

Medications in recovery: re-orientating drug dependence treatment

Appendix C – Opioid substitution treatment and its effectiveness: review of the evidence

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1 INTRODUCTION

1.1 This appendix reviews evidence concerning the factors enhancing the effectiveness of OST in promoting recovery from heroin addiction.

1.2 The distinctive aspect of this review of evidence is that it seeks to integrate, as far as is possible, the discourse of evidence-based practice (built on observation and measurement), with the humanitarian, recovery-based discourse based on values (such as responsibility, choice, and empowerment). The review identifies where the optimism which is central to recovery discourse needs to be tempered with evidence, and where the energy and focus on self-improvement associated with recovery can enhance the effectiveness of evidence-based practice. The approach taken has been to identify the broadly-agreed objectives of treatment, and to review the empirical evidence as to the effectiveness of OST. The paper then reviews the factors associated with variations in treatment effectiveness, and explores where the insights and dynamism of recovery can enhance the effectiveness of treatment.

1.3 The goals of treatment of heroin addiction

1.3.1 The foundation of treatment of heroin addiction is suppression of street heroin use. Other objectives are most likely to be achieved if patients stop or markedly reduce their use of street heroin and other drugs.

1.3.2 There are secondary objectives which are also critically important to build sustained recovery:

- reduction in other drug use – stimulants, cannabis, alcohol, benzodiazepines. Continuing misuse of, or dependence on, these drugs, is associated with poorer health and social outcomes
- for some participants, persisting mental and sometimes physical health problems are a barrier to recovery, and the extent to which treatment contributes to stabilisation and improvement in health is another critical determinant of recovery
- other critical steps towards sustained improvement are stable housing, employment, and development of social networks. Fostering 'recovery capital'

– the physical, social, emotional and cultural supports needed to sustain recovery – is an integral part of the treatment of heroin addiction.

1.4 Opioid Substitution Treatment (OST)

1.4.1 Opioid Substitution Treatment (OST) is the name given to treatment approaches which include prescribing and administration of a pharmaceutical opioid as a 'substitute' for illicit opioids. The most common form of OST is oral methadone treatment (MT), but there is a rapidly increasing experience with buprenorphine, and a small experience with prescribed injectable diamorphine (pharmaceutical heroin) in management of heroin addiction.

2 THE EFFECTIVENESS OF OPIOID SUBSTITUTION TREATMENT (OST)

2.1 A comprehensive Health Technology Assessment undertaken in the UK in 2007 reviewed the evidence for the effectiveness of methadone and buprenorphine, and concluded that both drugs were effective in treating opioid dependence (NICE, 2007b). This finding was based on a synthesis of randomised trials, observational evidence and expert opinion. The following analysis of effectiveness focuses on more specific issues, looking at a range of potential treatment outcomes, and providing an overview of the outcomes reported from major long-term observational studies. This has been undertaken because measuring the effectiveness of OST varies according to the outcome against which it is being evaluated. It focuses on three major studies, undertaken in differing countries – the Treatment Outcome Prospective Study (TOPS) (Hubbard et al., 1989) from the US, The National Treatment Outcome Research Study (NTORS) from the UK (Gossop et al., 2002), and the Australian Treatment Outcomes Study (ATOS) (Teesson, 2007). A later UK study, DTORS, is not included because results of multiple modalities of treatment are combined, making it impossible from the published report to identify outcomes of OST (Jones et al., 2009).

2.2 How effective is OST in suppressing use of street heroin?

2.2.1 There is evidence that all positive outcomes are to a large extent dependent on reduction of

heroin use (Gossop et al., 2001). Reduced risk of BBV transmission and reduced crime result from reduction in street heroin use (Bell et al., 1997). Cessation of heroin use during treatment is an essential step towards eventual successful withdrawal from OST (Milby, 1988).

2.2.2 The TOPS study followed for five years a sample of patients treated in residential rehabilitation (RR) and MT (Hubbard et al., 1989). Many RR patients were primarily cocaine users rather than heroin, which complicated interpretation of the results. At five years post index treatment, heroin use was sharply reduced in both cohorts. In the MT cohort, 65% had used heroin in the month prior to recruitment; at five years this had fallen to 16%. In the RR cohort 32% had used heroin in the month prior to enrolment, and at five years 11% had used heroin in the month prior to interview. Few in either group had achieved stable, prolonged abstinence – on average, subjects had four subsequent treatment episodes over five years follow-up, passing through episodes of treatment and episodes of relapse.

2.2.3 In the UK, NTORS used similar methodology to TOPS, interviewing patients from a range of treatment, and re-interviewing sub-samples out to four to five years. Heroin use at intake fell from 68% in the methadone sample to 23% at four to five years, while in the rehabilitation cohort it fell from 48% to 23% (Gossop et al., 2002). In the methadone sample 25.7% of subjects reported abstinence from illicit drugs (although cannabis use was not assessed) at five-year follow-up, compared to 38% of RR patients reporting abstinence from illicit drugs. Again, cycling through repeated episodes of treatment was common, making it difficult to attribute results to any particular modality of treatment.

2.2.4 ATOS (Teesson et al., 2007) reported on a cohort of 615 heroin users enrolled in a range of treatment modalities. The proportion who reported using heroin in the preceding month continued to decrease significantly from 99% at baseline to 35% at 24-month follow-up, with this rate remaining stable to 36-month follow-up. Positive outcomes were associated with more time in maintenance therapies and residential rehabilitation and fewer treatment episodes. Time spent in detoxification was not associated with positive outcomes. At each follow-up point, more than half the patients were in treatment.

2.2.5 These three large scale studies from different countries provide surprisingly consistent results. Heroin use was reduced, with 25-35% of heroin users

reporting continuing heroin use three to five years after beginning their index treatment. Many were still in treatment at follow up, and a high percentage had been through several episodes of treatment. Short-term treatment, and no treatment, were significantly less effective than MT. Residential rehabilitation was of similar effectiveness to MT, but as people switched between modalities, MT attracted and retained a higher proportion of heroin users than RR.

