INVESTIGATION OF METHADONE DOSING IN VICTORIA

FACTORS INFLUENCING DOSING LEVELS

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The responsibility for all statements made in this document lie with the authors. The views of the authors do not necessarily reflect the views and position of DHS.

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EXECUTIVE SUMMARY

The evidence regarding outcomes associated with different methadone doses has been systematically reviewed in a recent Cochrane Review which reported that high dose methadone (60mg and above) is associated with better treatment retention, less heroin use and less cocaine use than low dose methadone. Higher doses of methadone (>100mg) have been found to completely suppress opiate withdrawal and block the effects of heroin whereas lower doses (e.g. 30, 50) do not completely block the effects of heroin. It is not possible to identify therapeutic methadone plasma levels or dose ranges that will be effective for all patients.

National Clinical Guidelines reflect this research and recommend optimal doses for removing cravings for opioids, minimising the desire or need to continue illicit opioid use during treatment and improving retention in treatment. For methadone the guidelines state that effective maintenance doses typically exceed 60 mg per day. For buprenorphine, doses ranging from 12-24mg/day are recommended.

Despite these recommendations, research frequently reports doses below 60mg/day. Among studies reporting methadone doses for Victorian clients since 1995, the mean methadone dose has been lower than 60mg in all but one study. A similar tendency towards low doses has been reported in the UK, USA and Italy. Closer to home, it appears that much higher methadone doses are achieved in NSW methadone treatment programs, where a different model of service delivery is employed.

The few studies conducted into buprenorphine prescribing practices since its release in Victoria in 2002, have shown that doctors largely observed recommended daily maintenance doses of between 12 and 24 mg/day.

The Drugs Policy and Services Branch (DHS, Victoria) calculates mean daily doses of methadone and buprenorphine using data available through its census process and from the Office of Chemical Safety (OCS, Federal Department of Health and Ageing). The quarterly census provides an estimate of the number of OST patients in Victoria, while United Nations National Drug control System (UNNDS) data held by the OCS indicates the amount of methadone syrup and sublingual BPN tablets supplied to Victoria each year. Using these data sources, average daily doses of Victorian clients over the last two years have been estimated at approximately 50mg, although average doses have been as low as 32mg at other times (e.g. 1991, 2001, 2002). Average daily dose for BPN has been estimated at ranging from 6.8mg (2002) to 7.6mg (2005). The accuracy of these estimates is undetermined however, as it is not known to what extent the assumptions underlying the use of these data hold.

The aim of this research was to:

i. Estimate the proportion of Victorian methadone clients being prescribed less than 60 mg per day;
ii. Examine the validity of DRUMS data dose estimates by comparison of DRUMS estimates with community methadone and buprenorphine dose estimates;
iii. Identify key factors influencing daily methadone dose in Victoria;
iv. Identify barriers to optimal methadone dosing in Victoria; Explore the relationship between daily methadone dose and continued illicit opioid use while in treatment.

Seventeen pharmacies provided data to this study regarding methadone and buprenorphine doses dispensed to a total of 948 OST clients – 585 methadone and 363 buprenorphine clients. This accounts for approximately 8% of all OST clients in treatment across the state. The mean methadone dose was 54.0mg (range = 3 to 220, median = 50, SD = 32.0). This is lower than the 60mg/day recommended in treatment guidelines. The mean buprenorphine dose was 11.6 mg (range 0.4 to 36.0, median = 8.0, SD = 9.0). This dose is more consistent with treatment guidelines (12-24mg/day), however the modal buprenorphine dose was 8mg.

A strong theme to emerge from interviews with both prescribers and clients was that clients are the main drivers determining the size of their methadone dose. Thus, the primary reasons for low methadone dose are primarily client-related: client concern about side effects; and client focus on reducing off methadone as early as possible and the belief that lower doses are more suited to easier withdrawal and shorter term programs. Prescribers' experience of adequate / positive client outcomes on low doses and external pressure (e.g. from correctional services, child protection, families) for patients to be on low doses, also influence dosing practices.

Interviews revealed many misconceptions about determinants of appropriate dose size, mainly among clients, but also among some prescribers. In particular it is commonly believed that dose depends on patterns of heroin use (including duration of use, amount used and quality) body weight, age and gender.

Another strong theme to emerge from client interviews was considerable dissatisfaction with the amount of time doctors availed themselves for consultations, and the limited alternative supports for clients as part of treatment. Several clients and prescribers noted the value of support, especially counselling, for improving outcomes for OST clients.

Comparing the data collected by this study from pharmacies with DPSB estimates, it is apparent that the DRUMS system is adequate for estimating methadone dose, but inadequate for buprenorphine. Methadone estimates reasonably reflect actual dosing practices, while buprenorphine estimates are considerably lower than actual doses. The most likely reason for poor validity for BPN is that it is widely used for detoxification purposes (i.e. episodic short-term programs < 12-month duration) thereby breaching the assumptions of the DRUMS dose estimate system.

Having recognized that mean methadone doses in the Victorian program are well below the recommended range, the obvious question that follows is "does this matter"? It may be, as identified by some clients and doctors in this report, that some clients do well on low methadone doses, and perhaps this extends to a larger group. The extent to which treatment outcomes are affected by methadone dose was beyond the scope of this report. However, all previous research of methadone treatment outcomes in Victoria (Lintzeris et al., 1996; Lintzeris et al., 2004; Ritter et al., 2003) have been consistent with the international efficacy literature summarized in the recent Cochrane review (Faggiano et al 2003) – that methadone doses of below 60mg are less effective in retaining patients and reducing heroin use than dose above 60mg. This is such a consistent finding that it could be argued that methadone dose effectively acts as a surrogate marker for treatment effectiveness. Based on the findings of this study, the Victorian methadone program, as currently operating, is not attaining the optimal benefits that could be achieved for clients and the broader community.

1. METHOD

1.1. Project reference group

A Project Reference Group (PRG) was formed comprising members representing key bodies involved in or connected to methadone maintenance treatment and Turning Point's research team (see Appendix A). The group met three times during the course of the project, advising on method and key issues for investigation, reviewing draft documents, and participating in discussion of research findings and recommendations.

1.2. Literature review

A comprehensive literature review was conducted and comprises chapter two of this report. The review summarises the clinical treatment guidelines for methadone and buprenorphine and discusses the evidence regarding treatment outcomes associated with different methadone doses.

Searches were conducted using PubMed and the World Wide Web generally.

1.3. DRUMS data

Drugs Policy and Services Branch, DHS provided DRUMS data on the amount of methadone syrup and buprenorphine tablets supplied to Victoria each year for analysis. Methadone data were available from 1984-2006 and buprenorphine data from 2001-2006.

1.4. Pharmacy data

On a nominated 'census day' (2nd April 2007) de-identified methadone and buprenorphine dispensing records were collected from 17 pharmacies, across Victoria. Pharmacies were selected at random from a list provided by DHS. In order to collect data on at least 600 community dispensed methadone patients (approximately 10% of all Victorian methadone patients and the largest sample of methadone patients in Victoria) only pharmacies that dispense to at least 20 patients were included in the sample.

1.5. Key informant interviews

1.5.1 Prescribers

Twelve of Victoria's largest methadone prescribers (i.e. doctors who each prescribe to at least 50 clients) were selected at random and invited to participate in an individual face-to-face interview. Nine prescribers completed a semi-structure interview (see Appendix B for participating prescribers

and Appendix C for interview schedule), which took an average of 25 minutes to complete. Prescribers were paid $75[1] as reimbursement for their time participating in the project.

1.5.2 Clients

Eighty current methadone clients responded to an advertisement placed at pharmacies participating in the 'census'. From this group, 30 clients (aged over 18 years) participated in either a face-to-face or telephone, semi-structured interview (see Appendix D for interview schedule). Though the sample was not intended to be 'representative', clients were selected to cover a range of ages and locations. Furthermore, and as it was an aim of this project to identify barriers to optimal dosing, preference was given to those clients on methadone doses less than 60mg/day.

Interviews took an average time of 20 minutes to complete and clients were paid $30 in appreciation of their time.

1.6. Analysis

Quantitative data were analysed using Excel and SPSS. Qualitative data (notes from interviews) were analysed thematically using Nvivo 7.

1.7. Ethics

This project was approved by the Victorian Department of Human Services, Human Research Ethics Committee (DHS HREC).

[1] This rate is consistent with private general practitioner salary rates and an estimated interview time of one hour.

2. LITERATURE REVIEW

2.1. Introduction

Opioid substitution treatment (OST) remains a mainstay of Australian responses to heroin dependence. Methadone maintenance treatment for the management of opioid dependence was introduced in the 1960's in the USA, and in the early 1970's in Australia. Buprenorphine has been registered in Australia for this purpose since 2002, with significant uptake in Victoria, accounting for approximately 40% of OST places.

OST remains a controversial treatment approach amongst the alcohol and drug treatment sector, drug user and community groups – largely as it is often seen as merely 'swapping one drug for another', and that patients remain 'addicted' to a drug without addressing the 'real issues'. As a consequence, there has been extensive research examining the safety and efficacy of OST – more so than other treatment approaches for drug addiction, and as such, the components of effective OST have been well documented (Faggiano, Vigna-Taglianti, Versino, & Lemma, 2003; Mattick, Ali, & Lintzeris, Unpublished; Ward, Mattick, & Hall, 1998).These include:

- long term treatment approach, with an emphasis upon maintenance rather than detoxification (Ball & Ross, 1991; Kakko, Svanborg, Kreek, & Heilig, 2003; Sees et al., 2000)
- use of effective doses (Faggiano et al., 2003)
- access to psychosocial services, especially for those with co-morbid affective disorders (Faggiano et al., 2003)
- quality of the therapeutic relationships between service users and providers (Ward et al., 1998) for review)
- staff orientation and degree of structure within treatment programs (Ball & Ross, 1991; Ward et al., 1998) for review)

There has been considerably less research examining the *effectiveness* of OST programs – that is, the outcomes associated with actual treatment services, rather than services delivered under rarefied clinical trial conditions. This is particularly relevant given that the vast majority of research of OST has been conducted in specialist treatment settings (usually large multidisciplinary clinics providing a range of medical, psychosocial and dispensing services). In Australia however, and particularly in Victoria, OST has increasingly been delivered in community settings by general practitioners and pharmacies. The extent to which OST is delivered under optimised conditions is unclear (the last comprehensive review of community based methadone treatment in Victoria was conducted in 1995-96 (Lintzeris et al., 1996).

There are several areas of concern regarding the delivery of OST in Australia. Recent NSW data (Bell, Burrell, Indig, & Gilmour, 2006) identified that the median duration of treatment episodes is approximately 6 months – considerably lower than the recommendation that OST be long term treatment, with better outcomes associated with treatment of greater than 12 month duration (see (Ward et al., 1998) for review). Another area of concern has been the availability of psychosocial services for OST clients in community based programs (Lintzeris et al., 1996). Whilst new Medicare

items potentially enhance access to mental health services (e.g. registered clinical psychologists or social workers) in general practice settings, it remains to be seen the extent to which this addresses OST patient needs.

Another area of concern is the doses of methadone or BPN used in OST programs. There is no way at present of accurately identifying the mean dose of methadone or BPN treatment used in Victorian OST programs, however a number of previous studies conducted in Victorian OST programs suggests that mean doses of methadone are significantly lower than identified in the evidence base and recommended by national or state guidelines. This project aims to examine the methadone and buprenorphine doses used in Victorian OST programs, to explore reasons for doses used, and to identify strategies to optimise OST doses.

2.2. Evidence and Clinical Guidelines regarding methadone and BPN doses for OST

2.2.1 Evidence regarding treatment outcomes for methadone doses.

The evidence regarding the outcomes associated with different methadone doses has been systematically reviewed in a recent Cochrane Review (Faggiano et al., 2003). The review identified 21 studies - 11 Randomised Controlled Trials (RCT) (2279 participants), and 10 Controlled Prospective Studies (CPS) (3715 participants). The review categorised methadone doses as low (1-39mg), medium (40-59mg), high (60-109mg), and very high (110+mg). The main findings are tabulated below, and indicate that high dose methadone is associated with better treatment retention, less heroin use and less cocaine use than low dose methadone. There is less evidence (fewer studies) comparing very high or medium doses, however in general, there is a trend for higher doses to be associated with better outcomes than lower doses across these outcomes. There is insufficient evidence regarding other outcomes (e.g. side effects, criminal activity, mortality).

