Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification (Review)

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[Intervention Review]

Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification

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ABSTRACT

Background

Different pharmacological approaches aimed at opioid detoxification are effective. Nevertheless a majority of patients relapse to heroin use, and relapses are a substantial problem in the rehabilitation of heroin users. Some studies have suggested that the sorts of symptoms which are most distressing to addicts during detoxification are psychological rather than physiological symptoms associated with the withdrawal syndrome.

Objectives

To evaluate the effectiveness of any psychosocial plus any pharmacological interventions versus any pharmacological alone for opioid detoxification, in helping patients to complete the treatment, reduce the use of substances and improve health and social status.

Search strategy

We searched the Cochrane Drugs and Alcohol Group trials register (27 February 2008). Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 1, 2008), PUBMED (1996 to February 2008); EMBASE (January 1980 to February 2008); CINAHL (January 2003-February 2008); PsycINFO (1985 to April 2003) and reference list of articles.

Selection criteria

Randomised controlled trials which focus on any psychosocial associated with any pharmacological intervention aimed at opioid detoxification. People less than 18 years of age and pregnant women were excluded.

Data collection and analysis

Three reviewers independently assessed trials quality and extracted data.

Main results

Nine studies involving people were included. These studies considered five different psychosocial interventions and two substitution detoxification treatments: Methadone and Buprenorphine. The results show promising benefit from adding any psychosocial treatment to any substitution detoxification treatment in terms of completion of treatment relative risk (RR) 1.68 (95% confidence interval (CI)

1.11 to 2.55), use of opiate RR 0.82 (95% CI 0.71 to 0.93), results at follow-up RR 2.43 (95% CI 1.61 to 3.66), and compliance RR 0.48 (95% CI 0.38 to 0.59).

Authors' conclusions

Psychosocial treatments offered in addition to pharmacological detoxification treatments are effective in terms of completion of treatment, use of opiate, results at follow-up and compliance. Although a treatment, like detoxification, that exclusively attenuates the severity of opiate withdrawal symptoms can be at best partially effective for a chronic relapsing disorder like opiate dependence, this type of treatment is an essential step prior to longer-term drug-free treatment and it is desirable to develop adjunct psychosocial approaches that might make detoxification more effective. Limitations to this review are imposed by the heterogeneity of the assessment of outcomes. Because of lack of detailed information no meta analysis could be performed to analyse the results related to several outcomes.

PLAIN LANGUAGE SUMMARY

Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification

People who abuse opioid drugs and become dependent on them experience social issues and health risks. Medications such as methadone and buprenorphine are substituted to help dependent drug users detoxify and return to living drug free, by reducing physiological withdrawal symptoms (pharmacological detoxification). Yet psychological symptoms can occur during detoxification and may be distressing. It is often a personal crisis that led to a drug user deciding to detoxify. Furthermore the psychological reasons why a person became addicted are important. They may not be able to cope with stress and have come to expect that using mood modifying illicit substances helps. Even after successful return to a drug-free state, many people return to heroin use and re-addiction is a substantial problem in rehabilitation. The physiological, behavioural and social conditions in an individual's life that made them an opiate addict may still be present when physical dependence on the drug has been eliminated, which makes psychosocial therapy important. Psychosocial treatments include behavioural treatments, counselling and family therapy.

The review authors searched the medical literature and found evidence that providing a psychosocial treatment in addition to pharmacological detoxification treatment to adults who are dependent on heroin use is effective in facilitating opioid detoxification. This conclusion is based on nine controlled studies involving 634 adults, 32% men, with an average age of 34 years (28 to 41 years). The studies lasted 16 days to 26 weeks. The addition of a psychosocial treatment to substitution detoxification treatment improved the number of people who completed treatment (relative risk (RR) 1.68), use of opiate (RR 0.82), abstinence from drugs at follow up (RR 2.4), and halved the number of failures to attend clinic absences (RR 0.48). The findings of an improved rate of clinical attendance may help in suppressing illicit drug use and provides clinical staff with more opportunities to counsel patients in psychiatric, employment and other drug and non-drug related areas. Variations in the populations who are substance users and use of a wide range of different psychosocial interventions means that it is difficult to single out particular therapeutic interventions.

