

Preventing unauthorised use of medications prescribed for the treatment of opiate addiction

These notes are amended from a draft prepared in 2006 for the World Health Organization (WHO) in connection with a project to develop and publish minimum requirements and international guidelines on psychosocially assisted pharmacological treatment of persons dependent on opioids. They do not constitute a full or systematic review of the literature.

by **Mike Ashton**

phone +44 (0)2088886277, e-mail mike.ashton@blueyonder.co.uk

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Preventing unauthorised use of potent opioid agonist medications is a major priority for regulators, health planners and services. Control regimes are best decided locally in the light of all the circumstances. These notes are intended to inform that decision making. Whatever the circumstances, two measures are critical: requiring patients to consume their medication under clinical supervision ('supervised consumption'); and requiring each patient's treatment to be registered with a central authority.

Unauthorised use or 'diversion' of medications includes:¹

- use by the patient in ways not intended by the prescriber such as injection of 'non-injectable' formulations; skipping and 'hoarding' doses; sale; transfer or administration to other people;²
- use by other people to whom staff^{3 4} or the patient have directly or indirectly passed the medication;
- use by other people who find inadequately stored medication and consume it without the service's or the patient's knowledge or intention, especially children;⁵
- medication stolen from legitimate sources and directly consumed or sold on the illicit market.

Most forms of diversion undermine treatment because the patient is not taking their medication as intended in their care plan.⁶ Some also threaten their welfare through the injection of unsuitable preparations^{7 8 9 10 11 12 13 14} with potentially contaminated injecting equipment, by creating a gap in their medication 'shield' which enables a return to illegal opioid use,^{15 16} and through overdoses.^{17 18 19} Diversion also risks the lives of other people who acquire the medication,^{20 21 22} particularly those not as tolerant to opioids as the patient.²³ Especially when illicitly manufactured supplies are scarce, diverted medications can fuel the spread of dependent opioid use.²⁴ In a climate of antipathy to agonist maintenance, such incidents can threaten a particular service or the treatment as a whole.^{25 26}

Preventing diversion is for these reasons a priority. However, the attempt to do so can impede the achievement of other priority objectives (more below). By reducing its coverage and effectiveness, these 'side effects' undermine the gains expected from treatment. Less restrictive and more flexible regimes help achieve these gains by

permitting greater coverage but may risk diversion.^{27 28 29 30 31} Even when controls are relatively lax, making maintenance treatment widely available can save more lives than it costs.^{32 33}

How these dilemmas are resolved should depend on the extent and reality of the risks on either side. The risks of insufficiently controlled diversion are serious and real, but less so in some situations than others. Diverted medications may be taken largely by people already dependent on opioids who would otherwise be using illicitly produced drugs.³⁴ Many would be patients if treatment were more available, and take diverted medication for purposes similar to those promoted by treatment services – to maintain stability, prevent or manage withdrawal, and reduce use of illegal substances.^{35 36 37 38 39 40} These consumers risk death due to overdose and other causes, but not necessarily any more so than if they had used only illicit products.⁴¹ Patients who hoard doses or inject non-injectable preparations are arguably better off retained in imperfect treatment than excluded to avoid diversion.⁴² Where illicitly manufactured supplies are plentiful, a small amount of leakage from treatment services can have little impact on the extent of opioid addiction. Post-dispensing diversion may not be much of an issue at all when patients are integrated within conventional society rather than within drug using networks. Finally, some medications do not lend themselves to diversion and/or the consequences of diversion are less serious. Antagonists are an obvious example; buprenorphine combined with naloxone may prove to be another.⁴³

In these circumstances, stringent anti-diversion measures can unacceptably violate the patient's privacy and autonomy⁴⁴ and on balance do more harm than good.^{45 46 47} However, they may still be advisable to protect services from criticism and prescribers from legal challenges or professional disciplinary action.

How can the diversion be minimised?

Diversion can be curtailed by the implementation of regulations deriving from UN drug control conventions relating to the manufacture, trade, storage, transit and supply of medications controlled under those conventions, rigorous record-keeping of medication stocks and dispensing,⁴⁸ requiring proof of identity before prescription and dispensing, training staff in the implementation of these procedures, frequent dispensing of small amounts,⁴⁹ mandating supervised consumption for new and non-compliant patients,^{50 51 52 53 54} training on which patients can and should be allowed to consume their medications unsupervised or on long-interval dispensing, and by monitoring these patients' medication consumption. These safeguards should be systematised in an explicit service-wide policy.^{55 56} In their absence⁵⁷ (and particularly in the absence of supervised consumption) diversion can be widespread.^{58 59 60 61 62 63 64}

Diversion may also be minimised by developing good therapeutic relationships with patients⁶⁶ and providing treatment which stabilises their lifestyles and helps divorce them from drug using networks. Restrictions which impede this type of treatment risk being counterproductive. Options may be restricted to less 'divertable' medications which fail some patients who could otherwise cease illegal drug use. For example, many patients previously failed by oral methadone programmes have benefited from injectable heroin and methadone prescribing.⁶⁷ Clinic-imposed dosing limitations⁶⁸ undermine treatment's effectiveness and can lead patients to retain links

with illegal drug networks in order to supplement their prescriptions. Patients may be required to undergo demeaning urine collection procedures.^{69 70} Enforcing these procedures and limitations can dominate staff-patient interactions to the detriment of therapeutic interactions.^{71 72 73 74} Burdensome procedures also make services more costly, harder to establish and sustain, and divert resources from therapeutic activities.^{75 76} They also risk deterring would-be patients.

In balancing these competing priorities, patients have an ethical obligation to adhere to agreed treatment objectives and to avoid adversely affecting other people. Regulators and services have an obligation to impose only those restrictions commensurate with the risks being addressed and which do not unduly violate the privacy and autonomy of the patient, to take in to account the patient's ability to meet these requirements, to help them to do so, and to be sensitive to their situation including their neurobiological state and social circumstances.⁷⁷

All forms of post-dispensing diversion are most securely prevented by watching the patient ingest their medication. Supervised consumption and its opposite, take-away dispensing, are the subjects of the next section.

Under what circumstances can opioid maintenance patients take agonist medications away to be consumed without clinical supervision?

Take-away dispensing arrangements are usually considered suitable for patients whose dosage and social situation have been stabilised and who pose a low risk of diversion. The aims are to safely manage induction, prevent diversion, and retain patients who require this in regular and frequent clinical contact, while not unduly obstructing the social reintegration and autonomy of stabilised patients.

Supervised consumption entails being watched while taking one's medication and normally very frequent (from several times a day for short-acting medications to two or three times week for longer acting) visits to the dispensary. Done rigorously, it ensures that the patient is not left with any medication, eliminating post-dispensing diversion. It also safeguards the patient during induction, when patients are at greatest risk of overdose.

In respect of methadone, supervised consumption is commonly recommended until the patient's dosage has been titrated to an adequate and stable level and they have achieved social stability.^{78 79} The principal indicator is urine test results. Take-away dispensing is generally contingent on these indicating minimal illegal drug use and that methadone is being taken as per the treatment plan.⁸⁰ Other indicators of compliance with treatment (eg, attendance), of psychosocial stability (eg, employment, appropriate accommodation, no criminal activity) and of adequately controlled substance use (sobriety at appointments; alcohol breathalyser tests) may also be taken in to account.^{81 82} When programmes (such as US interim methadone programmes) are not resourced to make and monitor decisions on take-away dispensing, this may be banned altogether.⁸³ Patients are sometimes engaged in conversation after ingestion to stop methadone being retained in the mouth for later diversion,⁸⁴ though this is not foolproof.⁸⁵

Similar arrangements are suggested for buprenorphine, especially during induction,^{86 87 88 89 90 91} but its relative safety in overdose leads jurisdictions to be less prescriptive than with methadone.^{92 93 94 95} Supervised consumption of injectable medications

offers an opportunity to improve injecting technique and to prevent or manage complications but (in the case of heroin) means visiting the dispensary two or three times a day. Supervision may also be mandated or recommended in antagonist maintenance programmes, not to prevent diversion, but to ensure the patient takes the medication.⁹⁶

Alternative or additional means of preventing diversion (especially for patients on take-away dispensing) include inspecting veins and supplying diluted methadone mixtures to detect and deter injecting.^{97 98} Urinalysis is used to confirm that the patient has taken their medication and remains free of illicit drug use⁹⁹ but is a poor indicator. Take-away doses should be supplied in childproof bottles.¹⁰⁰ Patients are sometimes required to bring lockable containers to collect and store their medication.¹⁰¹ To deter and detect diversion, they may be required to return used bottles¹⁰² or ampoules¹⁰³ and called at random to return with unused medication.¹⁰⁴

Research confirms that anti-diversion regimes which include supervised consumption are associated with reduced diversion^{105 106 107 108} and that the risk of diversion is greatest among patients yet to achieve stability, marked for example by appropriate housing, employment, and reduced illegal drug use.^{109 110 111}

Research is contradictory with regard to the impact on outcomes and retention. This may be because two opposing influences are at play. Especially when it can be made convenient for the patient, supervised consumption can enhance retention by giving structure to lives newly devoid of the structure imposed by acquiring and using illegal drugs, by ensuring regular clinical contact,¹¹² and by preventing patients straying back to illegal drug use.¹¹³ Sometimes patients are aware of these dangers and resist increased take-away dispensing. Others relapse when take-aways are extended across the board rather than restricted to stabilised patients.¹¹⁴ On the other hand, patients find it difficult to comply with long-term attendance or supervision requirements leading to reduced compliance^{115 116} and premature drop-out or discharge.^{117 118 119 120 121}

Patients may understand the need for supervised consumption in the initial stages and for 'chaotic' patients, but object to its continuation when the individual has 'proved' themselves.¹²² Extended supervision is generally unpopular with patients.^{123 124 125 126 127} It contributes to long queues and congestion at busy clinics which foster disputes, facilitate drug-based social networks, and creates a counter-therapeutic environment.^{128 129 130} It also risks restricting the development of the patient's responsibility for their lives and displacing therapeutic activities and relationships with policing and control.^{131 132 133} Patient autonomy is undermined¹³⁴ because they are unable to control the timing and staging of their medication consumption.¹³⁵ This freedom might be exercised to facilitate illegal drug use, but may also be used to reduce it.¹³⁶ Frequent clinic or pharmacy visits obstruct reintegration in to employment and family responsibilities^{137 138 139 140 141 142 143 144 145} and make it difficult for patients to keep their condition secret.^{146 147 148}