Table 1: Key findings from Cochrane Review of methadone dose

Outcome	Findings
Retention rate	**Very high doses** not more effective than **high doses** but more effective than **medium dose** RR=1.67 [1.05, 2.26]. **High dose** more effective than **low dose** at short (<27 week) RR = 1.36 [1.13, 1.63] and longer term RR = 1.62 [0.95, 2.77] follow-up. **High dose** more effective than **medium dose** in longer term follow up (27+ weeks) RR=1.23 [1.05, 1.45], but not at shorter follow-up. **Medium dose** compared to **low dose**: inconclusive
Heroin use	**High dose** had significantly more periods of abstinence (3 weeks or more) than **low dose** RR=1.59 [1.16, 2.18]; **High dose** had trend for more periods of abstinence than **medium dose** RR=1.51 [0.63-3.61] **High dose** self-report less heroin use than **low dose** (by mean of 2.0 times / week) and **medium dose** (by mean of 1.89 times / week).
Cocaine use	**High dose** had significantly more periods of abstinence (3 continuous weeks or more) than **low dose** RR=1.81 [1.15, 2.85]

Laboratory evidence

The principles of opioid substitution treatment require that the opioid medication effectively minimises opiate withdrawal symptoms over the dosing interval, reduces cravings for illicit opioid use, and reduces the euphoric (reinforcing) effects of additional illicit opioid use.

Whilst two RCTs (Kosten, Schottenfeld, Ziedonis, & Falcioni, 1993; Preston, Umbricht, & Epstein, 2000) have reported that higher methadone doses were more effective in reducing opiate withdrawal symptoms than lower doses, neither study reported statistically significant findings – which may be due to methodological difficulties in such outpatient research where additional illicit heroin use (e.g. in lower dose groups) will impact upon the report of opiate withdrawal.

A number of laboratory studies have examined the extent to which different methadone doses reduce the subjective effects of additional opioid use. (Donny, Walsh, Bigelow, Eissenberg, & Stitzer, 2002) utilised an inpatient, double-blinded randomised within-subject design comparing the extent to which different methadone doses (30, 60, 120mg) impacted upon withdrawal symptoms and attenuated the agonist effects of 0,10 and 20mg intravenous heroin. 120mg methadone completely suppressed withdrawal symptoms and blocked the effects of heroin. Thirty and 60mg methadone were effective in suppressing opiate withdrawal, but did not completely block the effects of heroin.

A more recent study (Donny, Brasser, Bigelow, Stitzer, & Walsh, 2005) utilised a similar randomised inpatient double dummy within subject design, however examined the effects of 50, 100 and 150mg oral methadone upon intravenous heroin challenges (0, 10, 20mg). The authors reported similar findings - 100 and 150mg completely suppressed opiate withdrawal and blocked the effects of heroin, whereas 50mg methadone did not completely produce blockade effects.

Correlation between methadone dose, plasma levels and pharmacodynamic properties

A confounding factor in determining methadone dosages is the considerable individual variation in pharmacokinetic and pharmacodynamic effects of methadone. The bioavailaibility of oral methadone shows considerable individual variation, ranging from 40 to 100% (Dale, Hoffer, Sheffels, & Kharasch, 2002; Gourlay, Cherry, & Cousins, 1986; Nilsson, Meresaar, & Anggard, 1982). Methadone is largely metabolised by the hepatic CYP3A4 and 2D4 enzyme systems, which themselves are sensitive to a variety of hepatic morbidities (e.g. alcohol or HCV related hepatitis) and drug interactions. Furthermore, there appears to be genetic variation in the enzymes responsible for metabolising methadone – such that a proportion of individuals (estimated at between 10 to 30%) are considered 'rapid' metabolisers, who complain of opiate withdrawal and impaired mood states prior to dosing and cannot easily be maintained on once-a-day methadone dosing (Dyer & White, 1997; Dyer et al., 2001). This area is further complicated by the recent recognition of the different properties, side effects and metabolic pathways of the racemic isomers (R and S) of methadone (Mitchell, Dyer, Newcombe, Somogyi, & White, 2006).

There have been several attempts to examine the plasma concentrations of methadone in patients using heroin compared to those not-using heroin in treatment (Bell, Bowron, Lewis, & Batey, 1990; Tennant, 1987; Torrens et al., 1998). To date, these studies have found no relationship between plasma levels and heroin use, leading one author to conclude: "Therapeutic drug monitoring during methadone maintenance seems to be useful for assessing compliance with treatment but not for predicting heroin use and subjective withdrawal symptoms" (Torrens et al., 1998), p. 193).

In summary, it is not possible to identify therapeutic methadone plasma levels or dose ranges that will be effective for all patients. Rather, most commentators agree the need for individualisation of methadone doses according to clinical factors "There is no way of prescribing a single best methadone dose to achieve a specific blood level as a "gold standard" for all patients" (Leavitt, Shinderman, Maxwell, Eap, & Paris, 2000). Some case reports highlight the need for doses as high as 400mg/day; whereas others report significant rehabilitative effects for patients on doses as low as 30mg/day.

2.2.2 Australian Clinical Guidelines and recommendation regarding doses.

Methadone treatment

Since 2004, Victorian clinical guidelines regarding methadone treatment for the management of opioid dependence have referred to the National Methadone Clinical Guidelines (Henry-Edwards et al., 2003), endorsed by the National Drug Strategy Committee. These guidelines have been developed using systematic literature reviews and consensus expert opinion. Prior to this date, Victoria had state specific guidelines[2] describing dosing levels for induction, maintenance and termination of methadone maintenance treatment (Drugs and Poisons Unit, 2000), and made similar recommendations regarding methadone dosing levels. In summary, guidelines for methadone maintenance treatment are as follows:

- Induction and stabilisation. The initial methadone dose should generally be 20-30mg/day, less if the patient has low-level physical dependence, and with a maximum initial dose of 40mg. The dose is subsequently titrated (generally with increases of no more than 10mg per day or 30mg per week) according to clinical response, with regular reviews of clinical parameters including adverse events, continued drug use, cravings, and evidence of withdrawal or intoxication.
- Maintenance. Doses of at least 60 mg/day have been found to be more effective than lower doses in achieving the goals of treatment (such as decreased illicit drug use and treatment retention).
- Termination: recommended weekly dose reductions vary according to daily maintenance dose. Most patients can tolerate reductions as follows: doses over 50 mg/day, 5 mg/week; 30–50 mg, 2.5mg/week and less than 30 mg, 1–2 mg/week. It must be noted however, that methadone treatment is usually long-term and patients should be encouraged to remain in treatment for as long as they experience benefit. Evidence suggests benefits are maximised when the patient remains in treatment for at least 12 months.

Australian guidelines emphasise that doses be individualised for each patient, reflecting the importance of patient autonomy in clinical decision-making, individual variation in pharmacokinetic and pharmacodynamic profile; concomitant medical or psychiatric conditions, and continued levels of illicit opioid use and cravings.

Whilst internationally methadone is also used to assist in detoxification from opioids, this practice has had limited uptake in Australia (and particularly Victoria). In general, doses used for detoxification tend to be lower than maintenance treatment (e.g. maximum doses of between 30-40mg / day).

[2] The guidelines are consistent with national guidelines prepared by the National Methadone Committee and were endorsed by the National Drug Strategy Committee.

Buprenorphine treatment

In 2001, the Commonwealth Department of Health and Aged Care published national guidelines and procedures for the use of buprenorphine for treating heroin dependence (maintenance treatment and detoxification[3]) (Lintzeris et al., 2001). These have recently been updated (Lintzeris et al., 2006), and include the use of buprenorphine-naloxone combination product (Suboxone®) In summary, recommended dosing levels for buprenorphine maintenance treatment are as follows:

- Induction and stabilisation. The first dose of buprenorphine should be between 4 and 8 mg, with a target total day 1 dose of 8mg. The initial dose should be delayed until the patient is experiencing features of opiate withdrawal – typically at least 6-8 hours after last heroin use, 24-36 hours after low dose methadone (e.g. <40mg), and 36-72 hours after methadone doses of between 40-60mg. Transfers from higher doses are not recommended in community based programs. Thereafter, doses of BPN should be rapidly titrated upwards, reaching the target dose by day 2 or 3 of treatment.
- Maintenance. Doses ranging from 12-24mg/day are recommended, reflecting research that such doses are more effective in reducing heroin use and improving retention in treatment than lower doses.
- Termination. Rates of dose reduction vary with daily maintenance dose and are recommended as follows: doses over 16 mg/day, 4 mg/week or fortnight; 8-16 mg, 2-4 mg/week or fortnight and less than 8 mg, 2 mg/week or fortnight.

BPN is also widely used as a detoxification agent from illicit heroin use and methadone maintenance treatment. In Australia, heroin detoxification programs are generally recommended as short-term programs of one to two weeks duration, with maximum doses of 8 to 16mg per day, reducing by 2 to 4mg per day.

2.3. Estimating doses in OST programs.

At present, there is no mechanism to accurately identify the mean (or variance of) doses of methadone or buprenorphine used in Victorian OST. There have however been several studies of methadone and buprenorphine treatment conducted in Victorian treatment settings that enable some estimates of doses used. Furthermore, it is possible to estimate mean doses used by examining Victorian DHS data on number of OST clients registered annually and DRUMS data on the amount of methadone syrup and buprenorphine tablets supplied to Victoria each year.

2.3.1 Previous Victorian studies

Victorian research of community opioid substitution treatment programs provides some insights regarding actual methadone and buprenorphine dosing practices. These studies are summarised in Table 2.

[3] See guidelines (Lintzeris et al., 2001) for recommended doses for buprenorphine for the management of heroin detoxification.

Table 2: Summary of research of Victorian OST programs

Follow-up	CME (1995-96)	LIT (1999-2001)		BIT (1999-2001)		MWRP (2001)	ATOS (2004)
		INDUCTION	MAINTENANCE	INDUCTION	MAINTENANCE		
-	41.0 (Range=7-140)[4]		64.0[5]			46.6[6] (SD=24.2)	
3 mth		47 (SD=17.8)	65.5 (SD=34.8)	46.2 (SD=18.5)	37.8 (SD=13.1)		
6 mth		51.3 (SD=25.5)	65.3 (SD=36.2)	49.4 (SD=22)	51.2 (SD=17.6)		
12 mth		53.6 (SD=26.1)	64.6 (SD=38.5)				28.0 (SD=12)

Methadone

Although state and national guidelines describe doses of 60 mg/day and over as being most effective for reducing heroin use and retaining patients in treatment, research frequently reports doses below this level.

In 1993, the Victorian Drug Strategy Unit published data regarding the Victorian Methadone Program, including data on methadone dose. In the early 1990's, approximately 1500 (1991) to 2200 (1993) clients were registered with permits for methadone treatment. Dose data was extrapolated from permit applications and termination made by prescribing doctors. The mean methadone dose when doctors re-applied for a permit for an existing patient was 41.4mg. An alternative strategy for estimating mean dose was for the question 'highest dose prescribed' on the termination of permit forms – indicating a mean of 41.1 mg. Interestingly, doctors had to nominate a proposed maximum dose on permit applications. The proposed maximum was 66.3mg, well above the actual doses prescribed. It must be emphasised that this data may not accurately reflect clinical practice, as the data is reliant on doctors accurately reporting doses and fastidiously completing re-application and termination of permit forms.

The first large examination of community-based programs in Victoria was the Community Methadone Evaluation conducted in 1995-96 (Ezard et al., 1999; Lintzeris et al., 1996). This study involved postal surveys of Victorian community based methadone prescribers (with a 69% response rate) and pharmacists involved in OST (response rate 77%), and face-to-face interviews with 195 methadone clients in community based programs. Lintzeris et al. (Lintzeris et al., 1996) reported an average methadone dose of 41mg/day (range: 7-140mg/day, mode=30mg). 16% of clients were on doses of 20mg or less. Ten percent of these clients however, had only recently commenced methadone and so may have been on smaller doses that lowered the overall average.

Clients were asked about dose adequacy (whether they thought their current methadone dose was 'just right', 'too low', or 'too high'), and the results are shown in Table 3 below. Approximately 75 percent of the sample indicated that their methadone dose was 'just right', and approximately 13 percent indicated it was 'too low'. Interestingly, the highest level of satisfaction by clients was at lower doses (<40mg: 85% 'just right') compared to higher doses (>60mg) (60% 'just right').