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

any pharmacological detoxification treatment plus psychosocial compared to any pharmacological treatment alone for opioid dependent requiring detoxification

Patient or population: patients with opioid dependent requiring detoxification
Settings: outpatient and inpatient
Intervention: any pharmacological detoxification treatment plus psychosocial
Comparison: any pharmacological treatment alone

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	any pharmacological treatment alone	any pharmacological detoxification treatment plus psychosocial				
Completion of treatment (follow-up: mean 18 weeks)	**Low risk population**		**RR 1.68** (1.11 to 2.55)	184 (5)	[1,2]	
	253 per 1000	**425 per 1000** (281 to 645)				
use of opiate during treatment (follow-up: mean 018 weeks)	**Low risk population**		**RR 0.82** (0.71 to 0.93)	320 (4)	⊕⊕⊕◯ **moderate** [2,3]	
	Medium risk population					
	790 per 1000	**648 per 1000** (561 to 735)				

relapsed at follow-up (follow-up: mean 18 weeks)	**Medium risk population**	**RR 0.41** (0.27 to 0.62)	208 (3[1])	⊕⊕⊕◯ **moderate** [2,4]

*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 evidance
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] Four studies with unclear allocation concealment and one inadequate; 2 studies were single blind and 3 did not report data on blindness
[2] All studies were conducted in USA
[3] Four studies with unclear allocation concealment
[4] All studies with unclear allocation concealment, 2 single blind, 1 not blind

BACKGROUND

Abuse and dependence on opioid drugs are major health and social issues in most societies. Different interventions to deal with problems related to opiate abuse and dependence are available.

Data from literature and clinical experience, suggest that different pharmacological approaches aimed at detoxification are effective. Detoxification treatments may attenuate the withdrawal symptoms until the achievement of a drug free state. 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,Phillips 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).

The Cochrane Drugs and Alcohol Group has conducted five reviews on detoxification treatments of opioid dependence (Amato 2005, Gowing 2006, Gowing 2006 a, Gowing 2006 b, Gowing 2004). Some of the trials included in these reviews suggested that the provision of psychosocial support along with pharmacological therapy may help the success of the interventions (Hall 1979, Rawson 1983).

Improvements in the methadone withdrawal response may be achieved through the provision of more information, counseling and other supporting services. Indeed these other services, by encouraging realistic expectations and setting short term goals, might be as important as the pharmacological therapy in determining treatment outcomes.

In the published literature we did not find any systematic review assessing the effectiveness of psychosocial intervention plus pharmacological intervention aimed at detoxification.

Psychosocial treatments for opioid abuse or dependence are a critical component of the overall treatment package and require evaluation as stand-alone intervention but also in combination with pharmacotherapies. This current review focuses on psychosocial treatments delivered in association with pharmacological detoxification 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 other two partner reviews. The first looks at the effectiveness of psychosocial interventions plus pharmacological maintenance interventions for opiate dependence (Amato 2004). 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 during detoxification. 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 reviewed separately.

OBJECTIVES

To evaluate the effectiveness of any psychosocial plus any pharmacological interventions versus any pharmacological alone for opioid detoxification, in helping patients to complete the treatment, reduce the use of substances and improve health and social status.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials

Types of participants

Opiate addicts undergoing any psychosocial associated with any pharmacological intervention aimed at opioid detoxification.
People less than 18 years of age and pregnant women were excluded. These groups of people 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 pharmacological detoxification interventions of any kind (any psychosocial and any drug) compared to:
Control intervention - Pharmacological treatments (any drug) for opiate detoxification.
If information were available, studies with people using multiple drugs, were considered separately because these patients may respond differently to psychosocial interventions than those with less severe problems.

Types of outcome measures

Primary outcomes
(1) Completion of treatment as number of participants completing the detoxification program
(2) Use of opioid drugs measured as number of participants with positive urinalysis during the treatment
(3) Results at follow-up as number of participants abstinent at follow up
Secondary outcomes
(1) Compliance
(2) Use of other drugs
(3) Mortality

Search methods for identification of studies

See: Collaborative Review Group search strategy
We searched in the following electronic databases:

1. **Cochrane Drugs and Alcohol Group's Register of Trials (February 2008)**
2. **Cochrane Central Register of Controlled Trials (CENTRAL - The Cochrane Library issue 1, 2008)**
3. **PUBMED (1996 to February 2008)**
4. **EMBASE (January 1980 to February 2008)**
5. **PsycINFO (1985 to April Week 1 2003)**
6. **CINAHL (January 2003-February 2008)**

For details on searches *see* Appendix 1; Appendix 2; Appendix 3; Appendix 4; Appendix 5
Additional searches:
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-sperclin.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

Study selection:
One reviewer (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 three reviewers (Amato, Minozzi, Vecchi) independently assessed the article for inclusion. Doubts were resolved through discussion involving all three reviewers. The same authors worked at the update with the same modalities.