Though based on explicit criteria,^{149 150} decisions on whether to impose, continue with, or relax supervised consumption should be made on an individual basis taking in to account all the circumstances. Difficulties are exacerbated by stringent and inflexible criteria like total long-term abstinence from illegal drug use, or life changes like employment which are not under the patient's control and may not be achievable. These can mean very few patients qualify for take-away doses.^{151 152 153} Patients who

have curbed illegal drug use, and whose lifestyle and social circumstances suggest they will not be destabilised by the withdrawal of supervision, generally continue to remain stable and compliant when dispensed several doses at once and allowed to take their medication home.^{154 155 156 157} In some situations, supervision can be cautiously relaxed (eg, allowing weekend take-aways) without adverse consequences, even when patients have yet to achieve stability.¹⁵⁸

Supervised consumption can be made less onerous by transferring it from the clinic to a local pharmacy, but often at the cost of privacy for the patient while consuming their medication and protection from being recognised by other customers.¹⁵⁹ Longer acting medications like buprenorphine permit less frequent visits for supervised consumption¹⁶⁰ without risking diversion or undermining the effectiveness of the treatment.¹⁶¹

The unpopularity of frequent visits for supervised consumption gives clinics leverage to use its relaxation not just to recognise the patient's stability, but to prompt them towards it by rewarding their progress with take-away dispensing.¹⁶² The main limitation is that patients who control themselves enough to benefit from these arrangements tend already to be relatively stable

Supervised consumption is limited in the degree to which it can protect patients themselves from overdose. Checking for heavy drinking or intoxication prior to dosing does not eliminate the possibility that other drugs have been taken, nor prevent patients from taking these after they leave.¹⁶³

Whatever the objective balance of risks and benefits from supervised consumption, it may be considered necessary to overcome public and political misgivings about introducing or extending agonist maintenance programmes.¹⁶⁴

¹. Ritter A. and Di Natale R. "The relationship between take-away methadone policies and methadone diversion." *Drug and Alcohol Review*: 2005, 24(4), p. 347–352.

². Sometimes administration to another person is both permitted and intended, as in the use of naloxone for overdose prevention.

³. [US] Center for Substance Abuse Treatment. *Medication-assisted treatment for opioid addiction in opioid treatment programs*. Treatment Improvement Protocol (TIP) Series 43. Rockville, MD: [US] Substance Abuse and Mental Health Services Administration, 2005.

⁴. Inciardi J.A., Surratt H.L., Kurtz S.P., et al. "The diversion of prescription drugs by health care workers in Cincinnati, Ohio." *Substance Use & Misuse*: 2006, 41(2), p. 255–264. "Data from 1992 through 2002 show that opioids were the drugs most commonly diverted by health care workers ..."

⁵. This risk may be particularly acute when patients have unstable accommodation unsuited to secure storage (Ritter A. and Di Natale R. "The relationship between take-away methadone policies and methadone diversion." *Drug and Alcohol Review*: 2005, 24(4), p. 347–352).

⁶. Henry-Edwards S., Gowing L., White J., et al. *Clinical guidelines and procedures for the use of methadone in the maintenance treatment of opioid dependence*. Commonwealth of Australia, 2003.

⁷. Darke S., Ross J., Hall W. "Prevalence and correlates of the injection of methadone syrup in Sydney, Australia." *Drug and Alcohol Dependence*: 1996, 43(3), p. 191–198. "A sample of 312 heroin users was interviewed on their injection of methadone syrup. Methadone injecting was widespread, with 52% of subjects having injected methadone syrup, 29% in the preceding six months. Males and females were equally likely to report methadone injecting. Forty per cent of current methadone injectors reported weekly or more frequent methadone injecting over the preceding six months. A history of methadone injecting was associated with abscesses and infections in injection sites, having been diagnosed with a

venous thrombosis and a history of heroin overdose. Current methadone injectors were in poorer general health, had more injection-related symptoms, higher levels of psychological distress, were more likely to have recently passed on used injecting equipment and to have recently committed criminal acts.”

⁸. Ritter A. and Di Natale R. “The relationship between take-away methadone policies and methadone diversion.” *Drug and Alcohol Review*: 2005, 24(4), p. 347–352. In Australia “At a simplistic level, those states with restrictive and less flexible take-away policies tended to have the lowest reported prevalence of methadone injection.”

⁹. Southgate E., Kippax S. and Bammer G. *Methadone injection in New South Wales*. [Australian] National Centre in HIV Social Research, 2001. In Australia “Around 65% of respondents (n=134) qualified for weekly take-away doses of methadone and around 30% of those either always, usually or sometimes sold part of their methadone to others.” Commonly this was injected with resultant injecting related damage.

¹⁰. Darke S., Topp L., and Ross J. “The injection of methadone and benzodiazepines among Sydney injecting drug users 1996–2000: 5-year monitoring of trends from the Illicit Drug Reporting System.” *Drug and Alcohol Review*: 2002, 21, p. 27–32. In Australia “Both methadone and benzodiazepine injecting were independently associated with higher levels of injection-related health problems. Given the substantial harms associated with these practices, continued monitoring of their prevalence is warranted.... Diversion to the black market, and intravenous injection, has been shown to rise and fall in proportion to the extent of provision of take-away doses for unsupervised consumption.”

¹¹. Guichard A. Lert, F., Calderon C., *et al.* “Illicit drug use and injection practices among drug users on methadone and buprenorphine maintenance treatment in France.” *Addiction*: 2003, 98, p. 1585–1597. Cross sectional survey of opioid substitution patients in France over 18 years of age and in treatment for at least 6 months. Prescribed buprenorphine was far more likely to have been injected in the past month than prescribed methadone (40% v 15%).

¹². Obadia Y., Perrin V., Feroni I., *et al.* “Injecting misuse of buprenorphine among French drug users.” *Addiction*: 2001, 96(2), p. 267–272. “Thirty-nine sites where IDUs have access to sterile syringes in the city of Marseille (South-Eastern France). Among the 343 respondents (response rate 70.7%), 33.8% were polydrug users who occasionally injected buprenorphine in parallel to heroin and/or cocaine, while another 23.9% only injected buprenorphine in the previous 6 months ... 32.7% of respondents were on buprenorphine DMT, and a majority of them (70.5%) declared intravenous misuse of buprenorphine during the previous 6 months, while they were on DMT.” However, as the sample were all attending syringe outlets they were bound to be injecting something.

¹³. Valenciano M., Emmanuelli. J. and Lert F. “Unsafe injecting practices among attendees of syringe exchange programmes in France.” *Addiction*: 2001, 96, p. 597–606. Clients requesting syringes in 60 syringe exchanges in France. “During the last 6 months, 68.1% of the respondents had been under treatment substitution (buprenorphine-HD or methadone). Eighty-five percent were polydrug users and buprenorphine high-dosage was the substance most often used (73% in last month of whom 78.7% had injected it). In the previous month, 45% of the participants had re-used a syringe, 93% injected at least daily (mean 3.6 injections per day.), 18% shared a syringe and 71% shared injection paraphernalia. A striking finding is the high percentage of participants that reported injecting buprenorphine-HD, which is prescribed as sublingual oral tablets.”

¹⁴. Vidal-Trecañ G., Varescon I., Nabet N., *et al.* “Intravenous use of prescribed sublingual buprenorphine tablets by drug users receiving maintenance therapy in France.” *Drug and Alcohol Dependence*: 2003, 69, p. 175–181. “A cross-sectional survey was used to collect data from subjects on buprenorphine MT seeking treatment from health care networks, specialized structures, a prison and a hostel in three different regions of France (1998–1999). 66.3% were followed-up by a general practitioner in a healthcare network. About half (46.5%) of the subjects on MT (188/404) had ever injected buprenorphine. About half of all the subjects (49.4%) first injected buprenorphine within a month of the first prescription. Following the first injection, 84.6% of the injectors injected again and 79.4% during the following week.”

¹⁵. Spunt B., Hunt D.E., Lipton D.S., *et al.* “Methadone diversion: a new look.” *Journal of Drug Issues*: 1986, 16(4), p. 569–583. US study of heroin users in and out of methadone treatment. Regular diverters of methadone were significantly more likely to have recently used heroin and cocaine.

¹⁶. Gerra G., Ferri M., Polidori E., *et al.* “Long-term methadone maintenance effectiveness:

psychosocial and pharmacological variables." *Journal of Substance Abuse Treatment*: 2003, 25(1), p. 1–8. In Italy "Data were collected from 265 heroin-dependent patients in long-term methadone maintenance treatment ... Administration of methadone weekly or twice weekly ('home methadone') was less effective than daily administration." Multivariate analysis taking in to account a wide range of patient and treatment factors established that "The patients with the privilege of home-methadone administration had a higher rate of positive urine test results than patients who were required to attend the center daily. In our program, home-methadone was not a privilege based on good performance, but was initiated to reduce the number of patients attending outpatient units."

¹⁷. Henry-Edwards S., Gowing L., White J., *et al.* *Clinical guidelines and procedures for the use of methadone in the maintenance treatment of opioid dependence*. Commonwealth of Australia, 2003.

¹⁸. Ritter A. and Di Natale R. "The relationship between take-away methadone policies and methadone diversion." *Drug and Alcohol Review*: 2005, 24(4), p. 347–352.

¹⁹. Cooper G.A.A. *et al.* "A study of methadone fatalities in the Strathclyde region." *Medicine, Science and Law*: 1999, 39(3), p. 233–242.

²⁰. Roberts K. and Hunter C. "A comprehensive system of pharmaceutical care for drug misusers." *Harm Reduction Journal*: 2004, 1(6). In Scotland "Glasgow has a higher level of persons reported to the data-base and the higher level of prescribing of methadone than is the case in Edinburgh (Lothian), it has the lowest level of persons reported as using illicit methadone. Lothian Health Board area has a much lower level of supervised consumption of methadone than is the norm in Glasgow yet it has a much higher number of persons reported as being addicted to illicit methadone. A recently published report on the role of methadone in drug related deaths in the west of Scotland found that a growing prevalence of heroin misuse has resulted in an increase in the number of individuals entering methadone maintenance programs. Despite a continuing increase in the amount of methadone prescribed, methadone deaths in Strathclyde (the police area covering Glasgow and the West of Scotland) have decreased since 1996 due possible to changes both in prescribing and clinical care. The report concluded that, along with the findings of a Confidential Inquiry, 'increased and wide-spread supervision implemented by pharmacists have been major factors in decreasing deaths involving methadone'."

²¹. Southgate E., Kippax S. and Bammer G. *Methadone injection in New South Wales*. [Australian] National Centre in HIV Social Research, 2001. In Australia "Around 65% of respondents (n=134) qualified for weekly take-away doses of methadone and around 30% of those either always, usually or sometimes sold part of their methadone to others."