[4] Average time in current treatment = 26.5 months
[5] Average time in current treatment = 26 and 23.4 months for the control and experimental groups respectively.
[6] Average time in current treatment = 16.1 months

Table 3: Current methadone dose and client perception of dose

Current Dose	No.	%	% of clients who thought their dose was		
			Too low	Just right	Too high
0 - 40 mg	102	52	4	85	4
41 - 60 mg	51	26	15	75	6
>60mg	30	15	20	60	20
Don't know	12	6	n/a	n/a	n/a

Source: CME (Lintzeris et al., 1996)

The Victorian CME also reported client self-reported heroin, benzodiazepine, cannabis, and alcohol use in preceding month by methadone dose, shown in the figure below. The findings are consistent with the systematic review of methadone dose noted previously.

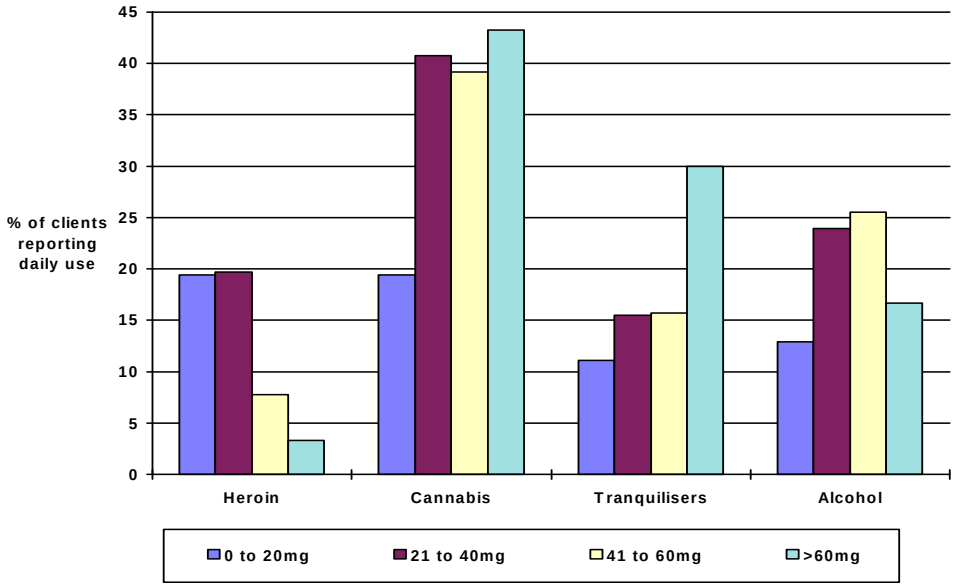

Figure 1: Proportion of clients reporting daily heroin, cannabis, tranquilliser or alcohol use by dose

In 1998, Turning point conducted surveys of clients and pharmacies involved in community methadone treatment as part of Stage 1 of the Methadone Withdrawal Research Project (Lenne et al., 2001). Pharmacists provided methadone dose data on 131 methadone clients. The clients sampled had been in their current methadone treatment episode for 16.1 (± 22.7) months. The mean current methadone dose was 46.6 (±24.2) mg. Clients had spent an average of 2.8 (± 4.9) months on their current methadone dose. 40% of clients had remained on a stable dose during the past 3 months, 35% were reducing their dose in the past 3 months, and 25% had increased their dose in the past 3 months. The highest and lowest average doses within the last three months were 51.1 (±22.5) and 41.6 (±22.4) respectively.

The next significant research conducted in Victorian OST settings was in 1999-2001, as part of the Buprenorphine Implementation Trial (BIT) (Lintzeris et al., 2004; Ritter et al., 2001b), and LAAM Implementation Trial (LIT) (Ritter et al., 2003). These trials together included approximately 25 prescribers, 30 pharmacies and 300 clients – with the majority in community settings. The trials utilised randomised designs, comparing BPN to methadone (BIT), and LAAM to methadone (LIT), recruiting both heroin users entering treatment, and methadone clients wishing to transfer.

In the BIT study, for the heroin users randomised to methadone maintenance treatment (n=36), average daily methadone doses of 46.2 mg (SD=18.5) and 49.4 mg (SD=22) were reported at three and six month follow-ups. For the patients (n=30) who entered the BIT study as methadone patients[7], and were randomised to stay in methadone treatment, the mean daily methadone doses of 37.8 mg (SD=13.1) and 51.2 mg (SD=17.6) were observed at 3 and 6 months respectively. It must however be noted that as this was a trial of buprenorphine, only methadone maintenance clients who were able to reduce to 60 mg/day or less[8] of methadone were eligible. Thus, these dose levels may be lower than in the general population of methadone clients on a maintenance regime.

Ritter et al., reported somewhat higher daily methadone doses among maintenance clients in the LIT study (2001a). Methadone patients (n=101) recruited into this study had an average daily dose of 64 mg at recruitment and had been undergoing methadone treatment for approximately two years[9]. Average daily methadone doses at three, six and 12 months were 65.5 mg (SD=34.8), 65.3 mg (SD=36.2) and 64.6 mg (SD=38.5) respectively. These doses were associated with (imputed) abstinence rates of 36.7%, 30.6% and 30.6%. The same study recruited a second group of patients (n=78) who were newly entering treatment for heroin dependence. Among those who were prescribed methadone only (control group) average daily doses at three, six and 12 months were 47.0 mg (SD=17.8), 51.3 mg (SD=25.5) and 53.6 mg (SD=26.1) respectively. These doses were associated with (imputed) abstinence rates of 22.8%, 14.3% and 17.1%.

Very low dosing practices were reported in the Victorian arm of the Australian Treatment Outcome Study (ATOS), however there were few methadone patients enrolled (n=8). The average daily dose on a maintenance regime at 12-month follow-up was 28mg (SD=12) (Holt et al., 2004). The small numbers prohibit the generalisability of this sample.

Other samples of Victorian methadone clients have been reported in other studies – largely the Illicit Drug Reporting System surveys. However, as these epidemiological studies have targeted active illicit drug users, there is a good possibility that they are biased towards individuals on low methadone doses (given the previous findings regarding methadone dose and continued illicit drug use); and consequently are not included in this review.

Thus, in the previous studies reporting methadone doses in Victorian clients, the mean methadone dose has been lower than 60mg in all but one study (see Figure 2).

[7] In treatment for at least eight weeks.
[8] 60 mg is the maximum daily methadone dose from which transfer to buprenorphine is recommended (see summary of guidelines above).
[9] Average duration of methadone treatment for this episode was 112.8 weeks for the control group and 102.6 weeks for the experimental group.

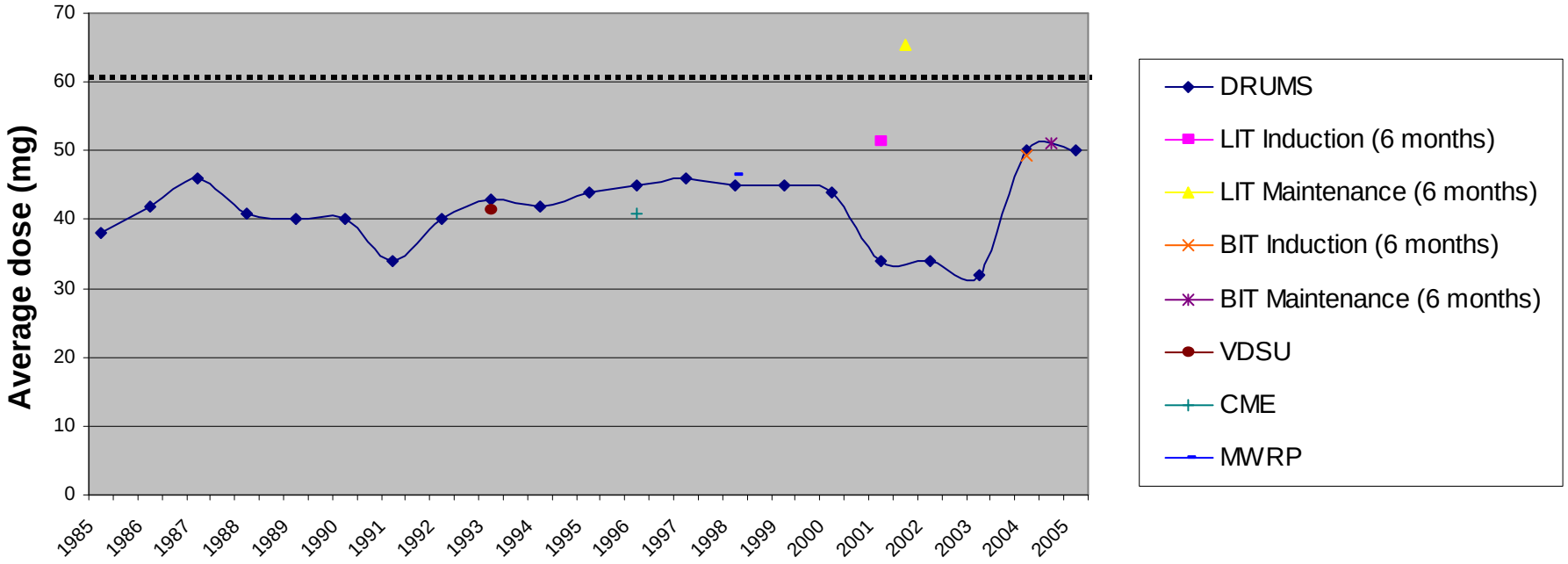

Figure 2: Mean daily methadone dose, reported studies 1985 - 2006 against 60mg recommended dose

Buprenorphine

Lintzeris et al. (Lintzeris et al., 2004) reported general adherence to buprenorphine guidelines among prescribing doctors in the buprenorphine implementation trial. For patients transferring from methadone to buprenorphine, equivalent daily buprenorphine doses were 15.9 mg (SD=12.7) and 15.7 mg (SD=14.7) at three and six month follow-ups. For heroin users entering treatment, equivalent daily buprenorphine doses were 13.1 mg (SD=5.8) and 13.2 mg (SD=5.6) at three and six month follow-ups. Thus, doctors largely observed recommended daily maintenance doses of between 12 and 24 mg/day.

The ATOS 12-month follow up reported an average daily buprenorphine dose for maintenance clients of 10mg (SD=8), with an average highest dose of 13mg (SD=7) and average lowest dose of 4mg (SD=3) (Holt et al., 2004). However, there were only 18 BPN clients involved, limiting the extent to which findings are generalised.

2.3.2 Population data estimates of methadone and buprenorphine doses - DRUMS

A potentially innovative approach to determining mean methadone and BPN dose is the use of DHS data regarding number of registered OST patients and total amounts of methadone and buprenorphine utilised annually through DRUMS data.

In Victoria, medical practitioners and pharmacies must be authorised and registered with the Drugs and Poisons Unit of the DHS in order to prescribe and dispense methadone or buprenorphine for opioid substitution treatment. Authorised doctors apply for a permit to prescribe methadone or buprenorphine for each individual patient. However, the number of active permits is not a true reflection of the number of active patients as doctors do not always terminate permits when patients cease treatment. Consequently, the number of active permits is probably an overestimate of the number of patients in these forms of treatment. Furthermore, the permit system does not differentiate between patients in methadone or buprenorphine treatment.

Consequently, the DPU conducts a census of all Victorian pharmacies authorised to dispense methadone (syrup) or buprenorphine (sublingual tablets) for OST. This is conducted by telephone by officers from the DPU at quarterly intervals, in order to ascertain the total number of patients dispensed methadone syrup or buprenorphine sublingual tablets for OST. This provides a more accurate estimate of the number of OST patients in Victoria.

Linked to this is the amount of methadone syrup and sublingual BPN tablets supplied to Victoria each year using the DRUMS data system. In accordance with international treaties, data regarding the amount of opioid medication used by each state is recorded by the Treaties and Compliance Section of the Office of Chemical Safety, Federal Department of Health and Ageing.

This data is available dating back to 1985. It is possible therefore to estimate the mean dose as follows:

$$\textbf{Mean methadone dose (mg)} = \frac{\textbf{total annual methadone dose (kg) / 365 days}}{\textbf{number of methadone patients (N)}}$$

This model makes certain assumptions. These include:

1. The number of patients in methadone treatment remains stable over the course of the year, and is reflected at the census dates
2. Methadone patients remain in treatment over the course of the year (i.e. a stable treatment population) – with limited 'gaps' in treatment over the year
3. The methadone dose for patients remains relatively stable over the course of the year. This assumes that there is limited duration of induction or termination (when methadone doses are lower than at maintenance levels)
4. There is little 'off-label' use of methadone preparations – specifically little use of methadone tablets for OST, and limited use of methadone syrup for management of chronic pain

This model therefore assumes a relatively stable treatment population, and with limited use of methadone or BPN for detoxification purposes (short term use, and where doses used are typically lower than for maintenance). It is unclear the extent to which these assumptions hold.