Assessment of the methodological quality:
Three reviewers (LA, SM, SV) assessed the quality of the studies. In determining our approach to assessing study quality, we considered the criteria indicated in Cochrane Reviewers' Handbook 4.2;

- ***Selection bias:*** empirical research has shown that lack of adequate allocation concealment is associated with bias (Chalmers 1993; Moher 1998; Moher 1999; Schulz 1995). Indeed, concealment has been found to be more important in preventing bias than other components of allocation, such as the generation of the allocation sequence
- ***Performance bias:*** systematic differences in the care provided to the participants in the comparison groups and the placebo effect could effectively take place in the addiction field. On the other hand is very unlikely that trials on the effectiveness of psychosocial treatments could be blinded.
- ***Attrition bias:*** loss of follow up and drop out from the study is one of the biggest problems in the field of addiction; in fact the retention in treatment is very often the primary outcome measure in these trials; for these reason the information on people who left the study has not been used as a validity criterion.
- ***Detection bias*** : to keep blind the people who will assess outcomes is particularly important when subjective outcome measures are used, but this is not the case for these studies, where the primary outcomes are the retention in treatment rate or the use of substances measured by bioanalysis.

Thus, study quality has been judged on the basis of the method of allocation concealment and was rated as follows:

- A. Low risk of bias: adequate allocation concealment, i.e. central randomization (e.g. allocation by a central office unaware of participant characteristics), computer file that can be accessed only after the characteristics of an enrolled participant have been entered or other description containing elements suggesting adequate concealment.
- B. Moderate risk of bias: unclear allocation concealment, in which the authors either did not report an allocation concealment approach at all or report an approach that did not fall in the category A or C.
- C. High risk of bias: inadequate allocation concealment, such as alternation or reference to case numbers or dates of birth.

- D. When allocation concealment has not been used to evaluate the quality of the study (i.e when it does not apply because of a study design other than RCT)

The methodological quality was not used as a criterion for inclusion or for subgroup analysis; in order to assess the effect of the low quality studies we performed a sensitivity analysis, either including or excluding the class C ones from meta-analysis.

Data extraction:

Three reviewers (LA, SM, SV). 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.

Data synthesis:

Dichotomous outcomes (retention in treatment, number of participants with negative urinalysis) were analysed by calculating the Relative risk (RR) for each trial with the uncertainty in each result being expressed by their confidence intervals. The RR from the individual trials were combined through meta-analysis where possible (comparability of intervention between trials) using a fixed effect model unless there was significant heterogeneity, in which case we used a random effects model. A P-value of the chi square test less than 0.05 indicated a significant heterogeneity.

The completion of treatment was reported as the number of patients that completed the detoxification program. The use of primary substance was reported as number of participants with positive urinalysis during the treatment. The results at follow up were reported as the number of participants abstinent at follow up (follow up period: six months).

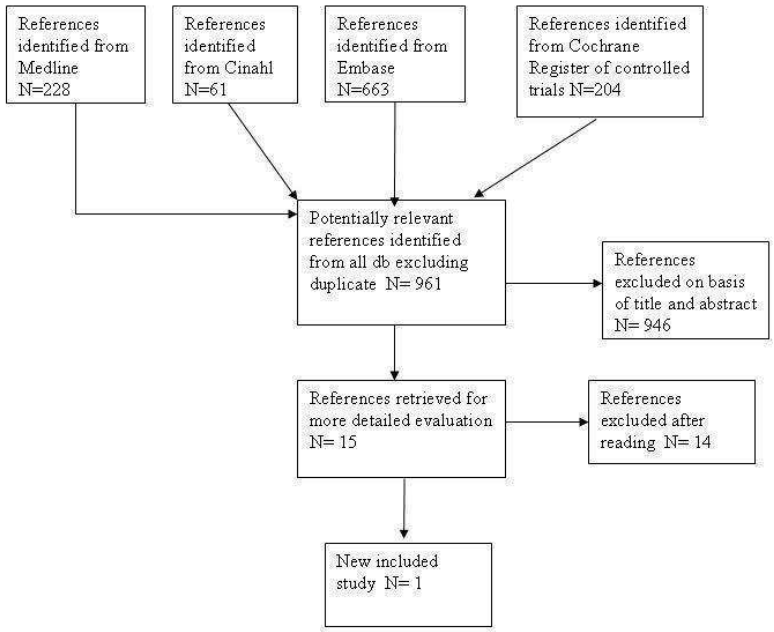
RESULTS

Description of studies

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

In the first publication of the review (search strategies ended in April 2003), we identified 83 reports relating to 77 different studies, with the new search (ended February 2008) we identified 961 new different studies *see* Figure 1, with treatment regimes involving the administration of pharmacological treatment associated with some psychosocial intervention.