2.2.6 The strength of OST has been in reducing the harm associated with heroin addiction – in particular, reducing overdose deaths and reducing acquisitive crime associated with dependence on street heroin. Participation in MT protects against death by overdose (Clausen et al., 2008; Davoli et al., 2007; Kimber et al., 2010). A further public health benefit of OST is that it reduces the risk of BBV, particularly in conjunction with availability of clean needles and syringes (Turner et al., 2011). The reduction in risk for those entering treatment translates into a public health benefit. This was powerfully illustrated in France in the 1990s. In 1994, there were only 52 people in treatment with methadone, and an estimated 160,000 people injecting illicit opioids in France. Five years later, there had been an expansion in methadone treatment to 7,000 people, and 60,000 people were being prescribed buprenorphine. Heroin overdose deaths in France fell from 505 in 1994 to 92 in 1999 (Bell et al., 2002). A similar, if less dramatic observation was made in Sweden following liberalisation of access to OST (Romelsjo et al., 2010). The number of patients in treatment increased more than threefold from 2000 to 2006, with the greatest increase for buprenorphine, introduced in year 2000. There was a significant 20-30% reduction in opiate-related mortality and inpatient care between 2000-2002 and 2004-2006 but not of other drug-related mortality and inpatient care. A small but significant increase in buprenorphine- and methadone-related mortality occurred. The authors concluded that liberalization of Sweden's drug policy, and expanded access to OST, contributed to a decrease in overall opiate-related mortality and inpatient care. Although the overall mortality rate declined due to a fall in heroin overdoses, there was a small but significant increase in buprenorphine- and methadone-related mortality – the trade-off involved in introducing OST.

2.2.7 There is also extensive data on the reduction in criminal activity after entry to methadone treatment; to the extent that people in treatment reduce their use of illicit drugs (and therefore reduce expenditure), the level of acquisitive crime by individuals in treatment

diminishes (Bell et al., 1997). An Australian analysis of community rates of offending has demonstrated a statistically significant link between increased numbers in MMT and falling levels of acquisitive crime in the community (Moffatt et al., 2005).

2.3 How effective is OST in suppressing misuse of drugs other than heroin?

2.3.1 There are few users of heroin only – most people entering treatment have misused, or are misusing, multiple drugs (Robins, 1993). Results of large-scale, observational studies suggest OST is minimally effective at suppressing use of drugs other than heroin.

2.3.2 Ball and Ross (1991) found no reduction in use of most non-opioid drugs with longer treatment. The TOPS study did find a fall in non-opioid drug use (except alcohol) in patients remaining in methadone maintenance, and that the reduction was greatest in those subjects who used least heroin (Fairbanks et al., 1993). However, five years after enrolment in the index episode of treatment, 35% of TOPS subjects were smoking cannabis (with slightly lower levels in the MT group than in RR), and heavy drinking was common in both groups – 28% of RR group, and 19% of the MT group. At five years, around 27% of the MT cohort had “minimal” use of any drug (Hubbard, 1989).

2.3.3 NTORS reported no significant reduction in use of cocaine over the five-year period in methadone-treated cohort, but a significant reduction in the RR cohort (a proportion of whom had sought treatment for cocaine rather than heroin addiction). In both groups, there was no reduction in heavy drinking. In the methadone sample 25.7% of subjects reported abstinence from all illicit drugs at five-year follow-up (although cannabis use was not measured, and had cannabis use been included, the rate of abstinence from all drugs would have been considerably lower).

2.3.4 The ATOS study (Teesson et al., 2007) reported that at baseline, >90% of participants were using other drugs in addition to heroin. At three-year follow-up, 77% were still using drugs other than heroin. This was the only outcome not positively associated with longer duration in maintenance treatment.

2.3.5 In summary, although using somewhat different criteria, these three observational studies found strikingly similar results – around ¾ of patients in OST were using other drugs, predominantly alcohol and cannabis, at long-term follow-up.

2.4 How effective is OST in improving physical and mental health?

2.4.1 Other than reduced risk of overdose and BBV, there is relatively little data on which to assess health outcomes. Residential rehabilitation programmes usually incorporate an emphasis on attitude change and growth of a new consciousness. However, in TOPS, at five years post-treatment, improvements in depression were identical in the MT and RR cohorts. The ATOS study (Teesson et al., 2007) reported substantial self-reported reductions in risk-taking, injection-related health problems and improvements in general physical and mental health. Positive outcomes were associated with more time in maintenance therapies and residential rehabilitation and fewer treatment episodes.

2.4.2 A recent review of studies of quality of life among opioid-dependent individuals identified 38 articles addressing the topic (de Maeyer et al., 2010). The results were mixed, but a few conclusions emerged. The subjective quality of life (QoL) and health-related Quality of life (HRQoL) of opioid-dependent individuals is relatively low as compared with the general population, and is most comparable with the QoL of individuals with psychiatric problems. Opiate users reported lower scores on mental health in particular, while their physical well-being was less affected.

2.4.3 Quality of life generally improved promptly on entry to OST. Reno and colleagues (1993) studied life activities in heroin users at the time of entry to MMT, and over the ensuing eight months. Subjects reported a prompt and substantial improvement in life activities (such as “spending more time with family”) in the two months following entry to treatment. There was little discernible change in the following six-month interval. Similarly, while there are improvements from baseline in reported well-being, for people with psychological distress, cross-sectional research has demonstrated very little evidence of continuing improvement with greater duration of treatment (Ball and Ross, 1991; Craig et al., 1990).

2.5 How effective is OST in improving social reintegration of marginalised heroin users?

2.5.1 There is very little quantitative data available on which to assess the extent to which people in MT are able to achieve social reintegration.

2.5.2 Qualitative interviews with a group of patients maintained on methadone (de Maeyer, 2011) provide an idea of the role of MT in enhancing social reintegration. Participants’ attitudes towards

the impact of methadone on QoL were characterised by a strong ambivalence. Gaining control over one's life and daily functioning and no longer being sick when no heroin is available, were only some of the frequently mentioned benefits of following a methadone treatment. The respondents emphasized that methadone does not cause changes in their lives, but allowed change to occur in important areas such as relationships. Methadone treatment can create the necessary preconditions to deal with a number of issues (e.g. developing one's skills to practice a job) that can enhance individuals' QoL. Opiate-dependent individuals valued methadone's ability to help them function normally, overcome their psychological problems and dependence on illicit opiates, and support them in achieving certain life goals. On the other hand, stigmatisation, discrimination, dependence on methadone and unpleasantness of withdrawing from methadone, were mentioned as having a negative impact on QoL.

2.5.3 In addition respondents referred to methadone having a "paralysing effect" on their emotions. This may reflect the change that occurs when a previously "busy" lifestyle and identity of the active heroin addict is removed, leaving difficult adjustment issues and a loss of sense of purpose and identity.