²². Scherbaum N., Kluwig J., Meiering C., *et al.* "Use of illegally acquired medical opioids by opiate-dependent patients in detoxification treatment." *European Addiction Research*: 2005, 11(4), p. 193–196. "Take-home dosages in maintenance treatment are of great therapeutic importance, but they include the risk of the substitute being distributed illegally. The authors of this article reviewed the extent of consumption of illegally acquired medical opiates by 142 opiate- or poly-addicted patients consecutively admitted to a detoxification ward. 76 (53.5%) of them admitted to taking illegally acquired medical opiates, usually methadone, at least once. The cumulative duration was 30 days (median) ... The results prove the necessity of stringent conditions for take-home dosages, and illustrate deficits in the health care system."

²³. Henry-Edwards S., Gowing L., White J., *et al.* *Clinical guidelines and procedures for the use of methadone in the maintenance treatment of opioid dependence*. Commonwealth of Australia, 2003.

²⁴. As in the UK in the 1960s. Spear B. "The early years of Britain's drug situation in practice." In: Strang J. and Gossop M., *eds.* *Heroin addiction and the British system. Volume 1: origins and evolution*. Routledge, 2005, p. 17–42.

²⁵. Henry-Edwards S., Gowing L., White J., *et al.* *Clinical guidelines and procedures for the use of methadone in the maintenance treatment of opioid dependence*. Commonwealth of Australia, 2003.

²⁶. Roberts K. and Hunter C. "A comprehensive system of pharmaceutical care for drug misusers." *Harm Reduction Journal*: 2004, 1(6). In Glasgow Scotland supervised consumption was introduced partly because "Public opinion was extremely antagonistic to methadone as a treatment modality. Great caution was thus required to gain acceptance of its reintroduction as a treatment option. To this day there is still a high level of public resistance to the concept that methadone is the drug of choice for the treatment of opiate dependence".

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- ²⁷. Brugal M.T. *et al.* "Evaluating the impact of methadone maintenance programmes on mortality due to overdose and AIDS in a cohort of heroin users in Spain." *Addiction*: 2005, 100, p. 981–989. Extract from Findings entry: "In the '90s the life expectancy of heroin users entering treatment in Barcelona increased by 21 years, seemingly largely due to the expansion of low threshold oral methadone maintenance programmes. From 1994 the city's clinics adopted a low threshold philosophy which seems likely to have maximised access and retention, abandoning limits on dose levels or duration, not penalising patients who continued to use illicit drugs, and commonly (for 60% of doses) allowing patients to take their medication away for consumption at home. Nearly all the study's methadone patients had been on take-home regimes..."
- ²⁸. Auriacombe M. "Buprenorphine prescribed by general practitioners." In: *Maintenance treatment of heroin addiction: evidence at the crossroads*. Oslo: Cappellans, 2003. p.190–204.
- ²⁹. Reisinger M. "Role of doctors: experiences in France and Belgium." In: *Maintenance treatment of heroin addiction: evidence at the crossroads*. Oslo: Cappellans, 2003. p.184–189.
- ³⁰. Auriacombe M., Franques P., Tignol J. "Deaths attributable to methadone vs buprenorphine in France." *Journal of the American Medical Association*: 2001, 285(1), p. 45.
- ³¹. Emmanuelli J. *Contribution à l'évaluation de la politique de réduction des risques*. SIAMOIS, Institut National de Veille Sanitaire, tome I, 2001. Cited in: Coppel A. "Good practice, good results. Maintenance treatment outcomes in France." *Heroin Addiction and Related Clinical Problems*: 2005, 7(2), p. 19–24.
- ³². Caplehorn J.R.M. and Drummer O.H. "Mortality associated with New South Wales methadone programs in 1994: lives lost and saved." *Medical Journal of Australia*: 1999; 170: 104–109. "Despite 10 people dying from iatrogenic methadone toxicity and diverted methadone syrup being involved in 26 fatalities, in 1994 NSW maintenance programs are estimated to have saved 68 lives." This was when unsupervised consumption was the rule in private programmes.
- ³³. Auriacombe M., Fatséas M., Dubernet J., *et al.* "French field experience with buprenorphine." *American Journal on Addictions*: 2004, 13(Suppl. 1), p. S17–S28.
- ³⁴. McCabe S.E., Cranford J.A., Boyd C.J., *et al.* "Motives, diversion and routes of administration associated with nonmedical use of prescription opioids." *Addictive Behaviors*: 2007, 32(3), p. 562–575.
- ³⁵. [US] National Institutes of Health. *Effective medical treatment of opiate addiction*. NIH Consensus Statement: 1997, 15(6), p. 1–38.
- ³⁶. Ritter A. and Di Natale R. "The relationship between take-away methadone policies and methadone diversion." *Drug and Alcohol Review*: 2005, 24(4), p. 347–352.
- ³⁷. Spunt B., Hunt D.E., Lipton D.S., *et al.* "Methadone diversion: a new look." *Journal of Drug Issues*: 1986, 16(4), p. 569–583. US study of heroin users in and out of methadone treatment. Of those not in treatment over half had used methadone in the previous week and of these 60% used to prevent withdrawal and 40% to get high. Others used it to cut down on their heroin use or detoxify or (if in treatment) because their dose was not preventing withdrawal or giving them the desired euphoria.
- ³⁸. Rettig R.A. and Yarmolinsky A., *eds.* *Federal regulation of methadone treatment*. Washington DC: National Academy Press, 1995. Such methadone as is diverted "has mainly served as a way to avoid or end withdrawal symptoms, as a form of self-treatment for heroin addiction, or as a substitute for heroin or other opiates when they are in short supply".
- ³⁹. Thiesen H. and Hesse M. "Buprenorphine treatment in Denmark." *Nordic Studies on Alcohol and Drugs* (English Supplement): 2004, 21, p. 152–155. Diverted buprenorphine in Denmark was used as self-medication by people who wanted to "detoxify and free themselves from opiate abuse without contacts with the treatment system".
- ⁴⁰. Scherbaum N., Kluwig J., Meiering C., *et al.* "Use of illegally acquired medical opioids by opiate-dependent patients in detoxification treatment." *European Addiction Research*: 2005, 11(4), p. 193–196. "The authors of this article reviewed the extent of consumption of illegally acquired medical opiates by 142 opiate- or poly-addicted patients consecutively admitted to a detoxification ward. 76 (53.5%) of them admitted to taking illegally acquired medical opiates, usually methadone, at least once. The cumulative duration was 30 days (median). Motivation was usually due to difficulties in acquiring heroin, however one third reported use in an attempt at self-detoxification or as transition before entering maintenance treatment."

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- ⁴¹. Best D., Man L-H., Zador D., *et al.* "Overdosing on opiates." *Drug and Alcohol Findings*: 2001, 5. See p. 17 "The Scottish experience". "Unlike the Lothian service on which it was based, from the start the Glasgow service introduced supervised consumption of methadone which from 1996 was strongly encouraged in the city and spread through the rest of the region. Almost certainly as a result, the rate of methadone deaths per year of treatment then fell steeply. However, the overall number of deaths from drugs seems to have changed little from the 97 deaths recorded in 1994, the first year of the current recording system. As well as the number of deaths, the type of drugs involved has also changed little, still being dominated by heroin and benzodiazepines. If, as suggested, the number of injectors in the city has decreased over the 1990s, this cannot be considered a good outcome."
- ⁴². Auriacombe M., Fatséas M., Dubernet J., *et al.* "French field experience with buprenorphine." *American Journal on Addictions*: 2004, 13(Suppl. 1), p. S17-S28.
- ⁴³. Auriacombe M., Fatséas M., Dubernet J., *et al.* "French field experience with buprenorphine." *American Journal on Addictions*: 2004, 13(Suppl. 1), p. S17-S28.
- ⁴⁴. Carter A. and Hall W. *The ethical use of psychosocially assisted pharmacological treatments for opioid dependence*. World Health Organization, 2006.
- ⁴⁵. [US] National Institutes of Health. *Effective medical treatment of opiate addiction*. NIH Consensus Statement: 1997, 15(6), p. 1-38.
- ⁴⁶. Joseph H. *et al.* "Methadone maintenance treatment (MMT): a review of historical and clinical issues." *Mount Sinai Journal of Medicine*: 2000, 67(5-6), p. 347-364. "Thus, diverted methadone is purchased primarily to withdraw and maintain an untreated heroin-addicted population. Primary addiction to methadone is rare, since methadone does not produce the sharp euphoria of heroin. Therefore, regulations based solely on fears of diversion can be counterproductive."
- ⁴⁷. Rettig R.A. and Yarmolinsky A., *eds.* *Federal regulation of methadone treatment*. Washington DC: National Academy Press, 1995. "The committee concludes that the risks to public safety and the public health of diverted methadone do not outweigh the benefits of making methadone treatment more easily available"
- ⁴⁸. [US] Center for Substance Abuse Treatment. *Medication-assisted treatment for opioid addiction in opioid treatment programs*. Treatment Improvement Protocol (TIP) Series 43. Rockville, MD: [US] Substance Abuse and Mental Health Services Administration, 2005.
- ⁴⁹. Report of the International Narcotics Control Board for 2003 (E/INCB/2003/1), paragraph 109.
- ⁵⁰. Roberts K. and Hunter C. "A comprehensive system of pharmaceutical care for drug misusers." *Harm Reduction Journal*: 2004, 1(6). In Scotland "Glasgow has a higher level of persons reported to the database and the higher level of prescribing of methadone than is the case in Edinburgh (Lothian), it has the lowest level of persons reported as using illicit methadone. Lothian Health Board area has a much lower level of supervised consumption of methadone than is the norm in Glasgow yet it has a much higher number of persons reported as being addicted to illicit methadone. A recently published report on the role of methadone in drug related deaths in the west of Scotland found that a growing prevalence of heroin misuse has resulted in an increase in the number of individuals entering methadone maintenance programs. Despite a continuing increase in the amount of methadone prescribed, methadone deaths in Strathclyde (the police area covering Glasgow and the West of Scotland) have decreased since 1996 due possible to changes both in prescribing and clinical care. The report concluded that, along with the findings of a "Confidential Inquiry, 'increased and widespread supervision implemented by pharmacists have been major factors in decreasing deaths involving methadone'."
- ⁵¹. Gerra G., Ferri M., Polidori E., *et al.* "Longterm methadone maintenance effectiveness: psychosocial and pharmacological variables." *Journal of Substance Abuse Treatment*: 2003, 25(1), p. 1-8. In Italy "Data were collected from 265 heroin-independent patients in longterm methadone maintenance treatment ... Administration of methadone weekly or twice weekly ("home methadone") was less effective than daily administration." Multivariate analysis taking in to account a wide range of patient and treatment factors established that "The patients with the privilege of home-methadone administration had a higher rate of positive urine test results than patients who were required to attend the center daily. In our program, home-methadone was not a privilege based on good performance, but was initiated to reduce the number of patients attending outpatient units."
- ⁵². Darke S., Topp L., and Ross J. "The injection of methadone and benzodiazepines among Sydney

injecting drug users 1996–2000: 5-year monitoring of trends from the Illicit Drug Reporting System.” *Drug and Alcohol Review*: 2002, 21, p. 27–32. In Australia “Both methadone and benzodiazepine injecting were independently associated with higher levels of injection-related health problems. Given the substantial harms associated with these practices, continued monitoring of their prevalence is warranted ... Diversion to the black market, and intravenous injection, has been shown to rise and fall in proportion to the extent of provision of take-away doses for unsupervised consumption.”

