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Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence (Review)

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TABLE OF CONTENTS

[Intervention Review]

Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

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ABSTRACT

Background

Maintenance treatments are effective in retaining patients in treatment and suppressing heroin use. Questions remain regarding the efficacy of additional psychosocial services.

Objectives

To evaluate the effectiveness of any psychosocial plus any agonist maintenance treatment versus standard agonist treatment for opiate dependence

Search methods

We searched the Cochrane Drugs and Alcohol Group trials register (June 2011), Cochrane Central Register of Controlled Trials (CENTRAL) (Issue 6, 2011), PUBMED (1996 to 2011); EMBASE (January 1980 to 2011); CINAHL (January 2003 to 2011); PsycINFO (1985 to 2003) and reference list of articles.

Selection criteria

Randomised controlled trials and controlled clinical trial comparing any psychosocial plus any agonist with any agonist alone for opiate dependence.

Data collection and analysis

Two authors independently assessed trial quality quality and extracted data.

Main results

35 studies, 4319 participants, were included. These studies considered thirteen different psychosocial interventions. Comparing any psychosocial plus any maintenance pharmacological treatment to standard maintenance treatment, results do not show benefit for retention in treatment, 27 studies, 3124 participants, RR 1.03 (95% CI 0.98 to 1.07), abstinence by opiate during the treatment, 8 studies, 1002 participants, RR 1.12 (95% CI 0.92 to 1.37), compliance, three studies, MD 0.43 (95% CI -0.05 to 0.92), psychiatric

symptoms, 3 studies, MD 0.02 (-0.28 to 0.31), depression, 3 studies, MD -1.70 (95% CI -3.91 to 0.51) and results at the end of follow up as number of participants still in treatment, 3 studies, 250 participants, RR 0.90 (95% CI 0.77 to 1.07) and participants abstinent by opioid, 3 studies, 181 participants, RR 1.15 (95% CI 0.98 to 1.36). Comparing the different psychosocial approaches, results are never statistically significant for all the comparisons and outcomes.

Authors' conclusions

For the considered outcomes, it seems that adding any psychosocial support to standard maintenance treatments do not add additional benefits. Data do not show differences also for contingency approaches, contrary to all expectations. Duration of the studies was too short to analyse relevant outcomes such as mortality. It should be noted that the control intervention used in the studies included in the review on maintenance treatments, is a program that routinely offers counselling sessions in addition to methadone; thus the review, actually, did not evaluate the question of whether any ancillary psychosocial intervention is needed when methadone maintenance is provided, but the narrower question of whether a specific more structured intervention provides any additional benefit to a standard psychosocial support. These interventions probably can be measured and evaluated by employing diverse criteria for evaluating treatment outcomes, aimed to rigorously assess changes in emotional, interpersonal, vocational and physical health areas of life functioning.

PLAIN LANGUAGE SUMMARY

Combined psychosocial and agonist maintenance interventions for treatment of opioid dependence

The abuse of opioid drugs and drug dependency are major health and social issues. Maintenance treatments with pharmacological agents can help to reduce the risks associated with the use of street drugs for drug addicts who are unable to abstain from drug use. Methadone is effective in retaining patients in treatment and reducing heroin use but re-addiction remains as a substantial challenge. Opiate addicts often have psychiatric problems such as anxiety and depression and may not be able to cope with stress. Psychosocial interventions including psychiatric care, psychotherapy, counselling, and social work services are commonly offered as part of the maintenance programs. Psychological support varies from structured psychotherapies such as cognitive behavioural therapy and supportive-expressive therapy to behavioural interventions and contingency management.

This review addressed whether a specific psychosocial intervention provides any additional benefit to pharmacological maintenance treatment. The control intervention was a maintenance program, which routinely offers counselling sessions in addition to pharmacological treatment. Present evidence suggests that adding psychosocial support does not change the effectiveness of retention in treatment and opiate use during treatment. Findings on retention in treatment were for 12 different psychosocial interventions including contingency management. These conclusions are based on 34 randomised trials involving 3777 opiate addicts, some 73% of whom were male. All but three studies were conducted in the USA.

The previous version of this review showed a reduction in opiate use during treatment that was no longer the case with the addition of new studies and the same is for the number of participants abstinent at the end of follow up. The psychosocial interventions are likely to require rigorous assessment of any changes in emotional, interpersonal, vocational and physical health areas of life functioning that may indirectly reduce drug use over longer periods of time.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Any Psychosocial intervention plus pharm versus pharm standard for treatment of opioid dependence

Patient or population: patients with treatment of opioid dependence
Settings:
Intervention: Any Psychosocial intervention plus pharm versus pharm standard

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	Any Psychosocial intervention plus pharm versus pharm standard				
Retention in treatment Objective Follow-up: mean 17 weeks	**Study population**		**RR 1.02** (0.97 to 1.07)	2582 (26 studies)	⊕⊕⊕⊕ **high**	
	683 per 1000	**696 per 1000** (662 to 730)				
	Moderate					
	738 per 1000	**753 per 1000** (716 to 790)				
Opioid abstinence objective Follow-up: mean 17 weeks	**Study population**		**RR 1.19** (0.91 to 1.56)	667 (7 studies)	⊕⊕⊕⊕ **high**	
	502 per 1000	**597 per 1000** (456 to 782)				
	Moderate					
	527 per 1000	**627 per 1000** (480 to 822)				

Number of participants still in treatment at the end of follow-up objective Follow-up: mean 3 months	**Study population**		**RR 0.9** (0.77 to 1.07)	250 (3 studies)	⊕⊕⊕⊕ **high**
	713 per 1000	**641 per 1000** (549 to 763)			
	Moderate				
	771 per 1000	**694 per 1000** (594 to 825)			
Number of participants abstinent at the end of follow-up objective Follow-up: mean 3 months	**Study population**		**RR 1.15** (0.98 to 1.36)	181 (3 studies)	⊕⊕⊕⊕ **high**
	724 per 1000	**833 per 1000** (710 to 985)			
	Moderate				
	429 per 1000	**493 per 1000** (420 to 583)			
Compliance objective Follow-up: mean 17 weeks		The mean compliance in the intervention groups was **0.43 higher** (0.05 lower to 0.92 higher)		685 (3 studies)	⊕⊕⊕○ **moderate**[1]

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: Confidence interval; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1] studies were judged at unclear risk of detection bias.

BACKGROUND

Description of the condition

Substance dependence continues to be a major clinical and social problem affecting millions of people worldwide and causing substantial costs to society.

Drug dependence has been described by the World Health Organization as "a cluster of physiological, behavioural and cognitive phenomena of variable intensity, in which the use of a psychoactive drug (or drugs) takes on a high priority. The necessary descriptive characteristics are preoccupation with a desire to obtain and take the drug and persistent drug-seeking behaviour. Determinants and the problematic consequences of drug dependence may be biological, physiological or social, and usually interact." (WHO 2009).

Abuse and dependence on opioid drugs are major health and social issues in most societies.The UNODC estimates the total number of opiates users at the global level between 15.2-21.1 million people (UNODC 2007). More than half of the world's opiates using population are thought to live in Asia. The highest levels of use (in terms of the proportion of the population aged 15-64 years) are found along the main drug trafficking routes out of Afghanistan. Trends in use appear to indicate a stabilisation of the overall number of heroin users in Europe, but recent data on drug induced deaths are mostly associated with opioid use (EMCDDA 2009). The largest heroin using population in the Americas is found in the USA where approximately 1.2 million heroin users (0.6% of the population aged 15-64) have been estimated (UNODC 2010).

Description of the intervention

Data from literature and clinical experience, suggest that methadone treatment aimed at maintenance is effective. Maintenance treatments, for those who are not yet able to achieve a drug free state, may help to reduce the risks associated with the use of street drugs.

Nevertheless a majority of patients relapse in heroin use, and relapse from the drug-free state to re-addiction is a substantial problem in the rehabilitation of dependent heroin users.

The difficulty for drug addicts in maintaining a drug-free state makes the psychological process underlying addiction particularly important in developing treatments and their importance is becoming increasingly apparent (Farrell 1994; Philips 1986).

The continued use of illicit substance reflects the drug addict's continuing inability to cope with stress. In this category of patients, the process of affective states elaboration is often delegated to an external factor such as a substance mood modifier. The substance abuse is reinforced by the positive expectancies towards the drug's effectiveness in reducing the stress due to the deficiencies in coping with situational demands (Castellani 1997).

Why it is important to do this review

The Cochrane Group on Drugs and Alcohol has conducted six reviews on maintenance treatment of opioid dependence (Clark 2002; Faggiano 2003; Ferri 2010; Minozzi 2011; Mattick 2008; Mattick, 2009). These reviews highlight that methadone maintenance at proper doses is the most effective treatment in retaining patients in treatment and suppressing heroin use but shows weak evidence of effectiveness towards other relevant outcomes such as mortality, criminal activity and quality of life. However, perhaps the only component of methadone maintenance treatment that has been conclusively evaluated is the dose level of the medication itself (Faggiano 2003). While the dose of methadone is clearly an "active ingredient" in methadone maintenance treatment, questions remain regarding the efficacy and value of the support services such as psychiatric care, psychotherapies, drug abuse counselling, urine monitoring, and social work services that are commonly offered by most maintenance programs and by all other forms of substance abuse treatment.

Psychosocial treatments for opioid dependence are a critical component of the overall treatment package and require evaluation as stand-alone interventions but also in combination with pharmacotherapies. This current review focuses on psychosocial treatments delivered in association with pharmacological maintenance treatment, to determine if the psychosocial treatments are effective in influencing adherence to treatment and in reducing relapse rates. In parallel with this review, there are two other partner reviews. The first looks at the effectiveness of psychosocial interventions plus pharmacological interventions for opioid detoxification (Amato 2011). The second looks at the effectiveness of psychosocial interventions alone for opiate dependence and abuse (Mayet 2004).

Heterogeneity of the population with substance use disorders, and the wide range of different psychosocial interventions, makes it very difficult to identify a particular therapeutic intervention as the gold-standard in this area. Hence this review will be comprehensive in the list of interventions which will be considered with the aim of including every type of psychosocial intervention provided to patients in conjunction with agonist maintenance treatment. No a priori choice will be made, since the scope of the review is to explore if psychosocial treatments contribute to the achievements of the expected outcomes, rather than ranking the different treatments. Should one of the treatments considered appear to prevail, it will be separately reviewed.

OBJECTIVES

To compare the effectiveness of the combination of psychosocial plus agonist maintenance interventions of any kind to any agonist maintenance treatments for opiate dependence, in retaining pa-

tients in treatment, reducing the use of substances and improving health and social status.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials and controlled clinical trials

Types of participants

Opiate addicts undergoing any psychosocial associated with any agonist maintenance intervention.
People less than 18 years of age and pregnant women were excluded because the pharmacological treatments for these people are often different from those offered to the general population.
No restrictions for people with physical or psychological illness.

Types of interventions

Experimental Interventions: Psychosocial plus agonist maintenance interventions of any kind (any psychosocial and any drug) compared to:
Control intervention: Any agonist treatments alone for opiate maintenance therapy.
It was intended to consider outcomes for participants using multiple drugs separately because these people may respond differently to psychosocial interventions than those with less severe problems. However, insufficient information of this nature was available to make this comparison.
Psychosocial treatments in combination with antagonist maintenance (e.g. naltrexone) treatment is not included in this review. The aims and context of antagonist maintenance are in quite different to agonist maintenance therapy and it would be complex dealing with this diversity as well as the diversity in psychosocial interventions.

Types of outcome measures

Secondary outcomes:
(1) Compliance
(2) Craving
(3) Psychiatric symptoms/psychological distress
(4) Quality of life
(5) Severity of dependence
(6) Death

Primary outcomes

1. Retention in treatment as number of participants still in treatment at the end of the study
2. Abstinence by primary substance measured as number of participants with consecutive negative urinalysis for at least three weeks
3. Results at follow-up as number of participants still in treatment at the end of follow up or opioid abstinent at the end of follow up

Secondary outcomes

1. Compliance as number of psychosocial sessions attended
2. Craving
3. Psychiatric symptoms/psychological distress
4. Quality of life
5. Severity of dependence
6. Death

Search methods for identification of studies

Electronic searches

We searched in the following electronic databases:
1. Cochrane Drugs and Alcohol Group's Register of Trials (June 2011)
2. Cochrane Central Register of Controlled Trials (CENTRAL - The Cochrane Library issue 6, 2011)
3. PUBMED (1996 to June 2011)
4. EMBASE (January 1980 to June 2011)
5. PsycINFO (1985 to April Week 1 2003)
6. CINAHL (January 2003 to June 2011)

For details on searches *see* Appendix 1; Appendix 2; Appendix 3; Appendix 4; Appendix 5;

Searching other resources

We also searched:
- Reference lists of all relevant papers to identify further studies.
- Some of the main electronic sources of ongoing trials: National Research Register; Current Controlled Trials (http://www.controlled-trials.com/); Clinical Trials.gov; Osservatorio Nazionale sulla Sperimentazione Clinica dei Medicinali (https://oss-sper-clin.agenziafarmaco.it/); Trialsjournal.com
- Conference proceedings likely to contain trials relevant to the review.We contacted investigators seeking information about unpublished or incomplete trials.

All searches included non-English language literature and studies with English abstracts were assessed for inclusion. When considered likely to meet inclusion criteria, studies were translated

Data collection and analysis

Selection of studies

One author (Amato) inspected the search hits by reading the titles and the abstracts. We obtained the full text of each potentially relevant study located in the search and two authors (Amato, Minozzi) independently assessed the articles for inclusion. Doubts were resolved through discussion Multiple publications were collated and assessed as one study.

Data extraction and management

Two authors (LA, SM) independently extracted data.Any disagreement was discussed and resolved by consensus. Key findings have been summarized descriptively in the first instance and assessed for possible meta-analysis.

Assessment of risk of bias in included studies

The risk of bias assessment for RCTs were performed using the criteria recommended by the Cochrane Handbook (Higgins 2011). The recommended approach for assessing risk of bias in studies included in Cochrane Review is a two-part tool, addressing seven specific domains, namely sequence generation and allocation concealment selection bias), blinding of participants and providers (performance bias) blinding of outcome assessor (detection bias) , incomplete outcome data (attrition bias) selective outcome reporting (reporting bias) and other source of bias. The first part of the tool involves describing what was reported to have happened in the study. The second part of the tool involves assigning a judgement relating to the risk of bias for that entry, in terms of low, high or unclear risk. To make these judgments we will use the criteria indicated by the handbook adapted to the addiction field. *See* Appendix 6 for details.

The domains of sequence generation and allocation concealment (avoidance of selection bias) were addressed in the tool by a single entry for each study.

Blinding of participants and, personnel (avoidance of performance bias) were not assessed because it was not feasible for the kind of intervention. Blinding of outcome assessor (avoidance of detection bias) were considered separately for objective outcomes (e.g. retention, abstinence measured by urine-analysis, subjects still in treatment or abstinent at the end of follow up) and subjective outcomes (e.g. side effects, social functioning as integration at school or at work, family relationship).

Incomplete outcome data (avoidance of attrition bias) were considered for all outcomes except for the drop out from the treatment, which is very often the primary outcome measure in trials on addiction. See Appendix 6 for criteria used to assess risk of bias.

Grading of evidence

The quality of evidence was assessed according to GRADE method (Guyatt 2008; Guyatt 2011), a method systematic and explicit. In order to indicate the extent to which one can be confident that an estimate of effect is correct, judgments about the quality of evidence are made for each comparison and outcome. These judgments consider study design (RCT, quasi RCT or observational study), study quality (detailed study design and execution), consistency of results (similarity of estimates of effect across studies), precision of estimates, and directness (the extent to which people, interventions and outcome measures are similar to those of interest). The following definitions in grading the quality of evidence for each outcome are used: High: further research is very unlikely to change our confidence in the estimate of effect. Moderate: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low: further research is very likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Very low: any estimate of effect is very uncertain.

Measures of treatment effect

Dichotomous outcomes (retention, abstinence by primary substance, results at follow-up) have been analysed calculating the Relative risk (RR) for each trial with the uncertainty in each result being expressed by their confidence intervals.

Continuous outcomes (compliance, psychiatric symptoms, depression) have been analysed calculating the Mean Difference (MD) with 95%CI. Weighted mean differences and 95% confidence intervals (CI) were calculated comparing and pooled the mean score differences from the end of treatment to baseline for each group. In case of missing data about the standard deviation of the change we imputed this measure using the standard deviation at the end of treatment for each group.

Unit of analysis issues

We have not used data presented as number of positive urine tests over total number of tests in the experimental and control group as measure of substance abuse. This is because using tests instead of the participants as the unit of analysis violates the hypothesis of independence among observations. In fact, the results of tests done in each participant are not independent.

If all arms in a multi-arm trial are to be included in the meta-analysis and one treatment arm is to be included in more than one of the treatment comparisons, then we divided the number of events and the number of participants in that arm by the number of treatment comparisons made. This method avoid the multiple use of participants in the pooled estimate of treatment effect while retaining information from each arm of the trial. It compromises the precision of the pooled estimate slightly.

Assessment of heterogeneity

Statistically significant heterogeneity among primary outcome studies was assessed with Chi-squared (Q) test and I-squared

(Higgins 2011). A significant Q (P<.05) and I-squared of at least 50% was considered as statistical heterogeneity.

Assessment of reporting biases

We used funnel plots (plots of the effect estimate from each study against the sample size or effect standard error) to assess the potential for bias related to the size of the trials, which could indicate possible publication bias

Data synthesis

The outcome measures from the individual trials were combined through meta-analysis where possible (clinical comparability of intervention and outcomes between trials) using a fixed-effect model unless there is significant statistical heterogeneity, in which case a random-effects model was used.