Figure 3 shows the mean methadone (and BPN) doses calculated using this model over the past 15 years. During the last two years, average daily doses of Victorian clients have been estimated at approximately 50mg, although average doses have been as low as 32mg at other times (e.g. 1991, 2001, 2002).

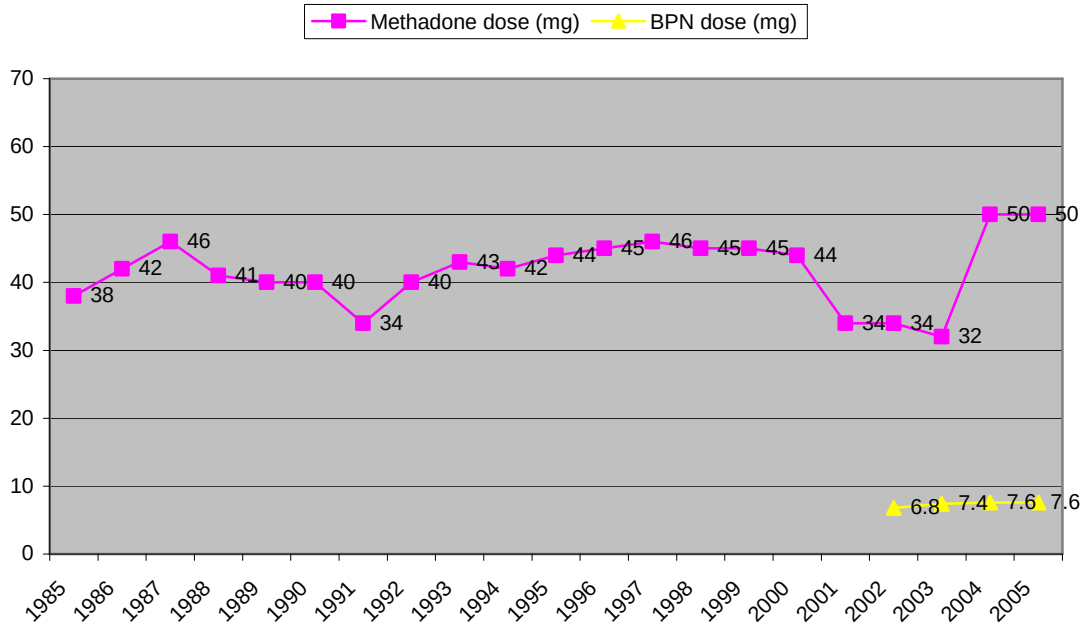

Figure 3: DRUMS daily dose estimates, Victoria: Methadone and Buprenorphine

Average daily dose of buprenorphine products (Subutex® and Suboxone®) is calculated by the same method. Data on these products is available from 2003 when total annual data is available (BPN was licensed and available on the PBS in mid 2002). As shown in Figure 3, average daily dose for BPN has been estimated at ranging from 6.8mg (2002) to 7.6mg (2005).

Figure 4 shows this data with superimposed data from the studies reported in section 2.3.1. It is apparent that this system of estimating methadone doses provides mean doses that are comparable with all the doses identified in previous studies.

In contrast, the limited data regarding buprenorphine (given the few research studies) suggest that the DRUMS method may under-estimate buprenorphine doses (see Figure 5).

However, given that the Victorian research studies have been relatively small numbers in clinical trials or surveys, it may be that these studies are not representative of broader methadone or buprenorphine patients.

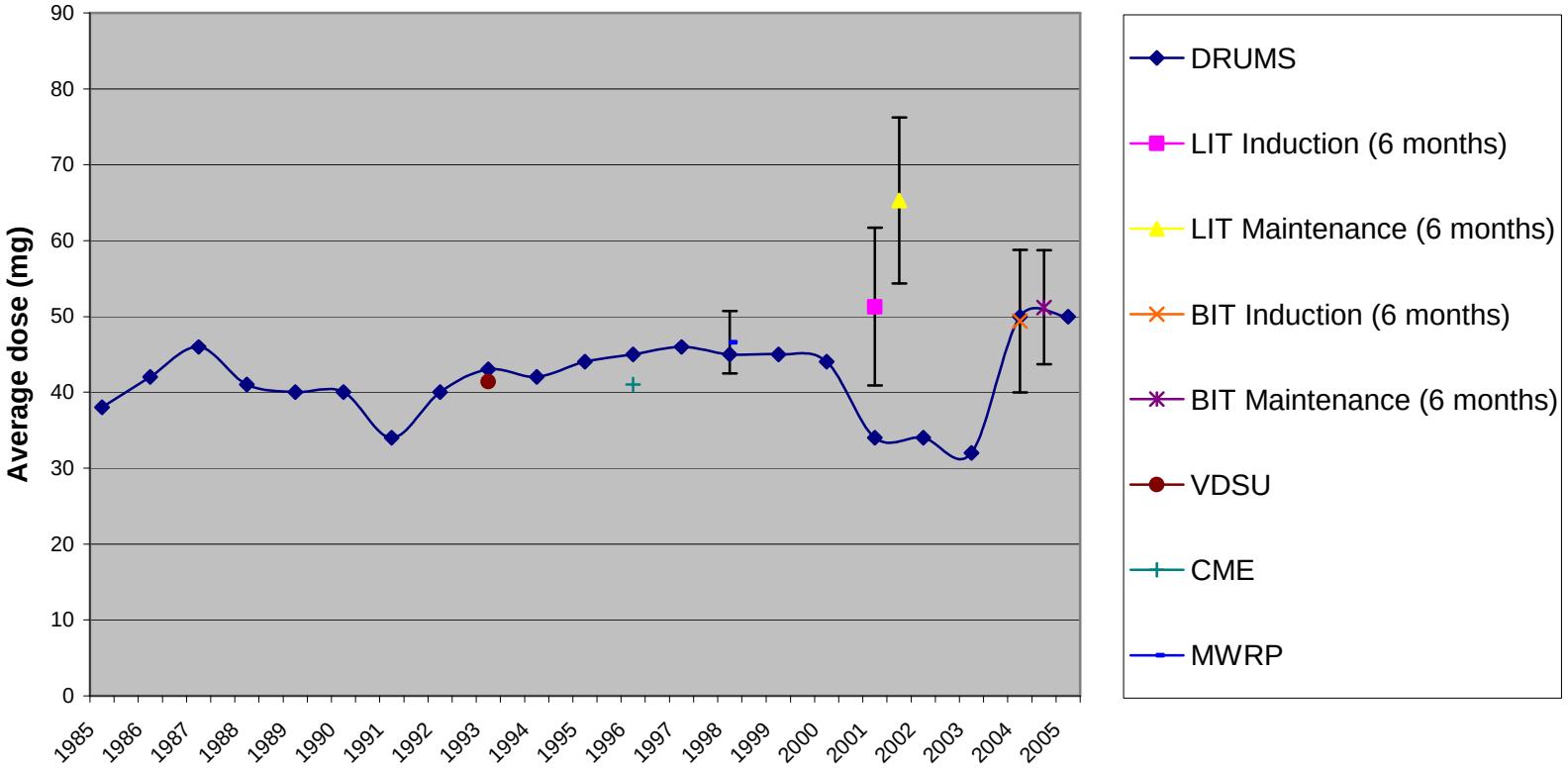

Figure 4:Daily methadone dose estimates of reported studies and DRUMS data, Victoria

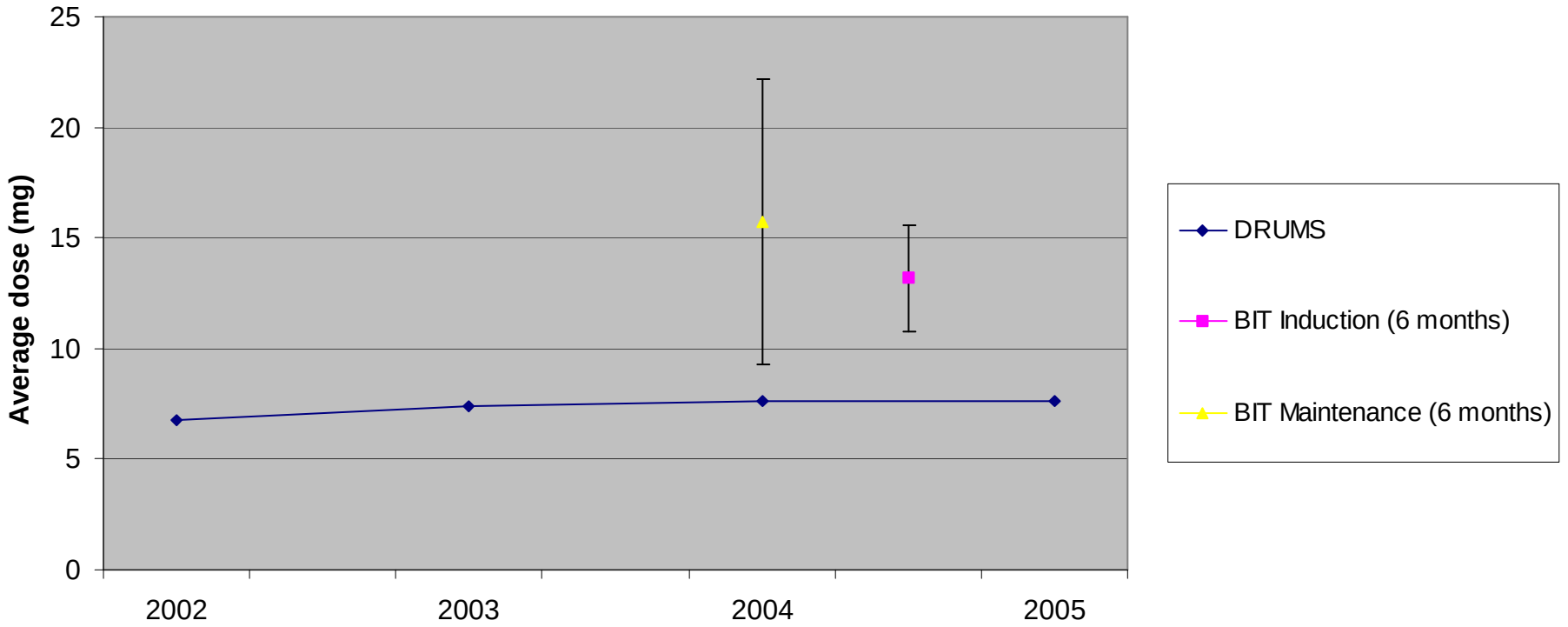

Figure 5: Daily buprenorphine dose estimates of reported studies and DRUMS data, Victoria

2.3.3 International data regarding methadone doses

Whilst the benefits associated with high dose methadone treatment are well established, a similar tendency towards Victorian low doses has been reported in a number of programs internationally.

In the UK, there have been a number of attempts at estimating. Perhaps the best estimates of methadone doses used in MMT come from the GP and pharmacy surveys from 1995 to 2005. These have been recently compiled (Strang et al., 2007). This project has involved postal mail outs to random sample of 25% of pharmacies across England and Wales using self-completion postal questionnaires regarding prescription data on opiate misusers treated during the preceding 4 weeks. Response rates have been between 75 and 95%. Over this decade, the mean methadone dose rose from 47.3 mg to 56.3 mg, which was also accompanied by increases in the proportion of patients having any supervised dispensing (from 0 to 36%), or daily dispensing (38% to 60%). Despite the increased mean daily dose, only 41.0% of prescriptions for methadone in 2005 were for daily doses in the recommended 60-120 mg dose range.

Interestingly, the same research group (Strang et al., 2005) surveyed 10% of all GPs in England and Wales in 2001, with a 66% response rate. Opiate misusers had been seen by 51% of GPs (mean of 4.1 such patients), for whom 50% had been prescribed an opioid substitution drug (oral methadone in 87% of cases). Of 1292 methadone prescriptions, the mean daily dose was 36.9 mg (SD=21.2, range 1 – 305mg, inter-quartile range 23-50mg). 48% were on 30 mg or less, and 71% on 40mg or less. Daily interval dispensing was stipulated by 45%, while 43% permitted weekly take-away supply. This data suggests that general practitioners may prescribe lower methadone doses than clinic programs, given that the mean methadone dose by GPs in 2001 (37mg) was considerably lower than nationwide methadone doses in 1995 (47mg) or 2005 (56mg).