⁵³. Southgate E., Kippax S. and Bammer G. *Methadone injection in New South Wales*. [Australian] National Centre in HIV Social Research, 2001. In Australia “Around 65% of respondents (n=134) qualified for weekly take-away doses of methadone and around 30% of those either always, usually or sometimes sold part of their methadone to others.” Commonly this was injected with resultant injecting related damage.

⁵⁴. Ritter A. and Di Natale R. “The relationship between take-away methadone policies and methadone diversion.” *Drug and Alcohol Review*: 2005, 24(4), p. 347–352. In Australia “At a simplistic level, those states with restrictive and less flexible take-away policies tended to have the lowest reported prevalence of methadone injection.”

⁵⁵. Spunt B., Hunt D.E., Lipton D.S., *et al.* “Methadone diversion: a new look.” *Journal of Drug Issues*: 1986, 16(4), p. 569–583. US study of heroin users in and out of methadone treatment. Diversion was rare. Diverters were rarely those with extensive take-home privileges suggesting effective selection and supervision.

⁵⁶. Rettig R.A. and Yarmolinsky A., *eds.* *Federal regulation of methadone treatment*. Washington DC: National Academy Press, 1995. Describes the various measures which have reduced methadone diversion since the early 1970s in the USA and which now [1995] keep this at a “low level”.

⁵⁷. Bouchez J. and Vignau J. “The French experience – the pharmacist, general practitioner and patient perspective.” *European Addiction Research*: 1998, 4(suppl. 1), p. 19–23. In France in 1997 “pharmacists reported that although supervised dispensing is advised during the induction phase, nearly 60% of buprenorphine patients took their medication without the supervision of the pharmacist”. GPs said that “In the induction phase, prescription was ‘often’ or ‘always’ dispensed by the pharmacist in 40% of cases. However, in the maintenance phase this was not considered necessary for many subjects and ‘never’ occurred in 50% of cases”.

⁵⁸. Duburcq A., Charpak Y., Blin P., *et al.* “Two years follow-up of a heroin users cohort treated with high dosage buprenorphine. Results of the SPESUB study.” *Rev. Epidemiol. Sante Publique*: 2000, 48(4), p. 363–373. [Article in French] In France “Each GP, known to be involved in drug user management, had to include the first 10 opioid drug addict patients to whom he prescribed high dosage buprenorphine, with a maximum inclusion period of 3 months... Between May and July 1996, 919 patients (664 men and 255 women, mean age: 30 years) were included by 101 GPs ... Two years later ... 14% of patients had declared intravenous injection of high dosage buprenorphine in the previous month.”

⁵⁹. Obadia Y., Perrin V., Feroni I., *et al.* “Injecting misuse of buprenorphine among French drug users.” *Addiction*: 2001, 96(2), p. 267–272. “Thirty-nine sites where IDUs have access to sterile syringes in the city of Marseille (South-Eastern France). Among the 343 respondents (response rate 70.7%), 33.8% were polydrug users who occasionally injected buprenorphine in parallel to heroin and/or cocaine, while another 23.9% only injected buprenorphine in the previous 6 months ... 32.7% of respondents were on buprenorphine DMT, and a majority of them (70.5%) declared intravenous misuse of buprenorphine during the previous 6 months, while they were on DMT.” However, as the sample were all attending syringe outlets they were bound to be injecting something.

⁶⁰. Valenciano M., Emmanuelli. J. and Lert F. “Unsafe injecting practices among attendees of syringe exchange programmes in France.” *Addiction*: 2001, 96, p. 597–606. Clients requesting syringes in 60 SEPs in France. During the last 6 months, 68.1% of the respondents had been under treatment substitution (buprenorphine-HD or methadone). Eighty-five percent were polydrug users and buprenorphine high-dosage was the substance most used (73% in last month of whom 78.7% had injected it). In the previous month, 45% of the participants had re-used a syringe, 93% injected at least daily (mean 3.6 injections per day), 18% shared a syringe and 71% shared injection paraphernalia. A striking finding is the high percentage of participants that reported injecting buprenorphine-HD, which is prescribed as sublingual oral tablets.”

⁶¹. Vidal-Trecan G., Varescon I., Nabet N., *et al.* “Intravenous use of prescribed sublingual

buprenorphine tablets by drug users receiving maintenance therapy in France." *Drug and Alcohol Dependence*: 2003, 69, p. 175–181. "A cross-sectional survey was used to collect data from subjects on buprenorphine MT seeking treatment from health care networks, specialized structures, a prison and a hostel in three different regions of France (1998–1999). 66.3% were followed-up by a general practitioner in a healthcare network. About half (46.5%) of the subjects on MT (188/404) had ever injected buprenorphine. About half of all the subjects (49.4%) first injected buprenorphine within a month of the first prescription. Following the first injection, 84.6% of the injectors injected again and 79.4% during the following week."

⁶². Guichard A. Lert, F., Calderon C., *et al.* "Illicit drug use and injection practices among drug users on methadone and buprenorphine maintenance treatment in France." *Addiction*: 2003, 98, p. 1585–1597. Cross sectional survey of opioid substitution patients in France over 18 years of age and in treatment for at least 6 months. Prescribed buprenorphine was far more likely to have been injected in the past month than prescribed methadone (40% v 15%).

⁶³. Southgate E., Kippax S. and Bammer G. *Methadone injection in New South Wales*. [Australian] National Centre in HIV Social Research, 2001. In Australia "Around 65% of respondents (n=134) qualified for weekly take-away doses of methadone and around 30% of those either always, usually or sometimes sold part of their methadone to others." Commonly this was injected with resultant injecting related damage.

⁶⁴. Ritter A. and Di Natale R. "The relationship between take-away methadone policies and methadone diversion." *Drug and Alcohol Review*: 2005, 24(4), p. 347–352. In Australia "At a simplistic level, those states with restrictive and less flexible take-away policies tended to have the lowest reported prevalence of methadone injection."

⁶⁵. Darke S., Ross J., Hall W. "Prevalence and correlates of the injection of methadone syrup in Sydney, Australia." *Drug and Alcohol Dependence*: 1996, 43(3), p. 191–198. "A sample of 312 heroin users was interviewed on their injection of methadone syrup. Methadone injecting was widespread, with 52% of subjects having injected methadone syrup, 29% in the preceding six months."

⁶⁶. Feroni I., Peretti-Watel P., Paraponaris A., *et al.* "French general practitioners' attitudes and prescription patterns toward buprenorphine maintenance treatment: does doctor shopping reflect buprenorphine misuse?" *Journal of Addictive Diseases*: 2005, 24(3), p. 7–22. "Doctor shopping was lower among GPs who reported inducing BMT with 8 mg of buprenorphine per day or more, and was higher for GPs endorsing a stringent attitude toward patients. Thus doctor shopping should not be understood exclusively as a deviant behaviour. It is partially physician-driven, and further research is needed to assess whether it reflects patients' dissatisfaction toward inappropriate care supply and the difficulty to establish a good therapeutic relationship between an opiate-dependent patient and a general practitioner."

⁶⁷ Ashton M. "Role Reversal". *Drug and Alcohol Findings*: 2003, 9, p. 16–23.

⁶⁸. Extract from Findings entry: "What the featured study (Robles E., Miller F.B., Gilmore-Thomas K.K., *et al.* "Implementation of a clinic policy of client-regulated methadone dosing." *Journal of Substance Abuse Treatment*: 2001, 20, p. 225–230) shows is that when the other controls are in place and for stable patients, a limit on dose levels can be waived without undue escalation or diversion of methadone on to the illicit market. This and other studies (Maddux J.F *et al.* "Patient self-regulated dose and optional counseling in methadone maintenance." *American Journal of the Addictions*: 1995, 4(1), p.18–32; Resnick R.B. *et al.* "Patient self-adjustment of methadone maintenance dose." In: Harris L.S. ed. *Problems of drug dependence*. NIDA, 1981, p. 327–330) have also indicated that when other anti-diversion controls are retained, there is also no need to automatically bar take-home doses beyond a certain dose level."

⁶⁹. Ege P. "Control procedures: evidence for effectiveness." In: Waal H. and Haga E., eds. *Maintenance treatment of heroin addiction: evidence at the crossroads*. Oslo: Cappellans, 2003, p. 175–183.

⁷⁰. Goldstein A., Brown B.W. "Urine testing in methadone maintenance treatment: applications and limitations." *Journal of Substance Abuse Treatment*: 2003, 25(2), p. 61–63.

⁷¹. Resnick R.B. *et al.* "Patient self-adjustment of methadone maintenance dose." In: Harris L.S. ed. *Problems of drug dependence*. NIDA, 1981, p. 327–330. Extract from Findings entry: A US study also concluded that average methadone doses did not increase under self-regulation. Before the shift to self-regulation this clinic was already operating a flexible dosing regime and approved most patient requests, but the process entailed considerable staff time and some frustration for patients who had to

wait to see a doctor. The justification for this process was to prevent clinically contraindicated dose levels. However, none of the self-regulated doses went beyond clinically appropriate levels. Given this experience, the more streamlined method of simply doing what the patient asks within certain limits and continuing to monitor reactions was made standard practice at the clinic.”

⁷². Goldstein A. *et al.* “Control of methadone dosage by patients.” *Journal of the American Medical Association*: 1975, 234, p. 734–737. US study. “We have long believed that dosage negotiation in a methadone program is destructive because it focuses excessive time and energy of both patients and staff on medication, at the expense of matters more germane to the rehabilitation process. Moreover, it places the patient and staff in adversary roles, to the detriment of a therapeutic relationship. One way to eliminate dosage negotiation is to make the dosage blind and fixed, but in our experience this generates suspicion and mistrust among the patients, who feel helpless with respect to the medication of their own bodies. We sought, therefore, to discover what would happen if patients were given knowledge and control of their own dosages, with certain safeguards built in. The main finding was that nothing remarkable happens.”

⁷³. Lilly R. *et al.* “Juggling multiple roles: staff and client perceptions of key worker roles and the constraints on delivering counselling and support services in methadone treatment.” *Addiction Research*: 1999, 7(4), p. 267–289. English study. Extract from Findings entry: “Clients who feared that illegal drug use would meet with a disciplinary reaction and possible dose reduction reacted by withholding information, creating distrust and tension. Some key workers tried to avoid such conflict by distancing themselves from decisions over dose.”