Flow chart showing identification of trials for the update of the review.



For substantive descriptions of studies please Characteristics of excluded studies and Characteristics of included studies tables
This review has a parallel one on Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence Amato 2004, the search strategy was common for the two reviews, then we separate the trials considering detoxification treatments from trial considering maintenance treatments.
The excluded studies described above are those that, on the basis of title and abstract were evaluate as probably considering psychosocial interventions associated with detoxification pharmacological interventions.

Excluded studies

49 studies did not meet the criteria for inclusion in this review, the grounds for exclusion were: study design not in the inclusion criteria: sixteen studies; type of intervention not in the inclusion criteria: sixteen studies; type of participants not in the inclusion criteria: six studies; type of participants and type of intervention not in the inclusion criteria: five studies; the outcomes reported not those defined for this review: three studies; type of design and type of participants not in the inclusion criteria: three studies.

Included studies

Nine studies met the inclusion criteria for this review. In the studies were considered:

- four different psychosocial interventions
- two detoxification treatments: Methadone Detoxification Treatment (seven studies) and Buprenorphine Detoxification Treatment (two studies)

Type of psychosocial treatments:

The four psychosocial intervention considered in the eight included studies were:

- two behavioural treatments: Contingency Management, Community Reinforcement
- one form of structured counselling: Psychotherapeutic Counseling
- one Family Therapy

Below there is a brief description of these intervention

- ***Contingency Management Approaches:***

Contingency Management is a behavioural treatment based on positive/negative reinforcers used to promote abstinence in participants in treatment. With positive reinforcers, the participants can obtain payment for drug-free urine (Hall 1979; Katz 2004; McCaul 1984; Robles 2002), or methadone dose increases (Higgins 1984; Higgins 1986). A variant of this approach is the Community Reinforcement Approach, a behavioural treatment that consists of two interventions: Community Reinforcement associated with Contingency Management. The Community Reinforcement consists of two to three individual counselling sessions of one hour per week; during therapy sessions, participants were provided with relationship and employment counselling, instructions on antecedents and consequences of their opiate use, assistance in developing new or reinitiating old recreational activities (Bickel 1997).
These interventions are both behavioural approaches, which are in line with the reinforcement principles. Contingency Management uses formal clinic-managed reinforcers (vouchers), while in the Community Reinforcement Approach often significant others are mobilised to administer reinforcers contingent on non-substance using behavior (alternatives) of the patient.

- ***Psychotherapeutic Counselling:***

This counselling entails the assessment of individual patient needs and the provision of services to meet these needs. The intervention does not consider intrapsychic processes. (Rawson 1983)

- ***Family Therapy:***

Family therapy is a structured and strategic approach which places particular emphasis on developing appropriate boundaries and limits before introducing a strategic intervention. If the patient was in a relationship, the therapist worked primarily with the couple. However, other significant relationships were also included in the discussion during the sessions, and other family members were also invited to attend some sessions (Yandoli 2002).

Duration of the trials: range 16 days to 26 weeks.

Participants: 634 opiate addicts: 32% (201) were male. Average age was 34 years (range 28 to 41).

Countries in which the studies were conducted: eight studies were conducted in USA, one study (Yandoli 2002) in UK.

Type of comparisons

- Any Psychosocial plus any Pharmachological Intervention versus any Pharmachological alone: eight studies, 634 participants (Bickel 1997; Hall 1979; Higgins 1984; Higgins 1986; Katz 2004; McCaul 1984; Rawson 1983; Robles 2002; Yandoli 2002).

- Any Psychosocial Intervention plus Methadone Detoxification Treatment (MDT) versus MDT alone: seven studies (Hall 1979;Higgins 1984;Higgins 1986; McCaul 1984;Rawson 1983;Robles 2002;Yandoli 2002) 384 participants
- Contingency Management Approaches plus MDT versus MDT alone: five studies (Hall 1979, Higgins 1984, Higgins 1986, McCaul 1984, Robles 2002), 215 participants
- Family Therapy plus MDT versus MDT alone versus Low Contact: one study (Yandoli 2002), 119 participants.
- Psychotherapeutic Counselling plus MDT versus MDT alone: one study (Rawson 1983), 50 participants.

Information on methadone doses was available for seven out of the nine included studies. The mean starting dose of methadone was 44.5 mg (range 30 to 76.4).