Sensitivity analysis

To incorporate assessment in the review process we first plotted intervention effects estimates stratified for risk of bias for each relevant domain. If differences in results were presents among studies at different risk of bias, we then performed sensitivity analysis excluding from the analysis studies with high risk of bias.We also performed subgroup analysis for studies with low and unclear risk of bias

RESULTS

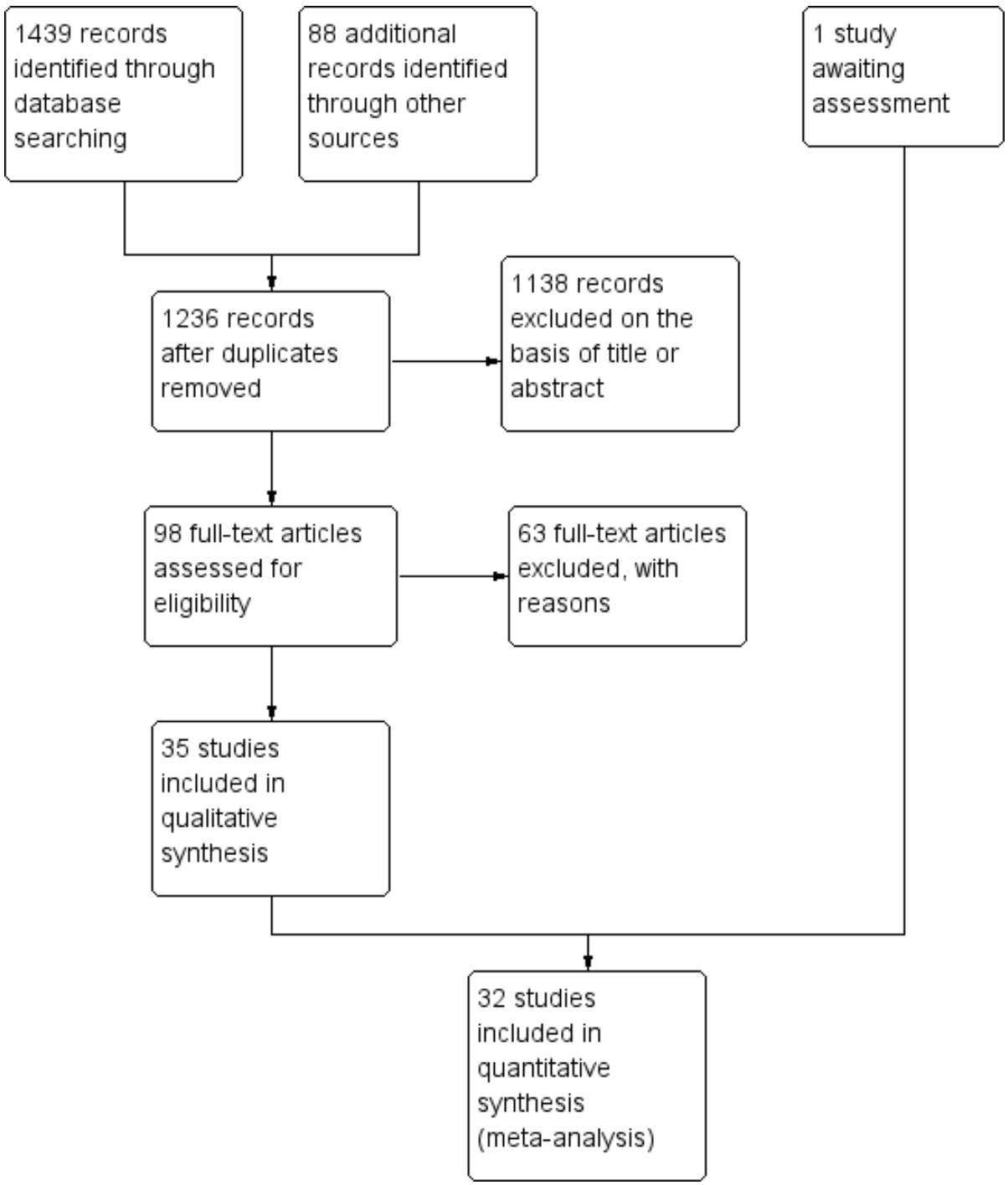
Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

The eligibility and relevance of 1138 trials was assessed on the basis of their abstracts retrieved from the electronic searches. 98 studies met the criteria of inclusion according to the abstract information and were retrieved in full text versions for a closer inspection. 63 studies were excluded, 35 included . The process of study identification and its results are outlined as a flow diagram Figure 1 according to the PRISMA statement (Moher 2009).

Figure 1. Study flow diagram.



For substantive descriptions of studies *see* Characteristics of excluded studies and Characteristics of included studies tables
This review has a parallel one on Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification (Amato 2011), the search strategies were common for the two reviews, then we separate the trials considering detoxification treatments from trial considering maintenance treatments.

Included studies

Thirty five studies, 4319 participants, met the inclusion criteria for this review, for substantive descriptions of studies *see* Characteristics of included studies .
The studies considered:

- Thirteen different psychosocial interventions;
- Three pharmacological maintenance treatment: Methadone Maintenance, Buprenorphime and LAAM

Type of psychosocial treatments:
The thirteen psychosocial interventions considered in the 34 included studies were:

- Five Behavioural interventions, twenty four studies: Acceptance and Commitment Therapy, Biofeedback, Cognitive-Behavioural Therapy, Contingency Management Approaches, Information-Motivation-Behavioral Skills Model
- Three psychoanalytic oriented interventions, four studies: Subliminal Stimulation, Supportive-Expressive Therapy, Short term Interpersonal Theray
- Three Counselling interventions,, seven studies: Customized Emplyement Support, Enhanced Methadone Services, Enhanced Pharmacy Services.
- Other interventions,, two studies: Relational Psychotherapies Mother's Group, Twelve Step Facilitation Therapy (ITSF)

For a brief description of these interventions Appendix 7.
Type of pharmacological treatments
Three pharmacological maintenance treatments: Methadone (28 studies), Buprenorphine (six studies), LAAM (one study)
Duration of the trials: range from 6 to 48 weeks, mean 17 weeks
Participants: 4319 opiate addicts: 73% were male, one study (Chawarski 2008) did not report information on gender. Average age was 35 years (range 27 to 45).
Countries in which the studies were conducted: 31 studies were conducted in USA, one in Germany and one in Malaysia, one in China, one in Scotland.
Type of comparisons

- Any psychosocial plus any pharmacological maintenance treatment versus any pharmacological maintenance treatment: 35 studies, 4319 participants.

- Any behavioural intervention plus any pharmacological maintenance treatment versus any pharmacological maintenance treatment: twenty four studies (Abbott 1998; Abrahms 1979; Avants 2004; Bickel 2008; Brooner 2004; Chopra 2009; Epstein 2009; Ghitza 2008; Gross 2006; Hayes 2004; Iguchi 1997; Khatami 1982; Kosten 2003; Milby 1978; Neufeld 2008; Oliveto 2005; Peirce 2006; Petry 2005; Petry 2007; Preston 2000; Scherbaum 2005; Silverman 2004; Stitzer 1992;

- Any psychoanalytic oriented interventions plus any pharmacological maintenance treatment versus any pharmacological maintenance treatment: four studies (Rounsaville 1983; Thornton 1987; Woody 1983; Woody 1995), 283 participants

- Any counselling intervention plus pharmacological maintenance treatment versus any pharmacological maintenance treatment:seven studies, (Chawarski 2008; Chawarski 2011; Czuchry 2009; Fiellin 2006; Magura 2007;Matheson 2010, McLellan 1993), 992 participants.

- Other psychosocial interventions plus pharmacological maintenance treatment versus any pharmacological maintenance treatment: two studies: Luthar 2000 (Relational Psychotherapy Mothers' Group) and Hayes 2004 arm b (Twelve-step facilitation), 143 participants; participants of control groups in Hayes 2004 arm b N.38 are considered twice in the statistical analysis.

For more detailed information *see* Appendix 7
Information on pharmacological doses: methadone information available for 17 out of 27, the mean dose varied from 37.6 to 100 mg/day; buprenorphine information available for all the six studies the mean doses varied from 10 to 16 mg/day; LAAM (one study) mean dose was 80 mg/3 times a week.

Excluded studies

Sixty three studies did not meet the criteria for inclusion in this review, for substantive descriptions of studies *see* Characteristics of excluded studies table
The grounds for exclusion were: type of intervention not in the inclusion criteria: 30 studies; type of participants not in the inclusion criteria: ten studies; type of outcomes not in the inclusion criteria: thirteen studies; study design not in the inclusion criteria: eight studies; type of participants and type of intervention not in the inclusion criteria: one study;

Risk of bias in included studies

Summary results across studies for each domain, Figure 2; Figure 3

Figure 2. Methodological quality graph: review authors' judgments about each methodological quality item presented as percentages across all included studies.

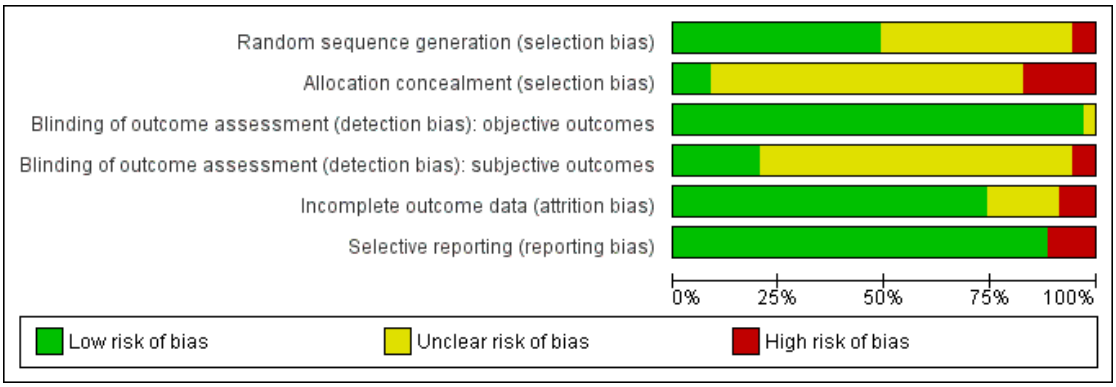
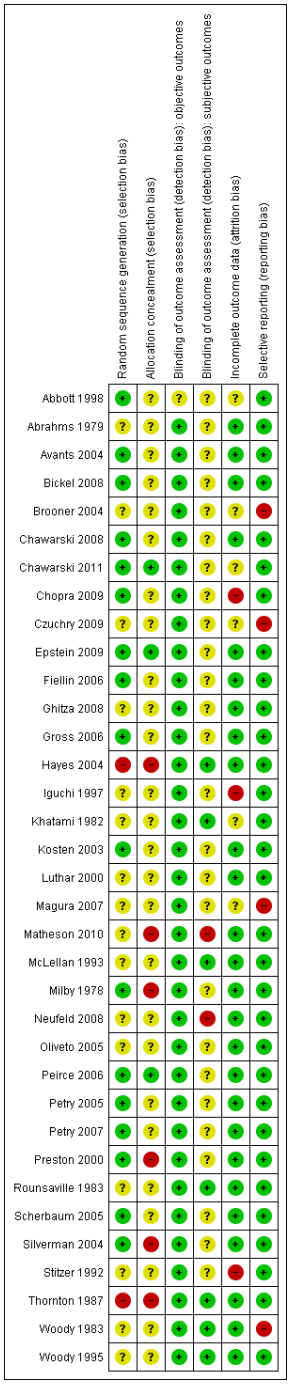


Figure 3. Methodological quality summary: review authors' judgments about each methodological quality item for each included study.



Allocation

Random sequence generation

Random sequence generation was judged as adequate in 17 studies, inadequate in two studies and unclear in the remaining trials

Allocation concealment

Only three studies were judged being at low risk of bias,three were judged at high risk of bias and remaining at unclear risk of bias

Blinding

Objective outcomes (retention, abstinence measured by patients with negative urine-analysis, still in treatment or abstinent at follow up): patients and participants were not blinded in all studies for the kind of interventions, but we judged that objective outcomes were not likely to be influenced by lack of blinding. All studies were judged to be at low risk of bias.

Subjective outcomes (Craving, Psychiatric symptoms/psychological distress, Quality of life, Severity of dependence) : patients and personnel were not blinded in all studies for the kind of interventions, 7 (20.5%) studies specified that outcome assessors were blinded and were judged to be at low risk of bias. Two studies reported that the outcome assessor was not blinding and were judged at high risk of bias; The remaining studies didn't specify if the outcome assessors were blinded and were judged at unclear risk

Incomplete outcome data

All outcomes except retention in treatment): 26 studies were judged to be at low risk of bias because there were few patients (not more than 10%) withdrawn from the studies , or there was a high rate of drop out but percentages were balanced across intervention groups and reason for withdrawn were given , or authors performed an intention to treat analysis. Three studies were judged to be at high risk of bias because of a high drop out rate unbalanced across groups and six were judged at unclear risk of bias.

Selective reporting

All included studies but four (Brooner 2004; Czuchry 2009; Magura 2007; Woody 1983) were judged as being a low risk of bias

For details, *see* risk of bias tables in Characteristics of included studies table.

Sensitivity analysis exploring the impact of risk of bias on results

Risk of bias for retention in treatment:

Considering Sequence generation and Allocation concealment, we didn't find significant difference in outcomes between studies with low and unclear risk of bias. We performed a sensitivity analysis including and excluding studies at high risk of bias, the results didn't change. For that we considered the results of all studies

Risk of bias for use of substance:

Considering Sequence generation, Allocation concealment and Incomplete outcome data, we didn't found significant difference in outcomes between studies with low and unclear risk of bias. We performed a sensitivity analysis including and excluding studies at high risk of bias, the results didn't change. For that we considered the results of all studies

Risk of bias for subjective outcomes

Because it was possible to pool data only of three studies, we couldn't explore the effect of bias on outcomes by sensitivity analysis.

Effects of interventions

See: **Summary of findings for the main comparison** Any Psychosocial intervention plus pharm versus pharm standard for treatment of opioid dependence

The results were summarized, with comparisons of quantitative data where possible, first comparing the presence of any kind of psychosocial versus pharmacological and then separately for the type of psychosocial treatment.

Eight studies had more than two arms of comparison, in this case we matched the groups with the same psychosocial intervention and the control groups if there was no psychosocial treatment. This was possible for seven out of eight studies. In one study (Woody 1983) in the first arm, participants were treated with a behavioural treatment, in the second arm with a psychoanalytic oriented treatment and in the third with a standard methadone maintenance treatment. This study was included for the first arm in the group of behavioural treatments and for the second arm in the group of psychoanalytic oriented treatment, participants of the third arm are considered twice; in any case these comparisons are kept separate preventing these participants from being counted twice. For details on the studies *see* Characteristics of included studies tables

For some outcomes reported in the included studies, it was impossible to make comparisons and pool results due the criteria adopted for reporting the results. Different rating instruments were used and for many of them the authors did not indicate the range of scores that were considered to represent mild, moderate and severe. This prevented comparison of results between studies. In addition, the results on urinalysis could not be summarised because these data were incongruous and the number of positive cases was unclear and possibly biased since the results are mainly based on number of positive tests rather than number of participants with positive tests.

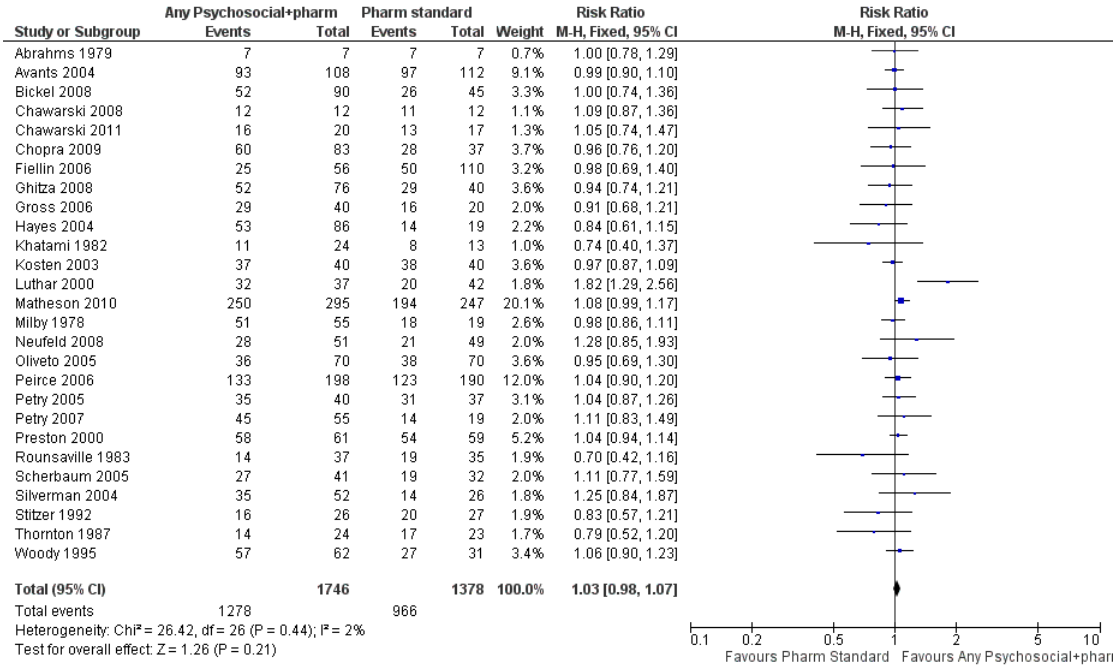
One study (Czuchry 2009) couldn't be included in any meta-analysis because the number of participants allocated to each group was not reported

1. Any Psychosocial interventions plus any pharmacological versus Standard pharmacological

1.1 Retention in treatment as number of participants still in treatment at the end of the study

Twenty seven studies, 3124 participants (Abrahms 1979; Avants 2004; Bickel 2008; Chawarski 2008;Chawarski 2011; Chopra 2009; Fiellin 2006; Ghitza 2008; Gross 2006; Hayes 2004; Khatami 1982; Kosten 2003; Luthar 2000; Matheson 2010; Milby 1978; Neufeld 2008; Oliveto 2005; Peirce 2006; Petry 2005; Petry 2007; Preston 2000; Rounsaville 1983; Scherbaum 2005; Silverman 2004; Stitzer 1992; Thornton 1987; Woody 1995), RR 1.03 (95% CI 0.98 to 1.07), the difference was not statistically significant *see* Analysis 1.1, or Figure 4

Figure 4. Forest plot of comparison: 1 Any Psychosocial intervention plus pharm versus pharm standard, outcome: 1.1 Retention in treatment.



1.2 Opioids Abstinence as Number of participants with consecutive negative urinalysis for at least three weeks:

Eight studies, 1002 participants (Abbott 1998; Avants 2004; Hayes 2004; Matheson 2010; McLellan 1993; Stitzer 1992; Thornton 1987; Woody 1995), RR 1.12 (95% CI 0.92 to 1.37), the difference was not statistically significant, *see* Analysis 1.2.

Furthermore, one study (Chopra 2009) reported the results in terms of median weeks of continuous abstinence (interquartile range): medication contingency: 6 (2,10); voucher contingency: 6 (3-12), control: 4 (2-12) ; Planned pair wise comparison revealed that both the medication and voucher contingency groups were each significantly better than standard treatment (P: 0.023 and P: 0.040 respectively). Another study (Epstein 2009) reported raw data about mean week of continuous abstinence only in a figure; in the text is reported that for patients receiving 70 mg of methadone, contingency had no effect on the frequency of opiate negative urine; For patients receiving 100 mg of methadone contingency on both opiate and cocaine negatives urine appeared to increase the frequency of opiate negative urine during the second week of intervention, but this effect quickly dissipated.