2.5.4 Thematic analyses undertaken in this study revealed five key themes contributing to a good QoL for opioid dependent individuals: (1) the availability of supportive and caring relationships, (2) holding an occupation, (3) feeling good about one's self, (4) being independent and (5) having a meaningful life. "Having a meaningful life" was associated with settling down, the security of a family and striving for stability in life (e.g. financial security, housing, basic comfort). The authors commented that in general, opiate-dependent individuals' expectations about life are low. In particular, the importance of enjoying the small, ordinary things in life (e.g. walk in the park, eating an ice cream) was frequently mentioned.

2.6 Is OST effective in promoting abstinence from all drugs, including OST medications?

2.6.1 Traditionally, treatment of dependence on alcohol and drugs has been based on two premises - that recovery from addiction required abstinence from drugs, and that it required a change of attitude and identity. The principle of OST - that people can recover while still dependent on an opioid - challenged the assumption that the objective of treatment should be abstinence from all drugs (including methadone).

2.6.2 International studies suggest that for opioid dependent persons in the criminal justice system, and those seeking treatment, addiction is often a chronic, relapsing and remitting condition. People cycle through differing episodes, and differing modalities of treatment. Hser and colleagues (2001) reported on a group of heroin addicts followed up 33 years after entering treatment. Forty percent were dead, many remained addicted. Among those who achieved prolonged abstinence, a quarter had eventually relapsed in subsequent observations. Indeed, relapse was observed even among patients abstinent as long as 15 years. Long term follow-up studies documenting the natural history of heroin addiction estimate that, among subjects who seek treatment, 2-5% per year achieve stable abstinence from opioids (Haastrup & Jepsen, 1984; Vaillant, 1988).

2.6.3 It has been argued that this view is overly pessimistic, and that many more people can and do recover from dependence on drugs. The phenomenon of spontaneous recovery from addiction has been well documented (Robins, 1993). Community surveys (notably, the ECA study from the US), have identified a number of respondents who report previous dependent use of drugs, but are no longer dependent, implying that many people "recover" from dependence. However, the prognosis for people who seek treatment for drug dependence is consistently worse than in non-treatment samples. Among people seeking treatment for addictive disorders - whether alcohol dependence (Dawson, 1996) or heroin addiction (Robins, 1993), the course of dependence tends to be chronic and relapsing, and recovery is less likely in this group than among people who never seek treatment. The reason for this disparity is most likely that people who present seeking treatment have more severe problems - "problems which will not be resolved just by getting them off drugs" (Robins, 1993).

2.6.4 The majority of patients aspire to an opioid-free life without methadone (de Maeyer, 2011), and an orientation to maintenance is not to suggest that people cannot leave MT and remain abstinent. People leaving MT are less likely to relapse if they have ceased injecting heroin, and have achieved a degree of social re-integration: employment, a stable relationship, or community connections, before the attempt to withdraw from methadone (Milby, 1988).

3 THE COMPONENTS OF EFFECTIVE OST

3.1 The evidence also indicates the treatment components more likely to deliver the benefits described above. As these are crucial to improving the

recovery orientation of treatment, they are considered in some detail below, starting at the organisational level and working down through to supervised consumption.

3.2 Clinical leadership and organisational functioning

3.2.1 Developing and maintaining clarity of goals and maintaining a therapeutic treatment context are the roles of clinical leadership. US studies on differences in effectiveness of clinics have identified engaged, stable clinical leadership as a predictor of better treatment outcomes (Ball and Ross, 1991; Magura et al., 1999). Leadership in clinical services is essential in maintaining the cohesion, focus and engagement of clinicians; without the presence of effective local leadership, it is unlikely that clinicians can sustain a therapeutic milieu in which to optimise recovery.

3.2.2 In addition to the outcomes literature for methadone maintenance, literature from the US on organisational readiness to change suggests that organisational change efforts, regardless of how effective they are initially, are unlikely to be maintained without a plan to sustain them (CSAT, 2009).

3.2.3 At the organisational level it is important that the programme has adequate resources, both financial and human. It is also important to have motivated staff with the attributes associated with successful long-term implementation of innovative and effective drug treatment programmes, including appropriate qualifications, confidence in their skills, a proportion in recovery themselves (CSAT, 2009).

3.2.4 Effective supervision of staff by competent clinicians and managers is an important conduit for leadership and a critical component in ensuring appropriate training, staff motivation, programme adherence, etc (Miller et al., 1995; Stitzer and Kellogg, 2008).

3.2.5 Moos (2007) also identified – and Gjersing et al. (2010) supported – that “common components of effective treatment include support, goal direction, and structure; an emphasis on rewards that compete with substance use, a focus on abstinence-oriented norms and models, and attempts to develop self-efficacy and coping skills”.

3.3 Duration of treatment

3.3.1 Among people seeking treatment for heroin addiction, the course of dependence tends to be prolonged, and relapse to opioid dependence is

common after leaving any form of treatment (Hser et al., 2001; Teesson et al., 2007). Longer duration in methadone treatment is associated with better outcome. Since the earliest large-scale outcome studies, such as DARP, longer retention in OST (up to one year or more) has consistently shown better – and better sustained – post treatment outcomes (Simpson and Sells, 1982; Zhang et al., 2003). After leaving treatment, relapse is usual (Milby, 1988). Time-limited methadone treatment is not effective (Gossop et al., 2003; Bell et al., 1995). For these reasons, there are risks associated with encouraging or pressuring people to withdraw from treatment, and OST is best regarded as long-term treatment. Moos (2003) reviewed several studies – of both OST and other drug treatment modalities – and concluded that the duration and continuity of care were more closely related to treatment outcome than was the intensity of care.

3.3.2 The importance of retention does not mean that people should be discouraged from seeking to move on from treatment if they are doing well, and have or can gain sufficient recovery capital to sustain long-term abstinence. Most patients do not wish to remain indefinitely in treatment. People remain for variable periods, commonly cycling in and out of episodes of treatment (Teesson et al., 2007). It is not possible to be definitive about how long an individual should remain in treatment - the appropriate duration of treatment depends on the severity of the individuals' problems, the extent of their supports, and the quality of the treatment. It may range from months to indefinite maintenance.

3.3.3 Those patients who have ceased heroin use, and have established supports (such as stable housing, employment, a stable relationship, affiliation with a support group) have a better prospect of sustaining abstinence after leaving treatment, but need to be aware that relapse is common (Milby, 1988).