- Behavioural Treatment plus Buprenorphine Detoxification Treatment (BDT): one study (Bickel 1997), 39 participants. The dose range was 2 to 8 mg/day.
- Contingency Management Approaches plus MDT versus MDT alone: one study (Katz 2004), 211 participants. 0.3 mg intramuscular buprenorphine daily for four days

Outcomes:

Primary outcomes:

1. Completion of treatment measured as number of subjects completing the detoxification program
2. Use of primary substance measured as number of subjects with positive urinalysis during the treatment
3. Results at follow as number of subjects abstinent at follow up

Secondary outcomes:

1. Compliance measured as clinic absences during the treatment
2. Use of other drugs
3. Mortality

Risk of bias in included studies

Only two studies (Bickel 1997, Rawson 1983) describe the randomisation method: Bickel 1997 use a stratified randomisation procedure to achieve balance between groups; Rawson 1983 describe the randomisation procedure as a random number table generated list. All the other studies simply state the participants were randomly assigned to the groups.

None of the included studies mention any allocation concealment approach. All but two studies were evaluated as studies with moderate risk of bias (class B).

Two studies (Robles 2002; Yandoli 2002) were evaluated as studies with inadequate allocation concealment (class C) as it appears that the people who recruited participants were aware of the assignment schedule and in some cases modified the assignment schedule for practical reasons: to ensure that participants in both groups received vouchers in equal amounts and temporal distributions (Robles 2002) or to put participants cohabiting in the same group (Yandoli 2002).

All studies but one (Hall 1979) give information on people who left the study or were lost at follow up.

Effects of interventions

See: **Summary of findings for the main comparison**

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

The only pharmacological treatments evaluated in the included studies were substitution treatment with the aim of detoxification: methadone and buprenorphine.

For some outcomes reported in the included studies, it was impossible to make comparisons and pool results due to the different ways of reporting the results. Different rating instruments were utilized and for many of them the authors did not indicate the scores considered to represent boundaries of mild, moderate and severe to allow comparison of results between studies.

Primary Outcomes

(1) Completion of treatment

Number of participants completing the detoxification program

Any Psychosocial plus any Pharmacological Intervention (a+d) versus any Pharmacological alone:

Five studies (Bickel 1997; Higgins 1984; McCaul 1984; Rawson 1983; Robles 2002), 184 participants relative risk (RR) 1.68 (95% confidence interval (CI) 1.11 to 2.55), *see* Analysis 1.1, the result is significantly in favour of any psychosocial associated with any pharmacological intervention. We performed a sensitivity analysis excluding the study with inadequate allocation concealment (class C) from meta-analysis (Robles 2002, 48 participants). The result did not change, remaining significantly in favour of the associated treatments (RR 2.17 (95% CI 1.26 to 3.72).

Any Psychosocial Intervention plus MDT (b+c) versus MDT alone:

Four studies (Higgins 1984; McCaul 1984; Rawson 1983; Robles 2002) 145 participants RR 1.48 (95% CI 0.93 to 2.35), *see* Analysis 2.1, the difference is not statistically significant but there is a clear trend in favour of psychosocial intervention associated with MDT. We performed a sensitivity analysis excluding the study with inadequate allocation concealment (class C) from meta-analysis (Robles 2002, 48 participants), the result did not change RR 1.96 (95% CI 1.02 to 3.77).

Contingency Management Approaches plus MDT versus MDT alone:

3 studies (Higgins 1984; McCaul 1984; Robles 2002), 95 participants, RR 1.51 (95% CI 0.93 to 2.46), *see* Analysis 3.1, the difference is not statistically significant but there is a clear trend in favour of contingency management associated with MDT. We performed a sensitivity analysis excluding the study with inadequate allocation concealment (class C) from meta-analysis (Robles 2002, 48 participants). The result became significant in favour of Contingency Management Approaches plus MDT RR 2.28 (95% CI 1.09 to 4.75).

Psychotherapeutic Counselling plus MDT versus MDT alone:

One study (Rawson 1983) 50 participants 4/25 (16%) participants in the associated treatment group completed withdrawal compared to 3/25 (12%) in the MDT alone group, RR 1.33 (95% CI 0.33

to 5.36). The difference is not statistically significant.

Contingency Management Approaches plus BDT versus BDT alone:

One study (Bickel 1997), 39 participants 10 out of 19 (53%) participants in the associated treatment group completed withdrawal compared to 4/20 (20%) in the BDT alone group, RR 2.63 (95% CI 0.99 to 6.98). The difference is in favour of the associated treatment.