1.3 Number of participants still in treatment at the end of the follow-up

Three studies, 250 participants (Iguchi 1997; Khatami 1982;

Woody 1983), RR 0.90 (95% CI 0.77 to 1.07), the difference was not statistically significant, *see* Analysis 1.3,

1.4 Number of participants opioid abstinent at the end of the follow-up

Three studies, (Hayes 2004; Khatami 1982; Woody 1983), 181 participants, RR 1.15 (95% CI 0.98 to 1.36), the difference was not statistically significant, *see* Analysis 1.4

1.5 Compliance as number of psychosocial sessions attended

Three studies (Avants 2004; Peirce 2006; Petry 2005), MD 0.43 (95% CI -0.05 to 0.92), the difference was not statistically significant, *see* Analysis 1.5

1.6 Psychiatric symptoms/psychological distress, measured by differences (post-pre treatment) in rating of Symptom Check List -90 scale,

Three studies, (Abbott 1998; Hayes 2004; Woody 1995), MD 0.02 (-0.28 to 0.31), the difference was not statistically significant, *see* Analysis 1.6

1.7 Depression measured by differences (post-pre treatment) in rating of Beck Depression Inventory

Three studies, (Abbott 1998; Hayes 2004; Woody 1995), MD -1.70 (-3.91 to 0.51), the difference was not statistically significant, *see* Analysis 1.7

2. Any Behavioural interventions plus any pharmacological versus Standard pharmacological

2.1 Retention in treatment

Nineteen studies, 2065 participants (Abrahms 1979; Avants 2004; Bickel 2008; Chopra 2009; Ghitza 2008; Gross 2006; Hayes 2004; Khatami 1982; Kosten 2003; Milby 1978; Neufeld 2008; Oliveto 2005; Peirce 2006; Petry 2005; Petry 2007; Preston 2000; Scherbaum 2005; Silverman 2004; Stitzer 1992), RR 1.01 (95% CI 0.95 to 1.06), the difference was not statistically significant, *see* Analysis 2.1.1

Considering only Contingency Reinforcement Approaches plus any pharmacological versus Standard pharmacological

Forteen studies, 1616 participants, (Bickel 2008; Chopra 2009; Ghitza 2008; Gross 2006; Kosten 2003; Milby 1978, Neufeld 2008; Oliveto 2005; Peirce 2006; Petry 2005; Petry 2007; Preston 2000; Silverman 2004; Stitzer 1992), RR 1.02 (95% CI 0.96 to1.08), the difference was not statistically significant, *see* Analysis 2.1.2

2.2 Opioid abstinence

Four studies, 448 participants (Abbott 1998; Avants 2004; Hayes 2004; Stitzer 1992), RR 1.04 (95% CI 0.89 to 1.21), the difference was not statistically significant, *see* Analysis 2.2

2.3 Continuous weeks of abstinence

Two studies, 138 participants (Gross 2006; Silverman 2004), MD 1.91 (95% 0.20 to 3.62), in favour of the associated treatment, see Analysis 2.3

2.4 Number of participants still in treatment at the end of the follow-up

Three studies, 218 participants, (Iguchi 1997; Khatami 1982; Woody 1983), RR 0.95 (95% CI 0.80 to 1.13), the difference was not statistically significant, see Analysis 2.4

2.5 Number of participants abstinent at the end of the follow-up

Three studies, 123 participants (Hayes 2004; Khatami 1982; Woody 1983), RR 1.18 (95% CI 0.98 to 1.41), the difference was not statistically significant, *see* Analysis 2.5

3. Psychoanalytic oriented interventions plus any pharmacological versus Standard pharmacological

3.1 Retention in treatment

Three studies, 212 participants, (Thornton 1987; Rounsaville 1983; Woody 1995), RR 0.90 (95% CI 0.75 to 1.07), the difference was not statistically significant, *see* Analysis 3.1

3.2 Opioid abstinence

Two studies, 127 participants (Thornton 1987; Woody 1995) RR 1.21 (95% CI 0.82 to 1.78), the difference was not statistically significant, see Analysis 3.2

4. Counselling plus any pharmacological versus Standard pharmacological

4.1 Retention in treatment

Four studies, 769 participants (Chawarski 2008;Chawarski 2011 Fiellin 2006, Matheson 2010), RR 1.07 [0.98, 1.15], the difference was not statistically significant, see Analysis 4.1

4.2 Opioid abstinence

One study, 335 participants (Matheson 2010) RR 0.98 [0.85, 1.14] the difference was not statistically significant, see Analysis 4.2

We added a Summary of findings for the main comparison to grade the quality of the evidence for the comparison "any Psychosocial interventions plus any pharmacological versus Standard pharmacological".

DISCUSSION

Summary of main results

Thirty five studies, 4319 participants, were included. These studies considered twelve different psychosocial interventions and three pharmacological maintenance treatments: Methadone, Buprenorphine, LAAM.

Comparing any psychosocial plus any maintenance pharmacological treatment to standard maintenance treatment, results do not show benefit for retention in treatment, 26 studies, 2582 participants, RR 1.03 (95% CI 0.98 to 1.07), abstinence by opiate during the treatment, 8 studies, 1002 participants, RR 1.12 (95% CI 0.92 to 1.37), compliance, measured as number of psychological sessions attended, three studies, MD 0.43 (95% CI -0.05 to

0.92), psychiatric symptoms, measured by differences (post-pre treatment) in rating of Symptom Check List -90 scale, 3 studies, MD 0.02 (-0.28 to 0.31), depression, measured by differences (post-pre treatment) in rating of Beck Depression Inventory, 3 studies, MD -1.70 (95% CI -3.91 to 0.51) and results at the end of follow up as number of participants still in treatment, 3 studies, 250 participants, RR 0.90 (95% CI 0.77 to 1.07) and participants abstinent by opioid, 3 studies, 181 participants, RR 1.15 (95% CI 0.98 to 1.36). The remaining outcomes were analysed only in single studies considering a limited number of participants.

Comparing the different psychosocial approaches, results are never statistically significant for all the comparisons and outcomes and this is true also for contingency approaches, contrary to all expectations. In fact results on retention in treatment for the 14 studies, 1616 participants, that considered contingency management approaches do not show any additional benefit in adding this intervention: RR 1.02 (95% CI 0.96 to1.08).

Duration of the studies was too short to analyse relevant outcomes such as mortality.

The previous versions of this review showed a reduction in opiate use during treatment that was no longer the case with the addition of new studies and the same is for the number of participants abstinent at the end of follow up.

Overall completeness and applicability of evidence

It should be noted that the control intervention used in the studies included in this review is a program that routinely offers counselling sessions in addition to pharmacological therapy; thus the present review did not evaluate the question of whether any ancillary psychosocial intervention is needed when pharmacological maintenance treatment is provided but the narrower question of whether a specific more structured intervention provides any additional benefit to a standard psychosocial support.

These interventions probably can be measured and evaluated by employing diverse criteria for evaluating treatment outcomes, aimed to rigorously assess changes in emotional, interpersonal, vocational and physical health areas of life functioning.

It is also worth mentioning that, like other patients who have been treated with some kind of psychotherapy, opiate addicts have significant psychiatric problems especially in the areas of depression and anxiety. To the extent that drug use is an attempt to self-medicate for these problems and to the degree that psychosocial intervention, especially psychotherapy, can reduce them, psychotherapy can, perhaps, reduce drug use indirectly in these people. Nevertheless to evaluate these effects it is necessary to observe these patients for long periods and to develop methods for standard assessments of specific outcomes.

Regarding the applicability it is probably good but it is important to note that 26/28 studies were conducted in the USA and this is a limit to the generalisability of the results because health effects of various substances of abuse seem to be strongly dependent on social context, and the location of the conduct of the studies could act as an effect modifier in the estimation of efficacy of treatment.

Quality of the evidence

Limitation in the study design:

Methodological quality of included studies was quite good: half of the studies had an adequate sequence generation and only two (5.8%) had it inadequate; 29/34 studies had an unclear allocation concealment and three had inadequate allocation concealment. None of the studies were double blind due to the kind of intervention assessed (psychosocial) which cannot be blinded. 20.5% of studies declared that the outcome assessor was blind. 76% of studies were judged at unclear risk of detection bias. For risk of bias related to incomplete outcome data, 73.5% of studies were judged to be at low risk of bias.

Considering risk of bias at an outcome level, we judged that objective outcomes (retention in treatment, use of substances) were at low risk of bias because they were not likely to be influenced by lack of blinding and because considering sequence generation and allocation concealment, we didn't found significant difference in results between studies with low and unclear risk of bias. Moreover, performing a sensitivity analysis including and excluding studies at high risk of bias, the results didn't change. For subjective outcomes nevertheless 76% of studies were judged at unclear risk of detection bias.

Indirectness of the evidence:

None of the included studies included indirect population, interventions, controls or outcomes, so we judged that the level of the body of evidence wasn't downgraded by this limitation.

Inconsistency in the results:

We didn't find unexplained heterogeneity or relevant inconsistency in the results.

Imprecision of the results:

Results for primary outcomes were not imprecise, whereas results of secondary outcomes had wide confidence intervals due to the low number of included studies and the small number of participants

The quality of evidence of any psychosocial plus any pharmacological Intervention versus any pharmacological standard, assessed according to GRADE method, be judged as high for dichotomous outcomes (retention, abstinence, results at follow up, compliance and moderate for dichotomous outcomes (compliance) see Summary of findings for the main comparison

Potential biases in the review process

A particularly important component of a review is the identification of relevant studies. Publication bias has long been recognised as a problem in this regard since it means that the likelihood of

finding studies is related to the results of those studies. One way to investigate whether a review is subject to publication bias is to prepare a funnel plot and examine this for signs of asymmetry. Funnel plot (plot of the effect estimate from each study against the sample size or effect standard error) was used to assess the potential for bias related to the size of the trials, demonstrating low probability of publication bias *see* Figure 4

Agreements and disagreements with other studies or reviews

Results of the parallel review on detoxification treatment (Amato 2011) shows more benefits of adding psychosocial interventions to the pharmacological one. This may be due to the most robust effects of methadone maintenance treatment itself, as compared to detoxification treatment and possibly to the fact that additional counselling is usually offered as well along with methadone maintenance and not with detoxification. Another possible explanation is that participants in detoxification are less stable - it is usually a personal crisis that brings them into detoxification - and they have more psychological issues that need to be dealt with. If psychosocial interventions delivered in association with detoxification helps them to deal with these issues, then it seems reasonable to expect that the provision of associated psychosocial interventions might improve the outcomes of detoxification.

AUTHORS' CONCLUSIONS

Implications for practice

For the considered outcomes, it seems that adding any psychosocial support to maintenance treatments do not add additional benefits. Data do not show differences between different psychosocial interventions also for contingency approaches, contrary to all expectations. Duration of the studies was too short to analyse relevant outcomes such as mortality.

It should be noted that the control intervention used in the studies included in the review on maintenance treatments, is a program that routinely offers counselling sessions in addition to methadone; thus the review, actually, did not evaluate the question of whether any ancillary psychosocial intervention is needed when methadone maintenance is provided, but the narrower question of whether a specific more structured intervention provides any additional benefit to a standard psychosocial support. These interventions probably can be measured and evaluated by employing diverse criteria for evaluating treatment outcomes, aimed to rigorously assess changes in emotional, interpersonal, vocational and physical health areas of life functioning.

It was not possible to find a specific psychosocial intervention with strong efficacy, in fact data do not show differences between different interventions also for contingency approaches, contrary to all expectations.

It is also worth mentioning that, like other patients who have been treated with some kind of psychotherapy, opiate addicts have significant psychiatric problems especially in the areas of depression and anxiety. To the extent that drug use is an attempt to self-medicate for these problems and to the degree that psychosocial intervention, especially psychotherapy, can reduce them, psychotherapy can, perhaps, reduce drug use indirectly in these people. Nevertheless to evaluate these effects it is necessary to observe these patients for long periods and to develop methods for standard assessments of specific outcomes.

Eventually, the results of the review on maintenance treatments clearly show that provision of methadone maintenance treatment should not be abandoned in the absence of resources for additional psychosocial treatment.

Implications for research

Eventually the review shows that psychosocial interventions can be evaluated in the context of randomised controlled trials, even though in order to study possible added value of any psychosocial treatment over an already effective treatment such as maintenance pharmacological interventions, only big multi site studies could be considered which define experimental interventions and outcomes in the most standardized way possible.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Abbott 1998

Methods	Randomised controlled trial. Patients recruited from consecutive admissions to a large urban drug treatment centre;
Participants	180 opiate dependent (DSM-III-R), residing stably in USA, age 18 or older, eligible for MMT according FDA requirements Exclusion Criteria: Acute psychosis, pregnancy, discharge from treatment at the centre within the past 6 months, grosses cognitive impairment Analysis on 166 (1) N 103, (2) N 63. Average age 37; 69% men; 79% Hispanic; mean use of heroin 11.73 years, mean use of cocaine 1.43 years, mean problematic alcohol use 4.13 years; 27% married, 39% widowed, divorced or separated, 34% single; average years of educational level 11.51, 33% < high school, 51% high school, 16% > high school; 55% employed, 31% unemployed, 14% not employed due to recent incarceration; 23% referred by probation
Interventions	All MMT 1. N= 103, Methadone mean 70.46 mg/day plus CM (CRA). 2. N= 63, Methadone mean 67.80 mg/day plus standard clinic counselling. For both weekly random urine drug screen with feed back. Duration 8 months + 6 months follow-up.
Outcomes	Retention in treatment assessed using a survival analysis. No data on the groups. Use of primary substance of abuse as % of opiate negative urine samples and as number of participants opiate negative for three consecutive weeks. Severity of dependence as ASI (mean composite scores) and as Risk Assessment Battery
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants were randomly assigned to one of the three treatment groups by a permuted block design. Bloks were formed by five dichotomized control factors: gender, ethnicity, ASI drug abuse, ASI psychiatric severity, admission mandated by criminal justice system
Allocation concealment (selection bias)	Unclear risk	Participants randomised within these blocks to balance the factors between treatment groups

Abbott 1998 (*Continued*)

Blinding of outcome assessment (detection bias) objective outcomes	Unclear risk	Research assistant, blind to treatment assignment, administered all assessment instruments
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Research assistant, blind to treatment assignment, administered all assessment instruments
Incomplete outcome data (attrition bias) all outcomes a part retention	Unclear risk	Of the 180 subjects who were randomly assigned, 166 were engaged in treatment. COMMENT: reason not given, not specified the number of subjects withdrawn from each group; the treatment outcome results are reported for the group which were followed for 6 months (91%)
Selective reporting (reporting bias)	Low risk	

Abrahms 1979

Methods	Randomised controlled trial. Patients recruited in a Methadone Maintenance Unit. Groups similar for drug use and demographic data
Participants	14 opiate dependent in MMT Average age 28; 87% men; 47% African-American, 53% White, mean number of previous treatments 2,5; mean use of drugs/alcohol 8 years; months of methadone maintenance treatment 9; 29% married; 64% high school; 100% history of criminal charges
Interventions	All MMT, no information on doses 1. N= 7 2 hour sessions of Cognitive-Behavioural Therapy per week 2. N= 7 Unstructured group discussion used as waiting list.
Outcomes	Use of primary substance as % of contaminated samples. Compliance as group attendance (scores). Psychiatric symptoms/psychological distress as: Internal-External Locus of Control, Interpersonal Trust, State-Trait Anxiety, Social Desirability, Depression, Assertion, Pleasant Events (all scores). Quality of life as % employed and/or academically involved
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Participants who completed the baseline test materials were randomly assigned to either the CB group or a nondirective meth-

Abrahms 1979 (*Continued*)

		adone maintenance group
Allocation concealment (selection bias)	Unclear risk	Participants who completed the baseline test materials were randomly assigned to either the CB group or a nondirective methadone maintenance group
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	No withdrawal from the study
Selective reporting (reporting bias)	Low risk	

Avants 2004

Methods	Randomised controlled study. Recruitment modality: patients who agreed to participate from 251 eligible consecutive admission to a inner city methadone maintenance programs
Participants	220 opiate dependent seeking methadone treatment Incl criteria: at least 18 years old, injecting drug users, not active suicidal, homicidal or psychotic 24% of the sample first time in methadone treatment. Mean Age (1)37.8 (2)36.0 years; Males (1)67% (2)70%; Race: White (1)66.7% (2)65.2%, African American (1)16.7% (2)14.3%, Hispanic (1)16.7% (2) 18.8%, Other minority (2)9%; Mean years of education (1)11.9 (2) 11.7; Employed full time (1)13.9% (2)18.8%; Mean years of opiate use (1)12.8 (2)12.3; cocaine users (1)79% (2)72%; Mean years of cocaine use (1)12.1 (2)11.5
Interventions	All MMT average dose 85.5 mg/day; 1. N= 108, Information-Motivation-Behavioural Skills Model; 2. N= 112, Standard care Duration 12 weeks.
Outcomes	Retention in treatment, use of opiates as at least three weeks with drug free urine, compliance
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

Avants 2004 (*Continued*)

Random sequence generation (selection bias)	Low risk	Participants were randomly assigned to one of two treatment conditions using a computerized randomisation program
Allocation concealment (selection bias)	Unclear risk	Participants were randomly assigned to one of two treatment conditions using a computerized randomisation program
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	All primary outcome analysis were conducted on the intention to treat sample defined as patients who attended at least one treatment session
Selective reporting (reporting bias)	Low risk	

Bickel 2008

Methods	randomised controlled trial
Participants	135 volunteer outpatients who met the DSM-IV criteria for opioid dependence; mean age: 29 years; male: 56%
Interventions	Buprenorphine maintenance for all patients: maintenance dose of either 6, 12, or 18 mg of buprenorphine/naloxone 1. Therapist delivered behavioral treatment based on CRA (community reinforcement approach) plus voucher based contingency management 2. Interactive self delivered computer based behavioral treatment based on CRA (community reinforcement approach) plus voucher based contingency management 3. Standard counselling Duration of the intervention: 23 weeks
Outcomes	retention in treatment, opioid and cocaine abstinence
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	Authors' judgement	Support for judgement

Bickel 2008 (*Continued*)

Random sequence generation (selection bias)	Low risk	quote: patients were randomly assigned to one of the three maintenance treatments using a computer generated stratified randomisation procedure"
Allocation concealment (selection bias)	Unclear risk	information not reported
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	drop out did not significantly differed across conditions
Selective reporting (reporting bias)	Low risk	

Brooner 2004

Methods	Randomised controlled trial. recruitment modality: "study participants were opioid-dependent patients new admitted to an outpatient treatment program in Baltimore
Participants	127 opioid dependent (DSM III-R); Mean age 38.2 years, males 46%, White 37%, African-American 63%; Current married 11%; average educations 11.4 years; unemployed 75%; almost 50% current diagnosis of cocaine dependence
Interventions	For all MMT mean dose across the study 60 mg/day 1. N= 65 CM (Motivated stepped care with behavioural contingencies); 2. N= 62 Standard stepped care. Duration 6 weeks
Outcomes	Treatment response, counselling attendance; use of substances
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Participants were randomly assigned to the MSC or the SSC control condition, after being stratified on baseline rates of cocaine positive urine specimens and lifetime psychiatric comorbidity status

Brooner 2004 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Participants were randomly assigned to the MSC or the SSC control condition, after being stratified on baseline rates of cocaine positive urine specimens and lifetime psychiatric comorbidity status
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Unclear risk	Information on drop out from the study not given
Selective reporting (reporting bias)	High risk	Data on retention in treatment not reported

Chawarski 2008

Methods	Randomised controlled trial. Recruitment modality: not described
Participants	24 opioid dependent (DSM IV) with positive urine toxicologic test, aged 18-65 years Excl Cr: Alcohol or benzodiazepines dependence, greater that three times normal liver enzymes, current suicide/homicide risk, current psychotic disorder, major depression, life-threatening or unstable medical problem
Interventions	For all BMT range 12-16 mg/day. 1. N= 12 Enhanced Methadone Services (nurse-delivered manual-guided behavioral drug and HIV risk reduction counselling (BDRC); 2. N= 12 Standard services. Duration 10 weeks.
Outcomes	Retention in treatment; use of opiates as long period of abstinence in weeks
Notes	Country of origin: Malaysia. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants were randomly assigned using a computer-generated simple randomisation procedure to either standard services or enhanced services

Chawarski 2008 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Participants were randomly assigned using a computer-generated simple randomisation procedure to either standard services or enhanced services
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	Only one participant in the standard service group drop out from study
Selective reporting (reporting bias)	Low risk	