3.4 Staff attitudes and the therapeutic alliance

3.4.1 In the evolution of methadone treatment in the US, two broad approaches to treatment evolved. One approach tolerated ongoing drug misuse, and was labelled “adaptive” or “an orientation to maintenance”. It generally featured high-dose, indefinite duration treatment. The other approach, labelled “change oriented” methadone or “an orientation to abstinence”, usually involved lower doses of methadone and sometimes time-limited treatment. It also featured “limit-setting” - rewards for abstinence, and punishments for persisting drug use

(such as dose reductions or removal from treatment). The underlying difference between the treatment philosophies was over the extent of patient autonomy, with "change-oriented" programs seeking to direct patients towards goals of treatment, while adaptive programs gave patients more autonomy. Paradoxically, efforts to promote positive change have at times been associated with poorer treatment outcomes (Ball and Ross, 1991).

3.4.2 These data have led many clinicians to assume that attempts to push people towards change are counterproductive. On this view, OST is primarily permissive, allowing patients to detach from the cycle of dependent drug use, and to reintegrate into society insofar as they are able and motivated. However, it would be erroneous to conclude on available evidence that the poorer outcomes from abstinence-oriented treatment relate to attempts to promote rehabilitation, and a recent Scandinavian study found that programs with more rehabilitation focus produced better outcomes (Gjersing et al., 2010). Rather, the limitations of "change-oriented" OST probably relate to use of low doses of medication. A study investigating differences in heroin use between two clinics, one oriented to abstinence and having a high rate of heroin-positive urine tests, the other oriented to maintenance and with a smaller proportion of positive tests, was able to demonstrate that the difference was attributable to methadone doses prescribed (Bell et al., 1995). An adequate dose of OST is an essential ingredient of OST, and the poor outcomes from some abstinence-oriented or change-oriented programs may be largely attributable to failure to provide a dose of OST medication sufficient to suppress street heroin use.

3.4.3 There is substantial evidence that the quality of interaction between service user and staff is a critical determinant of outcome (Ball & Ross, 1991). A critical issue is to identify what constitutes a 'good therapeutic relationship'. Therapists need to believe in the treatment they are delivering. In addition, to maintain a good therapeutic relationship, therapists should also have a genuine interest and concern for clients and respond empathically towards them (Rogers, 1957).

3.4.4 By the time they present for treatment, most dependent drug users are socially marginalised, lacking access to the rewards arising from employment, good personal relationships and family participation. Treating heroin dependence frequently involves the social reintegration of marginalised individuals having few and often tenuous social connections.

3.4.5 Four decades ago, Dole and Nyswander, pioneers of methadone treatment, recognised the critical importance of changing the 'addict' identity, a change encapsulated in Marie Nyswander's phrase "From Drug Addict to Patient". Their theme was that, freed from the cycle of dependence and treated with respect and dignity, heroin users can develop a different image of themselves, and behave with self-respect and dignity. They emphasised that negative assumptions about drug users need to be balanced by a belief in their capacity to change, and a sense of the practitioner's role in fostering that change (Dole & Nyswander, 1973).

3.4.6 A positive treatment alliance and a cohesive treatment setting may be helpful and perhaps even necessary conditions for change, but they are not sufficient conditions. Cohesion and support should not be seen simply as a matter of establishing a relationship, but as involving an orientation toward specific goals and structure (Moos, 2003).

3.5 Recovery focus

3.5.1 A programme focused only on retaining people in treatment – because of the benefits this is known to bring – lacks an adequate direction for that treatment. A focus on recovery sets out treatment objectives for OST that provide direction and structure for service users and clinicians.

3.5.2 An emphasis on recovery goes further. Moos (2003) also points out that cohesive, goal-directed, and well-organised intervention programmes can help distressed individuals recover and lead essentially normal lives – but they also need a supportive, stable social context. It is difficult to sustain positive steps toward recovery for individuals who lack community support, and fostering social reintegration – especially through employment – is a critical challenge in building sustainable recovery. There is also a potentially valuable role in community groups dedicated to promoting and supporting recovery.

3.6 Counselling and psychosocial interventions

3.6.1 In the evolution of methadone treatment, two broad approaches have evolved. The model proposed by Vincent Dole was a 'medical' model of treatment, in which methadone was medication for treating an acquired disease. Many people delivering treatment rejected this explanation, preferring a 'psychotherapeutic' paradigm. The psychotherapeutic paradigm has been prominent in the UK, where many clinicians have assumed that the prescription

of opiates merely served as the lure to attract drug misusers into the treatment services. In the words of one of the leading UK addiction specialists at the time, “regular contact between the addict and the doctor ... gives the opportunity for a relationship to be built up which may eventually lead to the addict requesting to be taken off the drug” (Connell, 1969).

3.6.2 Motivation is central to addictive disorders. Heroin users only enter treatment if they perceive it as offering some advantage, and it is an accurate insight to recognise that methadone is a lure, offering respite from withdrawal, and from the rigours of addicted lifestyle. The critical difference between the ‘psychotherapeutic’ and ‘medical’ paradigms lies in different assumptions about methadone dose. ‘Medical’ treatment has generally been high-dose, indefinite maintenance, whereas psychotherapeutic MT has involved lower doses.

3.6.3 All therapy requires a rationale, conceptual scheme, or myth that provides a plausible explanation for the patient’s symptoms, and the particular rationale needs to be accepted by the client and by the therapist (but need not be ‘true’). The client and therapist must believe in the treatment, or come to believe in it (Wampold, 2001). Dole’s “metabolic” theory of addiction had little evidence to support (although research into the neurobiology of addiction now provides some evidence for lasting changes in neural networks which leave former addicts vulnerable to relapse). However, Dole’s rationale provided an explanation which formed the basis for treatment.

3.6.4 The basis of methadone is pharmacological. However, while an adequate dose of methadone is necessary, it is usually not sufficient, for effective treatment. Ball and Ross’s influential study of USA methadone programmes concluded that those with a greater range and quality of counselling services had more favourable outcomes (Ball and Ross, 1991). McLellan et al. (1993) reported that the provision of psychosocial services, in a dose-dependent fashion, contributed to better outcomes. However, another study showed no difference in outcome between new entrants to OST offered no counselling, monthly counselling, or weekly counselling (Schwartz et al., 2011). Ball and Ross also reported that most of the work of methadone clinic staff can more properly be described as casework rather than counselling. And Dole and Nyswander reported that while counselling was offered to their patients, very few availed themselves of it (Dole and Nyswander, 1973).