Similar concerns have been raised in Italian programs (Schifano et al., 2006). A review of 8,378 patient treatment episodes in Rome indicated that of those receiving methadone maintenance, 50% of patients were on low doses (≤40mg), 31% medium (41-60mg) and only 19% above 60mg.

In the USA, Magura and colleagues reported on 1000 patients newly admitted to New York City methadone clinics. The mean dose at 3 months was 52mg (SD=20).

It is clear that despite available evidence, there is a common problem of methadone doses being prescribed that are consistently below doses of at least 60mg identified in the outcome literature as increasing treatment efficacy.

2.3.4 Data from other Australian states.

Victoria is unique in Australia and internationally in its emphasis (>98% of treatment places) upon private primary care services delivering non-custodial opioid pharmacotherapy treatment. In other Australian states, there is a much greater role for publicly-funded specialist clinics, and it may be that the low methadone and buprenorphine doses are a function of the model of service delivery.

NSW is the other state providing a large number of OST places. It differs in its model of service delivery from Victoria in that it has a significant public and private clinic model of treatment. Estimates suggest approximately one third of patients are treated in public clinics, a third in private and a third by

general practitioners. Two recent estimates of methadone maintenance doses in NSW OST suggest mean methadone doses in the range of 70 to 80mg.

In 2001, the NSW Health Department examined methadone take-away practices in the state (Hailstone, Indig, Lawrence, & Gill, 2004). A census of all dispensing pharmacies in May 2001 (12,943 patients) revealed a mean methadone dose of 73.0 mg. Thirty per cent of patients received no take away doses (mean dose 64.7mg), 5% received one take away dose per week (mean dose = 64.9mg), 13% received two take aways per week (mean dose = 66.3%), and 52% received 3 or more take-aways per week (mean dose = 74.2mg). Of those patients receiving any take aways, the mean dose was higher in private clinic (74.6mg) than public clinic (67.7mg) patients.

Broadly similar findings have recently been identified in a soon to be published paper examining methadone substitution patients across a range of public clinics in Sydney (Winstock, Lea, Madden, & Bath, 2007 in press). In surveying approximately 792 methadone patients (clinic and community pharmacy dispensed), the mean daily methadone dose was reported at 78.6mg for clinic clients, and 82.5mg for pharmacy clients, with 84% satisfaction by clients of dose adequacy. In surveying 164 buprenorphine clients (clinic and pharmacy), the mean daily dose was 12.0mg, with 90% satisfaction amongst clients regarding their dose.

These doses indicate that much higher methadone doses are achieved in NSW methadone treatment programs than in Victoria.

2.4. Understanding 'sub-optimal' dosing

There are a number of potential explanations for the low methadone doses routinely used in clinical practice. These have been variously posited by researchers and clinicians, however there has been little research directly examining this issue. Possible explanations include:

a) *Lack of clarity regarding the goals of long-term versus short-term methadone treatment*. There is a long standing debate as to the role of methadone treatment and indeed whether addiction is seen as an acute problem that requires only a short-term period (weeks to months) of medicated (e.g. methadone) treatment, or whether it is a chronic condition requiring long-term (years) 'medical' treatment. Whilst the original model of methadone treatment as proposed by Dole and Nyswander (1965) favoured the latter approach, by the 1980's, the predominant attitude was towards time-limited methadone treatment and that doses should be kept as low as possible, favouring a detoxification rather than a maintenance model. Whilst official Australian policy towards methadone treatment since the 1990's has emphasised the importance of the maintenance approach, patients and service providers may still hold ambivalence toward long-term treatment. Indeed recent findings from ATOS (Holt et al., 2004) and NSW (Bell et al., 2006) indicate that there is a high turnover of patients in OST, with many patients drifting in and out of short-term programs, rather than 'sticking' at continuous treatment episodes. Hence some authors have suggested (e.g. (Blaney & Craig, 1999) that some patients may enter methadone treatment with the goal of ceasing treatment within months and may therefore wish to remain on low doses of methadone in order to avoid difficult withdrawal symptoms from high dose methadone. Indeed, an examination of Australian methadone maintenance patient attitudes towards withdrawal found that

most patients (70%) were very interested in withdrawal from methadone treatment, despite the likely poor prognosis of such a course of action (Lenne et al., 2001). A comparable proportion of methadone patients in a New York City clinic (nearly 80%), identified that discontinuing methadone is an important goal (Stancliff, Myers, Steiner, & Drucker, 2002). Similar beliefs, that lower doses of methadone are associated with less 'dependence' and is better able "eventually engender opioid abstinence" may be held by clinicians working in the field (Leavitt et al., 2000), especially amongst generalist clinicians with limited training or experience in treating drug dependence, or in those without exposure to the principles of evidence-based clinical practice. Thus, low doses may be prescribed "more for philosophical, moral, or psychological reasons than for sound pharmacological and clinical ones" (Leavitt et al., 2000).

b) *Lack of clarity regarding the objectives of methadone treatment and changes in drug use*. The stated primary aim of methadone treatment in Australia is to "reduce or eliminate illicit heroin and other drug use by those in treatment" (Henry-Edwards et al., 2003), a goal that is probably supported by a majority of clinicians and clients associated with methadone treatment. However, not all patients entering methadone treatment may identify the cessation of all heroin use as a primary goal – and indeed may wish to continue to use heroin on a (ir)regular basis. As indicated by previous laboratory research (Donny et al., 2005; Donny et al., 2002), higher methadone doses (greater than 60mg) were more effective than lower doses (30 or 50mg) in suppressing the effects of additional heroin use. Thus for those patients who wish to continue their use of heroin, low methadone doses may be effective in achieving this aim.

c) For some prescribing doctors, their own *clinical experience of positive outcomes for some patients on lower doses*, guides them to reject research-based guidelines (Trafton, Minkel, & Humphreys, 2006). Again, this may be more likely to be a feature of clinicians with limited experience in treating dependence, or in those without exposure to the principles of evidence-based clinical practice.

d) *Desire to minimise side effects*. Whilst the systematic Cochrane review (Faggiano et al., 2003) was not able to identify any clear relationship between methadone dose and side effects, dose related side effects with all opioids have been identified and are well-recognised clinically. Many patients and their treating doctors may believe that low doses of methadone will be able to minimise the experience of certain side effects that may be problematic for individual patients (e.g. persistent nausea, constipation, sexual dysfunction, sweating, sleep disturbances). For other patients, a general anxiety about long-term methadone consumption may lead them to choose lower doses. For example, 80% of over 300 methadone patients in a survey of a New York City clinic were "certain or unsure" that methadone is bad for one's health (Stancliff et al., 2002).

These potential factors as to the use of low doses have been posited by various researchers and clinicians, however there has been very little systematic research examining these issues directly. The role of other factors, such as the logistics of treatment participation (e.g. cost, daily attendance, take away access), has not been examined.

Ultimately, the question as to whether methadone doses are 'suboptimal' can only be addressed through an evaluation of clinical outcomes:

> "The issue seems not whether the dose is low, medium or high, but rather what is the appropriate dose for the individual patient" (Blaney & Craig, 1999).

The available data from previous Victorian research, population estimates using DHS and DRUMS data, suggests that methadone doses are commonly prescribed in Victorian methadone program that are substantially lower than the research evidence regarding optimal dosing. This is an international trend, with similar observations in European and American programs. Various authors have suggested reasons for low doses, however, there has been little systematic research of this issue.

The aim of this research was to:

v. Estimate the proportion of Victorian methadone clients being prescribed less than 60 mg per day;

vi. Examine the validity of DRUMS data dose estimates by comparison of DRUMS estimates with community methadone dose estimates;

vii. Identify key factors influencing daily methadone dose in Victoria;

viii. Identify barriers to optimal methadone dosing in Victoria;

ix. Explore the relationship between daily methadone dose and continued illicit opioid use while in treatment.

By testing whether the DRUM estimated average dose of 50 mg/day actually corresponds to a significant number of treated patients, by investigating reasons for doses lower than 60 mg per day and by determining the extent to which such doses are associated with a need or desire to continue illicit opioid use while in treatment, an informed decision about the need for prescriber and/or client education programs can be made. If more clients can be moved safely to a dose that minimises illicit opioid use while in treatment, a further reduction in harm can be achieved above that already delivered through maintenance treatment.

3. RESULTS

3.1. Pharmacy data

Seventeen pharmacies sent data regarding methadone and buprenorphine doses dispensed on the census day (2nd April 2007) on a total of 948 OST clients – 585 methadone and 363 buprenorphine clients. This accounts for approximately 8% of all OST clients in treatment across the state. The total and regional breakdown of clients, and the mean ± standard deviation (SD) is shown in Table 4. There are no significant differences between the Health regions regarding mean methadone or buprenorphine doses ($F_{(4,580)}$=1.902, p=0.109 and $F_{(4,358)}$=1.213, p=0.305 respectively).

Table 4: Total and regional methadone and buprenorphine doses, pharmacy data

Region	Number of pharmacies	Number methadone clients	Methadone dose (mean ± SD)	Number buprenorphine clients	Buprenorphine dose (mean ± SD)
Geelong	1	22	52.5 ± 31.4	12	12.9 ± 9.0
Northern Region	3	74	63.3 ± 35.3	40	9.3 ± 8.7
Western Region	3	151	51.4 ± 29	88	10.7 ± 8.3
South Eastern Region	7	255	53.4 ± 31.8	193	12.3 ± 9.5
Eastern Region	3	83	52.4 ± 34.1	30	11.7 ± 7.8
Total	**17**	**585**	**54.0 ± 31.2**	**363**	**11.6 ± 9.0**

The mean methadone dose for the 585 clients was 54.0mg (range = 3 to 220, median = 50, SD = 32.0). Table 5 examines the proportion of patients on different dose ranges, and shows that more than two-thirds of clients are on doses less than 60mg/day, with most on doses between 21 and 60.

Table 5: Number of patients on different methadone dose ranges, pharmacy data

Methadone dose (mg/day)	Number	%	Cumulative %
1-20	70	12.0	12.0
21-40	175	29.9	41.9
41-60	161	27.5	69.4
61-80	90	15.4	84.8
81-100	50	8.5	93.3
101-120	21	3.6	96.9
>120	18	3.1	100.0
TOTAL	585	100.0	

Regarding buprenorphine doses, the mean dose dispensed on census day was 11.6 mg (range 0.4 to 36.0, median = 8.0, SD = 9.0). The range of doses is shown in Table 6. Most buprenorphine clients are on daily doses under 8mg.

Table 6: Number of patients on different buprenorphine dose ranges, pharmacy data

Buprenorphine dose (mg/day)	Number	%	Cumulative %
<2.0 mg	14	3.9	3.9
2.0 – 8.0	175	48.2	52.1
8.1 – 12.0	53	14.6	66.7
12.1- 16.0	38	10.5	77.1
16.1 – 20.0	26	7.2	84.3
20.1 – 24.0	21	5.8	90.1
>24.0	36	9.9	100.0
TOTAL	363	100.0	

Discussion

There are a number of potential sources of bias with this data. It is possible that the pharmacies themselves are not representative of general Victorian pharmacies. However, the pharmacies were randomly selected, and there is no reason to believe any undue bias. The sampling framework also included a mix of pharmacies from across the 4 metropolitan health regions, and one large regional centre (Geelong). Given that there were no significant differences in doses across the various health regions, there is little to suggest a sampling bias on geographical location.

Other potential sources of bias is that a number of patients may have had take-away doses on the census day, and that patients receiving take-away doses may have higher doses than those not getting take-aways (e.g. new to the program, low doses and using heroin and ineligible for take-aways). Indeed, the NSW review of take-away doses (Hailstone 2004) indicated that clients receiving take-aways had a higher methadone dose than those not receiving take-aways. This may lead to an under-representation of the mean methadone or buprenorphine dose from the survey.

Another potential source of bias regarding buprenorphine doses is that a small proportion of patients may have been receiving alternate day dispensing with BPN, and that the dose dispensed may represent double the daily dose[10]. This may lead to an over-representation of the mean BPN dose. However, whilst there is limited recent data, earlier Victorian data indicated that only a minority of BPN patients are sustained on alternate day dispensing (less than a third of patients). This is likely to have diminished further since the advent of Suboxone and take away doses diminishing the role of alternate day dispensing.