⁷⁴. Lilly R. *et al.* “Sociality in methadone treatment: understanding methadone treatment and service delivery as a social process.” *Drugs: Education, Prevention and Policy*: 2000, 7(2), p. 163–178. English study. Extract from Findings entry: “In another report from the same study staff tended to emphasise the importance of involving clients in decisions over their treatment including dose in order to safeguard or create a good relationship. Getting ‘bogged down’ in negotiations over dosage was seen as a distraction from productive counselling or therapy.”

⁷⁵. Gelkopf M., Bleich A. Hayward R., *et al.* “Patient outcomes after initiation of sabbath closure of a methadone maintenance clinic in Israel.” *Psychiatric Services*: 1998, 49, p. 1483–1485. “The findings suggest that clinics can permit themselves to close at least one day a week with no significant change in patient outcomes... Not having to attend the clinic for one day a week would make patients’ lives easier. In addition, a six-day schedule would reduce some of the workload and enable clinics to function more economically.”

⁷⁶. Senay E.C., Barthwell A.G., Marks R., *et al.* “Medical maintenance: a pilot study.” *Journal of Addictive Diseases*: 1993, 12, p. 59–67. In a one year study, 130 US methadone maintained subjects with a six-month history of good treatment performance (year’s retention, no positive urines, employed or equivalent, no criminal justice involvement, compliant with treatment plan) were assigned randomly to an experimental condition of one monthly non-random urine screen, one monthly counselling session, one monthly doctor visit, two times per month methadone pick up, a quarterly true random urine screen and participation in a diversion control program (random unused medication recall) or to a control condition of staying under standard conditions for six months (at least twice weekly pick-up) and then being transferred to the experimental condition for six months. Experimental conditions were cheaper such that resources freed up could be applied to the HIV epidemic.

⁷⁷. Carter A. and Hall W. *The ethical use of psychosocially assisted pharmacological treatments for opioid dependence*. World Health Organization, 2006.

⁷⁸. Uchtenhagen A., Ladjovic T. and Rehm J. *WHO Guidelines for psychosocially assisted pharmacological treatment of persons dependent on opioids. Background paper prepared for the ad-hoc expert meeting Geneva, 1–4 November 2005*. World Health Organization, 2005.

⁷⁹. Ward J., Bell J., Mattick R.P., *et al.* “Methadone maintenance therapy for opioid dependence: a guide to appropriate use.” *CNS Drugs*: 6(6), 1996, p. 440–449.

⁸⁰. [US] Center for Substance Abuse Treatment. *Medication-assisted treatment for opioid addiction in opioid treatment programs*. Treatment Improvement Protocol (TIP) Series 43. Rockville, MD: [US] Substance Abuse and Mental Health Services Administration, 2005.

⁸¹. [US] Center for Substance Abuse Treatment. *Medication-assisted treatment for opioid addiction in opioid treatment programs*. Treatment Improvement Protocol (TIP) Series 43. Rockville, MD: [US] Substance

Abuse and Mental Health Services Administration, 2005.

⁸². Some guidelines also recommend limiting the number of consecutive take-away doses regardless of the patient's stability. Henry-Edwards S., Gowing L., White J., *et al.* *Clinical guidelines and procedures for the use of methadone in the maintenance treatment of opioid dependence*. Commonwealth of Australia, 2003.

⁸³. [US] Center for Substance Abuse Treatment. *Medication-assisted treatment for opioid addiction in opioid treatment programs*. Treatment Improvement Protocol (TIP) Series 43. Rockville, MD: [US] Substance Abuse and Mental Health Services Administration, 2005. "No take-home doses are permitted for patients in short-term detoxification or interim maintenance treatment."

⁸⁴. Breslin K.T. and Malone S. "Maintaining the viability and safety of the methadone maintenance treatment program." *Journal of Psychoactive Drugs*: 2006, 38(2), p. 157–160. In USA requiring patients to talk after supervised consumption prevented methadone being retained in the mouth to be later spat out and sold.

⁸⁵. Spunt B., Hunt D.E., Lipton D.S., *et al.* "Methadone diversion: a new look." *Journal of Drug Issues*: 1986, 16(4), p. 569–583.

⁸⁶. [UK] Department of Health, Scottish Office Department of Health, Welsh Office, Department of Health and Social Services Northern Ireland. *Drug misuse and dependence – guidelines on clinical management*. HMSO, 1999.

⁸⁷. [UK] Royal College of General Practitioners. *Guidance for the use of buprenorphine for the treatment of opioid dependence in primary care*. Revised 2nd Edition 2004.

⁸⁸. Johnson R.E., Strain E.C., and Amass L. "Buprenorphine: how to use it right." *Drug and Alcohol Dependence*: 2003, 70(2, suppl.), p. S59–S77.

⁸⁹. Lintzeris N., Clark N., Winstock A., *et al.* "National clinical guidelines and procedures for the use of buprenorphine in the treatment of opioid dependence." Commonwealth of Australia, 2001.

⁹⁰. [US] Center for Substance Abuse Treatment. *Clinical guidelines for the use of buprenorphine in the treatment of opioid addiction*. Treatment Improvement Protocol (TIP) Series 40. Rockville, MD: [US] Substance Abuse and Mental Health Services Administration, 2004.

⁹¹. Verster A. and Buning E. *Buprenorphine: critical questions examined*. Amsterdam: Euro-Methwork Quest for Quality BV, 2005.

⁹². [UK] Department of Health, Scottish Office Department of Health, Welsh Office, Department of Health and Social Services Northern Ireland. *Drug misuse and dependence – guidelines on clinical management*. HMSO, 1999.

⁹³. Lintzeris N., Clark N., Winstock A., *et al.* "National clinical guidelines and procedures for the use of buprenorphine in the treatment of opioid dependence." Commonwealth of Australia, 2001.

⁹⁴. [US] Center for Substance Abuse Treatment. *Clinical guidelines for the use of buprenorphine in the treatment of opioid addiction*. Treatment Improvement Protocol (TIP) Series 40. Rockville, MD: [US] Substance Abuse and Mental Health Services Administration, 2004.

⁹⁵. Guichard A., Lert, F., Calderon C., *et al.* "Illicit drug use and injection practices among drug users on methadone and buprenorphine maintenance treatment in France." *Addiction*: 2003, 98, p. 1585–1597.

⁹⁶. Bell J., Kimber J., Lintzeris N., *et al.* *Clinical guidelines and procedures for the use of naltrexone in the management of opioid dependence*. Commonwealth of Australia, 2003. "There are many approaches to the delivery of supportive care. These include ... Supervised dosing – a family member or friend supervises the daily administration of naltrexone, sometimes administering the tablet crushed to minimise the risk of the patient spitting it out."

⁹⁷. Henry-Edwards S., Gowing L., White J., *et al.* *Clinical guidelines and procedures for the use of methadone in the maintenance treatment of opioid dependence*. Commonwealth of Australia, 2003. "All patients in receipt of takeaway doses should have an inspection of their veins at regular clinical review. People with evidence of continued injection should have takeaway doses suspended until they show evidence that injecting has ceased."

⁹⁸. Ritter A. and Di Natale R. "The relationship between take-away methadone policies and methadone diversion." *Drug and Alcohol Review*: 2005, 24(4), p. 347–352.

⁹⁹. [US] Center for Substance Abuse Treatment. *Medication-assisted treatment for opioid addiction in opioid treatment programs*. Treatment Improvement Protocol (TIP) Series 43. Rockville, MD: [US] Substance

Abuse and Mental Health Services Administration, 2005.

¹⁰⁰. [US] Center for Substance Abuse Treatment. *Medication-assisted treatment for opioid addiction in opioid treatment programs*. Treatment Improvement Protocol (TIP) Series 43. Rockville, MD: [US] Substance Abuse and Mental Health Services Administration, 2005. "Staff should ensure that patients can store medications safely in their homes (42 CFR, Part 8 β 12(I)(2)(vii)). All take-home medication must be labeled with the OTP name, address, and telephone number and packaged in a manner that is designed to reduce the risk of accidental ingestion, including child-proof containers."

¹⁰¹. Breslin K.T. and Malone S. "Maintaining the viability and safety of the methadone maintenance treatment program." *Journal of Psychoactive Drugs*: 2006, 38(2), p. 157–160. US patients may be required to bring secure, locked containers for their take-home medication and most programmes require return of empty take-home bottles.

¹⁰². Breslin K.T. and Malone S. "Maintaining the viability and safety of the methadone maintenance treatment program." *Journal of Psychoactive Drugs*: 2006, 38(2), p. 157–160. US patients may be required to bring secure, locked containers for their take-home medication and most programmes require return of empty take-home bottles.

¹⁰³. Metrebian N., Shanahan W., Wells B., *et al.* "Feasibility of prescribing injectable heroin and methadone to opiate-dependent drug users: associated health gains and harm reductions." *Medical Journal of Australia*: 1998, 168 (12), p. 596–600.

¹⁰⁴. [US] Center for Substance Abuse Treatment. *Medication-assisted treatment for opioid addiction in opioid treatment programs*. Treatment Improvement Protocol (TIP) Series 43. Rockville, MD: [US] Substance Abuse and Mental Health Services Administration, 2005. "Callbacks (see chapter 5) help prevent patient diversion of take-home medication. Callbacks require OTPs to select patients at random to return to the OTP with their remaining take-home medication. A random-callback policy avoids patient complaints of being unfairly picked on by staff members. Programs also can require patients to undergo drug tests when they bring in their medications. OTPs should document that patients have been informed of their responsibilities regarding callbacks (e.g., how much notice they will receive beforehand) and about the consequences of failure to respond or of discrepancies in medication amounts. The OTP callback policy should be stated clearly in the program DCP."

¹⁰⁵. Roberts K. and Hunter C. "A comprehensive system of pharmaceutical care for drug misusers." *Harm Reduction Journal*: 2004, 1(6). "Although Glasgow [Scotland] has a higher level of persons reported to the database and the higher level of prescribing of methadone than is the case in Edinburgh (Lothian), it has the lowest level of persons reported as using illicit methadone. Lothian Health Board area has a much lower level of supervised consumption of methadone than is the norm in Glasgow yet it has a much higher number of persons reported as being addicted to illicit methadone."

¹⁰⁶. Gerra G., Ferri M., Polidori E., *et al.* "Long-term methadone maintenance effectiveness: psychosocial and pharmacological variables." *Journal of Substance Abuse Treatment*: 2003, 25(1), p. 1–8. In Italy "Data were collected from 265 heroin-dependent patients in long-term methadone maintenance treatment ... Administration of methadone weekly or twice weekly ('home methadone') was less effective than daily administration." Multivariate analysis taking in to account a wide range of patient and treatment factors established that "The patients with the privilege of home-methadone administration [attending twice weekly or taking home a week's supply] weekly had a higher rate of positive urine test results than patients who were required to attend the center daily [presumed for supervised consumption]. [Tabulated results (rounded figures) were 45% of supervised patients urines free of illicit drugs in past month compared to 32% twice weekly and 24% weekly take-away patients though text says the last two categories averaged 22%] In our program, home-methadone was not a privilege based on good performance, but was initiated to reduce the number of patients attending outpatient units."