Chawarski 2011

Methods	randomised controlled trial
Participants	37 heroin dependents patients enrolling in two MMT clinics; mean age: 36.5; male: 81%
Interventions	for all MMT 45 mg daily 1. N= 20 Behavioral drug and HIV risk reduction counselling (BDRC) 2. N= 17 MMT only duration of intervention: three months
Outcomes	retention in treatment, use of substance of abuse
Notes	Country of origin: China, Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	quote: " patients were randomly assigned to condition using a simple randomisation procedure: a computer generated randomisation list in the US was used and randomisation codes were provided to the research personnel in China on the day of randomisation"
Allocation concealment (selection bias)	Low risk	quote: "a computer generated randomisation list in the US was used and randomisation codes were provided to the research personnel in China on the day of randomisation"

Chawarski 2011 (*Continued*)

Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Unclear risk	no significant difference in drop out rate between groups
Selective reporting (reporting bias)	Low risk	

Chopra 2009

Methods	randomised controlled trial
Participants	120 opioid dependent patients; mean age: 31 years, male: 58%,
Interventions	For all buprenorphine maintenance . doses of 12-18 mg daily 1. N= 42 Medication contingency condition with CRA (community reinforcement Approach) : thrice weekly dosing schedule vs. daily attendance and single-day 50% dose reduction imposed upon submission of an opioid and/ or cocaine positive urine sample 2. N= 41 Voucher contingency with CRA: escalating schedule for opioid and/ or cocaine negative samples with reset for drug-positive samples 3. N= 37 Programmed consequences for urinalysis results duration of the intervention: 12 weeks
Outcomes	retention in treatment;continuous week of abstinence
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	quote: " participants were randomly assigned to one of three treatment grups using minimum likelihood allocation (Aickin 1982). This method of permutation has been shown to achieve balance between treatment groups on patients characteristics likely to influence treatment outcome. Three characteristics were used to stratify patients: stabilization dose of buprenorphine, cocaine use in the past month, distance from the clinics
Allocation concealment (selection bias)	Unclear risk	information not reported

Chopra 2009 (*Continued*)

Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	High risk	"the proportions of patients completing the trial was significantly different among groups;
Selective reporting (reporting bias)	Low risk	

Czuchry 2009

Methods	randomised controlled trial
Participants	82 opioid dependent patients admitted to a private, for profit methadone maintenance clinic; mean age: 40 years; male: 70%; African American: 16%, Hispanic: 63%, white: 21%
Interventions	For all methadone maintenance; 1. N= Not reported Free map counselling: counsellors and clients cooperatively construct a node-link display over the course of counselling session. A marker board or large sheet of paper is used to provide a shared visualization.. The results display is reviewed and modified in subsequent session. 2. N= Not reported Free plus guide mapping: utilisation of a preformed "fill in the node" mapping which could halp patients and counsellors in examining treatment related issues 3. N= Not reported Treatment as usual
Outcomes	opiate use
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	quote: " patients were randomly assigned to condition"
Allocation concealment (selection bias)	Unclear risk	information not reported
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding

Czuchry 2009 (*Continued*)

Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Unclear risk	information not reported
Selective reporting (reporting bias)	High risk	no information on retention in treatment

Epstein 2009

Methods	randomised controlled trial
Participants	252 heroin and cocaine abusing patients; mean age: 38 years, male: 48%, African American: 66%
Interventions	1. N= 49 MMT 70 mg daily plus voucher for cocaine abstinence 2. N= 47 MMT 70 mg daily plus voucher for cocaine and heroin abstinence 3. N= 30 MMT 70 mg daily plus voucher non contingent 4. N= 38 MMT 100 mg daily plus voucher for cocaine abstinence 5. N= 47 MMT 100 mg daily plus voucher for cocaine and heroin abstinence 6. N= 31 MMT 100 mg daily plus voucher non contingent Duration of the intervention: 12 weeks
Outcomes	retention in treatment, use of substance
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	quote: " participants were first randomised to contingency management condition by a study technician who used a Microsoft Excel macro that stratified randomisation by race, sex, employment status, probation status, frequency of opiate and cocaine positive urine during baseline. Participants were then randomised to a dose condition using a similar macro with identical stratification variables"
Allocation concealment (selection bias)	Low risk	quote "randomisation was done by an investigator who had no contact with participants. Dose assignment were known only to her and to a in-house pharmacy staff who also had no contact with participants"
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding

Epstein 2009 (*Continued*)

Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	no significant difference in drop out rate among conditions
Selective reporting (reporting bias)	Low risk	

Fiellin 2006

Methods	Randomised controlled trial. recruitment modality: not described
Participants	166 opioid dependent (DSM IV) that met criteria for opioid agonist maintenance treatment Excl Cr:dependent on alcohol, benzodiazepines, sedatives; dangerous to themselves or others; psychotic or with major depression; unable to comprehend English; life-threatening medical problem; women of childbearing age agreed to use contraception and undergo monthly pregnancy monitoring Age (1) 35.1(2)36.4; White 127; full employed 79; high school graduate 134; never married 95
Interventions	For all BMT+naloxone combination (tablets which include buprenorphine and naloxone in a 4:1 ratio, average dose of buprenorphine 16 mg/day 1. N= 56 Enhanced Medical Management 2. N= 110 Standard Medical Management. Duration 24 weeks
Outcomes	Retention in treatment, use of opiate, use of cocaine, patient satisfaction, adherence to pharmacological treatment
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	An urn randomisation procedure were used to ensure that the groups were similar with regard to sex ratio, employment status, presence of cocaine abuse and presence of personality disorders
Allocation concealment (selection bias)	Unclear risk	An urn randomisation procedure were used to ensure that the groups were similar with regard to sex ratio, employment status, presence of cocaine abuse and presence of

Fiellin 2006 (*Continued*)

		personality disorders
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	High drop out rate. reason for drop out given for each group. drop out patients balanced among groups
Selective reporting (reporting bias)	Low risk	

Ghitza 2008

Methods	randomised controlled trial
Participants	116 heroin and cocaine users admitted to methadone maintenance treatment.Mean age: 37 years, male 56%; African American : 47%
Interventions	for all methadone maintenance ; daily maintenance dose ranged from 70 to 100 mg, adjusted based on feedback from the participant and on the clinical judgment of the staff. 1. N= 76 Contingent management for drug abstinence 2. N= 40 Methadone maintenance duration: 25 weeks
Outcomes	retention in treatment
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	quote "subjects were randomly assigned to experimental or control group: Randomisation was stratified by race, sex, employment status, probation status, frequency of opiate and cocaine positive urine at baseline"
Allocation concealment (selection bias)	Unclear risk	information not reported
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding

Ghitza 2008 (*Continued*)

Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	analysis done by the intention to treat principle
Selective reporting (reporting bias)	Low risk	

Gross 2006

Methods	Randomised controlled trial . Recruitment modality: "patients were recruited via a variety of advertisements"
Participants	60 opioid dependent (DSM-UIV), 18 years or older, in good health, met criteria for agonist maintenance treatment Exc Cr: evidence of acute psychosis or serious medical illness; pregnancy Males 33; Mean age 32.5 years; White 90%
Interventions	For all BMT 8-16 mg/day; 1. N= 20 CM voucher group; 2. N= 20 CM medication contingency; 3. N= 20 Standard treatment. Duration 12 weeks
Outcomes	Retention in treatment; use of opiates as weeks of continuous abstinence, use of cocaine, ASI scores
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants were randomly assigned to one of three treatments groups using minimum-likelihood allocation. This method was designed to achieve balance between treatment groups on patients characteristics likely to influence outcomes. Five characteristics were used to stratify patients: buprenorphine maintenance dose, history of injection use, gender, prior history of buprenorphine treatment, presence or not of cocaine use

Gross 2006 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Participants were randomly assigned to one of three treatments groups using minimum-likelihood allocation. This method was designed to achieve balance between treatment groups on patients characteristics likely to influence outcomes. Five characteristics were used to stratify patients: buprenorphine maintenance dose, history of injection use, gender, prior history of buprenorphine treatment, presence or not of cocaine use
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	20% of drop out. Reason for withdrawn not given. "there were no significant difference in the percentages of patients who completed the trial (X^2: 1.6; p= 0.49)
Selective reporting (reporting bias)	Low risk	

Hayes 2004

Methods	Randomised controlled trial. recruitment modality: patients who received methadone for at least 60 days and who had used opiates during that time were recruited from one of three community-based methadone clinics
Participants	124 opioid dependent (DSM IV), who had received MMT for at least 60 days and who had used opiates during that time Exc Cr: current DSM IV diagnosis of schizophrenia, schizoaffective disorder, psychosis not other specified, bipolar affective disorder, imminent criminal justice proceedings that might result in incarceration during the treatment Males 49%; ethnic minorities 13%; on average 42.2 years old; single 72%; unemployed 60%; mood disorder 40%; anxiety disorder 42%; dependent on alcohol 35%; cocaine 46%; other drugs 35%
Interventions	For all MMTdoses not reported; 1. N= 42 Acceptance and Commitment Therapy 2. N= 44 Intensive Twelve Steps Facilitation 3. N= 38 Standard care. Duration 16 weeks

Hayes 2004 (*Continued*)

Outcomes	Retention in treatment, use of opiates as number of subjects with urine negative at the end of treatment and at follow up; psychiatric symptoms/psychological distress measured with Beck Depression InventorY and with Symptom Check List-90
Notes	Country of origin: USA. Setting: outpatients The participants in the Standard care Group (n. 38) are considered both in arm a and in arm b

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Participants were randomly assigned in sequential waves of three to MM, ACT, ITSF
Allocation concealment (selection bias)	High risk	Participants were randomly assigned in sequential waves of three to MM, ACT, ITSF
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	All assessment were carried out by a team of assessors blind to the treatment condition of participants
Blinding of outcome assessment (detection bias) subjective outcomes	Low risk	All assessment were carried out by a team of assessors blind to the treatment condition of participants
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	At post, outcome data were available for 57%, 59% and 74% of each group, a non significant difference (Pearson X^2 2.76, p: ns). At follow up, outcome data were available for 43%, 57% and 68% of each group, which is also non significant, but barely so (Pearson X^2 5.49, p:<0.07)
Selective reporting (reporting bias)	Low risk	

Iguchi 1997

Methods	Randomised controlled trial. Recruitment modality: all patients admitted at the methadone maintenance treatment at a clinic. Groups similar for drug use and demographic data
Participants	103 opiate dependent at least 1 year of opiate use. Ex C: Significant medical condition, symptoms of active psychosis, involved in drug treatment within the past month Average age 36; 63% men; 85% White, 12% African-American; 3% Hispanic; mean use of heroin 5.8 years; 33% married, 17% widowed, divorced or separated, 50% single;

Iguchi 1997 (*Continued*)

	average years of educational level 11.4; 34% employed full time, 5% employed part time, 57% unemployed, 1% home workers, 1% retired, 2% disabled
Interventions	For all MMT, subjects stabilized for 6 weeks on methadone than randomised, (no information on doses), plus regularly scheduled individual counselling sessions along with a system of privilege levels for determining take home medication eligibility 1. N= 68 CM (vouchers for each free urine up to 30 vouchers per week or 30 vouchers per week for completing objectively defined and clearly verifiable treatment plan task. The tasks were weekly tailored on patient's characteristics) 2. N= 35 Control. Duration 12 weeks plus 12 weeks follow-up.
Outcomes	Results at follow-up as % of dropouts at the end of follow-up. Use of primary substance of abuse as % of drug-free urine samples. Compliance as clinic Attendance (mean number of counselling sessions attended)
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Participants were randomly assigned to one of the three treatment protocol
Allocation concealment (selection bias)	Unclear risk	Participants were randomly assigned to one of the three treatment protocol
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	High risk	Total attrition at the end of the study was 22%9 for the STD group and 33.3% for the UA group. COMMENT: high rate of drop out and unbalanced between group
Selective reporting (reporting bias)	Low risk	

Khatami 1982

Methods	Randomised controlled trial. Recruitment modality: drawn from the outpatient methadone clinic. Groups similar for drug use and demographic data.
Participants	37 opiate dependent, receiving maintenance doses of methadone for no more than 2 weeks Average age 29.5; 100% men; 43% not White; mean use of heroin 7.7 years; 65% high school; 32% employed
Interventions	For all MMT, mean dose 39.5 mg/day plus routine clinic counselling and ancillary therapies 1. N= 24 Biofeedback, 15 sessions. 2. N= 13 Control, 15 pseudo bio feed-back sessions in which participants had a recording of another individual biofeedback responses. Duration 15 sessions + 1 month follow-up
Outcomes	Retention in treatment as % of participants that completed all 15 sessions of treatment. Results at follow-up as no. of participants relapsed at 1 month only on participants that completed the 15 session, and as no. of participants in MMT at 1 month. Psychiatric symptoms/psychological distress as scores
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Those interested in participating were randomly assigned to either an experimental group or a control group
Allocation concealment (selection bias)	Unclear risk	Those interested in participating were randomly assigned to either an experimental group or a control group
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	The double blind design ensured that neither the patients nor those running the study were aware of subject's experimental status
Blinding of outcome assessment (detection bias) subjective outcomes	Low risk	The double blind design ensured that neither the patients nor those running the study were aware of subject's experimental status
Incomplete outcome data (attrition bias) all outcomes a part retention	Unclear risk	Drop out was high in both group: 54% in the experimental condition and 38% in the control condition but difference was not significant P:0.3. COMMENT: small sam-

Khatami 1982 (*Continued*)

		ple, perhaps the test had low power to detect significant difference
Selective reporting (reporting bias)	Low risk	

Kosten 2003

Methods	Randomised controlled trial. Recruitment modality: "cocaine abusing opiate dependent patients seeking opiate maintenance recruited from the general Greater New haven area"
Participants	80 opioid and cocaine dependent (DSM IV). Exc Cr: pregnancy, cardiac conduction problems, acute hepatitis, current suicidality or psychosis, inability to read or understand symptom check list, current alcohol or sedative dependence, use of medications that interact with study medication; women of childbearing age agreed to use contraception and undergo monthly pregnancy monitoring Males 51; aged 21-65; Withe 39, African American 30, Other 11; High school 54
Interventions	For all BMT 8-12 mg/day plus desipramine 150 mg/day 1. N= 40 CM (vouchers for opiate and cocaine free urine); 2. N= 40 Non Contingent Management (vouchers, less than in (1) with a non contingent schedule. Duration 6 weeks
Outcomes	Retention in treatment
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Simple randomisation to one of four treatment conditions
Allocation concealment (selection bias)	Unclear risk	Simple randomisation to one of four treatment conditions
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	High rate of drop out. reason for drop out given. "49% of patients completed the trial, which did not differ among the four treat-

		ment groups (Wilcoxon 0.4; p: ns)
Selective reporting (reporting bias)	Low risk	

Luthar 2000

Methods	Randomised controlled trial. recruitment modality: "patients recruited at three methadone clinics. Recruitment occurred via several means including referral from counsellors, visits made by research assistant to ongoing drug counselling groups and medication lines, referrals from mothers who had already participated in the study"
Participants	61 heroin addicted mothers. mothers had to have children less than 16 years of age and report subjective experience of problems with parenting Exc Cr: cognitive deficit, psychotic thought process, suicidality Single (1)63%, (2)70%; Caucasian (1)78%, (2)65%; African American (1)10%, (2) 30%; Hispanic (1)12%, (2)5%
Interventions	For all MMT, doses not reported; 1. N= 37 Relational Psychotherapy Mothers' group; 2. N= 24 Standard care (drug counselling). Duration 6 months
Outcomes	Retention in treatment
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Mothers were randomised to either the RPMG or comparison group
Allocation concealment (selection bias)	Unclear risk	Mothers were randomised to either the RPMG or comparison group
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	15% of drop out. Reason for withdrawal given. Drop out balanced between groups

Selective reporting (reporting bias)	Low risk	

Magura 2007

Methods	Randomised controlled trial. recruitment modality: "patients who applied to the study were either referred by their primary methadone treatment counsellors (about 85%) or were self referred (about 15%)
Participants	168 opiate dependents. Incl Cr: Unemployed, stabilized on appropriate methadone dose, opiate negative urine, absence of any condition that would preclude any work at all (i.e. severe mental illness, severe physical problem, willingness to enter in the study Males 58%; Minority group 75%; average age 45 years; in MMT on average of 5 years; never married 47%
Interventions	For all MMT doses not reported; 1. N= 78 Counselling (Customized Employement Support); 2. N= 90 Standard counselling. Duration 12 months; Follow up 12 months
Outcomes	Competitive and or informal employment, 6 and 12 months; any paid employment 6 and 12 months
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	A total of 213 patients were randomised during the study period". "Consenting subjects were randomised to either the CES Vocational model or the clinic standard vocational counselling
Allocation concealment (selection bias)	Unclear risk	A total of 213 patients were randomised during the study period". "Consenting subjects were randomised to either the CES Vocational model or the clinic standard vocational counselling
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.

Magura 2007 (*Continued*)

Incomplete outcome data (attrition bias) all outcomes a part retention	Unclear risk	45 patients out of 213 randomised drop out for reason explained in the text; but it is not specified how many participants dropped out from each group
Selective reporting (reporting bias)	High risk	Retention in treatment, a measure usually utilized in drug addiction trial, not reported for each group

Matheson 2010

Methods	cluster randomised controlled trial; randomisation by pharmacy
Participants	77 pharmacists and 542 opioid dependent patients ; mean age 32.5 years, male: 64 %
Interventions	motivational intervention delivered by pharmacists: 40 pharmacies, 295 participants control: no intervention: 36 pharmacies, 247 participants
Outcomes	retention in treatment, substance use, psychological and physical health
Notes	Country of origin: Scoltland; setting: outpatients; the full text of the study was obtained trough a correspondence with the first author

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	quote: " Pharmacies were then randomised to intervention or control groups by the Health Services Research Unit in the University of Aberdeen (independent of the study team)."
Allocation concealment (selection bias)	High risk	quote: " Pharmacies were then randomised to intervention or control groups by the Health Services Research Unit in the University of Aberdeen(independent of the study team)." But " Following randomisation, three pharmacies in the control group (each with one pharmacist) said they would only take part in the intervention group and four pharmacies (each with one pharmacist) in the intervention arm said they would only take part as controls (because they could not attend training)."