For both groups, and especially the buprenorphine group, it is likely that a proportion of patients are not on their stable maintenance dose on census day. This could be due to patients having just commenced treatment, are reducing off maintenance treatment, or are using buprenorphine as a detoxification program and hence using low doses. This will tend to under-estimate the mean dose.

Despite these limitations, it is apparent that the mean buprenorphine dose in this study (11.6mg) approaches the recommended National clinical guidelines of between 12 and 24 mg daily (Lintzeris et

[10] Some pharmacies indicated where a take-away dose was given and a daily dose was calculated accordingly, however this was not consistently done by all participating pharmacies.

al., 2006), and that a significant proportion of patients (47.9%) are on doses of 8mg or more – generally considered to be effective in reducing heroin use and retaining patients in treatment.

In contrast, the mean methadone dose of 54mg falls somewhat short of the recommended 60 to 100mg doses recommended in national clinical guidelines (Henry-Edwards et al., 2004). In particular, only a minority of patients (23.9%) are on recommended doses of 60 to 100mg.

The findings are remarkably similar to recent UK data regarding methadone doses (Strang et al., 2007), where a mean dose of 56.3mg was reported by pharmacies, and only 41% of patients being on doses of the recommended 60-120mg. The doses are lower than reported in other Australian states - most notably NSW, which is the other state with large numbers of OST service providers and clients, where the mean doses reported there appear to be in the range of 70 to 80mg.

DRUMS Data

When comparing the recent pharmacy data – the largest confirmed data source of methadone and buprenorphine doses in Victoria - to the recent estimates of mean methadone and buprenorphine dose using the DRUMS data system (described in section 2.3.2), it is apparent that the DRUMS system is adequate for estimating methadone dose, but inadequate for buprenorphine. The mean methadone dose estimated by DRUMS in 2006 was 50mg – compared to a mean dose of 54mg in this study. When combined with previous estimates of mean methadone doses (see section 2.3.1), it is apparent that with the exception of the LIT study, the DRUMS data estimate of mean methadone dose has always been within 5 mg of other data sources. The low mean methadone doses reported using the DRUMS data for the years 2001-2003 may reflect that this was the time at which buprenorphine was introduced in Victoria, and many methadone patients transferred to buprenorphine over this time, given the very rapid uptake of BPN in Victoria (Lintzeris et al., 2004). This may have led to a number of methadone patients dropping their dose (prior to transfer), and more importantly, that many patients would have interrupted their treatment year – breaking the assumptions of the DRUMS data system (see Literature Review Section 2).

The DRUMS system is less robust for buprenorphine. Whilst there are fewer data points for buprenorphine, findings from the BIT study and this more recent pharmacy survey indicate mean BPN doses of between 10 to 12mg, whereas the DRUMS system estimates the mean dose at under 8mg. There may be a number of reasons for the poor validity of the DRUMS system for BPN. The most likely reason is that BPN is widely used for detoxification purposes – both in structured inpatient settings, and also by patients cycling through multiple outpatient short programs. These episodic short-term programs will result in patients not being in treatment for the entire 12-month duration – breaching the assumptions of the DRUMS system (see Section 2.3.2).

3.2. Key stakeholder data

"The public view is not that methadone is a solution to anything, rather that it's one more thing that junkies do. All this together works towards a very negative stigma of methadone and people resist going up on the dose because of this and are getting worse because of it." (Prescriber)

3.2.1 Key stakeholder demographics

Prescribers

Nine methadone prescribers were interviewed for this study – eight males and one female. All prescribers were aged 40 years or older: three (33.3%) were aged 40-49 years; four (44.4%) were 50-59 years; and two (22.2%) were aged 60 years or above.

Prescribers had been prescribing methadone for an average of 11.2 years (range: 5-25; median=8).

Prescribers were asked how many *current* clients they have on methadone and buprenorphine. On average, prescribers reported 72 methadone and 79 buprenorphine clients (see Table 7). The maximum number of clients reported by a prescriber was 120 and 153 for methadone and buprenorphine, respectively.

Table 7: Client load of participating prescribers

Number of current clients	Mean	Median	Minimum	Maximum
Methadone	71.7	62	20	120
Buprenorphine	78.7	75	10	153

Prescribers were asked to estimate the proportion of their methadone clients on three different types of doses that may be considered unstable (see Table 8). Approximately one third (32.9%) of clients were estimated to be on an unstable dose. The largest group of unstable clients, comprising approximately one fifth (20.8%) of all methadone clients, was those withdrawing off methadone.

Table 8: Proportion of methadone clients estimated to be on unstable dose

Type of methadone dose	Mean %	Median %	Minimum %	Maximum %
Currently withdrawing off methadone	20.8	20.0	10.0	30.0
Recently commenced (yet to reach stable dose)	5.8	5.0	1.0	10.0
Reducing methadone dose in order to transfer to other medication (e.g. buprenorphine)	6.3	2.0	0.0	20.0
TOTAL (unstable dose)	32.9	35.0	13.0	50.0

Prescribers were asked to estimate the proportion of their clients on different sized methadone doses. Participating doctors reported that they had prescribed a dose between 21 and 40mg/day for more than one third (37.0%) of their clients and a dose between 21 and 60mg/day for almost two thirds (64.8%) of their clients (see Table 9). Prescribers reported giving higher doses to only a small proportion of their clients (e.g. 9.5% on doses over 80mg/day).

Prescriber estimates of their prescribing practices are consistent with reported doses obtained from pharmacies (see section 3.1 and Appendix E).

Table 9: Proportion of methadone clients estimated to be on different methadone doses

Methadone dose (mg/day)	Mean %	Median %	Minimum %	Maximum %
0-20 mg/day	8.8	5.0	2.0	20.0
21-40 mg/day	37.0	35.0	10.0	90.0
41-60 mg/day	27.8	25.0	5.0	50.0
61-80 mg/day	17.0	18.0	0	40.0
81-100 mg/day	5.8	5.0	0	10.0
>100 mg/day	3.7	4.0	0	10.0

Clients

The 30 clients interviewed for this study ranged in age from 22 to 52 years, with an average age of 33.8 years. Seventeen clients (56.7%) were male and 13 were female (43.3%).

On average, clients reported that they had been on methadone maintenance treatment on 3 occasions (including present treatment). Over one quarter (27.6%) were taking part in their first methadone treatment program while one client was on their twelfth treatment episode[11]. The average amount of time clients had been on their *current* methadone treatment program was 34.5 months, with a range of 2 weeks to 12 years.

Clients reported current methadone doses ranging from 5 to 180 mg/day. The average dose was 45.4 mg/day (median=30mg/day). Approximately half of clients (16, 53.3%) reported a current dose of 30 mg/day or less. Most clients (24, 82.8%) indicated that their current dose was "about right", while three (10.3%) felt their dose was "too low" and two (6.9%) felt their dose was "too high".

Clients were asked to report their highest ever, daily methadone dose. These ranged from 35 to 180mg, with an average "highest ever" dose of 78mg/day (median=67.5).

Clients were asked to identify the methadone dose they would most like to be on at present. Nine participants (30%) reported that they would like to be taking no methadone whatsoever. Among the remaining clients, preferred dose size ranged from 15 to 110mg/day with an average of 45.6mg/day (median=40).

3.2.2 What is the "right" methadone dose?

Both clients and prescribers identified that the primary indicator that an individual is on his/her ideal dose, is the absence of withdrawal symptoms. Clients described that they don't feel withdrawal symptoms such as nausea, aches and pains, difficulty sleeping, cold shivers, runny nose or lack of concentration, when their dose is "right". Clients explained that beyond not suffering these withdrawal symptoms, they feel "normal" when their dose is correct:

"I don't feel anything from it at all; I don't feel like I'm on anything while I'm taking it. I just feel normal…it doesn't feel like you have taken any drugs." (Client)

[11] This was the highest reported number of methadone treatment episodes.

Another dimension of this reported by clients is that the correct dose "lasts for the full 24 hours" and does not make them appear or feel drug-affected.

"The right dose is the one where you're not feeling withdrawal symptoms. You don't want to be feeling stoned. At some point you stop feeling euphoria with feeling stoned. Your pupils are not huge; no throbbing in your private parts. Not feeling depressed or anxious etc. With the right dose you sleep at night and you feel normal." (Client)

Clients and prescribers also identified that a dose is correct when the client does not feel over-sedated and has diminished cravings to use heroin or other drugs.

"You are satisfied on methadone alone." (Client)

"If dose is too low, you may not reach that "blockage" point so you might muck up and use." (Client)

Four of the nine prescribers interviewed reported a mg/day figure optimal dose for their clients: 45, 50-60, 50-70, 60-80. They described that at these doses, withdrawal symptoms, cravings and over-sedation are absent and the effects of heroin are sufficiently blocked.

The remaining five prescribers were of the view that there is no fixed "optimal dose", rather it is patient-specific and is whatever mg "dose gets them comfortable and stable."

Most clients as a rule felt that lower doses were preferable to higher doses (see discussion at section 3.2.5), but several articulated similar to the above, that what is important is that the dose holds them, rather than how many milligrams it is:

"There is no such thing as a perfect dose because I've felt quite well on other doses. There's no magic number. Rather than talking about low and high dose you should talk about the right dose - the one where you're not feeling withdrawal symptoms." (Client)

3.2.3 Determinants of dose size

Comments from clients revealed that most are under the belief that methadone dose depends on the following:

- Amount of heroin use (including quantity, frequency, strength of heroin and duration of use), with higher doses required by those using more heroin or for longer periods of time
- Body weight – with methadone doses being linked proportionally to body weight
- Age – with smaller doses being required by younger users (linked to duration and amount of use)
- Gender – with women requiring lower doses than men

"Depends on the amount of drugs they have used previously; more drug use would mean they would need a higher dose." (Client)

It depends on build; bigger man would need a bigger dose than a small woman." (Client)

Some clients gave specific examples:

"Low dose for people with a $50 habit; Medium dose if using $80-100 of heroin per day; and High dose for those with more than a $100 a day habit – heavy users and dealers." (Client)

"People who use a gram or more a day need the highest doses."(Client)

"Large proportion [should be on <40mg], especially because the gear is not very good at the moment." (Client)

Three prescribers indicated similar beliefs about indicators of appropriate dose size, reporting nature of heroin use (amount and duration), body weight and gender as important determinants. One of these prescribers also reported that patient expectations and lifestyle influence what a suitable dose would be.

"Some people need more than others - depends on amount of heroin used and depends on time aspects - people who have been using for 20 years would be on a much higher dose than people who started using two months ago." (Prescriber)

There was no discussion by either prescribers or clients regarding the importance of other factors such as differences in individual hepatic metabolism of methadone (as affected by liver function, concomitant medical conditions, pregnancy, or the use of other medications or drugs), or psychological profile of the individual (particularly the existence of concomitant psychiatric comorbidity). This is concerning given that these factors appear to be more closely related to methadone dose requirements than the factors identified by clients and prescribers such as age, gender or amount of heroin use – which have consistently been shown to be poorly correlated to methadone dose requirements.

3.2.4 Defining "high" and "low" doses

Prescribers characterised a low methadone dose as ranging between 20 to 40 mg/day, with an average of 32.78 mg/day (see Table 10). Clients defined a low dose somewhat lower, ranging from 2 to 45mg/day, with an average of 20.8mg/day (see Table 11). Prescribers defined high methadone doses as ranging between 50 and 100 mg/day, with an average of 75.11 mg/day. Similarly, 79.7mg/day was the average high dose defined by clients.

Table 10: Prescriber definitions of dose size

Dose size	Mean mg/day	Median mg/day	Minimum mg/day	Maximum mg/day
Low	32.8	30.0	20.0	40.0
Medium	51.2	55.0	40.0	70.0
High	75.1	70.0	50.0	100.0

Table 11: Client definitions of dose size

Dose size	Mean mg/day	Median mg/day	Minimum mg/day	Maximum mg/day
Low	20.8	20.0	2.0	45.0
High	79.7	75.0	20.0	180.0

Methadone doses as low as 50mg (prescribers) and even 20mg (clients) were identified as 'high doses'. In contrast, most international literature identifies 'high' methadone doses as greater than 60mg of methadone (and often greater than 80mg) (see Faggiano et al., 2003). This reflects a Victorian 'culture' amongst both clients and prescribers of identifying 'normal' methadone doses as ideally being below the recommended range of >60mg.

3.2.5 Explanations for "low" methadone doses

Interviews with clients and prescribers largely confirmed the explanations for low methadone doses posited in the literature review (see section 2.4). Client-related factors include a view of and preference for methadone as short-term treatment and a belief that higher doses are associated with greater side effects. Prescriber-related factors include selective clinical experience of positive client outcomes on low doses, external pressure to prescribe low doses and concerns about overdose and diversion. These and related side issues are discussed below.