¹⁰⁷. Ritter A. and Di Natale R. "The relationship between take-away methadone policies and methadone diversion." *Drug and Alcohol Review*: 2005, 24(4), p. 347–352. In Australia, "At a simplistic level, those states with restrictive and less flexible take-away policies tended to have the lowest reported prevalence of methadone injection."

¹⁰⁸. Darke S., Topp L., and Ross J. "The injection of methadone and benzodiazepines among Sydney injecting drug users 1996–2000: 5-year monitoring of trends from the Illicit Drug Reporting System." *Drug and Alcohol Review*: 2002, 21, p. 27–32. In Australia "Diversion to the black market, and intravenous injection, has been shown to rise and fall in proportion to the extent of provision of take-

away doses for unsupervised consumption.”

¹⁰⁹. Vidal-Trecan G., Varescon I., Nabet N., *et al.* “Intravenous use of prescribed sublingual buprenorphine tablets by drug users receiving maintenance therapy in France.” *Drug and Alcohol Dependence*: 2003, 69, p. 175–181. “A cross-sectional survey was used to collect data from subjects on buprenorphine MT seeking treatment from health care networks, specialized structures, a prison and a hostel in three different regions of France (1998–1999). Injectors [of buprenorphine, presumed largely from their own prescription] were more likely to be unemployed than non-injectors and were more likely to have an income other than a salary or no income than non-injectors (Table 3). They were more likely to have injected a substance other than buprenorphine and to have used cocaine, crack and cannabis during the month before inclusion in the study than the non-injectors. Having injected a substance other than buprenorphine, cannabis use and having a source of income other than salary were the only variables that were independently, positively associated with buprenorphine injection (Table 4).”

¹¹⁰. Spunt B., Hunt D.E., Lipton D.S., *et al.* “Methadone diversion: a new look.” *Journal of Drug Issues*: 1986, 16(4), p. 569–583. US study of heroin users in and out of methadone treatment. Regular diverters of methadone were significantly more likely to have recently used heroin and cocaine.

¹¹¹. Guichard A. Lert, F., Calderon C., *et al.* “Illicit drug use and injection practices among drug users on methadone and buprenorphine maintenance treatment in France.” *Addiction*: 2003, 98, p. 1585–1597. Cross-sectional survey of opioid substitution patients in France over 18 years of age and in treatment for at least 6 months. Whilst prescribed buprenorphine was far more likely to have been injected in the past month than prescribed methadone (40% v 15%) and was also more likely to have been prescribed by GPs than specialist centres. In the buprenorphine group, drug injection was particularly related to unstable housing and a higher daily dosage”

¹¹². Ritter A. and Di Natale R. “The relationship between take-away methadone policies and methadone diversion.” *Drug and Alcohol Review*: 2005, 24(4), p. 347–352.

¹¹³. Auriacombe M. *et al.* “Les modalités de mise a disposition d’un traitement de substitution par buprénorphine influencent-elles la réponse générale au traitement? Résultats préliminaires d’une étude.” *Courrier des Addictions*: 2002, 4, p. 104–106. Cited in: Auriacombe M., Fatséas M., Dubernet J., *et al.* “French field experience with buprenorphine.” *American Journal on Addictions*: 2004, 13(Suppl. 1), p. S17–S28. “Within the French treatment system, an important variable that may influence office-based treatment efficacy could be the frequency with which supervised — as opposed to take-home doses — of buprenorphine are administered. In a recent study examining this, 202 patients were assigned quasi-randomly to daily supervised dosing for either two weeks, three months, or six months, after which dosing was on a weekly schedule. Results from this study showed that retention in treatment at the six-month follow-up was highest for those patients in the six month daily supervised dosing group (80%) and lowest for those patients in the two-week daily supervised dosing group (46%). (The three-month daily supervised dosing group fell between these two [65%.]) Rates of opioid-positive urine samples were lowest for the six-month daily supervised dosing group (14%), compared to the three-month daily supervised (22%) and two-week daily supervised (18%) groups. Finally, average daily doses at the six-month assessment were similar for the three groups (7.9, 8.7, and 8.5 mg/day for the six-months, three-month, and two-week groups, respectively). These results suggest that initial efficacy for office-based buprenorphine treatment may be enhanced by a more closely supervised delivery of medication.” Note that the French system generally requires relatively convenient supervision at a nearby GP’s office or pharmacy.

¹¹⁴. Zisowitz C. Ambivalent response to extended take-homes at a methadone clinic. Abstract 35A. ASAM 36th Annual Conference, April 14–17, 2005, Dallas, TX. Take-Home Methadone Not Always Welcomed by Patients. Investigators at the University of Pittsburgh Medical Center methadone maintenance treatment clinic examined the beneficial effects of methadone take home privileges. The clinic made 3-day a week privileges for unemployed patients available for the first time and extended weekend take-homes available to those in MMT for only 3 months. A significant minority of patients were reluctant to accept the take-home privileges, and larger numbers experienced drug relapse shortly after gaining them.

¹¹⁵. Amass L., Kamien J.B., and Mikulich S.K. “Thrice-weekly supervised dosing with the combination buprenorphine-naloxone tablet is preferred to daily supervised dosing by opioid-dependent humans.” *Drug and Alcohol Dependence*: 2001, 61(2), p. 173–181. Of the three dosing regimens (daily supervised,

three times a week supervised no take-homes, three times a week supervised with intervening take-homes) patients preferred not to have come daily for buprenorphine and to be able take their drugs at home. Patients took more doses when they did not have to visit daily.

¹¹⁶. Borisova N.N. and Goodman A.C. "The effects of time and money prices on treatment attendance for methadone maintenance clients." *Journal of Substance Abuse Treatment*: 2004, 26(1), p. 345–352. US economic analysis indicates that the higher the burden patients have in terms of time and money to attend for treatment the less they will attend so treatment will be less effective.

¹¹⁷. Gaughwin M. *et al.* "Correlates of retention on the South Australian methadone program 1981–91." *Australian and New Zealand Journal of Public Health*: 1998, 22(7), p. 771–776. Extract from Findings entry: Being able to get one's prescription dispensed at a local chemist was associated with greatly reduced drop-out (by a factor of five) at methadone clinics in South Australia during the decade 1981 to 1991. The data ... could partly reflect clinical decisions to permit take-home doses to more cooperative patients, but clinic policies were probably also a factor. Those which required daily attendance forced some patients to travel very long distances and to devote much of their lives to obtaining their medication.

¹¹⁸. Rhoades H.M., Creson D., Elk R., *et al.* "Retention, HIV risk, and illicit drug use during treatment: methadone dose and visit frequency." *American Journal of Public Health*: 1998, 88, p. 34–39. Extract from Findings entry: "A US trial randomly allocated patients to visit twice a week or every day except weekends; on other days they received take-home doses. Within each set, patients were also randomly allocated to 50 or 80mg a day. About half were unemployed. Given more adequate doses, patients were prepared to attend every weekday; regardless of the attendance requirement, nearly six months later about 80% were still in treatment. But at the lower dose level retention fell to about 40% when take-home doses were limited to weekends."

¹¹⁹. Donmall M., Watson A., Millar T., *et al.* *Outcome of Waiting Lists (OWL) Study. Waiting for drug treatment: effects on uptake and immediate outcome.* University of Manchester, 2002. English study. "Clients who were always on supervised consumption were much less likely to still be in treatment at three months than those who were never put on this regime. ... There was no statistical difference in retention between clients who were supervised for some of the three months compared to those who were not supervised at all. It is of course possible that the clients who are put on supervised consumption are the less stable ones, and therefore the ones most likely to default. It is also possible that the discouraging effect of supervision stops people from staying with their treatment."

¹²⁰. Pani P.P. and Pirastu R. "Take home and compliance with methadone maintenance treatment." *Heroin Addiction and Related Clinical Problems*: 2000, 2(1), p 33–38; Pani P.P., Pirastu R., Ricci A., *et al.* "Prohibition of take-home dosages: negative consequences on methadone maintenance treatment." *Drug and Alcohol Dependence*: 1996, 41, p. 81–84. "In Italy the take-home of methadone has seen different law-related phases: allowed until January 1991; prohibited until April 1993; allowed again up to now. The two years of prohibition came from the enforcement of a national law (Decree 445) which stated that the ingestion of methadone had to take place in front of a health professional. Until the enforcement of the Decree 445, the therapeutic plan included the opportunity to take-home methadone doses. After six months of complete compliance with the program, negative morphinuria results included, patients could come to the service once a week to carry out urinalyses, clinical check ups, assume prescribed methadone dose and take-home methadone doses for the rest of the week. The maintenance of take-home privilege was subject to the maintenance of negative urine results for morphine. In order to study the consequences of the change of perspective on the patients who were allowed to take home part of their supply of methadone, at the end of the 6-month period following the notice of the new law we compared the retention in treatment of a group of 211 patients, chosen at random among those subjected to the new law, with that of a group of 200 patients, matched for demographic and clinical characteristics and chosen from 430 patients who were in take-home program one year before the announcement of the law. The two groups of patients were evaluated at the end of a 6-month period and according to the changes observed divided into four categories: those interrupting the program, those continuing on take-home dosages, those assuming methadone daily on the service premises, and those completing detoxification successfully. The results showed that in the group of patients subjected to the new law a significantly higher percentage dropped out of the treatment abruptly (19.9% versus 3.2%) or after detoxification (23.2% versus 3.6%). It does not seem that these negative consequences were counterbalanced by the percentage of patients who completed detoxification (23.2%). In fact, three years later, we noticed that of these patients 10 were again in

treatment and 5 had died.”

¹²¹. Ritter A. and Di Natale R. “The relationship between take-away methadone policies and methadone diversion.” *Drug and Alcohol Review*: 2005, 24(4), p. 347–352.

¹²². Stone E. and Fletcher K. “User views on supervised methadone consumption.” *Addiction Biology*: 2003, 8, p. 45–48. English study of patients seeking methadone maintenance in an area which had introduced supervised consumption as the norm. “In particular, they considered that supervision was important at the commencement of methadone treatment and for chaotic individuals who were still actively engaged in illicit street drug use. They were keen to see movement away from supervision when good progress was made and an individual had objectively demonstrated that they were refraining from street drug use, complying with appointments and making positive life-style changes ... Service users felt aggrieved at being put on to supervision if they had been using their medication responsibly ... the general opinion was that, in order to prevent black market leakage, ‘only those who had proved themselves trustworthy’ should be given unsupervised methadone.”