3.6.5 These contradictory findings underline the importance of staff having a coherent, well-accepted rationale for treatment – a treatment philosophy.

3.6.6 Possible explanations for the contradictory findings of the two randomised trials of counselling intensity are that treatment is more effective when staff believe in the treatment they are providing (Bell, 1998) and that client differences (those ready for and wanting counselling as opposed to those who aren’t and don’t) disguise the effectiveness for those able to benefit from it. Counselling should be properly and individually timed for maximum impact – offered only when clients have identified and owned concerns and issues they actually want help with.

3.6.7 NICE’s 2007 review of psychosocial interventions for drug misuse said that psychosocial interventions provide “an important element of the overall treatment package” for opioid misuse. It found good evidence that contingency management for people in OST is strongly and consistently associated with longer continuous periods of abstinence during treatment and point abstinence after six and 12 months of follow-up. Behavioural couples therapy and family based interventions were also associated with reductions in illicit drug use but relapse prevention and standard cognitive behavioural therapy (CBT) did not appear to be effective, although CBT for addressing common mental health problems was recommended. Benefits were also seen with active referral to self-help (12-step) groups, with better sustained attendance at groups after contact was actively facilitated by treatment staff (NICE, 2007d).

3.6.8 A recent Cochrane review analysed results of trials of psychosocial treatment in conjunction with OST, and found no significant benefit of adding a specific, more structured intervention to a standard psychosocial support in terms of retention, non-prescribed opioid use, psychiatric symptoms, compliance or depression. The authors suggest that more rigorous assessment may be needed to determine the subtle changes that psychosocial interventions may bring about in emotional, interpersonal, vocational and physical health areas of life functioning that may indirectly reduce drug use over longer periods of time (Amato et al., 2011).

3.7 Drug and dose

3.7.1 NICE (2007a) recommends oral formulations of methadone and buprenorphine as options for maintenance therapy in the management of opioid dependence, with the choice between the two being

determined by factors that include “the person’s history of opioid dependence, their commitment to a particular long-term management strategy, and an estimate of the risks and benefits of each treatment made by the responsible clinician in consultation with the person. If both drugs are equally suitable, methadone should be prescribed as the first choice.”

3.7.2 A dose of methadone means opioid-dependent individuals are no longer sick when they are not using heroin, and this increases their control over their heroin use (de Maeyer et al., 2011). Doses of methadone 30-50mg/day are sufficient to block withdrawal for 24 hours in the majority of dependent heroin users. However, such doses are not adequate for effective suppression of heroin use. For only around 10% of heroin users seeking treatment, respite from withdrawal is sufficient to enable them to cease drug seeking and drug use (Chan et al., 1998).

3.7.3 For those who continue to use street heroin ‘on top’, increasing the daily methadone dose increases their tolerance to opioids, attenuating the response to injected heroin. Heroin becomes less reinforcing, helping to extinguish the habit. Current UK guidelines recommend maintenance doses of 60-120mg/day, and a reasonable approach to dose setting is that after entry to treatment, methadone dose should be progressively raised until heroin use ceases, or a dose of 120mg/day is reached. Once heroin use has ceased for a period, it may be reasonable to lower the dose if side effects are problematic, but there is a likelihood that, as doses are lowered, there will be a return to heroin use (Chan et al., 1998).

3.7.4 In practice, many people report reluctance to take high doses of methadone, fearing it will make them ‘more addicted’, and less able to eventually withdraw from methadone. There is evidence which suggests that this concern may not be justified. A follow-up study of subjects treated at three clinics – two ‘high dose’ clinics (mean doses 95mg and 82mg) and one low dose clinic (mean dose 43mg) – found that, six to seven years after entry to treatment, higher doses were more likely to be associated with eventual abstinence (McGlothlin and Anglin, 1981).

3.7.5 A meta-analysis suggested that higher methadone doses, and service users having control over their doses, were independently predictive of better retention in treatment (Bao et al., 2009). This poses a dilemma for clinicians trying to suppress heroin use with higher doses, as there is a risk that this will provoke resistance among service users, and lead to

some people dropping out of treatment and returning to high-risk heroin use. While evidence supports the efficacy and safety of higher doses, it requires skill, persistence and patience to persuade some patients of the need for an effective higher dose.

3.7.6 Not everyone responds to adequate doses of methadone. Up to one third of heroin users metabolise methadone sufficiently rapidly that they experience low-grade withdrawal symptoms in the latter half of the dosing interval, when blood concentration of methadone is falling. These people experience feeling unsettled and out-of-sorts (withdrawal dysphoria), low mood, craving, and are more likely to persist in heroin use and to misuse other drugs (Dyer et al., 1999; Holmstrand et al., 1978). Increasing the methadone dose in these subjects is unlikely to be effective, as the problem is not the absolute blood concentration of methadone, but the rate at which the concentration is falling (Dyer et al., 1999). In those who have continued to use heroin despite receiving doses of methadone of 100mg/day, splitting the same daily dose into two or three –doses taken at intervals during the day, or use of an alternate agent such as buprenorphine, may be more effective in suppressing withdrawal symptoms and heroin use.

3.7.7 Methadone is more effective than buprenorphine in retaining people in treatment but buprenorphine is a valuable treatment option, firstly because some people tolerate methadone poorly and, importantly, because buprenorphine treatment is associated with a lower risk of death by overdose than methadone treatment (Bell et al., 2009). Current UK guidelines recommend buprenorphine doses in the range 12-24mg (and up to 32mg) per day.

3.7.8 For a small proportion of people, who persist in heroin use despite OST, injectable diamorphine has been shown to be effective in reducing street heroin use and improving self-reported quality of life (Strang et al., 2010; Haasen et al., 2007; Oviedo-Joekes et al., 2009). For some, who have lost family support and are so entrenched in a daily cycle of drug seeking and drug use they have little other reward in life, and little capacity to imagine things might ever be different, the transition from ‘addict’ to ‘patient’ begins a process of social reintegration that is made possible because sufficient incentive is offered to participate in structured treatment.

3.8 Supervised consumption

3.8.1 In the US, OST has always been a tightly regulated treatment system, with regulations stipulating supervision of administration, counselling,

and monitoring of treatment (Jaffe et al., 2003). In particular, the randomised trials establishing the effectiveness of methadone, buprenorphine and diamorphine treatment have all involved daily attendance for supervised administration.