Short-term vs. long-term methadone treatment

Most clients approach MMT as a short-term rather than long-term treatment option, holding the goal of reducing and getting off methadone as soon as possible. The following are typical client statements regarding duration of their methadone treatment:

"Some people are on it for years… Doctors should encourage trying to decrease your dose."

"I kept reducing because I don't like being on too high a dose but it takes so long and I don't want to be one of those people on it for 10 years. I don't want to be on it forever! Although I was doing better on a higher dose."

"My idea was to be off methadone within 6 months if things went well."

This presents a significant challenge to doctors. As stated by one prescriber:

"I explain [to clients] you have to be on the program for a period of time for it to be effective. At least 1-2 years. It can be difficult for them to accept that. They'd prefer a few months."

Reasons stated by clients for wishing to minimise the time they are taking methadone include the side effects of methadone (see below) and that the program is burdensome (cost and daily/frequent visits to pharmacy).

"Apparently long term use of it (methadone) gets into your bones and makes your bones brittle". (Client)

Also emerging from the interview data is a strong resistance to or even fear of being "hooked" on methadone and "hooked" for a long time.

"I met an old man who was 67 and he was on methadone and he said 'do you think you can ever get off?' I don't want to be 67 and be stuck on this." (Client)

"There are people who have been on it for 25 years and they say they can never get off it now." (Client)

Clients believe that they will be able to minimise their time on the methadone program by maintaining a lower rather than higher dose. They believe that high doses are more difficult to reduce from and take longer to come off.

"The higher you go the harder it is to get off… On a low dose of methadone it is easy to get off it." (Client)

"If you're on too high of a dose it will take longer (2-4 years) to get off it – this is a major drawback." (Client)

Client interviews revealed an interesting phenomenon – while methadone treatment is initiated in order to reduce/stop heroin use, it appears that for many clients, the focus soon shifts. Methadone treatment ceases to be about quitting heroin and comes to be driven first and foremost, by the desire to get off methadone as soon as possible.

"Some people have such a keenness to get off that it tempers what is realistic…what will stop them from using [heroin]."(Prescriber)

As succinctly put by one client:

"Its not about using drugs anymore its about getting off the program."

The high importance placed by Australian clients on wishing to cease methadone treatment has been previously reported (e.g. Lenne et al., 2001), and can be understood in a number of ways – the daily inconvenience, and significant financial burden of the Victorian methadone program for clients, and the general problem of a young patient population accepting the need for long term treatment of a chronic condition parallels the poor adherence to treatment seen in other chronic conditions affecting young people such as Type I diabetes mellitus. Furthermore, an alcohol and drug treatment system which fragments treatment and continuity of care for patients is bound to cause confusion for patients as to their appropriate treatment. In the current Victorian service system, methadone treatment is largely disconnected from the remainder of the A&D service sector, such that different aspects of a client's treatment journey are delivered by separate service providers, often with quite oppositional ideological perspectives (e.g. detoxification, rehabilitation, Narcotics Anonymous, methadone) – hence, a detoxification service may encourage a client to withdraw off their methadone program (despite their continuing to use heroin) without consultation with the methadone service provider.

Whilst there is a considerable literature examining the safety and efficacy of methadone treatment, there is a much smaller research base and literature identifying optimal methods of withdrawal off methadone maintenance. There is poor clarity in the research literature, and this appears to also be present amongst service providers and clients about when to withdraw off methadone, the optimal methods of withdrawal, the role of newer approaches such as transfer to buprenorphine or rapid antagonist detox, and strategies to optimise post-withdrawal abstinence. The limited resources available (e.g. the client booklet "Coming off methadone" (Dunlop et al., 1996)) are out of date, and

are expensive for clients. Further, the limited psychosocial components of treatment in the Victorian methadone program limits the capacity for such interventions as part of the treatment program – and is reliant on referral to alternative service providers, rather than enabling continuity of care.

It is important that the field develop effective strategies in addressing genuine client and community concerns about being 'stuck' on methadone. It will be easier to optimise methadone treatment through the use of effective doses if clients can be assured that there is an 'exit strategy', and that 'coming off methadone' is achievable – and that it is more likely to occur successfully (i.e. without relapse to heroin use) if clients have achieved stability during their treatment – which is more likely to occur if clients are on more effective doses that enable them to stop using heroin.

Minimising side effects

There is a strong belief among clients that fewer side effects are suffered on lower, compared with higher methadone doses.

"I put on weight on a higher dose."

"Your teeth and bones deteriorate with higher doses of methadone."

"You feel sicker if you're on a high dose than a small dose, your body craves it, needs it more."

"[When I'm on a low dose] my sleeping and eating patterns go back to normal. My sex drives increases. My mental clarity increases. There are a lot of benefits to a low dose. More clarity in your head."

Clients reported that as dose increases, constipation, drowsiness, sexual dysfunction, sweating and problems with dry mouth worsen, consistent with much of the literature regarding methadone. Indeed, there is a growing understanding of methadone related side effects in recent years, with greater examination of the effects of methadone upon sleep, respiratory function, immune function, bone metabolism, cardiac function, cognition, driving performance, and interactions with other medications. This has led many researchers and clinicians to be more reticent in dismissing client complaints of methadone related side effects as 'methadone myths' or 'junkie folklore'. A review of this growing literature and its dissemination to key audiences is warranted.

Clinical experience of positive outcomes on low dose

Prescribers reported that they dose according to what clients report holds them stable (i.e. without withdrawal symptoms and cravings) and/or what the client wants (e.g. wanting to reduce off methadone; continuing low level heroin use). Taking this approach, prescribers reported that lower doses (<60mg) are appropriate for some clients.

"I don't go by any figure - whether it is 50 or 60 or any "average". I go purely on what the patient says is holding them. Many patients are happy to get down to a 40-50mg dose because they find it sufficient."

"I have one patient who functions well on 120mg and one that functions very well on 35mg and people in between so I don't think that there is one optimal dose, it is very much up to the individual…There is no hard and fast rule." (Prescriber)

Nonetheless, most prescribers estimated that 10-25% of their clients continue to use heroin and other drugs because their dose is too low.

"We are happy to drop them on the lowest dose but there are patients that would probably benefit from a higher dose because of the use of cannabis and benzos or street opiates but they decline." (Prescriber)

One long-time prescriber described himself as having "been on the low dose side all the way through" and described benefits of the continued drug use associated with low doses. This prescriber reported that his preferred dose is generally around 45mg and challenged total abstinence during methadone treatment as a useful goal, explaining his view that a better aim of treatment is:

"For people to learn about their drug use [through relapse] and understand why they are in that situation… I would prefer a patient to be on 40mg and using once a month than 80mg and not using because then they can learn from their relapse… Many people on 40 will use a few times, learn something and then stop."

Regardless of any preferred dose size, all prescriber interviews revealed that their dosing practices are driven primarily by their own clinical practice experience. It is interesting to note that, even though prescribers were not specifically asked how they use the clinical treatment guidelines in their practice, that none reported that their dosing decisions were influenced by research evidence (as reported in the clinical guidelines). This may reflect that the prescribers interviewed all had considerable experience in treating methadone clients.

External pressures faced by prescribers

Several prescribers reported pressure from DHS, corrections officers, and child protection to reduce clients' doses.

"We get phoned from DHS and child protection all the time seeing if they [patients] have reduced their dose. Patients often come in and want proof that they are reducing their dose and this has crept into the culture of providers around social issues of methadone and I'm sure this influences many prescribers as well as the patients." (Prescriber)

"I think that the pressure from DHS, possibly from corrections officers and various providers on patients to prove that they are over the drug thing by getting down off their methadone dose is wrong." (Prescriber)

Concerns about overdose and diversion

Three of the nine doctors interviewed indicated that concern about overdose and diversion influences doctors to prescribe lower doses. This is linked in part to concerns about patient reliability and full disclosure of drug use.

"There's a certain amount of worry about diversion if more than necessary is being prescribed." (Prescriber)

"[Average dose is less than 60mg because some] doctors are being cautious in using a dangerous drug - wanting to keep it to a minimum level."

"People lie to their doctor about use…People exaggerate using so they can get stoned." (Client)

Abstinence vs. continued heroin use

Three prescribers noted that there is a cohort of methadone clients who wish to continue using heroin either occasionally, or regularly at a low level, and hence "don't want a total blockade dose". They indicated that for some clients, the goal is to manage their heroin use at a lower level rather than to abstain completely.

"Some people think that using two times a week is great; they're ok with continuing to use." (Prescriber)

"A … proportion of people on methadone still like to have that option of scoring, be it for a celebration or to deal with some problem. [Being on a low dose] leaves the door open for use." (Prescriber)

None of the clients interviewed reported continued heroin use as a reason for themselves preferring a low dose, and only three (out of 30 clients) noted this as a reason for other clients.

"I reckon people are using it as a fall back. [On a low dose] you can still use if you want to or you can use methadone as a backup so you're not hanging out." (Client)

The majority view of clients however, is that the aim is to be on a dose that eliminates cravings and "stops you from using". It is interesting that continued use was not stated by any clients in the interviews, but was identified by a quarter of the doctors. Certainly previous Victorian research indicates that a considerable proportion of clients continue to use some heroin whilst in methadone treatment (up to half based on Lintzeris et al., 1996), and that heroin use is more common in those on lower doses (less than 40mg); and it is unlikely that the client interviewees would have been unaware of this phenomenon. This highlights the need for interpretation of subject responses in any qualitative research.

3.2.6 Treatment delivery

Client autonomy and decision-making

A strong theme to emerge from interviews with both prescribers and clients was that clients are the main drivers determining the size of their methadone dose. Doctors reported that they prescribe according to client feedback about how well their dose is holding them and client goals around withdrawing from methadone (vs. maintaining a stable dose for a period). Most clients participating in this study reported that it is their experience that they are the main drivers of their dose size and believe they should be so.

"You go to your doctor and ask them and that's it. The next day you are on a higher dose. When it comes to methadone anytime you go to the doctor they ask 'how are you feeling?', 'Do you need to go lower or higher, what do you want?'. You just have to tell your doctor that you are not coping and it needs to go higher." (Client)

"Patient should have some input; they are entitled to input – I tend to be guided by the patient – the patient decides if they want to go up or down. They very rarely ask, "What do you suggest?"" (Prescriber)

"I can discuss with them if they would like to increase so they're not using, but if they say, 'No I'm happy where I am' I'm not going to force the issue. It's up to the patient." (Prescriber)

"When patients think they need a higher or lower dose we just change them." (Prescriber)

While a handful of clients reported experiences with doctors who refused to adjust their dose as per their request, all of the prescribers interviewed described that they usually explain the course of treatment they believe is most appropriate to achieve abstinence, but ultimately it is up to the patient[12].

"If a person comes along who is on 50mg and says that they are using occasionally, perhaps weekly, I'd suggest that they increase their dose. I could explain to them that increasing the dose would have them use less often or not at all and not have the consequences or physical risks of injecting and the expense, which often leads to crime. One can only point out to people but you can't force them to increase their dose." (Prescriber)

This study indicates that the majority of methadone prescribing doctors allows their clients considerable autonomy in determining their OST. This raises the ethical and philosophical question: "what is the doctor's role in dealing with clients whose condition by its very nature indicates loss of control and reduced capacity to make good decisions about their own health?" Should doctors allow their patients to make treatment decisions that are likely to result in "failure" or should they step in and be more directive in treatment decision making, as the expert who "knows best"? Ultimately, clinical decision making should be a collaborative process between service providers and informed clients who have capacity. This process requires time and resources, and frequent reviews of treatment plans. The extent to which the current model of methadone treatment in Victoria allows this to occur is addressed in the next section.

Appointments – duration and content

Another theme to emerge from client interviews was considerable dissatisfaction with the amount of time doctors availed themselves for consultations. The following client comment is typical of the complaints made:

"Doctors need to have time to talk to you and treat you like a person. If he understood what was going on in my life her would put it [dose] down. We suffer because he gives us a smaller appointment."

[12] Two clients noted the absence of a regulatory body with powers of enforcement to respond to consumer complaints about prescribers or pharmacy staff. It is beyond the scope of the current project to comment on the need or otherwise to empower a complaints body, however consideration of such may arise under the review of the OST service provision model recommended at the end of this report (recommendation 4).