¹²³. Amass L., Kamien J.B., and Mikulich S.K. “Thrice-weekly supervised dosing with the combination buprenorphine-naloxone tablet is preferred to daily supervised dosing by opioid-dependent humans.” *Drug and Alcohol Dependence*: 2001, 61(2), p. 173–181. Of the three dosing regimens (daily supervised, three times a week supervised no take-homes, three times a week supervised with intervening take-homes) patients preferred not to have come daily for buprenorphine and to be able take their drugs at home.

¹²⁴. Christo G. *Response client satisfaction survey 2004*. Study of an English methadone prescribing service. In 2004 71% of clients had to pick up their medication six times a week but just 19% of these wished to do so. 69% of patients preferred to be dispensed weekly. 19% of the 2004 clients were on supervised administration of methadone. 75% of these felt it was an unreasonable requirement.

¹²⁵. Cox W.M. “Evaluation of a shared-care program for methadone treatment of drug abuse: an international perspective.” *Journal of Drug Issues*: 2002, p. 1115–1124. English study. “The great majority of all three categories of professional respondents (physicians, pharmacists, and community drug workers) indicated that they were “in favour of” or “very much in favour of” community pharmacist supervision. In contrast, the majority of patients indicated that they ‘objected’ or ‘strongly objected’ to the supervision.”

¹²⁶. Smith I. and Honor S. *The estate they’re in*. Trafford: The Edge, 2004. English study. “Significant numbers of users oppose [supervised ingestion] (although a minority everywhere accept it)”

¹²⁷. Stone E. and Fletcher K. “User views on supervised methadone consumption.” *Addiction Biology*: 2003, 8, p. 45–48. English study of patients seeking methadone maintenance in an area which had introduced supervised consumption as the norm. “Some individuals ... commented adversely on the lack of private areas in pharmacies saying that this had caused ‘great embarrassment and humiliation’.”

¹²⁸. Personal communication from Dr Fred Rotgers, Associate Professor of Psychology at the Philadelphia College of Osteopathic Medicine. “Each dose is carefully regulated and must be taken in view of program personnel. Clients often have to stand in line for hours to get their dose. And, they have to ‘qualify’ for limited ‘take homes’ by ‘proving’ their motivation by being completely free of all other drugs ... for months. It is an awful, dehumanizing system designed more because of fear of diversion than any attempt to treat opioid dependence.”

¹²⁹. Senay E.C., Barthwell A.G., Marks R., *et al.* “Medical maintenance: an interim report.” *Journal of Addictive Diseases*: 1994, 13(3), p. 65–69. US report. “Common clinical experience in methadone maintenance programs indicates that there are many patients who stabilize on methadone and do well for long periods of time. Many of these patients appear not to need intensive levels of care to maintain their stability. They experience constant exposure to non-recovering patients as burdensome as these are the very people they are trying to avoid.”

¹³⁰. Fraser S. “The chronotope of the queue: methadone maintenance treatment and the production of time, space and subjects.” *International Journal of Drug Policy*: 2006, 17(3), p. 192–202. Australian research. “The paper argues that in the context of the methadone dosing point, time and space co-produce each other as a chronotope of the queue, and that this chronotope helps materialise particular methadone subjects. Often, these are the very kinds of subjects considered undesirable; that is, the ‘unproductive’, the ‘disorderly’, the ‘illicit’ ... the queue is a site of anxiety as well as of boredom and frustration for clients. ”

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- ¹³¹. Bell J., Byron G., Gibson A., *et al.* "A pilot study of buprenorphine-naloxone combination tablet (Suboxone) in treatment of opioid dependence." *Drug and Alcohol Review*: 2004, 23(3), p. 311–317. Australian study. "Employed patients on buprenorphine maintenance, who had ceased heroin use, were switched to Suboxone and provided with weekly supplies of medication to take without supervised administration ... Therefore it was not surprising that freedom from the clinic also contributed to the sense of having 'moved on'. Receiving medication to self-administer without supervision was also seen as an expression of trust and responsibility, and contributed to a changed (and much improved) relationship with clinic staff."
- ¹³². Bell J., Byron G., Gibson A., *et al.* "A pilot study of buprenorphine-naloxone combination tablet (Suboxone) in treatment of opioid dependence." *Drug and Alcohol Review*: 2004, 23(3), p. 311–317. "One of the problems which arises with supervised administration of methadone and buprenorphine is that the immediate task of delivering a daily dose to patients tends to become the focus of treatment, displacing concerns over patients' well-being and functioning ... For health professionals, supervised administration creates a treatment system in which, inevitably, the focus becomes the logistics of administering daily doses to large numbers of people, and much clinical interaction becomes a process of haggling over take-away doses."
- ¹³³. Senay E.C., Barthwell A.G., Marks R., *et al.* "Medical maintenance: a pilot study." *Journal of Addictive Diseases*: 1993, 12, 59–67. "In a one year study, 130 methadone maintained subjects with a six month history of good treatment performance (year's retention, no positive urines, employed or equivalent, no criminal justice involvement, compliant with treatment plan) were assigned randomly to an experimental condition of one monthly non-random urine screen, one monthly counselling session, one monthly doctor visit, two times per month methadone pick up, a quarterly true random urine screen and participation in a diversion control program (random unused medication recall) or to a control condition of staying under standard conditions for six months (at least twice weekly pick-up) and then being transferred to the experimental condition for six months. Experimental conditions were cheaper such that resources freed up could be applied to the HIV epidemic."
- ¹³⁴. Henry-Edwards S., Gowing L., White J., *et al.* *Clinical guidelines and procedures for the use of methadone in the maintenance treatment of opioid dependence*. Commonwealth of Australia, 2003.
- ¹³⁵. Smith I. and Honor S. *The estate they're in*. Trafford: The Edge, 2004. English study. "The major issues [with supervised ingestion] are ... the way it interferes with split dosing".
- ¹³⁶. Stone E. and Fletcher K. "User views on supervised methadone consumption." *Addiction Biology*: 2003, 8, p. 45–48. English study of patients seeking methadone maintenance in an area which had introduced pharmacy-based supervised consumption as the norm. "Some individuals reported increased heroin use because they were no longer able to split the dose of methadone."
- ¹³⁷. Stone E. and Fletcher K. "User views on supervised methadone consumption." *Addiction Biology*: 2003, 8, p. 45–48. English study of patients seeking methadone maintenance in an area which had introduced pharmacy-based supervised consumption as the norm. "There were complaints about daily pick-up (this would not be limited to supervised consumption) causing inconvenience and difficulties with work or finding work."
- ¹³⁸. Quaglio G., Lugoboni F., Pattaro C., *et al.* "Patients in long-term maintenance therapy for drug use in Italy: analysis of some parameters of social integration and serological status for infectious diseases in a cohort of 1091 patients." *BMC Public Health*: 6, 2006. "Seventy-nine percent of subjects were employed and 16% were unemployed. it is the general opinion of the personnel in treatment centres that patients have higher levels of employment today than in the past. This could be the result among other possible factors of the different approach to substitutive treatment (methadone and buprenorphine) compared to the past, with higher doses and easier access to it, for example by supplying one or more weeks of methadone take-home doses ... Clinicians routinely reduce the frequency of centre visits for patients who improve and prescribe sufficient quantities of medication to cover the increased time intervals between visits."
- ¹³⁹. Cox G. and Lawless M. "Maintaining or enabling? Evaluation of a methadone prescribing service in Dublin City." In: *Pieces of the jigsaw: six reports addressing homelessness and drug use in Ireland*. Dublin: Merchants Quay, 2004. Irish study. "Many who were employed reported that it was very difficult to meet the competing requirements of both a full-time job and the methadone treatment services. In general, those with full-time work feared that their employers would discover that they were on a methadone treatment programme and that they would lose their position."

¹⁴⁰. Spunt B., Hunt D.E., Lipton D.S., *et al.* "Methadone diversion: a new look." *Journal of Drug Issues*: 1986, 16(4), p. 569–583. US study of heroin users in and out of methadone treatment. Compliant clients relied on take-home doses to normalise their lives. Daily visits threatened anonymity and employment.

¹⁴¹. Fraser S. "The chronotope of the queue: methadone maintenance treatment and the production of time, space and subjects." *International Journal of Drug Policy*: 2006, 17(3), p. 192–202. Australian study. "Each morning people would arrive long before opening hours, sometimes as early as 4 a.m., to place themselves near the front of the queue, some because they needed to get to work, and the clinic's opening time of 8 a.m. allowed for little scope if they were expected at work at 8:30 or 9. ... This is one of many ways in which the queue is a site of anxiety as well as of boredom and frustration for clients. Others include waiting causing lateness for work."

¹⁴². King V.L., Kidorf M.S., Stoller K.B., *et al.* "A 12-month controlled trial of methadone medical maintenance integrated into an adaptive treatment model." *Journal of Substance Abuse Treatment*: 2006, 31(4), p. 385–393. In USA stable employed patients who had not tested positive for illegal drugs on the past 12 months were eligible for random allocation "routine care, MMM at the methadone maintenance program, and MMM at a physician's office. Methadone medical maintenance patients received a 28-day supply of methadone, whereas routine care patients received five or six take-home methadone doses each week. All patients performed a medication recall once a month and submitted two urine samples each month. MMM patients initiated more new employment or family/social activities than did routine care patients over the study period."

¹⁴³. Senay E.C., Barthwell A.G., Marks R., *et al.* "Medical maintenance: an interim report." *Journal of Addictive Diseases*: 1994, 13(3), 65–69. US study: "Common clinical experience in methadone maintenance programs indicates that there are many patients who stabilize on methadone and do well for long periods of time. They find a job, or if they are from disadvantaged communities where jobs are hard to get, they do odd jobs, make repeated attempts to get a job, and demonstrate that they are trying to make major changes in their lives. They stop using drugs, avoid drug users, cease criminal activity, and are frequently married to or in a relationship with a nondrug using person. Many of these patients appear not to need intensive levels of care to maintain their stability. They report that the time spent in traveling to a clinic two or three times a week and then waiting in lines for methadone, as well as attending groups and counseling, takes up enough time to create problems in getting or holding a job and significantly limits their ability to relate to their family."

¹⁴⁴. Smith I. and Honor S. *The estate they're in*. Trafford: The Edge, 2004. English study. "The major issues [with supervised ingestion] are ... the difficulties for those in employment and who have children."