Blinding of outcome assessment (detection bias) objective outcomes	Low risk	outcome assessed by the researcher. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	High risk	outcome assessed by the researcher.
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	Drop out balanced between groups. 38% of participants did not completed the follow up questionnaire in each group
Selective reporting (reporting bias)	Low risk	

McLellan 1993

Methods	Randomised controlled trial. recruitment modality: sample drawn from patients admitted to a methadone maintenance clinic. Groups similar for all the 36 variables but 3.
Participants	92 opiate dependent. Ex C: Need for medical or psychiatric hospitalisation at the time of admission, plan for an imminent move from the Philadelphia area .Average age 41; 100% men; 74% African-American; 27% married; average years of educational level 12; 47% employed; mean use of heroin 11 years, mean use of cocaine 3 years, mean problematic alcohol use 7 years
Interventions	For all MMT, 60 to 90 mg/day. 1. N= 31 Enhanced Methadone Services; 2. N= 29 Standard Methadone Services; 3. N= 32 Only methadone (especially permitted by FDA) Duration 24 weeks.
Outcomes	Use of primary substance of abuse as % of opiate positive urine samples and as % of subjects with opiate free urine samples per 8, 12, 16 consecutive weeks. Use of other drugs as % of cocaine positive urine samples. Severity of dependence as ASI (composite scores).
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Following the orientation period, patients were randomly assigned to one of the three intervention

McLellan 1993 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	Following the orientation period, patients were randomly assigned to one of the three intervention
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	The pretreatment and post treatment evaluation were performed by project technician who were independent of the treatment process
Blinding of outcome assessment (detection bias) subjective outcomes	Low risk	The pretreatment and post treatment evaluation were performed by project technician who were independent of the treatment process
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	10% of the all sample drop out; withdrawn from the study balanced between groups
Selective reporting (reporting bias)	Low risk	

Milby 1978

Methods	Randomised controlled trial. recruitment modality: patients on methadone maintenance treatment Information on comparability at baseline not given.
Participants	74 opiate dependent in program for 90 days and had verifiable narcotic addiction history of 2 years. Age range between 21-54; 82% men; 48% White; 52% African-American
Interventions	For all: MMT, no information on doses 1. N= 55 CM (take-home privilege if they had 7 consecutive clean urine, were engaged in productive activity full time, continued the program without violating rules; 2. N= 19 Control. Duration 7 weeks, follow-up at 2 months.
Outcomes	Retention in treatment as participants attended 14 consecutive weeks (7 before and then the contingency). Use of primary substance of abuse as % of opiate negative urine samples and as number of patients who met 7 consecutive clean urine samples before and after contingency
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants were randomly assigned to group I or II by a coin toss

Milby 1978 (*Continued*)

Allocation concealment (selection bias)	High risk	In four cases a husband and wife were randomly assigned as a unit rather than individually
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified..COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	No withdrawn from the study
Selective reporting (reporting bias)	Low risk	

Neufeld 2008

Methods	Randomised controlled trial. Recruitment modality: "patients recruited from the Addiction Treatment Services program"
Participants	100 opioid dependent and Antisocial Personality Disorder (DSM IV) Exc Cr: pregnancy, bipolar disorder, schizophrenia. Male 77%; Mean age 39; Caucasian 40%; Married 12%; Average years of education 10. 7; Employed 34%
Interventions	For all MMT mean 55 mg/day; 1. N= 51 Contingency Management 2. N= 49 Standard Treatment. The contingent intervention was highly structured designed to reinforce abstinence and adherence to scheduled counselling sessions. The protocol incorporated 9 steps to provide rapid delivery of predictable and increasingly positive consequences for attendance and abstinence (step +1 to +4) and increasingly negative consequences for missed counselling sessions and ongoing drug use (step -1 to -4) Duration 14 weeks
Outcomes	Retention in treatment, compliance, use of substances, ASI
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Participants were stratified on race, gender, baseline urine results, presence of other psy-

		chiatric diagnoses and therapist assignment and were randomised to one of two treatment conditions. COMMNENT: authors state that they stratified patients but do not described how they randomised people within each strata
Allocation concealment (selection bias)	Unclear risk	Participants were stratified on race, gender, baseline urine results, presence of other psychiatric diagnoses and therapist assignment and were randomised to one of two treatment conditions
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Outcome assessor not blinded. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	High risk	Outcome assessor not blinded
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	High drop out rate. Reason for withdrawn from the study not given. Drop out rate balanced between group (55% vs 43%; OR: 1.62, CI95% 0.74-3.58, p: ns)
Selective reporting (reporting bias)	Low risk	

Oliveto 2005

Methods	Randomised controlled trial. Recruitment modality: "cocaine abusing opioid dependent patients seeking opioid maintenance treatment were recruited from the greater New haven area"
Participants	140 opioid and cocaine dependents (DSM IV). Exc Cr: pregnancy, respiratory conditions such as asthma, abnormal liver enzyme level, use of other drugs that interact with LAAM, current diagnosis of other drugs dependence, history of major psychiatric disorders (psychosis, schizophrenia, bipolar), current suicidality and inability to read and understand the consent form; women of childbearing age agreed to use contraception and undergo monthly pregnancy monitoring Age 21-55; females 45; Africa American 39%, Hispanic 10%, Caucasian 91%
Interventions	For all LAAM maintenance (range 30-130 mg/three times a week), N= 70 Contingency Management (voucher for opiate and cocaine free urine); N= 70 Standard treatment. Duration 12 weeks
Outcomes	Retention in treatment, use of substances, withdrawal and depression symptoms

Oliveto 2005 (*Continued*)

Notes	Country of origin: USA. Setting: outpatients	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Participants were randomised by sex to one of the four treatment condition
Allocation concealment (selection bias)	Unclear risk	Participants were randomised by sex to one of the four treatment condition
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified..COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified..
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	The intent to treat sample of 140 participants were used for the statistical analysis. In any case reason for premature termination of the studies are given and group are balanced for drop out rate (log rank: 2. 77;p:<0.44)
Selective reporting (reporting bias)	Low risk	

Peirce 2006

Methods	Randomised controlled trial. Recruitment modality: "patients were recruited from six methadone maintenance community treatment programs that were members of the Clincal Trial Network"
Participants	388 stimulant abusing patients enrolled in MMT for at least one month and no more than three years Exc Cr: recovery for gambling problems (because the potential similarity between gambling and the prize draw incentive procedure) Participants were enrolled from 6 MMT sites and their characteristics are described for each site
Interventions	For all MMT from 67.9 to 108 mg/day; N= 190 Contingency Management (chance to win prizes for free urine); N= 108 Standard care Duration 12 weeks; follow up 6 months
Outcomes	retention, drug use, incentives earned

Peirce 2006 (*Continued*)

Notes	Country of origin: USA. Setting: outpatients	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Results of the first urine sample were used to stratify patients according to two variables: presence or absence of a stimulant drug, presence or absence of opioids. Stratification and random assignment were conducted independently at each site and accomplished by a computer program using a dynamic balanced randomisation procedure
Allocation concealment (selection bias)	Low risk	Research staff did not know the randomisation sequence, but were aware of individual group assignment
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified..COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	High drop out rate. Reason for withdrawn not given. "the decline in study retention over time was virtually identical for the two groups"
Selective reporting (reporting bias)	Low risk	

Petry 2005

Methods	Randomised controlled trial: Recruitment modality: not described
Participants	77 cocaine dependents in MMT treatment (DSM IV) on stable dose of methadone and English speaking Exc Cr: severe dementia, active uncontrolled psychosis or bipolar disorder, recovery for pathological gambling (because the potential similarity between gambling and the prize draw incentive procedure) Men (1)27.5%, (2) 27%; mean age (1)40, (2) 39; mean years of education (1)10.5, (2) 10.9; Hispanic (1)47.5%, (2)43.2%; African America (1)37.5%, (2) 32.4%; Cucasian (1)15%, (2)24.3%; full employed (1)27.5%, (2)21.6%; never married (1)62.5%, (2)

	73%
Interventions	For all MMT (1)71.5 mg/day, (2) 78.4 mg/day; 1. N= 40 Contingency Management (chance to win prizes for cocaine free urine) plus MMT 71.5 mg/day; 2. N= 37 Standard MMT 78.4 mg/day. Duration 12 weeks
Outcomes	Retention in treatment, compliance as N. of therapy sessions attended
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Minimum likelihood allocation was used to randomise patients to condition. Group were allocated on the following variables: gender, race, age (less than 35), presence of cocaine negative samples in three months prior the study initiation, attendance at more than three groups in the three months prior the study initiation
Allocation concealment (selection bias)	Unclear risk	Minimum likelihood allocation was used to randomise patients to condition. Group were allocated on the following variables: gender, race, age (less than 35), presence of cocaine negative samples in three months prior the study initiation, attendance at more than three groups in the three months prior the study initiation
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified..
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	Few drop out from the study. reason for withdrawn given. Drop out balanced between groups
Selective reporting (reporting bias)	Low risk	

Petry 2007

Methods	Randomised controlled trial. Recruitment modality: not described
Participants	74 opiate and cocaine dependents (DSM IV) in MMT, 18 years or older, spoke English Exc Cr: psychotic disorder (schizophrenia, bipolar), current suicidal, recovery for pathological gambling (because the potential similarity between gambling and the prize draw incentive procedure) Male 52; average age of education 12%; current married 2%; employed full or part time 11% European American 16%; African American 34%; Hispanic American 23%; Other 1%.;
Interventions	1. N= 28 Contingency management (chance to win prizes for cocaine free urine) plus MMT mean 83 mg/day; 2. N= 27 Contingency management (vouchers for cocaine free urine) plus MMTmean 78.4 mg/day; 3. N= 19 Standard Treatment MMT mean 81.2 mg/day. Duration 12 weeks
Outcomes	Retention in treatment, use of drugs, adverse events
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants randomly assigned to one of the three conditions. A computer urn randomisation procedure balanced groups on gender, ethnicity, employment status and baseline cocaine results
Allocation concealment (selection bias)	Unclear risk	Participants randomly assigned to one of the three conditions. A computer urn randomisation procedure balanced groups on gender, ethnicity, employment status and baseline cocaine results"
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified..COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified..
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	Data analysis were conducted on an intent to treat basis. The proportion of patients drop out from treatment were not significantly different among groups (X^2: 2.55;

		p: 0.28)
Selective reporting (reporting bias)	Low risk	

Preston 2000

Methods	Randomised controlled trial. Recrutiment modality: subjects selected from 285 patients consecutively admitted to a methadone maintenance program . Factorial design Groups similar for all the 43 variables but 2.
Participants	120 opiate dependent Ex C: Current major psychiatric illness, unstable serious medical illness, current physical dependence on alcohol or benzodiazepines Age between 18 and 65 years, eligible for MMT according to FDA requirements. (1)29 (2)31 (3)32 (4)28. Average age 37.6; 67.5% men; 42% African-American, 58% White; mean use of heroin 12.6 years; 17% married, 41.5% widowed, divorced or separated, 41. 5% never married; 28% employed full time, 14% employed part time 58% unemployed
Interventions	For all MMT, 50 mg/day dose constant plus 1 session of counselling per week 1. N= 61 Contingency management (vouchers based on results of the 3 times weekly urine tests); 2. N= 59 Control Duration, 13 weeks (5 weeks baseline + 8 weeks intervention)
Outcomes	Retention in treatment as number of participants completing 8 week intervention. Use of primary substance of abuse as % of opiate negative urine, % of patient abstinent on 39 successive urine test as graph, number of consecutive opiate negative urine samples, self-reported opiate use as mean frequency per day. Craving as self-reported opiate craving as scores. Quality of life as positive lifestyle changes and criminal activity (scores). Use of other drugs as graph
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Two studies were conducted concurrently: one on cocaine dependent patients and one on heroin dependent. Patients who met the criteria for both studies were randomised to one of them by a coin toss. This was followed by assignment to contingent or non contingent; the first 10 patients were assigned to contingent vouchers yo allow for yoking of non contingent patients. Thereafter, patients were assigned to a voucher condition by coin flip. Dose randomisa-

Preston 2000 (*Continued*)

		tion was then conducted separately for contingent and non contingent group by the study pharmacist, using a random number table
Allocation concealment (selection bias)	High risk	The first 10 patients were assigned to contingent vouchers yo allow for yoking of non contingent patients. Thereafter, patients were assigned to a voucher condition by coin flip. Dose randomisation was then conducted separately for contingent and non contingent group by the study pharmacist, using a random number table. COMMENT: not concealed for contingent, non contingent assignment, concealed for dose increase, not dose increase assignment. Because the objective of the review is to assess the effect of psychosocial intervention (i.e. contingent vs non contingent) the study has been considered with high risk of bias for this comparison
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified..COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified..
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	"93.3% of participants completed the intervention. No significant between group differences were noted in retention"
Selective reporting (reporting bias)	Low risk	

Rounsaville 1983

Methods	Randomised controlled trial. recruitment modality: patients members of the New have methadone maintenance program. Groups significantly different for race
Participants	72 methadone maintained opiate addicts, in treatment for a minimum of 6 weeks, Exc Cr: Schizophrenic and manic patients Current psychiatric disorder or a personality disorder.57%; age over 27; men 61%; White 58%; single, divorced or separated 61%; high school 95%; employed full time 50%.
Interventions	For all MMT, no information on doses, daily contact with the clinic, monitoring of urine for illicit substance use and mandatory weekly 90-min group psychotherapy sessions as

Rounsaville 1983 (*Continued*)

	minimal core components of the treatment plan 1. N= 37 Short term Interpersonal Psychotherapy , 1 hour per week; 2. N= 35 Control Low-contact Treatment, 20 min session per month during which the clinician generally reviewed the patient's current social situation. Duration 6 months.
Outcomes	Retention in treatment as number of voluntary and of symptomatic failure drop outs, number completed. Use of primary substance of abuse as number of urine positive samples. Psychiatric symptoms/psychological distress as scores
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Participants were randomly assigned to one of the two treatment
Allocation concealment (selection bias)	Unclear risk	Participants were randomly assigned to one of the two treatment
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Clinical evaluators were blind to the treatment the subjects were receiving and the patients were instructed not to inform the raters of the treatment received
Blinding of outcome assessment (detection bias) subjective outcomes	Low risk	Clinical evaluators were blind to the treatment the subjects were receiving and the patients were instructed not to inform the raters of the treatment received
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	High drop out rate in both group. But reason for attrition clearly described. Because of the large number of early drop out, it was possible that the two groups were no longer comparable. To evaluate this, demographic characteristics, diagnosis and a range of variables that might predispose to terminate early(symptoms, drug use, legal history) were compared between the two remaining group. The two group remained similar except for ethnic composition
Selective reporting (reporting bias)	Low risk	

Scherbaum 2005

Methods	Randomised controlled trial. Recruitment modality:"subjects recruited from individuals seeking MMT ay the urban centre for the assignment of heroin addicts to various MMT clinics and general practitioners"
Participants	73 opiate addicts Male 53; mean age 30 years; duration of dependence mean 7 years; additional psychiatric disorder 71%; additional current addiction or poly drug dependence 83%; employed 66%; single 22%
Interventions	For all MMT 1. N= 41 CBT, mean methadone dose 99.9 mg/day; 2. N= 32, Standard MMT, mean methadone dose 98.9 mg/day Duration 6 months and 6 months follow up
Outcomes	Retention in treatment
Notes	Country of origin: Germany. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Each participant was randomly allocated to one of two group by flipping a coin
Allocation concealment (selection bias)	Unclear risk	Each participant was randomly allocated to one of two group by flipping a coin
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified. COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	The analysis was made according to the intention to treat principle (ITT), meaning that the data of all included studies were analysed, whether they had completed the study or not. Missing data at months 6 and 12 were substituted by the last available urine samples
Selective reporting (reporting bias)	Low risk	

Silverman 2004

Methods	Randomised controlled trial. recruitment modality: "patients selected from newly admitted patients to a methadone treatment program"
Participants	78 opiate dependents, 18-50 years old Excl Cr: pregnant women, serious psychiatric illness Mean age (1)39.3, (2)40.9; Men (1)50%, (2)65%; African American (1)71%, (2)69%; White (1)29%, (2)31%; 12 years of education (1)46%, (2)38%; married (1)15%, (2) 15%; employed (1)15%, (2)23%
Interventions	For all MMT mean 60 mg/day; 1. N= 52 CM (take home plus voucher or voucher alone for cocaine free urine); 2. N= 26 Usual care Duration 24 weeks
Outcomes	Retention in treatment, use of opiates as longest duration of abstinence, compliance as mean hours of counselling received
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants were stratified for five variables: urine sample positive for cocaine, urine sample positive for opiates, criteria for antisocial personality disorders, full time employment, race . A computerized random number generator accomplished random assignment
Allocation concealment (selection bias)	High risk	The same staff person identified potential participants as eligible, stratified and randomly assigned them and introduced them to their study condition
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified.COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	High drop out rate. Reason for withdrawn given. "There were no significant difference among groups in study retention"

Selective reporting (reporting bias)	Low risk	

Stitzer 1992

Methods	Randomised controlled trial. recruitment modality: all patients admitted to methadone maintenance treatment during the recruitment period and eligible. No differences between groups on baseline drug use.
Participants	53 opiate dependent eligible for MMT. Average age 34; 72% men; 66% White; mean use of heroin 15 years; 23% married; 34% employed; 77% high school; 40% legally free, 38% on probation, 22% pending trial. Ex C: Psychiatric and behavioural problem
Interventions	For all MMT, mean dose 51.4 mg/day, all stabilized for 12 weeks and then randomised plus counselling session 1 per week 1. N= 26 Contingent Treatment, opportunity to receive methadone takes-home, maximum 3 take-home doses per week after drug free urine. 2. N= 27 Non Contingent, receive random from 0 to 3 take home doses per week. Duration 6 months.
Outcomes	Retention in treatment as n. of drop-outs. Use of primary substance of abuse as % of positive urine and as % of subjects with at least 12 consecutive free urine
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Participants were stratified for gender and race and than randomly assigned to one of two condition. COMMNENT: authors state that they stratified patients but do not described how they randomised people within each strata
Allocation concealment (selection bias)	Unclear risk	Participants were stratified for gender and race and than randomly assigned to one of two condition
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	Blindness of outcome assessor not specified.COMMENT: the outcomes are unlikely to be influenced by lack of blinding
Blinding of outcome assessment (detection bias) subjective outcomes	Unclear risk	Blindness of outcome assessor not specified.

Incomplete outcome data (attrition bias) all outcomes a part retention	High risk	Final attrition included 38% of patients from the contingent group and 26% form the non-contingent group. COMMENT: reason from drop out not given. High rate of drop out. Unbalanced between group
Selective reporting (reporting bias)	Low risk	

Thornton 1987

Methods	Randomised controlled trial. Recruitment modality:not described. Groups similar for drug use and demographic data
Participants	47 opiate dependent in MMT. Average age 38; 100% men; 34% Hispanic, 21% White, 45% African-American; 47% participated in previous treatment program
Interventions	All MMT. 1. N= 24 Subliminal Stimulation Group, Methadone mean 44.0 mg/day plus experimental stimulus MOMMY AND I ARE ONE. 2. N= 23 Control, Methadone mean 47.0 mg/day plus exposure with the same modalities of the control to the neutral message PEOPLE ARE WALKING. Duration 6 weeks.
Outcomes	Retention in treatment as no. of drop-outs. Use of primary substance of abuse as chi square results on data and as no. of participants opiate-free at 2,3 weeks. Psychiatric symptoms/psychological distress as positive dream feelings (chi square results) and as results to a questionnaire designed by the authors to tap their own assessment of changes (scores and chi square results). Results at follow-up as no. of participants with negative urine samples at 2 and 3 weeks post-experimental period presented as chi square statistical analysis results
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Participants were assigned to the experimental or control group n a random fashion, except for an attempt to keep relatively balanced the average age and racial distribution of the two group
Allocation concealment (selection bias)	High risk	Participants were assigned to the experimental or control group on a random fashion, except for an attempt to keep relatively balanced the average age and racial distri-

Thornton 1987 (*Continued*)

		bution of the two group
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	In a large number of prior studies under the same conditions, no subjects could recognize the content of the stimulus. Since the experimenters were also blind , the current study can be said to have been carried out under double blind conditions
Blinding of outcome assessment (detection bias) subjective outcomes	Low risk	In a large number of prior studies under the same conditions, no subjects could recognize the content of the stimulus. Since the experimenters were also blind , the current study can be said to have been carried out under double blind conditions
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	Of the 58 participants, 11 dropped out during the course of the study (6 control and 5 experimental) for reason ranging from feeling of disinterest to absenteeism from the clinic. The remaining members were comparable for demographic and background characteristics. COMMENT: reasons described; drop out balanced
Selective reporting (reporting bias)	Low risk	

Woody 1983

Methods	Randomised controlled trial. Recruitment modality:patients recruited by their counsellor or by the author of the study from patients receiving methadone for at least two weeks but no more than six month. No differences between groups on baseline drug use.
Participants	110 opiate dependent, age between 18 and 55 years, met the FDA requirements for MMT, and had been receiving methadone for at least 2 weeks but no more than 6 months. Average age 32.5; 100% men; 39% White, 61% African-American; mean use of heroin 9.4 years; mean prior treatment 3.6; 34% married, 34% divorced or separated, 32% never married; average years of educational level 12.3; criminal convictions 3. Ex C: Psychosis, persistent or clinically significant organic brain syndrome
Interventions	For all MMT. 1. N= 32 Supportive-Expressive Therapy, Methadone mean dose 36 mg/day plus in the first 6 weeks 3 appointments with the counsellor plus 3 appointments with the therapist 2. N= 39 Cognitive-Behavioural Therapy, Methadone mean dose 42mg/day plus in the first 6 weeks 3 appointments with the counsellor plus 3appointments with the therapist.