3.8.2 In the 1990s, when preventing the spread of HIV among injecting drug users became the public health priority driving the expansion of treatment, 'low-threshold' treatment was introduced in several jurisdictions, with relaxed requirements for attendance and monitoring. A study of low-threshold methadone in the Netherlands found that the erratic attendance of participants did not allow doses to be raised to effective levels, and the treatment was not effective in suppressing heroin use and HIV transmission (van Ameijden et al., 1994).

3.8.3 Further moves towards unsupervised consumption have been driven by pressure to expand treatment while reducing costs. Although the benefits of supervised consumption as a behavioural component of treatment are recognised and understood by service users (Neale, 1999), it has received relatively little study. Reports from France have shown that less clinical monitoring was associated with more heroin use and more injecting of prescribed buprenorphine (Barau et al., 2001), and that less supervision was associated with worse retention and more heroin use (Auriacombe et al., 2004).

3.8.4 Supervised consumption is associated with reduced diversion, and the risk of diversion is greatest among people yet to achieve stability (housing, employment, and reduced illegal drug use).

3.8.5 Extending supervision for those still assessed as at risk needs to be balanced against the gains that can be made from letting service users control the timing and staging of their medication consumption.

4 BEYOND THE LIMITATIONS OF OST

4.1 The critical limitation of OST – and of all forms of treatment – is that individuals need long-term social supports and personal psychological resources to sustain recovery. Formal treatment can be a powerful factor in building these social supports and psychological resources to facilitate positive change, but on its own it typically does not have a lasting influence (Moos, 2003).

4.2 People need alternate rewards in their lives if they are to recover from drug dependence. The rewards of everyday life – for most people, a stable,

intimate relationship, fulfilling work, and family life – are less accessible for people marginalised, and lacking in interpersonal and vocational skills, entrenched by drug dependence.

4.3 Linking people in treatment to recovery-orientated community organisations outside of treatment is a potentially valuable way to enhance social reintegration.

4.4 There is some evidence that participation in training and employment can be fostered by treatment. One early randomised trial comparing treatment with methadone to drug-free treatment included intensive vocational retraining, and limit setting in relation to continued drug use. It demonstrated that OST, in a package with other measures, can dramatically improve social reintegration (Gunne & Grondbladh, 1981).

4.5 OST, like all forms of treatment for drug dependence, relies on motivation: willingness to accept treatment, and more importantly, the willingness, personal resources and social opportunities to take advantage of the respite from dependence to make steps towards sustained recovery. All of these factors can be enhanced by service and staff factors, and psychosocial interventions described earlier.

4.6 Unless arrested, heroin users typically only enter treatment if it is perceived to offer some advantage over their drug-using state (Gerstein et al., 1990). Often this means entering treatment during crisis, and only remaining in treatment until the crisis passes. Participation in treatment is often patchy, with people cycling in and out, having periods of heavy drug use, periods of treatment, periods of abstinence or controlled drug use, relapse to dependent use, and return to treatment (Bell, 2006). Better outcomes (reductions in heroin and other drug use, risk-taking, crime, and injection-related health problems and improvements in general physical and mental health) are associated with people remaining in a single, extended episode of treatment, rather than cycling through multiple treatment episodes (Teesson, 2007).

4.7 A focus on recovery can enhance the effectiveness of treatment through clarity of therapeutic goals. Every clinical interaction is most useful if focused on specific performance goals related to the person's circumstances (Moos, 2003). Specific treatment protocols can enhance such focus, and implementation of treatment concordant with treatment guidelines can enhance outcomes (Barnett et al., 2010).

REFERENCES

- Amato L, Minozzi S, Davoli M, Vecchi S (2011) Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence. *Cochrane Database of Systematic Reviews Issue 10*. Art. No.: CD004147. DOI: 10.1002/14651858.CD004147.pub4.
- Auriacombe M, Fatséas M, Dubernet J, et al. (2004) French field experience with buprenorphine. *American Journal on Addictions: 13(Suppl. 1)*, p. S17-S28.
- Barau K, Thirion X, Micallef J, Chuniaud-Louche C, Bellemin B, San Marco J (2001) Comparison of methadone and high dosage buprenorphine users in French care centres. *Addiction*, 96 (10); 1433-1441
- Ball JC and Ross A (1991) The effectiveness of methadone maintenance treatment: patients, programs, services and outcome. New York: Springer-Verlag.
- Barnett PG, Trafton JA, Humphreys K (2010) The cost of concordance with opiate substitution treatment guidelines. *Journal of Substance Abuse Treatment*. 39(2):141-9
- Bao YP, Liu ZM, Epstein DH, Du C, Shi J & Lu L (2009) A meta-analysis of retention in methadone maintenance by dose and dosing strategy. *The American Journal of Drug and Alcohol Abuse* 35:1,28-33
- Bell J (1998) Delivering effective methadone treatment. In Ward, J., Mattick, R.P., and Hall, W. (eds) *Methadone Maintenance Treatment and Other Opioid Replacement Therapies*. Amsterdam: Harwood Academic Publishers
- Bell J, Mattick RP, Chan J, Hay A, Hall W (1997) Methadone maintenance and drug related crime. *Journal of Substance Abuse Treatment* 9; 15-25
- Bell J, Chan J, Kuk A (1995) Investigating the effect of treatment philosophy on outcome of methadone maintenance. *Addiction*, 90; 823-830
- Bell J, Dru A, Fischer B, Levit S, & Sarfraz, MA (2002) Substitution therapy for heroin addiction. *Substance Use and Misuse* 37 (8-10); 1145-1174
- Bell J, Burrell T, Indig D, & Gilmour S (2006) Cycling in and out of treatment; participation in methadone treatment in NSW, 1990-2002. *Drug and Alcohol Dependence* 81; 55-61
- Bell J, Shanahan M, Mutch C, Rea F, Ryan A, Batey R, Dunlop A, Winstock A (2007) A randomised trial of effectiveness and cost effectiveness of observed versus unobserved administration of buprenorphine-naloxone for heroin dependence. *Addiction* 102; 1899-1907
- Bell J, Butler B, Lawrance A, Batey R, Salmelainen P (2009) Comparing overdose mortality associated with methadone and buprenorphine treatment. *Drug and Alcohol Dependence* 104; 1-2:73-77
- Chan JSK, Kuk AYC, Bell J, & McGilchrist C (1998) The analysis of methadone clinic data using marginal and conditional logistic models with mixture or random effects. *The Australian and New Zealand Journal of Statistics*, 40 (1): 1-10
- Clausen T, Anchersen K, & Waal H (2008) Mortality prior to, during and after opioid maintenance treatment (OMT); a national, prospective cross-registry study. *Drug and Alcohol Dependence* 94; 151-57
- Connell PH (1969) Drug dependence in Great Britain: a challenge to the practice of medicine. In: Steinberg, H. (Eds.), *Scientific basis of drug dependence*. London: Churchill Livingstone
- Craig R, Olson R, Shalton G (1990) Improvement in psychological functioning among drug abusers: inpatient treatment compared to outpatient methadone maintenance. *Journal of Substance Abuse Treatment*, 7; 11-19, 1990
- CSAT (2009) *Implementing Change in Substance Abuse Treatment Programs*. Technical Assistance Publication Series 31. Rockville, MD: SAMHSA
- Davoli M, Bargagli AM, Preuccil CA, Schifano p, Belleudi V, Hickman M, Salamina G, Decidue R, Vigna-Tagliante F, Faggiano F, and the VEdeTTE study group (2007) Risk of fatal overdose during and after specialist drug treatment: the VEdeTTE study, a national multi-site prospective cohort study. *Addiction*, 102, 1954-1959
- Dawson DA (1996) Correlates of past-year status among treated and untreated persons with former alcohol dependence: United States, 1992. *Alcoholism, Clinical and Experimental Research*, 20, 771-779
- De Maeyer J, Vanderplasschen W, Broekaert E (2010) Quality of life among opiate-dependent individuals: A review of the literature. *International Journal of Drug Policy* 21; 364-380