¹⁴⁵. Güttinger, F.P., Schulte G.B., Rehm, J., *et al.* "Evaluating long-term effects of heroin-assisted treatment: the results of a 6-year follow-up." *European Addiction Research*: 2003, 9, 73–79. "Surprisingly, the results show a minor increase in unemployed persons compared to the data from the short-term and mid-term course of treatment ... A further reason for the high rates of unemployment could be the very structured and time-intensive nature of the heroin prescription program. On average, clients get their pharmaceutical dose 2–3 times a day, which may make pursuing a regular occupational activity quite difficult."

¹⁴⁶. Bell J., Byron G., Gibson A., *et al.* "A pilot study of buprenorphine-naloxone combination tablet (Suboxone) in treatment of opioid dependence." *Drug and Alcohol Review*: 2004, 23(3), p. 311–317. Australian study. "Employed patients on buprenorphine maintenance, who had ceased heroin use, were switched to Suboxone and provided with weekly supplies of medication to take without supervised administration. Freedom from the anxiety and shame associated with daily attendance at the clinic for dosing was consistently identified as a major benefit."

¹⁴⁷. Smith I. and Honor S. *The estate they're in*. Trafford: The Edge, 2004. English study. "The major issues [with supervised ingestion] are lack of privacy and confidentiality ..."

¹⁴⁸. Spunt B., Hunt D.E., Lipton D.S., *et al.* "Methadone diversion: a new look." *Journal of Drug Issues*: 1986, 16(4), p. 569–583. US study of heroin users in and out of methadone treatment. Daily visits threatened anonymity and employment.

¹⁴⁹. Ward J., Bell J., Mattick R.P., *et al.* "Methadone maintenance therapy for opioid dependence: a guide to appropriate use." *CNS Drugs*: 6(6), 1996, p.440-449.

¹⁵⁰. King V.L., Kidorf M.S., Stoller K.B., *et al.* "A 12-month controlled trial of methadone medical maintenance integrated into an adaptive treatment model." *Journal of Substance Abuse Treatment*: 2006, 31(4), p. 385-393. In USA stable employed patients who had not tested positive for illegal drugs on the past 12 months (98 of 380 patients at one clinic) were eligible for random allocation "routine care, MMM at the methadone maintenance program, and MMM at a physician's office. Methadone medical maintenance patients received a 28-day supply of methadone, whereas routine care patients received five or six take-home methadone doses each week. All patients performed a medication recall once a month and submitted two urine samples each month. An adaptive stepped-care system of treatment intensification was used for patients who failed recall or who had drug-positive urine specimens. Seventy-seven patients completed the 12-month study period. Dropout was caused primarily by problems with handling methadone and disliking the recall frequency. There were low rates of drug use or failed medication recall. Overall, 42% (14/33) of those who required stepped-up care received only one episode of intensified treatment and had no further problem during the study period."

¹⁵¹. Bell J., Byron G., Gibson A., *et al.* "A pilot study of buprenorphine-naloxone combination tablet (Suboxone) in treatment of opioid dependence." *Drug and Alcohol Review*: 2004, 23(3), p. 311-317. Australian study. "Employed patients on buprenorphine maintenance, who had ceased heroin use, were switched to Suboxone and provided with weekly supplies of medication to take without supervised administration ... Only 11% of people receiving buprenorphine met eligibility criteria ... using access to unsupervised dosing to promote abstinence from heroin probably limits the potential benefits of unsupervised administration to a very small proportion of patients"

¹⁵². King V.L., Kidorf M.S., Stoller K.B., *et al.* "A 12-month controlled trial of methadone medical maintenance integrated into an adaptive treatment model." *Journal of Substance Abuse Treatment*: 2006, 31(4), p. 385-393.

¹⁵³. King V.L., Kidorf M.S., Stoller K.B., *et al.* "A 12-month controlled trial of methadone medical maintenance integrated into an adaptive treatment model." *Journal of Substance Abuse Treatment*: 2006, 31(4), p. 385-393. In USA stable employed patients who had not tested positive for illegal drugs on the past 12 months (98 of 380 patients at one clinic) were eligible for random allocation "routine care, MMM at the methadone maintenance program, and MMM at a physician's office."

¹⁵⁴. Bell J., Byron G., Gibson A., *et al.* "A pilot study of buprenorphine-naloxone combination tablet (Suboxone) in treatment of opioid dependence." *Drug and Alcohol Review*: 2004, 23(3), p. 311-317. "Employed patients on buprenorphine maintenance, who had ceased heroin use, were switched to Suboxone and provided with weekly supplies of medication to take without supervised administration ... Seventeen subjects were recruited. Fifteen were retained for the full six months. No subject appeared destabilized by unsupervised dosing."

¹⁵⁵. King V.L., Kidorf M.S., Stoller K.B., *et al.* "A 12-month controlled trial of methadone medical maintenance integrated into an adaptive treatment model." *Journal of Substance Abuse Treatment*: 2006, 31(4), p. 385-393. In USA stable employed patients who had not tested positive for illegal drugs on the past 12 months were eligible for random allocation to "routine care, MMM at the methadone maintenance program, and MMM at a physician's office. Methadone medical maintenance patients received a 28-day supply of methadone, whereas routine care patients received five or six take-home methadone doses each week. All patients performed a medication recall once a month and submitted two urine samples each month. An adaptive stepped-care system of treatment intensification was used for patients who failed recall or who had drug-positive urine specimens. There were low rates of drug use or failed medication recall. No condition difference was observed in the percentage of patients requiring more intensive treatment for submitting drug-positive urine samples or failing medication recalls".

¹⁵⁶. Senay E.C., Barthwell A.G., Marks R., *et al.* "Medical maintenance: a pilot study." *Journal of Addictive Diseases*: 1993, 12, 59-67. In a one year study, 130 US methadone maintained subjects with a six month history of good treatment performance (year's retention, no positive urines, employed or equivalent, no criminal justice involvement, compliant with treatment plan) were assigned randomly to an experimental condition of one monthly non-random urine screen, one monthly counselling session, one monthly doctor visit, two times per month methadone pick up, a quarterly true random urine screen and participation in a diversion control program (random unused medication recall) or to a control condition of staying under standard conditions for six months (at least twice weekly pick-up) and then being transferred to the experimental condition for six months. Results of urine screens and

scores on the Addiction Severity Index (ASI) at entrance and six month intervals showed no differences between groups. Three out of four subjects completed the year in good standing and there was no difference in this between the groups.

¹⁵⁷. Spunt B., Hunt D.E., Lipton D.S., *et al.* "Methadone diversion: a new look." *Journal of Drug Issues*: 1986, 16(4), p. 569–583. US study of heroin users in and out of methadone treatment. Diverters were rarely the patients on extended take-away arrangements since they were the compliant clients.

¹⁵⁸. Gelkopf M., Bleich A. Hayward R., *et al.* "Patient outcomes after initiation of Sabbath closure of a methadone maintenance clinic in Israel." *Psychiatric Services*: 1998, 49, p. 1483–1485." The study examined whether closing of a methadone maintenance clinic in Israel on the Sabbath was associated with adverse patient outcomes. One take-home dose of methadone was given to all patients for that day regardless of whether they had earned take-home privileges. No difference was found in dropout rates for the six-month periods before and after Saturday closure was initiated. Results of random, twice-weekly urinalyses for all patients did not indicate increased use of heroin. The findings suggest that closure of a methadone clinic at least one day a week does not jeopardize patient outcome. Cutting hours of operation would reduce workload and enable clinics to function more economically.... The retention rates for the two periods were examined using a survival analysis, with time in treatment as the dependent covariate. Of the 131 patients attending the clinic in the six months before the Saturday take-home dose was introduced, 14 left treatment, for a dropout rate of 10.7 percent. Of the 133 patients attending in the six months after, seven left treatment, for a dropout rate of 5.3 percent. Although the rate was roughly halved during the second period, the difference was not statistically significant ... Giving the responsibility for self-administration of methadone – even for one day a week – to patients who may not be ready to assume this responsibility was a concern of many staff members at our clinic. They feared that patients would resume or increase their use of drugs. However, this study has shown that these fears were not realized ... We believe that this finding can be attributed to two factors – maintenance of our patients at the appropriate methadone dosage and the 'holding' function of the clinic."

¹⁵⁹. Stone E. and Fletcher K. "User views on supervised methadone consumption." *Addiction Biology*: 2003, 8, p. 45–48. English study of patients seeking methadone maintenance in an area which had introduced pharmacy-based supervised consumption as the norm. "Some individuals ... commented adversely on the lack of private areas in pharmacies saying that this had caused 'great embarrassment and humiliation'. There were complaints about daily pick-up (this would not be limited to supervised consumption) causing inconvenience and difficulties with work or finding work."

¹⁶⁰. Carter A. and Hall W. *The ethical use of psychosocially assisted pharmacological treatments for opioid dependence*. World Health Organization, 2006. "Drugs like methadone that act for 24 hours will require daily dosing unless take away doses are allowed. Longer acting partial agonists like buprenorphine may allow alternate day supervised dosing or once weekly dosing with takeaways."

¹⁶¹. Amass L., Kamien J.B., and Mikulich S.K. "Thrice-weekly supervised dosing with the combination buprenorphine-naloxone tablet is preferred to daily supervised dosing by opioid-dependent humans." *Drug and Alcohol Dependence*: 2001, 61(2), p. 173–181. Of the three dosing regimens (daily supervised, three times a week supervised no take-homes, three times a week supervised with intervening take-homes) patients preferred not to have come daily for buprenorphine and to be able take their drugs at home. Most doses were taken in the three times a week schedules.

¹⁶². Griffith J.D. *et al.* "Contingency management in outpatient methadone treatment: a meta-analysis." *Drug and Alcohol Dependence*: 2000, 58, p. 55–66. Extract from Findings entry: "A meta-analysis combining results from 30 studies of contingency management in the context of methadone programmes found that these regimens make a modest but worthwhile contribution to improving drug use outcomes. Of the variables investigated in several studies, the greatest reductions in positive urine tests were associated with using take-home doses as a reinforcer, delivering the reinforcer immediately after the relevant urine test result, and testing at least three times a week."

¹⁶³. Squires T. *et al.* *National Confidential Enquiry into Methadone Related Deaths (Scotland) 2000*. "Of those on a prescription, 60% were on supervised consumption at the time of their death. It is important to emphasise that supervised consumption does not protect an individual user from a drug-related death. The cost-benefit of the further extension of supervised consumption should, therefore, be defined."

¹⁶⁴. Roberts K. and Hunter C. "A comprehensive system of pharmaceutical care for drug misusers." *Harm Reduction Journal*: 2004, 1(6). "Another reason for supervised consumption of methadone in

Glasgow [Scotland] was previous experience of an unstructured and unsupervised system in the late 1970s–early 1980s. Public opinion was extremely antagonistic to methadone as a treatment modality. Great caution was thus required to gain acceptance of its reintroduction as a treatment option. To this day there is still a high level of public resistance to the concept that methadone is the drug of choice for the treatment of opiate dependence”.