	3. N= 39 Standard Drug Counseling, Methadone mean dose 35 mg/day plus in the first 6 weeks 3 appointments with the counsellor. Duration: 7 months plus 12 months follow-up.
Outcomes	Use of primary substance of abuse as urinalysis results as value of F. Psychiatric symptoms/ psychological distress as scores. Severity of dependence as mean methadone dose (graph), % of participants receiving ancillary medications (graph), ASI (scores). Results at follow-up as number still in treatment, number of lost and number of abstained
Notes	Country of origin: USA. Setting: outpatients The participants in the Standard Drug Counseling (n. 39) are considered both in arm a and in arm b

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Participants were randomly assigned to three treatment conditions
Allocation concealment (selection bias)	Unclear risk	Participants were randomly assigned to three treatment conditions
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	The interviews were done by independent technicians who were not part of the treatment staff and were not aware of patients group assignments
Blinding of outcome assessment (detection bias) subjective outcomes	Low risk	The interviews were done by independent technicians who were not part of the treatment staff and were not aware of patients group assignments
Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	Participants randomised were required to complete three appointments with their counsellors or therapists. If they failed to complete the appointments they were considered not engaged and their were dropped from the study. Approximatively 80% of patients keep these initial appointments. There were no significant differences (p>0. 1) between groups in the proportion of patients who completed initial appointments. All patients who completed these initial appointments underwent subsequent evaluation and were include in the analysis regardless of their subsequent attendance

Woody 1983 (*Continued*)

Selective reporting (reporting bias)	High risk	Retention in treatment, a measure usually utilized in drug addiction trial, not reported

Woody 1995

Methods	Randomised controlled trial. recruitment modality: not described Groups similar for all the 38 variables but 2.
Participants	93 opiate dependent age between 18 and 55 years, met the FDA requirements for MMT, had been receiving methadone for at least 2 weeks but no more than 6 months. Average age 41; 100% men; 60 % White, 57% African-American, 43% Caucasian; average years of educational level 12; 36% employed; 46% had been incarcerated. 13% on probation. Ex C: Psychosis, persistent or clinically significant organic brain syndrome
Interventions	For all MMT, no information on doses 1. N= 62 Supportive-Expressive Therapy, 26 sessions of 30 min in the 24 weeks. 2. N= 31 Standard Drug Counseling, in the first 6 weeks 3 appointments with the counsellor. Duration: 24 weeks, follow-up at 1 and 6 months.
Outcomes	Retention in treatment as n. of retained. Use of primary substance of abuse as % of opiate positive urine samples by graph and as % of participants with positive urine samples. Use of other drugs as % of cocaine positive UA and as no. participants with positive UA for other drugs
Notes	Country of origin: USA. Setting: outpatients

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Participants were randomly assigned to supportive expressive therapy or drug counselling
Allocation concealment (selection bias)	Unclear risk	Participants were randomly assigned to supportive expressive therapy or drug counselling
Blinding of outcome assessment (detection bias) objective outcomes	Low risk	All measures were completed by independent research technicians who were not part od the treatment programs or the therapy
Blinding of outcome assessment (detection bias) subjective outcomes	Low risk	All measures were completed by independent research technicians who were not part od the treatment programs or the therapy

Woody 1995 (*Continued*)

Incomplete outcome data (attrition bias) all outcomes a part retention	Low risk	Participants were required to complete three appointments with their counsellor in order to be considered engaged.76% of the psychotherapy group and 76% of the counsellor group became engaged. 92% of psychotherapy group patients and 87% of counselling group were contacted at follow up. COMMENT: reason for drop out given; drop out balanced between group
Selective reporting (reporting bias)	Low risk	

ASI scores: Addiction Severity Index scores
BMT: Buprenorphine Maintenance Treatment
CRA: Community Reinforcement Approach
DSM-III-R: Diagnostic and Statistical Manual of Mental Disorders, American Psychiatric Association Washington DC
Ex Cr: Exclusion Criteria
FDA: Food and Drug Administration
MMT: Methadone Maintenance Treatment

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Arani 2010	excluded as outcome measures not in the inclusion criteria
Ball 2007	excluded as participants not in the inclusion criteria: only 19% of participants were opioid dependents
Barnett 2009	excluded as outcome measures not in the inclusion criteria
Brooner 2005	Excluded as type of intervention not in the inclusion criteria: there is not a group with pharmacological alone
Brooner 2007	Excluded as type of intervention not in the inclusion criteria: there is not a group with pharmacological alone
Calsyn 1994	Excluded as study design not in the inclusion criteria: it is impossible to evaluate the effects of the single interventions not knowing the number of participants for each group
Carpenedo 2010	excluded as : intervention (both group received psychosocial intervention) and outcome (cocaine use) not in the inclusion criteria
Carrol 2006	excluded as participants not in the inclusion criteria: only 5% of participants were opioid dependents
Conrod 2000	Excluded as the type of participants not in the inclusion criteria: females dependent/abusing alcohol, prescription drugs or both

(*Continued*)

Correia 2003	Excluded as type of intervention not in the inclusion criteria: no group with pharmacological alone
Coviello 2009	excluded as the intervention is nor in the inclusion criteria: both groups received psychosocial intervention
Czuchry 2000	Excluded as type of participants and intervention not in the inclusion criteria: participants were drug dependent (any drug) and the treatments compared were both psychosocial without pharmacological intervention
Czuchry 2004	Excluded as the type of intervention not in the inclusion criteria: aim is to address cognitive deficits that may impede substance abuse treatment within the criminal justice system
Epstein 2003	Excluded as type of outcomes not in the inclusion criteria: cocaine negative urine
Fals-Stewart 1996	Excluded as the type of participants not in the inclusion criteria: substances abusers (any drug)
Fiellin 2006b	Excluded as type of intervention not in the inclusion criteria: no group with pharmacological alone
Fiorentine 2000	Excluded as the study design not in the inclusion criteria: review article
Galanter 2004	Excluded as type of intervention not in the inclusion criteria: two groups, one only network therapy and the other only medication management (buprenorphine)
Gandhi 2009	excluded as study design not in the inclusion criteria: cross sectional survey
Greenwald 2009	excluded as outcome measures not in the inclusion criteria
Griffith 2000	Excluded as the study design not in the inclusion criteria: overview
Hanson 2008	excluded as outcome measures not in the inclusion criteria
Havassy 1979	Excluded as the outcomes not in the inclusion criteria: effects of regulation of dosage and increased number of take-home doses to decrease the methadone dose
Havens 2009	excluded as the intervention not in the inclusion criteria: engagement in a maintenance treatment is the outcome
Hawkins 1989	Excluded as the type of participants not in the inclusion criteria: not only opiate addicts in the final stages of their residential drug treatment program
Iguchi 1996a	Excluded as the type of intervention not in the inclusion criteria: no pharmacological intervention alone
Ingram 1990	Excluded as the type of participants not in the inclusion criteria: residents of an alcohol and drug treatment centre
Jenkins 2007	Excludes as study design not in the inclusion criteria: cohort study
Joe 1997a	Excluded as outcomes not in the inclusion criteria: results only on sub group of participants, likely to be selected

(*Continued*)

Kakko 2007	Excluded as type of intervention not in the inclusion criteria: two groups, (1) methadone (2) stepped treatment initiated with buprenorphine/naloxone and escalated to methadone if needed
Kang 2006	Excluded as type of intervention not in the inclusion criteria: no pharmacological intervention alone
Kidorf 2007	Excluded as type of outcomes not in the inclusion criteria: rates of cannabis use and the effectiveness of an adaptive stepped care intervention for reducing cannabis use
Kidorf 2009	excluded as type of intervention not in the inclusion criteria: no maintenance treatment
Kinlock 2007	Excluded as type of intervention not in the inclusion criteria: no group with pharmacological treatment alone
Kinlock 2009	excluded as type of intervention not in the inclusion criteria: all groups receive psychosocial intervention
Kirby 2006	Excluded as type of intervention not in the inclusion criteria: cocaine abstinence
Kuhn 2007	Excluded as study design not in the inclusion criteria: no randomisation for allocate participants in the groups
Ledgerwood 2006	Excluded as outcomes not in the inclusion criteria: effect of Contingency Management on motivation to change substance use
Magura 1999	Excluded as study design not in the inclusion criteria: performance analysis through benchmark comparison
McLellan 1997	Excluded as type of participants not in the inclusion criteria: participants were dependent on alcohol, drugs (any) or both
Montoya 2005	Excluded as study design not in the inclusion criteria: no randomisation for psychosocial interventions
Morgenstern 2001	Excluded as the type of participants not in the inclusion criteria: substance abusers (any drug)
Morgenstern 2009	excluded as type of intervention not in the inclusio criteria: not all patients receive maintenance treatment
Nurco 1995	Excluded as outcomes not in the inclusion criteria: responses on an interview contained 15 agree/disagree questions tapping orientations to locus-of-control beliefs about drug misuse
Olmstead 2009	excluded ad outcome measures not in the inclusion criteria
Page 1982	Excluded as the type of participants not in the inclusion criteria: participants were drug dependent (any drug)
Pantalon 2004	Excluded as type of intervention not in the inclusion criteria: no pharmacological alone
Petry 2005b	Excluded as type of participants not in the inclusion criteria: opiate or cocaine abusers, analysis not separated
Petry 2008	excluded as study design not in the inclusion criteria: secondary analysis of already included or excluded studies
Poling 2006	Excluded as type of intervention not in the inclusion criteria: no group with pharmacological alone

(*Continued)*

Preston 2008	excluded as : intervention not in the inclusion criteria: both groups received psychosocial treatment
Rhodes 2003	Excluded as type of intervention not in the inclusion criteria: no group with pharmacological alone
Rowan-Szal 2005	Excluded as type of intervention and outcomes not in the inclusion criteria: counselling on cocaine use and cocaine use as outcome
Saunders 1995	Excluded as type of intervention not in the inclusion criteria: no information available on pharmacological intervention
Schottenfeld 2005	Excluded as type of intervention not in the inclusion criteria:no pharmacological alone
Schroeder 2003	Excluded as type of intervention not in the inclusion criteria:no pharmacological alone
Schroeder 2006	Excluded as type of outcome not in the inclusion criteria: HIV risk behaviours
Sigmon 2004	Excluded as type of outcomes not in the inclusion criteria: cocaine negative urine
Silverman 2007	Excluded as the type of intervention: (1) abstinence-and-work and (2) work-only
Sorensen 2007	Excluded as type of intervention not in the inclusion criteria: contingency management intervention designed to improve medication adherence
Stitzer 1980	Excluded as type of intervention not in the inclusion criteria: 3 groups, (1) $ 15.00 cash, (2) 2 methadone take-home doses, (3) the opportunity of self-regulate methadone doses

MMT= Methadone Maintenance Treatment
CC: contingency contracting
NC: no contingencies

Characteristics of ongoing studies *[ordered by study ID]*

DATA AND ANALYSES

Comparison 1. Any Psychosocial intervention plus pharm versus pharm standard

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Retention in treatment	27	3124	Risk Ratio (M-H, Fixed, 95% CI)	1.03 [0.98, 1.07]
2 Opioid abstinence	8	1002	Risk Ratio (M-H, Random, 95% CI)	1.12 [0.92, 1.37]
3 Number of participants still in treatment at the end of follow-up	3	250	Risk Ratio (M-H, Random, 95% CI)	0.90 [0.77, 1.07]
4 Number of participants abstinent at the end of follow-up	3	181	Risk Ratio (M-H, Fixed, 95% CI)	1.15 [0.98, 1.36]
5 Compliance	3	685	Mean Difference (IV, Random, 95% CI)	0.43 [-0.05, 0.92]
6 Psychiatric symptoms SCL-90	3	279	Mean Difference (IV, Fixed, 95% CI)	0.02 [-0.28, 0.31]
7 Depression (BDI)	3	279	Mean Difference (IV, Fixed, 95% CI)	-1.70 [-3.91, 0.51]

Comparison 2. Any Behavioural interventions plus pharm versus pharm standard

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Retention in treatment	19		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Any behavioural plus pharm versus pharm standard	19	2065	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.95, 1.06]
1.2 Contingency management plus pharm versus pharm standard	14	1616	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.96, 1.08]
2 Opioid abstinence	4	448	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.89, 1.21]
3 Continuous weeks of abstinence	2	138	Mean Difference (IV, Fixed, 95% CI)	1.91 [0.20, 3.62]
4 Number of participants still in treatment at the end of follow-up	3	218	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.80, 1.13]
5 Number of participants abstinent at the end of follow-up	3	123	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [0.98, 1.41]

Comparison 3. Psychoanalytic oriented treatments plus pharm versus pharm standard

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Retention in treatment	3	212	Risk Ratio (M-H, Fixed, 95% CI)	0.90 [0.75, 1.07]
2 Opioid abstinence	2	127	Risk Ratio (M-H, Fixed, 95% CI)	1.21 [0.82, 1.78]

Comparison 4. Counselling plus pharm versus pharm standard

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 retention in treatment	4	769	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.98, 1.15]
2 opioid abstinence	1	335	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.85, 1.14]

Analysis 1.1. Comparison 1 Any Psychosocial intervention plus pharm versus pharm standard, Outcome 1 Retention in treatment.

Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 1 Any Psychosocial intervention plus pharm versus pharm standard

Outcome: 1 Retention in treatment

Study or subgroup	Any Psychoso-cial+pharm n/N	Pharm standard n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Abrahms 1979	7/7	7/7		0.7 %	1.00 [0.78, 1.29]
Avants 2004	93/108	97/112		9.1 %	0.99 [0.90, 1.10]
Bickel 2008	52/90	26/45		3.3 %	1.00 [0.74, 1.36]
Chawarski 2008	12/12	11/12		1.1 %	1.09 [0.87, 1.36]
Chawarski 2011	16/20	13/17		1.3 %	1.05 [0.74, 1.47]
Chopra 2009	60/83	28/37		3.7 %	0.96 [0.76, 1.20]
Fiellin 2006	25/56	50/110		3.2 %	0.98 [0.69, 1.40]
Ghitza 2008	52/76	29/40		3.6 %	0.94 [0.74, 1.21]
Gross 2006	29/40	16/20		2.0 %	0.91 [0.68, 1.21]

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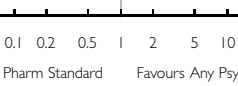
Study or subgroup	Any Psychoso-cial+pharm n/N	Pharm standard n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Hayes 2004	53/86	14/19		2.2 %	0.84 [0.61, 1.15]
Khatami 1982	11/24	8/13		1.0 %	0.74 [0.40, 1.37]
Kosten 2003	37/40	38/40		3.6 %	0.97 [0.87, 1.09]
Luthar 2000	32/37	20/42		1.8 %	1.82 [1.29, 2.56]
Matheson 2010	250/295	194/247		20.1 %	1.08 [0.99, 1.17]
Milby 1978	51/55	18/19		2.6 %	0.98 [0.86, 1.11]
Neufeld 2008	28/51	21/49		2.0 %	1.28 [0.85, 1.93]
Oliveto 2005	36/70	38/70		3.6 %	0.95 [0.69, 1.30]
Peirce 2006	133/198	123/190		12.0 %	1.04 [0.90, 1.20]
Petry 2005	35/40	31/37		3.1 %	1.04 [0.87, 1.26]
Petry 2007	45/55	14/19		2.0 %	1.11 [0.83, 1.49]
Preston 2000	58/61	54/59		5.2 %	1.04 [0.94, 1.14]
Rounsaville 1983	14/37	19/35		1.9 %	0.70 [0.42, 1.16]
Scherbaum 2005	27/41	19/32		2.0 %	1.11 [0.77, 1.59]
Silverman 2004	35/52	14/26		1.8 %	1.25 [0.84, 1.87]
Stitzer 1992	16/26	20/27		1.9 %	0.83 [0.57, 1.21]
Thornton 1987	14/24	17/23		1.7 %	0.79 [0.52, 1.20]
Woody 1995	57/62	27/31		3.4 %	1.06 [0.90, 1.23]
Total (95% CI)	**1746**	**1378**		**100.0 %**	**1.03 [0.98, 1.07]**

Total events: 1278 (Any Psychosocial+pharm), 966 (Pharm standard)

Heterogeneity: Chi^2 = 26.42, df = 26 (P = 0.44); I^2 =2%

Test for overall effect: Z = 1.26 (P = 0.21)

Test for subgroup differences: Not applicable



Analysis 1.2. Comparison 1 Any Psychosocial intervention plus pharm versus pharm standard, Outcome 2 Opioid abstinence.

Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 1 Any Psychosocial intervention plus pharm versus pharm standard

Outcome: 2 Opioid abstinence

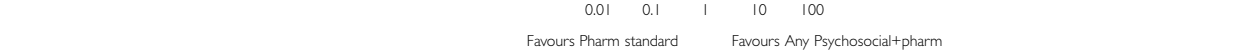
Study or subgroup	Any Psychoso-cial+MMT n/N	Pharm standard n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Avants 2004	51/108	59/112		17.2 %	0.90 [0.69, 1.17]
McLellan 1993	23/31	24/61		13.2 %	1.89 [1.30, 2.74]
Stitzer 1992	8/25	2/25		1.8 %	4.00 [0.94, 17.00]
Abbott 1998	46/52	52/67		21.2 %	1.14 [0.97, 1.34]
Woody 1995	31/57	16/27		12.6 %	0.92 [0.62, 1.36]
Hayes 2004	25/45	9/14		10.4 %	0.86 [0.54, 1.38]
Thornton 1987	9/22	2/21		1.9 %	4.30 [1.05, 17.61]
Matheson 2010	123/182	105/153		21.7 %	0.98 [0.85, 1.14]
Total (95% CI)	**522**	**480**		**100.0 %**	**1.12 [0.92, 1.37]**

Total events: 316 (Any Psychosocial+MMT), 269 (Pharm standard)

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 20.70$, df = 7 (P = 0.004); $I^2 = 66\%$

Test for overall effect: Z = 1.13 (P = 0.26)

Test for subgroup differences: Not applicable



Analysis 1.3. Comparison 1 Any Psychosocial intervention plus pharm versus pharm standard, Outcome 3 Number of participants still in treatment at the end of follow-up.

Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 1 Any Psychosocial intervention plus pharm versus pharm standard

Outcome: 3 Number of participants still in treatment at the end of follow-up

Study or subgroup	Any Psychoso-cial+pharm n/N	Pharm Standard n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Iguchi 1997	50/68	27/35		51.8 %	0.95 [0.76, 1.20]
Khatami 1982	17/24	11/13		22.9 %	0.84 [0.59, 1.18]
Woody 1983	38/71	24/39		25.2 %	0.87 [0.63, 1.21]
Total (95% CI)	**163**	**87**		**100.0 %**	**0.90 [0.77, 1.07]**
Total events: 105 (Any Psychosocial+pharm), 62 (Pharm Standard)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.45$, df = 2 (P = 0.80); $I^2 = 0.0\%$					
Test for overall effect: Z = 1.19 (P = 0.23)					
Test for subgroup differences: Not applicable					

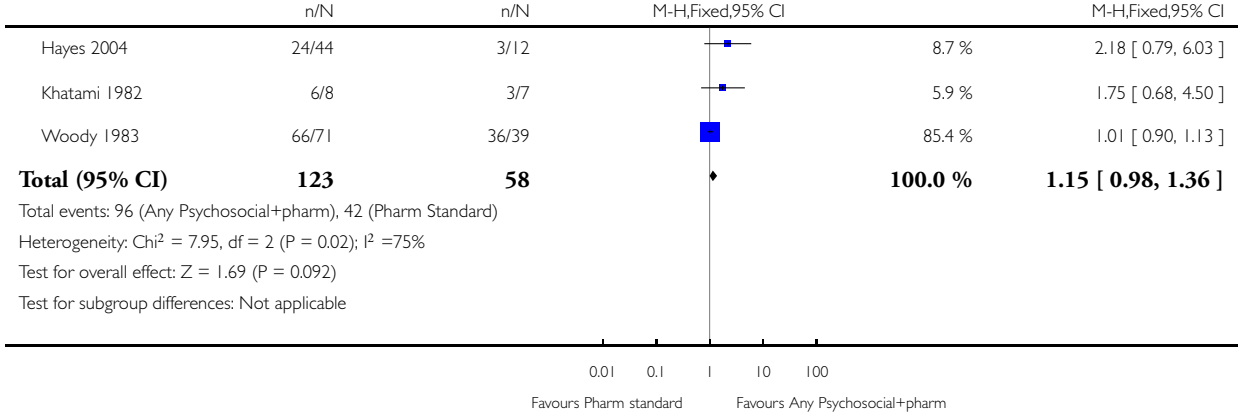
Analysis 1.4. Comparison 1 Any Psychosocial intervention plus pharm versus pharm standard, Outcome 4 Number of participants abstinent at the end of follow-up.

Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 1 Any Psychosocial intervention plus pharm versus pharm standard

Outcome: 4 Number of participants abstinent at the end of follow-up

Study or subgroup	Any Psychoso-cial+pharm n/N	Pharm Standard n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Hayes 2004	24/44	3/12		8.7 %	2.18 [0.79, 6.03]
Khatami 1982	6/8	3/7		5.9 %	1.75 [0.68, 4.50]
Woody 1983	66/71	36/39		85.4 %	1.01 [0.90, 1.13]
Total (95% CI)	**123**	**58**		**100.0 %**	**1.15 [0.98, 1.36]**
Total events: 96 (Any Psychosocial+pharm), 42 (Pharm Standard)					
Heterogeneity: Chi^2 = 7.95, df = 2 (P = 0.02); I^2 =75%					
Test for overall effect: Z = 1.69 (P = 0.092)					
Test for subgroup differences: Not applicable					



Analysis 1.5. Comparison 1 Any Psychosocial intervention plus pharm versus pharm standard, Outcome 5 Compliance.

Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 1 Any Psychosocial intervention plus pharm versus pharm standard

Outcome: 5 Compliance

Study or subgroup	Any Psychoso-cial+pharm N	Mean(SD)	Pharm standard N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Peirce 2006	198	8.6 (8)	190	10.3 (11.9)		5.3 %	-1.70 [-3.73, 0.33]
Petry 2005	40	4 (0.5)	37	3.4 (1)		48.0 %	0.60 [0.24, 0.96]
Avants 2004	108	5.3 (1.4)	112	4.8 (1.45)		46.7 %	0.50 [0.12, 0.88]
Total (95% CI)	**346**		**339**			**100.0 %**	**0.43 [-0.05, 0.92]**

Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 4.81$, df = 2 (P = 0.09); $I^2 = 58\%$

Test for overall effect: Z = 1.75 (P = 0.081)

Test for subgroup differences: Not applicable

Analysis 1.6. Comparison 1 Any Psychosocial intervention plus pharm versus pharm standard, Outcome 6 Psychiatric symptoms SCL-90.

Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 1 Any Psychosocial intervention plus pharm versus pharm standard

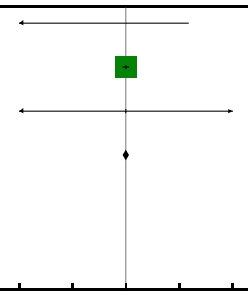
Outcome: 6 Psychiatric symptoms SCL-90

Study or subgroup	Any Psychoso-cial+pharm N	Mean(SD)	Pharm Standard N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Abbott 1998	96	-21.12 (48.45)	55	-10 (52.86)		0.0 %	-11.12 [-28.12, 5.88]
Hayes 2004	28	-0.08 (0.64)	16	-0.1 (0.365)		100.0 %	0.02 [-0.28, 0.32]
Woody 1995	57	-11 (51)	27	-11 (68)		0.0 %	0.0 [-28.86, 28.86]
Total (95% CI)	**181**		**98**			**100.0 %**	**0.02 [-0.28, 0.31]**

Heterogeneity: Chi² = 1.65, df = 2 (P = 0.44); I² =0.0%

Test for overall effect: Z = 0.11 (P = 0.91)

Test for subgroup differences: Not applicable



Analysis 1.7. Comparison 1 Any Psychosocial intervention plus pharm versus pharm standard, Outcome 7 Depression (BDI).

Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 1 Any Psychosocial intervention plus pharm versus pharm standard

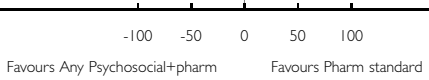
Outcome: 7 Depression (BDI)

Study or subgroup	Any Psychoso-cial+pharm N	Mean(SD)	Pharm Standard N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Abbott 1998	96	-6.97 (7.88)	55	-4.92 (8.07)		69.7 %	-2.05 [-4.70, 0.60]
Hayes 2004	28	-2.45 (12.23)	16	-2.35 (5.46)		17.7 %	-0.10 [-5.36, 5.16]
Woody 1995	57	-6 (10)	27	-4 (15)		12.6 %	-2.00 [-8.23, 4.23]
Total (95% CI)	**181**		**98**			**100.0 %**	**-1.70 [-3.91, 0.51]**

Heterogeneity: Chi² = 0.43, df = 2 (P = 0.81); I² =0.0%

Test for overall effect: Z = 1.50 (P = 0.13)

Test for subgroup differences: Not applicable



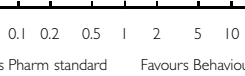
Analysis 2.1. Comparison 2 Any Behavioural interventions plus pharm versus pharm standard, Outcome 1 Retention in treatment.

Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 2 Any Behavioural interventions plus pharm versus pharm standard

Outcome: 1 Retention in treatment

Study or subgroup	Behavioural+Pharm n/N	Pharm standard n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Any behavioural plus pharm versus pharm standard					
Abrahms 1979	7/7	7/7		1.1 %	1.00 [0.78, 1.29]
Avants 2004	93/108	97/112		13.9 %	0.99 [0.90, 1.10]
Bickel 2008	52/90	26/45		5.1 %	1.00 [0.74, 1.36]
Chopra 2009	60/83	28/37		5.6 %	0.96 [0.76, 1.20]
Ghitza 2008	52/76	29/40		5.5 %	0.94 [0.74, 1.21]
Gross 2006	29/40	16/20		3.1 %	0.91 [0.68, 1.21]
Hayes 2004	53/86	14/19		3.3 %	0.84 [0.61, 1.15]
Khatami 1982	11/24	8/13		1.5 %	0.74 [0.40, 1.37]
Kosten 2003	37/40	38/40		5.5 %	0.97 [0.87, 1.09]
Milby 1978	51/55	18/19		3.9 %	0.98 [0.86, 1.11]
Neufeld 2008	28/51	21/49		3.1 %	1.28 [0.85, 1.93]
Oliveto 2005	36/70	38/70		5.5 %	0.95 [0.69, 1.30]
Peirce 2006	133/198	123/190		18.3 %	1.04 [0.90, 1.20]
Petry 2005	35/40	31/37		4.7 %	1.04 [0.87, 1.26]
Petry 2007	45/55	14/20		3.0 %	1.17 [0.85, 1.60]
Preston 2000	58/61	54/59		8.0 %	1.04 [0.94, 1.14]
Scherbaum 2005	27/41	19/32		3.1 %	1.11 [0.77, 1.59]
Silverman 2004	35/52	14/26		2.7 %	1.25 [0.84, 1.87]
Stitzer 1992	16/26	20/27		2.9 %	0.83 [0.57, 1.21]
Subtotal (95% CI)	**1203**	**862**		**100.0 %**	**1.01 [0.95, 1.06]**
Total events: 858 (Behavioural+Pharm), 615 (Pharm standard)					
Heterogeneity: Chi^2 = 9.29, df = 18 (P = 0.95); I^2 =0.0%					
Test for overall effect: Z = 0.27 (P = 0.79)					
2 Contingency management plus pharm versus pharm standard					
Bickel 2008	52/90	26/45		6.6 %	1.00 [0.74, 1.36]
Chopra 2009	60/83	28/37		7.3 %	0.96 [0.76, 1.20]



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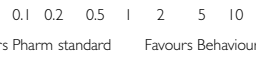
Study or subgroup	Behavioural+Pharm n/N	Pharm standard n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Ghitza 2008	52/76	29/40		7.2 %	0.94 [0.74, 1.21]
Gross 2006	29/40	16/20		4.0 %	0.91 [0.68, 1.21]
Kosten 2003	37/40	38/40		7.2 %	0.97 [0.87, 1.09]
Milby 1978	51/55	18/19		5.1 %	0.98 [0.86, 1.11]
Neufeld 2008	28/51	21/49		4.1 %	1.28 [0.85, 1.93]
Oliveto 2005	36/70	38/70		7.2 %	0.95 [0.69, 1.30]
Peirce 2006	133/198	123/190		23.8 %	1.04 [0.90, 1.20]
Petry 2005	35/40	31/37		6.1 %	1.04 [0.87, 1.26]
Petry 2007	45/55	14/20		3.9 %	1.17 [0.85, 1.60]
Preston 2000	16/26	20/27		3.7 %	0.83 [0.57, 1.21]
Silverman 2004	35/52	14/26		3.5 %	1.25 [0.84, 1.87]
Stitzer 1992	58/61	54/59		10.4 %	1.04 [0.94, 1.14]
Subtotal (95% CI)	**937**	**679**		**100.0 %**	**1.02 [0.96, 1.08]**
Total events: 667 (Behavioural+Pharm), 470 (Pharm standard)					
Heterogeneity: Chi^2 = 6.86, df = 13 (P = 0.91); I^2 =0.0%					
Test for overall effect: Z = 0.56 (P = 0.57)					



Analysis 2.2. Comparison 2 Any Behavioural interventions plus pharm versus pharm standard, Outcome 2 Opioid abstinence.

Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 2 Any Behavioural interventions plus pharm versus pharm standard

Outcome: 2 Opioid abstinence

Study or subgroup	Behavioural + pharm n/N	Pharm standard n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Abbott 1998	46/52	52/67		38.2 %	1.14 [0.97, 1.34]
Avants 2004	51/108	59/112		48.6 %	0.90 [0.69, 1.17]
Hayes 2004	25/45	9/14		11.5 %	0.86 [0.54, 1.38]
Stitzer 1992	8/25	2/25		1.7 %	4.00 [0.94, 17.00]
Total (95% CI)	**230**	**218**		**100.0 %**	**1.04 [0.89, 1.21]**

Total events: 130 (Behavioural + pharm), 122 (Pharm standard)

Heterogeneity: Chi^2 = 6.38, df = 3 (P = 0.09); I^2 =53%

Test for overall effect: Z = 0.47 (P = 0.63)

Test for subgroup differences: Not applicable

Analysis 2.3. Comparison 2 Any Behavioural interventions plus pharm versus pharm standard, Outcome 3 Continuous weeks of abstinence.

Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 2 Any Behavioural interventions plus pharm versus pharm standard

Outcome: 3 Continuous weeks of abstinence

Study or subgroup	Behavioural+Pharm N	Mean(SD)	Pharm standard N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Gross 2006	40	4.4 (3.95)	20	4 (3.2)		84.8 %	0.40 [-1.46, 2.26]
Silverman 2004	52	15.1 (14.2)	26	4.8 (5.44)		15.2 %	10.30 [5.91, 14.69]
Total (95% CI)	**92**		**46**			**100.0 %**	**1.91 [0.20, 3.62]**

Heterogeneity: Chi² = 16.56, df = 1 (P = 0.00005); I² =94%

Test for overall effect: Z = 2.18 (P = 0.029)

Test for subgroup differences: Not applicable

Analysis 2.4. Comparison 2 Any Behavioural interventions plus pharm versus pharm standard, Outcome 4 Number of participants still in treatment at the end of follow-up.

Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 2 Any Behavioural interventions plus pharm versus pharm standard

Outcome: 4 Number of participants still in treatment at the end of follow-up

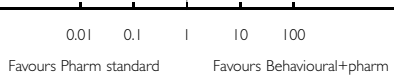
Study or subgroup	Behavioural+pharm n/N	Pharm standard n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Iguchi 1997	50/68	27/35		48.2 %	0.95 [0.76, 1.20]
Khatami 1982	17/24	11/13		19.3 %	0.84 [0.59, 1.18]
Woody 1983	24/39	24/39		32.5 %	1.00 [0.70, 1.42]
Total (95% CI)	**131**	**87**		**100.0 %**	**0.95 [0.80, 1.13]**

Total events: 91 (Behavioural+pharm), 62 (Pharm standard)

Heterogeneity: Chi² = 0.58, df = 2 (P = 0.75); I² =0.0%

Test for overall effect: Z = 0.63 (P = 0.53)

Test for subgroup differences: Not applicable



Analysis 2.5. Comparison 2 Any Behavioural interventions plus pharm versus pharm standard, Outcome 5 Number of participants abstinent at the end of follow-up.

Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 2 Any Behavioural interventions plus pharm versus pharm standard

Outcome: 5 Number of participants abstinent at the end of follow-up

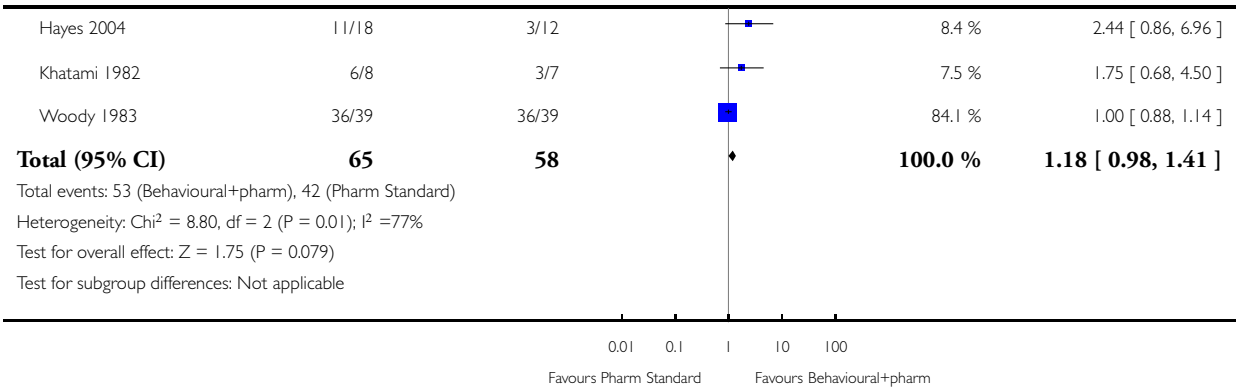
Study or subgroup	Behavioural+pharm n/N	Pharm Standard n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Hayes 2004	11/18	3/12		8.4 %	2.44 [0.86, 6.96]
Khatami 1982	6/8	3/7		7.5 %	1.75 [0.68, 4.50]
Woody 1983	36/39	36/39		84.1 %	1.00 [0.88, 1.14]
Total (95% CI)	**65**	**58**		**100.0 %**	**1.18 [0.98, 1.41]**

Total events: 53 (Behavioural+pharm), 42 (Pharm Standard)

Heterogeneity: Chi^2 = 8.80, df = 2 (P = 0.01); I^2 =77%

Test for overall effect: Z = 1.75 (P = 0.079)

Test for subgroup differences: Not applicable



Analysis 3.1. Comparison 3 Psychoanalytic oriented treatments plus pharm versus pharm standard, Outcome 1 Retention in treatment.

Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 3 Psychoanalytic oriented treatments plus pharm versus pharm standard

Outcome: 1 Retention in treatment

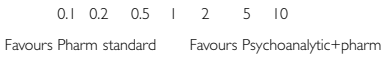
Study or subgroup	Psychoanalytic+pharm n/N	Pharm Standard n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rounsaville 1983	14/37	19/35		26.8 %	0.70 [0.42, 1.16]
Thornton 1987	14/24	17/23		23.8 %	0.79 [0.52, 1.20]
Woody 1995	57/62	27/31		49.4 %	1.06 [0.90, 1.23]
Total (95% CI)	**123**	**89**		**100.0 %**	**0.90 [0.75, 1.07]**

Total events: 85 (Psychoanalytic+pharm), 63 (Pharm Standard)

Heterogeneity: $Chi^2 = 5.61$, df = 2 (P = 0.06); $I^2 = 64\%$

Test for overall effect: Z = 1.24 (P = 0.22)

Test for subgroup differences: Not applicable



Analysis 3.2. Comparison 3 Psychoanalytic oriented treatments plus pharm versus pharm standard, Outcome 2 Opioid abstinence.

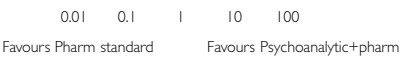
Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 3 Psychoanalytic oriented treatments plus pharm versus pharm standard

Outcome: 2 Opioid abstinence

Study or subgroup	Psychoanalytic+pharm n/N	Pharm standard n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Thornton 1987	9/22	2/21		8.6 %	4.30 [1.05, 17.61]
Woody 1995	31/57	16/27		91.4 %	0.92 [0.62, 1.36]
Total (95% CI)	**79**	**48**		**100.0 %**	**1.21 [0.82, 1.78]**

Total events: 40 (Psychoanalytic+pharm), 18 (Pharm standard)
Heterogeneity: Chi² = 4.99, df = 1 (P = 0.03); I² =80%
Test for overall effect: Z = 0.96 (P = 0.34)
Test for subgroup differences: Not applicable



Analysis 4.1. Comparison 4 Counselling plus pharm versus pharm standard, Outcome 1 retention in treatment.