- De Maeyer J, Vanderplasschen W, Camfield L, Vanheule S, Sabbe B, Broekaert E (2011) A good quality of life under the influence of methadone: A qualitative study among opiate-dependent individuals. *International Journal of Nursing Studies* 48 (2011) 1244-1257
- Dole VP, Robinson JW, Orraca, J et al (1969) Methadone treatment of randomly selected criminal addicts. *New England Journal of Medicine* 280; 1372-75
- Dole VP, & Nyswander M (1973) Rehabilitation of patients on methadone programs. *Proceedings of the 5th National Conference on Methadone Treatment*. NAPAN, New York
- Dyer KR, Foster DJ, White JM, Somogyi AA, Menelaou A, Bochner F (1999) Steady-state pharmacokinetics and pharmacodynamics in methadone maintenance patients: comparison of those who do and do not experience withdrawal and concentration-effect relationships. *Clinical Pharmacology & Therapeutics* 65(6):685-94
- Fairbanks JA, Duntzman GH, Condelli WS (1993) Do methadone patients substitute other drugs for heroin? Predicting substance use at 1-year follow-up. *American Journal of Drug & Alcohol Abuse* 19(4):465-74
- General Accounting Office (1990) Methadone maintenance: Some treatment programs are not effective; greater federal oversight needed. Report to the chairman, Select Committee on Narcotic Abuse and Control, House of Representatives. Washington DC: General Accounting Office
- Gerstein DR, & Harwood HJ (1990) *Treating Drug Problems. Vol 1: A study of effectiveness and financing of public and private drug treatment systems*. Washington DC: National Academy Press
- Gibson AE, Doran CM, Bell JR, Ryan A, & Lintzeris N (2003) A comparison of buprenorphine treatment in specialist and primary care settings: a randomised trial. *Medical Journal of Australia* 179; 38-42
- Gjersing L, Waal H, Caplehorn JR, Gossop M, Clausen T (2010) Staff attitudes and the associations with treatment organisation, clinical practices and outcomes in opioid maintenance treatment. *BMC Health Services Research* 10:194
- Gossop M, Marsden J, Stewart D, Treacy S (2001) Outcomes after methadone maintenance and methadone reduction treatments: two-year follow-up results from the National Treatment Outcome Research Study. *Drug & Alcohol Dependence* 62(3):255-64
- Gossop M, Marsden J, Stewart D & Kidd T (2002) The National Treatment Outcome Research Study (NTORS): 4-5 year follow-up results. *Addiction* 98; 291-303
- Gossop M, Stewart D, Browne N, Marsden J (2003) Methadone treatment for opiate dependent patients in general practice and specialist clinic settings: Outcomes at 2-year follow-up. *Journal of Substance Abuse Treatment*. 24(4):313-21
- Gunne, L.M. & Grondbladh, L. (1981). The Swedish methadone maintenance programme: a controlled study. *Drug and Alcohol Dependence*, 7(3), 249-256.
- Haasen C, Verthein U and Degkwitz P (2007) Heroin-Assisted Treatment for Opioid Dependence: Randomised Controlled Trial. *Br J Psychiatry* 2007 191: 55-62
- Haastруп S & Jepsen PW (1988) Eleven year follow-up of 300 young opioid addicts. *Acta Psychiatrica Scandinavica*, 77(1), 22-26.
- Hartel DM, Shoenbaum EE, Selwyn PA, Kline J, Davenny K, Klein RS, & Friedland GH (1995) Heroin use during methadone maintenance treatment: the importance of methadone dose and cocaine use. *American Journal of Public Health* 85; 83-88.
- Holmstrand J, Anggard E & Gunne LM (1978) Methadone maintenance: Plasma levels and therapeutic outcome. *Clinical Pharmacology and Therapeutics*, 23; 175-180
- Hser YI, Hoffman V, Grella CE, & Anglin MD (2001) A 33-year follow-up of narcotics addicts. *Archives of General Psychiatry*, 58, 503-508
- Hubbard RL, Marsden ME, Rachel JV et al. (1989) *Drug Abuse Treatment: A National Study of Effectiveness*. Chapel Hill, NC: University of North Carolina Press
- Jaffe J & O'Keeffe C (2003) From morphine clinics to buprenorphine; regulating opioid agonist treatment of addiction in the United States. *Drug and Alcohol Dependence* 70; S3-S11
- Jones A, Donmall M, Millar T, Moody A, Weston S, Anderson T, Gittins M, Abeywardana V and D'Souza J