(2) Use of primary substance

Number of participants with opiate positive urinalysis during the treatment

Any Psychosocial plus any Pharmacological Intervention (a+d) versus any Pharmacological alone:

Four studies (Bickel 1997; Katz 2004; McCaul 1984; Rawson 1983) 320 participants, RR 0.82 (95% CI 0.71 to 0.93), *see* Analysis 1.2, in favour of the associated treatment .

Any Psychosocial Intervention plus MDT (b+c) versus MDT alone:

Two studies (McCaul 1984; Rawson 1983) 70 participants RR 0.68 (95% CI 0.43 to 1.07), *see* Analysis 2.2, the difference is not statistically significant.

Contingency Management Approaches plus MDT versus MDT alone:

One study (McCaul 1984), 20 participants, 5/10 (50%) participants in the associated treatment group with opiate positive urine samples during the treatment compared to 10 out of 10 (100%) in the MDT alone group, RR 0.50 (95% CI 0.27 to 0.93). The difference is in favour of the associated treatment.

Psychotherapeutic Counselling plus MDT versus MDT alone:

One study (Rawson 1983) 50 participants, 10/25 (40%) participants in the associated treatment group with opiate positive urine samples compared to 12 out of 25 (48%) in the MDT alone group, RR 0.83 (95% CI 0.44 to 1.56). The difference is not statistically significant, but there is a trend in favour of the associated treatment.

Contingency Management Approaches plus BDT versus BDT alone:

Two studies (Bickel 1997; Katz 2004), 230 participants, RR 0.47 (95% CI 0.25 to 0.91) *see* Analysis 4.1, in favour of the associated treatment.

(3) Results at follow-up

Number of subjects abstinent at follow up

Any Psychosocial plus any Pharmacological Intervention (a+d) versus any Pharmacological alone:

Three studies (Bickel 1997; Rawson 1983; Yandoli 2002), 208 participants, RR 2.43 (95% CI 1.61 to 3.66), *see* Analysis 1.3, in favour of the associated treatments. We performed a sensitivity analysis excluding the study with inadequate allocation concealment (class C) from meta-analysis (Yandoli 2002, 119 participants). The result was no longer statistically significant RR 2.03 (95% CI 0.84 to 4.92).

Any Psychosocial Intervention plus MDT (b+c) versus MDT alone:

Two studies (Rawson 1983; Yandoli 2002), 129 participants RR 1.40 (95% CI 1.10 to 1.80), *see* Analysis 2.3, in favour of the associated treatments.

Psychotherapeutic Counselling plus MDT versus MDT alone:

One study (Rawson 1983), 50 participants 18 out of 25 (72%) participants in the associated treatment group were abstinent at follow-up compared to 13/25 (52%) in the MDT alone group, RR 2.00 (95% CI 0.69 to 5.80). The difference is not statistically significant.

Family Therapy plus MDT versus MDT alone:

One study (Yandoli 2002), 119 participants, 29 out of 41 (71%) participants in the associated treatment group were abstinent at follow-up compared to 39/78 (50%) in the MDT alone group, RR 1.41 (95% CI 1.05 to 1.90). The result is significantly in favour of the associated treatment.

Contingency Management Approaches plus BDT versus BDT alone:

One study (Bickel 1997), 39 participants, 4 out 19 (21%) participants in the associated treatment group were abstinent at follow-up compared to 2/20 (10%) in the BDT alone group, RR 2.11 (95% CI 0.43 to 10.19), the difference is is not statistically significant, but there is a trend in favour of the associated treatment.

Secondary outcomes

(1) Compliance

Measured as Clinic Attendance:

Any Psychosocial Intervention plus MDT versus MDT alone:

Three studies (Higgins 1984; Higgins 1986; Rawson 1983). The outcome is reported as number of clinic absences during the treatment. RR 0.48 (95% CI 0.38 to 0.59), *see* Analysis 2.4, the result is significantly in favour of the associated intervention.

Contingency Management Approaches plus MDT versus MDT alone:

Three studies (Higgins 1984; Higgins 1986; McCaul 1984). It was possible to pool data only for 2 of these studies (Higgins 1984; Higgins 1986), that reported this outcome as number of clinic absences during the treatment. RR 0.29 (95% CI 0.15 to 0.56), *see* Analysis 3.2, the result is significantly in favour of the associated intervention.

The other study that reported this outcome (McCaul 1984), did not report data, but reported that no difference was found in missed clinic days attendance between groups, t(18)=0.41 not statistically significant.