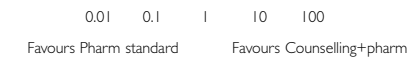
Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 4 Counselling plus pharm versus pharm standard

Outcome: 1 retention in treatment

Study or subgroup	Counselling+pharm n/N	Pharm standard n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Chawarski 2008	12/12	11/12		4.3 %	1.09 [0.87, 1.36]
Chawarski 2011	16/20	13/17		5.2 %	1.05 [0.74, 1.47]
Fiellin 2006	25/56	50/110		12.5 %	0.98 [0.69, 1.40]
Matheson 2010	250/295	194/247		78.1 %	1.08 [0.99, 1.17]
Total (95% CI)	**383**	**386**		**100.0 %**	**1.07 [0.98, 1.15]**

Total events: 303 (Counselling+pharm), 268 (Pharm standard)
Heterogeneity: Chi² = 0.33, df = 3 (P = 0.95); I² =0.0%
Test for overall effect: Z = 1.57 (P = 0.12)
Test for subgroup differences: Not applicable



Analysis 4.2. Comparison 4 Counselling plus pharm versus pharm standard, Outcome 2 opioid abstinence.

Review: Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence

Comparison: 4 Counselling plus pharm versus pharm standard

Outcome: 2 opioid abstinence

Study or subgroup	Counselling+pharm n/N	Pharm standard n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Matheson 2010	123/182	105/153		100.0 %	0.98 [0.85, 1.14]
Total (95% CI)	**182**	**153**		**100.0 %**	**0.98 [0.85, 1.14]**
Total events: 123 (Counselling+pharm), 105 (Pharm standard)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.20 (P = 0.84)					
Test for subgroup differences: Not applicable					

APPENDICES

Appendix 1. Cochrane Drug and Alcohol Group Specialised Register search strategy

Diagnosis=opioid or opiate* or heroin

Appendix 2. CENTRAL search strategy

1. MeSH descriptor Substance-Related Disorders explode all trees
2. ((opioid or opiate*) next (abuse* or addict* or dependen*))
3. #1 or #2
4. (opiat* or opioid* or heroin* or narcoti*):ti,ab
5. MeSH descriptor Heroin explode all trees
6. #4 or #5
7. MeSH descriptor Psychotherapy explode all trees
8. psychother*:ti,ab
9. psychosocial:ti,ab
10. (social near/2 skill*):ti,ab
11. (coping near/2 skill):ti,ab
12. Counseling:ti,ab
13. (behavi* near/2 therap*):ti,ab
14. MeSH descriptor Reinforcement (Psychology) explode all trees
15. (contingent near manage*):ti,ab
16. (brief near motivational):ti,ab
17. (marital near therapy):ti,ab
18. (community near reinforcement):ti,ab
19. (stress near management near training):ti,ab
20. (drug near counseling):ti,ab
21. (supportive near expressive near therapy):ti,ab
22. (neurobehavioral next treatment*):ti,ab
23. voucher:ti,ab
24. reinforcement:ti,ab
25. communit*:ti,ab
26. social*
27. #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26
28. #3 and #6 and #27

Appendix 3. PUBMED search strategy

1. "Substance-Related Disorders"[Mesh]
2. "Opioid-Related Disorders"[Mesh]
3. (substance* or drug*) AND (abuse* or dependen* or use* or disorder* or addict*)
4. #1 OR #2 OR #3
5. (opiat* or opioid* or morphin*)
6. ("Heroin"[Mesh]) or (heroin) [tiab]
7. narcotic*
8. #5 OR #6 OR #7
9. Psychotherapy [Mesh]
10. psychotherap*[tiab]
11. Cognitive [tiab]
12. contingent* [tiab]
13. voucher* [tiab]
14. "Social Adjustment"[Mesh]
15. "Socialization"[Mesh]
16. "Teaching"[Mesh]
17. "social skill training"
18. "Adaptation, Psychological"[Mesh]
19. "coping skill*"

20. “self-control training”
21. “Counseling”[Mesh]
22. counsel*[tiab]
23. “marital therapy”
24. “Community Mental Health Services”[Mesh]
25. “Community Networks”[Mesh]
26. “Reinforcement, Social”[Mesh]
27. reinforcement [tiab]
28. “Social Support”[Mesh]
29. “community reinforcement”
30. “Relaxation Therapy”[Mesh]
31. “stress management”
32. “Case Management”[Mesh]
33. (Therapeutic[tiab] and Communit*[tiab])
34. #9 OR #10 OR #11 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33
35. “Randomized Controlled Trial ”[Publication Type]
36. “Controlled Clinical Trial” [Publication Type]
37. randomized [tiab]
38. placebo [tiab]
39. drug therapy [sh]
40. randomly [tiab]
41. trial [tiab]
42. groups [tiab]
43. #37 or #38 or #39 or #40 or #41 or #42
44. animals [mh] NOT humans [mh]
45. #43 NOT #44
46. #4 AND #8 AND #34 AND #45

Appendix 4. EMBASE search strategy

1. substance abuse/exp
2. narcotic dependance/exp
3. ((((’drug’/de OR ’drug’) OR substance) AND (abuse* OR depend* OR addict*))
4. #1 OR #2 OR #3
5. (opioid* OR opiate*)
6. (’heroin’/de OR ’heroin’)
7. ((’diamorphine’/exp OR ’diamorphine’)
8. Narcotic*
9. #5 OR #6 OR #7
10. #4 AND #9
11. psychotherapy/exp
12. psychotherap*
13. community care/exp
14. therapeutic community/exp
15. (therapeutic* AND communit*)
16. counselling/exp
17. reinforcement/exp
18. reinforc*
19. (contingent* AND manag*)
20. (voucher AND reinforce*)
21. case management/exp

22. ((case OR care) AND management)
23. counsel*
24. psychosoc*
25. community mental health/exp
26. (social AND skill*)
27. ((social AND support) OR 'social support'/exp
28. #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27
29. random*
30. placebo*
31. (((singl* OR doubl* OR trebl* OR tripl*) AND (blind* OR mask*))
32. crossover*
33. randomized controlled trial/exp
34. phase 2 clinical trial/exp
35. phase 3 clinical trial/exp
36. double blind procedure/exp
37. single blind procedure/exp
38. crossover procedure/exp
39. latin square design/exp
40. placebo/exp
41. multicenter study/exp
42. controlled clinical trial/exp
43. (clinic* AND trial*)
44. #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43
45. #10 AND #28 AND #44
46. #45 limit to humans

Appendix 5. CINAHL search strategy

1. (MH "Substance Use Disorders+")
2. ((drug or substance) and (addict* or dependen* or abuse*or disorder*))
3. ((opioid* or opiate*) and (abuse* or addict* or dependen*))
4. #1 or #2 or #3
5. (opioid* or opiate*)
6. (MH "Methadone") or methadone
7. (MH "Heroin") or heroin
8. #5 or #6 or #7
9. MW randomi* or TI randomi* or AB randomi* or IN randomi*
10. MW Clin* or TI Clin* or AB Clin* or IN Clin*
11. MW trial* or TI trial* or AB trial* or IN trial*
12. #10 and #11
13. (MH "Single-Blind Studies")
14. (MH "Double-Blind Studies")
15. (MH " Triple-Blind Studies")
16. #13 or #14 or #15
17. MW singl* or TI singl* or AB singl* or IN singl*
18. MW doubl* or TI doubl* or AB doubl* or IN doubl*
19. MW tripl* or TI tripl* or AB tripl* or IN tripl*
20. MW trebl* or TI trebl* or AB trebl* or IN trebl*
21. MW mask* or TI mask* or AB mask* or IN mask*
22. MW blind* or TI blind* or AB blind* or IN blind*
23. #17 or #18 or #19 or #20

24. #21 or #22
25. #23 AND #24
26. (MH "Crossover Design")
27. MW crossover or AB crossover or TI crossover or IN crossover
28. MW allocate* or AB allocate* or TI allocate* or IN allocate*
29. MW assign* or AB assign* or TI assign* or IN assign*
30. #28 or #29
31. MW random* or TI random* or IN random* or AB random*
32. #30 AND #31
33. (MH "Random Assignment")
34. (MH "Clinical Trials")
35. #9 or #12 or #16 or #25 or #26 or #27 or #30 or #31 or #33 or #34
36. #4 and #8 and #35

Appendix 6. Criteria for risk of bias assessment

Item	Judgment	Description
1. random sequence generation (selection bias)	low risk	The investigators describe a random component in the sequence generation process such as: random number table; computer random number generator; coin tossing; shuffling cards or envelopes; throwing dice; drawing of lots; minimization
	high risk	The investigators describe a non-random component in the sequence generation process such as: odd or even date of birth; date (or day) of admission; hospital or clinic record number; alternation; judgement of the clinician; results of a laboratory test or a series of tests; availability of the intervention
	Unclear risk	Insufficient information about the sequence generation process to permit judgement of low or high risk
2. allocation concealment (selection bias)	low risk	Investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based, and pharmacy-controlled, randomisation); sequentially numbered drug containers of identical appearance; sequentially numbered, opaque, sealed envelopes
	high risk	Investigators enrolling participants could possibly foresee assignments because one of the following method was used: open random allocation schedule (e.g. a list of random numbers); assignment envelopes without appropriate safeguards (e.g. if envelopes were unsealed or nonopaque or not sequentially numbered); alternation or rotation; date of birth; case record number; any other explicitly unconcealed procedure
	Unclear risk	Insufficient information to permit judgement of low or high risk This is usually the case if the method of concealment is not described or not described in sufficient detail to allow a definite judgement

(*Continued*)

3. blinding of outcome assessor (detection bias) Objective outcomes	low risk	No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; Blinding of outcome assessment ensured, and unlikely that the blinding could have been broken
4.blinding of outcome assessor (detection bias) Subjective outcomes	low risk	No blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; Blinding of outcome assessment ensured, and unlikely that the blinding could have been broken
	high risk	No blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; Blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding
	Unclear risk	Insufficient information to permit judgement of low or high risk;
5. incomplete outcome data (attrition bias) For all outcomes except retention in treatment or drop out	low risk	No missing outcome data; Reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias); Missing outcome data balanced in numbers across intervention groups, with similar reasons for missing data across groups; For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk not enough to have a clinically relevant impact on the intervention effect estimate; For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes not enough to have a clinically relevant impact on observed effect size; Missing data have been imputed using appropriate methods All randomised patients are reported/analysed in the group they were allocated to by randomisation irrespective of non-compliance and co-interventions (intention to treat)
	high risk	Reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; For dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention effect estimate; For continuous outcome data, plausible effect size (difference in means or standardized difference in means) among missing outcomes enough to induce clinically relevant bias in observed effect size; 'As-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation;
	Unclear risk	Insufficient information to permit judgement of low or high risk (e.g. number randomised not stated, no reasons for missing data provided; number of drop out not reported for each group);

(*Continued*)

6 selective reporting (reporting bias)	low risk	The study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the pre-specified way; The study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon)
	high risk	Not all of the study's pre-specified primary outcomes have been reported; One or more primary outcomes is reported using measurements, analysis methods or subsets of the data (e.g. subscales) that were not pre-specified; One or more reported primary outcomes were not pre-specified (unless clear justification for their reporting is provided, such as an unexpected adverse effect); One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis; The study report fails to include results for a key outcome that would be expected to have been reported for such a study
	Unclear risk	Insufficient information to permit judgement of low or high risk

Appendix 7. Description of psychosocial interventions utilized in the included studies

- **Behavioural Interventions (20 studies)**

1 Acceptance and Commitment Therapy (Hayes 2004 arm a)
A behavioural therapy with emphasis on acceptance, spirituality, mindfulness and behaviour changes. The attempt is to regulate thoughs, feelings or other private experiences.
2. Biofeedback (Khatami 1982 *)*
A behavioural treatment based on the assumption that environmental stimuli can act as cues for drug-taking behaviour. These stimuli appear to cause anxiety in addicts who are trying to abstain from drugs and such anxiety may in turn motivate further drug use. The biofeedback procedure aims to relieve anxiety. Electromyography (EMG) biofeedback consists of teaching participants to control their EMG activity.
3. Cognitive-Behavioural Therapy (Abrahms 1979; Scherbaum 2005; Woody 1983 arm b)
Cognitive-Behavioural Therapy is an active, directive, time-limited system of psychotherapy that focuses on uncovering and understanding the relationship and influence of automatic thoughts and underlying assumptions on problematic feelings and behaviours. The behavioural component consists of deep muscular relaxation training with imaginal and actual approach of conflict situations; identification and practice of verbal and non verbal components of assertiveness; identification of and engagement in pleasant events; isolation and graduated rehearsal of small units of behaviour leading to goal attainment. The Cognitive component includes identification and disputation of irrational assumptions; sensitisation to aversive consequences of drug use; lowering of expectations and restructuring of goal setting strategies; development and contingent application of positive self-statements and evaluations.
4. Contingency Management Interventions (Abbott 1998; Bickel 2008; Brooner 2004;Chopra 2009; Epstein 2009; Ghitza 2008; Gross 2006; Iguchi 1997; Kosten 2003; Milby 1978; Neufeld 2008; Oliveto 2005; Peirce 2006; Petry 2005; Petry 2007; Preston 2000; Silverman 2004; Stitzer 1992)
Contingency Management is a behavioural treatment based on positive/negative reinforcers used to promote abstinence in in participants in treatment. Many are the contingencies utilized in the included studies both, single or combined. Participants can obtain payment, or win prizes or a (c) take-home pharmacological treatment (methadone or bupreborphine) dose, for drug-free urines or for completing a treatment plan task; furthermore participants can receive half of their pharmacological treatment for clinical attendance and the other half for remaining abstinent. A variant of this approach is the Community Reinforcement Approach, a behavioural treatment intervention based on a social learning theory model intended to rearrange personal and community reinforces. Specific abstinence

reinforces in all major aspects of the patient's life are examined; positive reinforces are identified and presented as alternatives to drug use.

5. Information-Motivation-Behavioural Skills Model (Avants 2004)

A model of behaviour change that focused on reducing both drug and sex risks.

All these interventions are behavioural approaches, which are in line with reinforcement principles.

- **Psychoanalytic Interventions (4 studies)**

1. Subliminal Stimulation (Thornton 1987)

Is based on a psychoanalytic theory that states that unconscious wishes and fantasies have a direct impact on overt behaviour particularly pathological behaviour. The experimental stimuli are designed to activate unconscious wishes and fantasies that have affected behaviour in ways that neutral stimuli have not. The stimuli MOMMY AND I ARE ONE was chosen to activate "symbiotic-like fantasies" of oneness with the "good mother of infancy". This fantasy allays anxiety and mobilizes positive affect, very likely because the unconscious fantasy, the idea of oneness with the mother leaves the person feeling comforted and protected. Furthermore this fantasy enables participants to feel more 'connected' to the therapist and more able to respond to treatment.

2. Supportive-Expressive Therapy (Woody 1983 arm a; Woody 1995)

The supportive techniques aim to help the participant feel comfortable in discussing his or her personal experiences. The expressive techniques aim to help the participant identify and work through problematic relationship themes. Special attention is paid to themes that are involved in drug dependence, the role of drugs in relation to problem feelings and behaviours and how problems may be solved without recourse to drugs.

3. Short-term Interpersonal Psychotherapy (Rounsaville 1983)

A treatment based on the concept that psychiatric disorders, including opiate addiction, are intimately associated with disturbances in interpersonal functioning, which may be associated with the genesis and perpetuation of the disorder.

- **Counselling Interventions (4 studies)**

1. Customized Employment Supports (Magura 2007)

An intervention in which counsellors work intensively with a small caseload of patients to overcome the vocational as well a non-vocational barriers that hinder employment, with the goal of attaining rapid job placement.

2. Enhanced Methadone Services (Chawarski 2008;Chawarski 2011 McLellan 1993)

This intervention consists of counselling plus on site medical, psychiatric, employment and family therapy services. The intervention is composed also by educational, directive, and prescriptive component (BDRC) and uses short-term behavioral contracts aimed at improving treatment adherence and getting patients to make initial lifestyle
changes, including cessation/reduction of drug use and cessation/reduction of
drug- and sex-related risk behaviours

3. *Enhanced Medical Management* (Fiellin 2006)

Extended sessions of manual guided, medical focused counselling

4.Free Mapping and Free plus guide Mapping: (Czuchry 2009)

Counsellors and clients cooperatively construct a node-link display over the course of counselling session in order to facilitate engagement of patients in treatment, positive feeling about self and treatment, therapeutic alliance . A marker board or large sheet of paper is used to provide a shared visualization.. The results display is reviewed and modified in subsequent session.

In free plus guide mapping the utilisation of a preformed "fill in the node" mapping could help patients and counsellors in examining treatment related issues

- **Other Interventions (2 studies)**

1. Relational Psychotherapy Mothers' Group (Luthar 2000)

Is a developmental informed, supportive psychotherapy designed to serve heroin-addicted mothers with children less than 16 years of age, aims at addressing psychosocial vulnerabilities and facilitating optimal parenting, among at risk mothers.

2. Twelve-step facilitation (Hayes 2004 arm b)

Is a structured, manualized psychosocial intervention designed to both parallel and facilitate a 12-step prospective. The treatment emphasizes acceptance of the addiction problem, surrender of control and active participation in 12-step meetings and a program of recovery.

In 25 out of 28 of the included studies, the standard control treatment consisted of the provision of agonist maintenance treatment associated with the availability of standard counselling sessions. The counselling sessions consisted of: clear statements of the program's rules, comprehensive treatment plans, information on HIV and, when needed, other relevant specific issues. This counselling is standard

for all agonist maintenance treatments and is offered to all subjects independently from the group of treatment in which they are included, although the frequency of the session is variable within the studies
For more details see 'Characteristics of included studies' table.

WHAT'S NEW

Last assessed as up-to-date: 31 July 2011.

Date	Event	Description
1 August 2011	New citation required but conclusions have not changed	New studies included and excluded, new analysis
1 August 2011	New search has been performed	New searches, new studies included, excluded

HISTORY

Protocol first published: Issue 2, 2003

Review first published: Issue 4, 2004

Date	Event	Description
11 November 2008	Amended	to be corrected
20 October 2008	Amended	Contact details updated
7 August 2008	New search has been performed	the review is updatet and conclusion changed, new citation
25 June 2008	New citation required and conclusions have changed	new search, new trials, new valuation of included studies, conclusions changed
17 April 2008	Amended	Converted to new review format.
26 July 2004	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

For the update, Laura Amato inspected the search hits by reading the titles and the abstracts. Laura Amato and Silvia Minozzi independently assessed the articles for inclusion and wrote the review. Silvia Minozzi assessed the methodological quality of the included studies. Marina Davoli and Simona Vecchi commented on the draft.

DECLARATIONS OF INTEREST

None known

SOURCES OF SUPPORT

Internal sources

- Department of Epidemiology, ASL RM E, Italy.

External sources

- EDAP Project (Evidence for Drugs and Alcohol Policy) sponsored by the European Community- Directorate Public Health (Grant Agreement SPC.2002454), Not specified.

INDEX TERMS

Medical Subject Headings (MeSH)

Combined Modality Therapy [methods]; Narcotics [*therapeutic use]; Opioid-Related Disorders [psychology; *rehabilitation]; Psychotherapy [*methods]; Randomized Controlled Trials as Topic

MeSH check words

Humans