- (2009) The Drug Treatment Outcomes Research Study (DTORS): Final outcomes report 2nd Edition Research report 24. London: Home Office
- Kimber J, Copeland L, Hickman M, Macleod J, McKenzie J, De Angelis D, Robertson JR (2010) Survival and cessation in injecting drug users: prospective observational study of outcomes and effect of opiate substitution treatment. *BMJ* 340:c3172 doi:10.1136/bmj.c3172
- McGlothlin WH & Anglin MD (1981) Long-term follow-up of clients of high- and low-dose methadone programs. *Archives of General Psychiatry* 38; 1055-1063
- McLellan AT, Arndt IO, Metzger DS, Woody GE and O'Brien CP (1993) The effects of psychosocial services in substance abuse treatment. *Journal of the American Medical Association* 269(15): 1953-9.
- Magura S, Nwakeze PC, Kang S-Y, Demsky S (1999) Program quality effects on patient outcomes during methadone maintenance: a study of 17 clinics. *Substance Use & Misuse*. 34(9): 1299-1324
- Marsden J, Eastwood B, Bradbury C, Dale-Perera A, Farrell M, Hammond P, Knight J, Randhawa K, Wright C (2009) Effectiveness of community treatments for heroin and crack cocaine addiction in England: a prospective, in-treatment cohort study. *Lancet* 374; 1262-70
- Mattick RP, Breen C, Kimber J, Davoli M (2009) Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence. *Cochrane Database of Systematic Reviews*. (3):CD002209, 2009
- Milby JB (1988) Methadone maintenance to abstinence: how many make it? *Journal of Nervous and Mental Disease*, 176(7), 409-422
- Miller WR, Zweben A, DiClemente CC and Rychtarik RG (1995) *Motivational Enhancement Therapy Manual: A Clinical Research Guide for Therapists Treating Individuals with Alcohol Abuse and Dependence*. National Institute on Alcohol Abuse and Alcoholism. Project MATCH Monograph Series. Volume 2
- Moffatt S, Weatherburn D & Donnelly N (2005) What caused the recent drop in property crime? *Crime and Justice Bulletin* 85, NSW Bureau of Crime Statistics and Research, Sydney
- Moos RH (2003) Addictive Disorders in Context: Principles and Puzzles of Effective Treatment and Recovery. *Psychology of Addictive Behaviors* 17; 1: 3-12
- Moos R (2007) Theory-Based Processes That Promote The Remission of Substance Use Disorders. *Clin Psychol Rev* 27(5): 537-551
- Neale J (1999) Drug users' views of substitute prescribing conditions. *International Journal of Drug Policy* 10 (1999) 247-258
- NICE (2007a) Drug misuse: opioid detoxification. NICE clinical guideline 52
- NICE (2007b) Methadone and buprenorphine for the management of opioid dependence. NICE technology appraisal guidance 114
- NICE (2007c) Drug misuse: psychosocial interventions. NICE clinical guideline 51. London: National Institute for Health and Clinical Excellence
- NICE (2009) Needle and syringe programmes: providing people who inject drugs with injecting equipment. NICE public health guidance 18
- Orford J (2008) Asking the right questions in the right way: the need for a shift in research on psychological treatments for addiction. *Addiction* 103; 875-885
- Oviedo-Joekes E, Brissette S, Marsh DC, Lauzon P, Guh D, Anis A, Schecter MT (2009) Diacetylmorphine versus methadone for the treatment of opioid addiction. *New England Journal of Medicine* 361; 8: 777-786
- Reno RR & Aiken LS (1993) Life activities and life quality of heroin addicts in and out of methadone treatment. *International Journal of the Addictions* 28(3):211-32
- Robins L (1993) Vietnam veterans rapid recovery from heroin addiction: a fluke, or normal expectation? *Addiction* 88; 1041-1054
- Rogers CR (1957) The Necessary and Sufficient Conditions of Therapeutic Personality Change. *Journal of Consulting Psychology*, 21: 95-103.
- Romelsjo A, Engdahl B, Stenbacka M, Fugelstad A, Davstad I, Leifman A, Thiblin I (2010) Were the changes to Sweden's maintenance treatment policy

- 2000-06 related to changes in opiate-related mortality and morbidity? *Addiction* 105(9):1625-32
- Ryrie I, Ford C (2001) The primary care treatment of drug users: is shared care really the best approach? *Journal of Substance Use* 6; 3-6
- Schwartz RP, Kelly SM, O'Grady KE, Gandhi D, Jaffe J (2011) Interim methadone treatment compared to standard methadone treatment: 4-Month findings. *Journal of Substance Abuse Treatment* 41, 21-29
- Simpson DD & Sells SB (1982) Effectiveness of treatment for drug abuse: an overview of the DARP research program. *Advances in Alcohol and Substance Abuse* 2(1): 7-29
- Stimson GV (1995) AIDS and injecting drug use in the UK: the policy response and the prevention of the epidemic. *Social Science and Medicine*, 41(5), 699-716.
- Stitzer ML and Kellogg S (2008) Large scale dissemination efforts in drug abuse treatment clinics. In Higgins ST, Silverman K and Heil SH (eds.) *Contingency Management in Substance Abuse Treatment*. New York: Guilford Press
- Strang J, Metrebian N, Lintzeris N, Potts L, Carnwath T, Mayet S, et al. (2010) Supervised injectable heroin or injectable methadone versus optimised oral methadone as treatment for chronic heroin addicts in England after persistent failure in orthodox treatment (RIOTT): a randomised trial. *The Lancet* 375(9729):1885-95
- Teesson M, Mills K, Ross J, Darke S, Williamson A & Havard A (2007) The impact of treatment on 3 years' outcome for heroin dependence: findings from the Australian Treatment Outcome Study (ATOS). *Addiction*, 103, 80-88
- Torrens M, San L, Martinez A, Castillo C et al (1997) Use of the Nottingham Health Profile for measuring health status of patients in methadone maintenance treatment. *Addiction* 92(6):707-16
- Turner KME, Hutchinson S, Vickerman P et al. (2011) The impact of needle and syringe provision and opiate substitution therapy on the incidence of hepatitis C virus in injecting drug users: pooling of UK evidence. *Addiction* 106, 1978-1988
- Van Ameijden EJC, van den Hoek AAR & Couthino RA (1994) Injecting risk behaviour among injecting drug users in Amsterdam, 1986-1992, and its relationship to AIDS prevention programs. *American Journal of Public Health*, 84; 275-281
- Vaillant GE (1988) What can long-term follow-up teach us about relapse and prevention of relapse in addiction? *British Journal of Addiction*, 83(10), 1147-1157
- Wampold BE (2001) *The great psychotherapy debate: models, methods, and findings*. Lawrence Erlbaum Associates Inc.
- Zhang Z., Friedmann PD & Gerstein DR (2003) Does retention matter? Treatment duration and improvement in drug use. *Addiction*, 98, 673-684