Psychotherapeutic Counselling plus MDT versus MDT alone:

One study (Rawson 1983), 50 participants, outcome reported as number of clinic absences during the treatment. Participants in the associated treatment group missed 83/460 (18%) scheduled clinic attendances compared to 169/482 (35%) in the MDT alone group, RR 0.51 (95% CI 0.41 to 0.65), the difference is statistically significant in favour of the associated treatment.

(2) Use of other drugs

Contingency Management Approaches plus BDT versus BDT alone:

One study (Bickel 1997), 39 participants; the data are on subjects with positive urine samples for each substance in both groups. Barbiturates: 9 out of 19 (47%) participants in the associated treatment group compared to 6/20 (30%) in the BDT alone group; Benzodiazepines: 17 out of 19 (89%) participants in the associated treatment group compared to 15 out of 20 (75%) in the BDT alone group; Cannabinoids: 9 out of 19 (47%) participants in the associated treatment group compared to 11 out of 20 (55%) in the BDT alone group; Cocaine: 12/19 (63%) participants in the associated treatment group compared to 11/20 (55%) in the BDT alone group. The differences were never statistically significant for any of the substances.

(3) Mortality

Family Therapy plus MDT versus MDT alone:

One study (Yandoli 2002), 119 participants, 2 out of 41 (5%) participants in the associated treatment group had died at 1 year follow-up compared to 0 out of 78 in the MDT alone group; 3 out of 41 (7%) participants in the associated treatment group had died at 5 year follow-up compared to 2 out of 78 (2.5%) in the MDT alone group.

DISCUSSION

The results of this review show promising benefit from adding any psychosocial treatment to any substitution detoxification treatment in terms of completion of treatment, use of opiate, results at follow-up and compliance. For results at follow-up, if we exclude the study evaluated as class C from meta-analysis, , the result become not statistically significant but the trend in favour of associated treatment is confirmed.

For the other two outcomes considered in the included studies (use of other drugs and mortality) it was not possible to pool the data. The use of other drug was considered only in Bickel 1997 and the results for all the substances considered were never significant; mortality was considered only in Yandoli 2002 but the low number of events did not permit the use of statistical analysis.

The results of this review are different from the results of the parallel review on maintenance treatment (Amato 2004). That review showed that patients in treatment with standard methadone maintenance therapy do not need adjunctive intervention to improve on standard outcomes of retention in treatment or results at follow-up. This may be because methadone maintenance treatment has robust effects and furthermore counselling is usually offered along with methadone. 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 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.

In fact, there is no evidence that detoxification can substitute for long term treatment in the management of opiate addiction. Research suggests that relapse to opiate use is not entirely determined by avoidance of, or escape from withdrawal symptoms. Therefore a treatment that exclusively attenuates the severity of opiate withdrawal symptoms can be at best partially effective. Many if not most of the physiological, behavioural and social conditions prevailing during an individual's life as an opiate addict will still be present when the physical dependence has been eliminated.

Furthermore, once methadone has been removed, opiates will likely recover the reinforcing properties that previously sustained self administration and it is under those conditions that relapse is likely to occur. Yet, outpatient detoxification from opiate is a quick, inexpensive and common procedure that helps individuals by ameliorating withdrawal symptoms, and by temporarily reducing health risk associated with drugs. In addition, detoxification constitutes the first instance of contact of many addicts with the various treatment services available, and may facilitate transition into long term care. Given that methadone detoxification is such a widely used procedure, it appears reasonable to attempt to develop more efficacious detoxification techniques and to add psychosocial interventions to detoxification techniques seems to improve this procedure.

Particularly interesting are the findings of a high rate of clinical attendance by participants with the associated interventions, not only for suppressing illicit drug use, but also because it provides clinical staff with more opportunities to counsel patients in psychiatric, employment and other drug and non-drug related areas.

AUTHORS' CONCLUSIONS

Implications for practice

Psychosocial treatments offered in addition to pharmacological detoxification treatments are effective in term of completion of treatment, use of opiate, results at follow-up and compliance. Although a treatment, like detoxification, that exclusively attenuates the severity of opiate withdrawal symptoms can be at best partially effective for a chronic relapsing disorder like opiate dependence, this form of treatment is an essential step prior to longer-term drug-free treatment and it is desirable to develop adjunct psychosocial approaches that might make detoxification more effective.

Implications for research

Limitations to this review are imposed by the heterogeneity of the assessment of outcomes. Due to lack of detailed information, it was not possible to perform a meta analysis to analyse the results related to several outcomes.