The main reason that clients gave for wanting more time with their doctor, is to enable discussion, planning and support for reducing off methadone.

"Doctors should encourage trying to decrease dose and see how it goes instead of just getting people in and out - some doctors don't have time to see how you are going." (Client)

"It should be the goal of every doctor to examine the patient and to see if they are doing well and ask them to reduce. The goal should be to get off methadone not to stay on it. There should be a time limit, it should be something that your doctor works with you. Doctors should set a time limit and help you develop a plan to get off it." (Client)

As above (1.3.2.1), these types of comments compel consideration of the proper role of the methadone-prescribing doctor. For these participants, a proactive and even interventionist approach is favoured – an approach that requires greater resources for service providers to either spend more time with patients, or to have support staff who can do so (see 'Ancillary support' below). The Victorian methadone treatment system is almost entirely reliant upon general practitioners operating in a fee-for-service Medicare based consultation system, with limited or no support from ancillary workers such as nurse practitioners, counsellors or case managers. The responses by clients here suggest that this is an inadequate model for managing this population of patients with chronic and often complex medical, psychiatric and social conditions.

Ancillary support

Several clients and prescribers noted the value of support, especially counselling, for improving outcomes for OST clients.

"It would be good if counselling was given at same time because methadone doesn't address the problems.
It's a good program but people need more." (Client)

More broadly, there was a call for assistance that enhances stability.

"More counselling. I'd love to have someone attached to our practice - a social worker/psychologist - to deal with any issues (housing, emotional, financial). We try to do it but have minimal time." (Prescriber)

"Being on the program gives you so much hope. But you need follow up and a network of support such as counselling, good doctor, housing, employment and people to talk to." (Client)

In essence, these study participants are calling for a more robust model of treatment for opioid users.

4. SUMMARY OF KEY FINDINGS

Methadone maintenance treatment

- The average methadone dose of Victorian clients is lower than recommended in treatment guidelines (54mg/day vs. >60mg)
- The primary reasons for low dose are
    - Client concern about side effects
    - Client focus on reducing off methadone as early as possible and the belief that lower doses are more suited to easier withdrawal and shorter term programs
    - Prescribers' experience of adequate / positive client outcomes on low doses
- There are many misconceptions about determinants of appropriate dose size, in particular that dose depends on the following: patterns of heroin use, including duration of heroin use, amount used and quality of heroin available; body weight; age; and gender.
- Clients are the main drivers determining the size of their methadone dose.

Having recognized that the mean methadone dose in the Victorian program is below the recommended range, a question that follows is "does this matter?" It may be, as identified by some clients and doctors in this report, that some clients can do well on low methadone doses. The extent to which treatment outcomes are affected by methadone dose was beyond the scope of this report or methodology. However, previous research of methadone treatment outcomes in Victoria (Lintzeris et al., 1996; Lintzeris et al., 2004; Ritter et al., 2003) have been consistent with the efficacy literature summarised in the recent Cochrane review (Faggiano et al., 2003) – that methadone doses of below 60mg are less effective in retaining patients and reducing heroin use than dose above 60mg. This is such a consistent finding that it could be argued that methadone dose acts as a surrogate marker for treatment effectiveness. Based on the findings of this study, the Victorian methadone program, as currently operating, is not attaining the optimal benefits that could be achieved for clients and the broader community.

Buprenorphine

- Buprenorphine dosing is more consistent with treatment guidelines than methadone. Almost half of clients are receiving a dose greater than 8mg/day.

DRUMS data - Population data estimates of methadone and buprenorphine doses

- Methadone estimates reasonably reflect actual dosing practices.
- Buprenorphine estimates are considerably lower than actual doses.

5. RECOMMENDATIONS

The following recommendations emerged from the data:

1. Better information for doctors, pharmacists and clients about methadone treatment is required. This should address:

    a. How to optimise methadone treatment

    An accessible compilation of the existing evidence about "what works" to be produced. Important areas to highlight include: long-term treatment outcomes are better than short-term; and the components of effective treatment – such as the role (and determinants) of dose and psychosocial services; the need to identify and respond to mental health comorbidity; and de-bunking 'methadone myths' where appropriate. Consideration should be given as to how existing state, national and international materials could be made more accessible to clients and service providers.

    It is important that any such campaign is not seen as 'window dressing'. It is detrimental to identify that effective methadone treatment requires a holistic approach with psychosocial services if such services are largely unavailable to patients. Without structural reforms to the Victorian methadone treatment system, criticisms that methadone treatment 'merely replaces one drug with another' will remain somewhat justified and undermine efforts to enhance treatment.

    b. Addressing patient identified barriers to optimal treatment

        i. Side effects

    A review of recent research regarding side effects of methadone and other opioid substitution treatment is required. This should then inform (a) a research plan examining responses to side effects and (b) dissemination of information regarding the short- and long-term side effects of methadone and other opioids.

    Clients need better information about coping with side effects. Information needs to be succinct, accurate, consistent, authoritative and informed by good research that addresses client concerns and experiences. Information needs to be readily available and in accessible formats (e.g. patient literature, DVDs, user magazines and websites). Peer based education strategies should be included in these efforts.

        ii. Coming off methadone

    Further research is required examining optimal methods to successfully withdraw off methadone without relapse to heroin use.

    Clients need better information about when and how to approach coming off methadone. Information needs to be succinct, accurate, consistent, authoritative and informed by good research. Information needs to free for patients and readily

available. Existing materials, such as the "Coming off methadone" booklet (Dunlop et al., 1999) could be updated to this end. Peer based strategies for information dissemination should also be considered.

2. Training and continuing professional development for service providers.

   There is limited training or professional development opportunities for existing methadone service providers in Victoria. The "Fundamentals Training Program" targets new prescribers and pharmacists, however there needs to be forums and opportunities for training existing providers addressing both knowledge and skills on these issues.

3. Education of other service providers, families and community groups

   There is considerable stigma against methadone treatment – affecting the recruitment and retention of both service providers and clients. Some important public services (e.g. child protection and corrections), as well as a sizeable proportion of the general public, are poorly informed about the nature of OST. Misconceptions foster intolerance and increase stigma and pressure for suboptimal dosing. Education and awareness campaigns targeting key service systems (including mental health, corrections, child protection) and families and carers regarding the nature of effective methadone treatment are required.

4. Structural aspects of treatment delivery

   Strategies are required to enhance and evaluate a more robust model of OST service provision in Victoria. This reports calls for a widespread and comprehensive review of the Victorian methadone treatment system, with particular attention on how to continue to meet demand for treatment and deliver comprehensive care, consistent with evidence based practice. A review should include the following areas:

   a. Capacity for existing service providers (doctors, pharmacists) to provide more resources and have a better skills base in working with clients to address goal-oriented treatment plans, client perceptions of treatment, side effects, and broader psychosocial needs.

   b. Numbers of service providers. A key driver of the current limitations in the Victorian service model is the reliance on a small number of general practitioners (fewer than 30) who currently treat the majority of methadone clients in Victoria. This limits their capacity to provide comprehensive care to patients. Strategies to recruit and diversify the methadone workforce are required.

   c. Multidisciplinary teams. The almost exclusive reliance on general practitioners (funded largely through Medicare) and community pharmacies (funded through patient payment) is inconsistent with the evidence regarding optimal methadone treatment. More effective and cost effective strategies are required to broaden the capacity and skills base of the methadone service industry in Victoria. Consideration should be given as to how multidisciplinary teams can be engaged into the Victorian methadone treatment system including nurses, counsellors, allied health and specialist medical practitioners. A review of the role of the small Specialist Pharmacotherapy Service system, and its capacity to support community-based programs should be included.

d. Other supports for clients: including improved access to counselling, welfare services, case management, and assistance for clients in responding to a range of medical, psychiatric and social problems commonly seen in this patient group, and in dealing with methadone related issues that serve as barriers to optimal treatment (such as side effects and assistance in withdrawal off methadone). This is linked to recommendation c. above

5. Evaluation

Any interventions implemented must be evaluated; evaluation planning to be included in project implementation plans. In any evaluation of the impact of interventions upon methadone and buprenorphine doses (which in turn act as a surrogate measure of treatment effectiveness), DRUMS data dose estimates are adequate for estimating the impact upon methadone doses, but poorly reflect actual buprenorphine doses.

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7. APPENDICES

Appendix A – Project reference group members

Dr Michael Aufgang	RACGP
Chris Boag	Manager, Pharmacotherapy Development, Drugs Policy and Services, DHS
Dr Malcolm Dobbin	Senior Medical Adviser, Drugs Policy and Services, DHS
Sarah Lord	Pharmacotherapy Liaison Officer, PAMS @ VIVAIDS Inc.
Dr Nick Lintzeris	Senior Staff Specialist, Drug Health Services, Sydney South West Area Health Service
Irvine Newton	PSA

Appendix B – Participating prescribers

Dr J. Guy Churchman

Dr Noah Diner

Dr Peter J Drake

Dr Beng H Eu

Dr Douglas M. Gee

Dr Elaine L. Ogilvie

Dr Marcus T. Weyland

Appendix C – Questions for methadone prescribers

1. Demographic & practice details

a. Age group: 30-39 40-49 50-59 60+

b. Gender: male / female

c. Years prescribing methadone: _____

d. Number of methadone patients: _____

e. Number buprenorphine patients: _____

2. Please estimate the proportion (%) of methadone patients in your practice on the following doses:

0-20	____
21-40	____
41-60	____
61-80	____
81-100	____
>100	____
	100%

3. What proportion of your methadone patients would you describe are

- Currently withdrawing off methadone (and less than 40mg) ____%
- Recently commenced methadone (and yet to reach stable dose) ____%
- Reducing methadone dose in order to transfer to other medication (e.g. buprenorphine) ___%

4. What kinds of methadone doses would you characterise as

Low	_____ mg/day
Medium	_____ mg/day
High	_____ mg/day

5. What do you think the optimal methadone dose is for your patients?
Please discuss

6. Are there some of your patients who you think would do better if they were on a higher or a lower methadone dose? If so, what proportion, and why?

7. What are the factors that may prevent patients from being on their optimal methadone dose?

8. What are the kinds of reasons stated by patients as to why they do not want a dose increase?

9. How do you try to address these concerns?

10. The average methadone dose in Victoria seems to be about 50mg. Most of the research evidence tells us that most people use less heroin when they are on doses of >60mg. Why do you think the Victorian average is less than recommended in guidelines?

11. Are there strategies (clinical, training, written literature) that you can think of that would enhance patients being on more effective methadone doses?

Appendix D – Questions for methadone clients

1. Demographic & treatment issues (for descriptive purposes only)
   (a) Age:
   (b) Gender: male / female
   (c) Length of this episode of methadone treatment so far: _____ months _____ days
   (d) Total number of methadone treatment episodes (including this one): _____
   (e) Current methadone dose: _____ mg/day
   (f) Highest ever methadone dose: _____mg/day

2. Do you think your current methadone dose is:
   ☐ too much
   ☐ about right
   ☐ too low

3. What dose would you like to be on at the moment? _____mg/day
4. What are the reasons you are not on your ideal dose?
5. How does a person know when he/she is on the correct dose of methadone? Please explain.
6. What kind of dose would you call a LOW dose? ____mg/day
7. What kind of dose would you call a HIGH dose? ____mg/day
8. Are there BENEFITS from being on a LOW dose?
9. Are there PROBLEMS from being on a LOW dose?
10. Are there BENEFITS from being on a HIGH dose?
11. Are there PROBLEMS from being on a HIGH dose?
12. Have you heard of any other positive or negative experiences people have had related to the size of their methadone dose?
13. What proportion of clients need the following doses?
    0 – 40 mg/day ____
    41 – 60 mg/day ____
    61 – 100 mg/day ____
    > 100mg/day ____
    100%
14. Do you think clients sometimes have problems getting good methadone doses from their doctors? If so, why do you think this may happen? [Probe – dose too small or too big?]
15. Do you think anything should be done to INCREASE client's doses? If yes, what kinds of things should be done?
16. Do you think anything should be done to DECREASE client's doses? If yes, what kinds of things should be done?

Appendix E – Methadone doses: Prescriber estimates cf. pharmacy data

Table 12: Proportion of patients on different methadone dose ranges, prescriber estimates compared with pharmacy reported doses

Methadone dose (mg/day)	Prescriber estimates %	Pharmacy data %
1-20	8.8	12.0
21-40	37.0	29.9
41-60	27.8	27.5
61-80	17.0	15.4
81-100	5.8	8.5
>100	3.7	6.7