health, the guidelines are jointly agreed between the four UK jurisdictions.

considers that limiting the input of expertise to Glasgow and Edinburgh is too restrictive.

Recommendation 8: Initial dosage levels should be monitored very closely. DHSSPS implement a flexible methadone dosing policy.

DHSSPS Response: Accept.

The Department accepts that the evidence in the report is clear in that trying to use minimalist prescribing which is not flexible to user need is counterproductive. This applies to any substitute drug, not just methadone.

Recommendation 9: Prescribers must be provided with very detailed information on drug interactions.

DHSSPS Response: Accept.

The Department acknowledges that this is essential.

Recommendation 10: Where possible, it is recommended that shared care protocols for the treatment of heroin dependence be implemented.

DHSSPS Response: Accept with qualification.

In light of small numbers of problem users likely to avail of treatment, and the fact that substitute prescribing is new in Northern Ireland, it will be appropriate that in the initial phases of the policy for secondary care should have the responsibility for the initiation of maintenance treatment and that GPs should liaise with secondary care in the treatment of patients as appropriate. The Department is of

the view that, at least initially, one shared care monitoring group would be appropriate for all of Northern Ireland.

Recommendation 11: Persons who are dependent on heroin should be provided with various methods for accessing substitute drugs.

DHSSPS Response: Accept with qualification.

The setting up of substitute prescribing services from a low baseline may initially restrict points of access on a purely logistical/resource basis. The Implementation Group will have to take these factors into account.

Recommendation 12: Methadone consumption should be supervised for the first six months of treatment, and perhaps longer for some clients.

DHSSPS Response: Accept with qualification.

Experience from elsewhere suggests that diversion of drugs prescribed for substitution purposes can be a significant problem and that supervised consumption is an effective measure which can be used to reduce the risk of this occurring. Supervised consumption also acts as a reassurance to prescribers as it minimises the likelihood that medicines that they prescribe will subsequently end up being used by anybody other than the patient for whom it was intended. The Department thus supports the contention that the consumption of substitute drugs, including methadone and buprenorphine, be supervised.

The Department is also of the view that in the initial stages of the implementation of a substitute prescribing regime consumption should continue to be supervised indefinitely. This practice of supervised consumption should continue until the

Department is persuaded that a policy of allowing take-home doses can be operated that minimises the likelihood of any one other than the patient taking the substitute medication. The Implementation Group should draw up guidelines bearing this position in mind. Take-home doses should be minimised so that they are allowed only in exceptional circumstances, and guidelines need to be clear on precisely when this can occur and the safeguards that need to be introduced if take-home doses are to be permitted.

Recommendation 13: Implement a monitoring system for tracking methadone-related deaths.

DHSSPS Response: Accept with qualification

The Department recognises that if substitute prescribing is implemented then it will be necessary to try and ascertain if any subsequent deaths are related to substitute medication. Collating such data retrospectively is complicated and it should be noted that patients who are under a maintenance therapy regime might also have access to drugs from another source.

Recommendation 14: Urinalysis should be used only as a method to monitor treatment progress and as a tool to assist with the prevention of overdose.

DHSSPS Response: Accept.

Positive urine tests should be discussed with user and not automatically lead to treatment termination. The Department also considers that urinalysis results have a place in the wider monitoring and evaluation of substitute therapy regimes.

Recommendation 15: The number of persons in receipt of methadone and other substitute drugs for maintenance should be monitored closely.

DHSSPS Response: Accept.

The Department accepts this recommendation. This seems to support the need for some form of register unlike Recommendation 3.

Recommendation 16: Develop outreach teams in various parts of Northern Ireland.

DHSSPS Response: Accept.

The Implementation Group should determine the best way of achieving this.

Recommendation 17: Counselling should be offered to clients in receipt of methadone.

DHSSPS Response: Accept.

The Department consider that counselling should be offered, but not made compulsory for clients to accept. It would also be essential to ensure that counsellors are appropriately qualified and have access to clinical supervision.

Recommendation 18: Counselling should address issues pertaining to post-traumatic stress.

DHSSPS Response: Not accept.

This recommendation is written specifically in the context of political situation in Northern Ireland and in particular the high level of violence that has pertained over the past 30 years or so. The Department considers that post-traumatic stress disorder has a number of other causes, eg road traffic accidents, family deaths, serious illness etc. Counselling should address all of patient's relevant needs where appropriate and it cannot be assumed that post-traumatic stress disorder is a factor in each case of drug misuse and/or the desire for maintenance therapy. For this reason Department believes that counselling should only consider this issue if the need is identified.

Recommendation 19: It is recommended that crèche facilities be implemented at specialised drug treatment centres, to enable parents with young children to have greater access to treatment.

DHSSPS Response: Accept with qualification.

The Department accepts this but acknowledges that there will be logistical issues for treatment centres and there is also the issue of resources which will need to be addressed.