Problems in generalisation of the results call for further research, which should be conducted in a way that standardizes the way in which specific outcomes are measured and reported.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Bickel 1997

Methods	Allocation: randomised controlled trial; Randomization: minimum likelihood allocation. Blindness: only for pharmacological intervention. No difference between groups.
Participants	39 opiate dependent, (DSM-III-R), stable, residing in USA, age 18 or older, eligible for MMT according to FDA requirements. (1)19 (2)20. Average age 33.5; 64% men; 97% White; mean use of heroin 10 years; mean age at the first use 20; 41% never married; 92% high school; 41% employed. Ex C: Psychosis, dementia, major medical disorder, pregnancy.
Interventions	For all BDT, dose-taper 4 mg/70 kg, dose increased to 8 mg if withdrawal, after the first week patients were maintained for an additional 42 hours, 72 hours or 7 days for the 2, 4, or 8 mg/70 kg dose respectively; then the dose was decreased gradually 10% every 5 days for the remainder 160 days. (1) Behavioural Therapy. (2) Standard counselling sessions once per week for 37 min. Duration 26 weeks.
Outcomes	Retention in treatment as % of participants that completed the treatment. Use of primary substance of abuse as % of continued abstinent at 4, 8, 12 and 16 weeks and as % of abstinent from opioids at 23 and 26 weeks. Use of other drug as n. of positive participants (at least 1 positive urine specimen during the 26 weeks). Results at follow-up as no. of opioid abstinent at 29 weeks.
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Hall 1979

Methods	Allocation: randomised controlled trial; Randomization:method not reported. Blindness: not possible.
Participants	81 opiate users, no detail of use, (1)41 (2)40. Average age 28; 65% men; 53% Caucasian, 12% African-American, 24% Hispanic; 27% treated previously.
Interventions	For all methadone detoxification, starting from 40 mg/day and tapered from day 3 of 5 mg every second day, the final dose on day 16 was 5 mg. (1) Contingency Management, participants paid for drug-free urine 6 times during treatment. (2) Control , participants paid for each urine given. Duration 16 days.

Hall 1979 (*Continued*)

Outcomes	Use of primary substance of abuse as % of positive urine samples. Retention in treatment as days in treatment but only statistical test results reported. Psychiatric symptoms/psychological distress, no data only conclusions of the authors.
Notes	Community Oriented Program Environment Scale (COPES) on days 3-5 and 11-13. Participants also completed Client Satisfaction Questionnaire

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Higgins 1984

Methods	Allocation: randomised controlled trial; Randomization: method not reported. Blindness: methadone doses double blind.
Participants	27 opiate dependent, had to provide 50% or more opiate-free urine during the first 3 weeks of the detoxification before the start of the trial. (1)9 (2)8 (3)10. 100% men; no other information available on the characteristics of the participants.
Interventions	For all methadone detoxification, all stabilized on 30 mg/day during 21 days, trial starts on day 22; methadone dose was reduced in alternating 2 and 3 mg/day steps until 0 mg reached at the end of 63 days (week 9). (1) Contingency Management, participants could increase their clinic dose of methadone if their most recent urine sample was opioid free. (2) Non Contingency Management, the same amount of extra methadone available as contingent group but the dose increase is independent of the urinalysis results. Duration 13 weeks.
Outcomes	Retention in treatment as % of participants terminating the treatment. Use of primary substance of abuse as average % of positive tests (3 tests per participant per week). Compliance as % of clinic absence.
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Higgins 1986

Methods	Allocation: randomised controlled trial; Randomization: method not reported. No differences between groups.
Participants	39 opiate dependent, had to provide 50% or more opiate free urines during the first 3 weeks after treatment enrolment. (1)13, (2)13, (3)13. Average age 32; 100% men; 51% White; 49% African-American; mean years of continuous opiate use: 9.2; average years of educational level 11.6; 46% employed; legal state free 69%, parole/probation/pending trial 31%.
Interventions	For all: During the first 3 weeks, patients were stabilized on 30 mg/day of methadone; from week 4, methadone dose decreased in alternating 2 mg and 3 mg steps until 0 mg was reached on week 10. (1) Contingency Management, participants could increase their methadone dose by 5, 10, 15 or 20 mg on a daily basis from day 22-77 of detoxification but only if their most recent urine sample was opiate free. (2) Non Contingency Management , participants could increase their methadone dose by 5, 10, 15 or 20 mg on a daily basis from day 22-77 of detoxification independent of their urinalysis results. (3) Control, participants did not receive dose increase. Duration 13 weeks.Retention in treatment as average number of days in treatment. Compliance as % of missing clinic visits and as withdrawal symptoms (scores). Use of primary substance of abuse as % of opiate positive urine samples and as average daily amount of supplemental methadone received.
Outcomes	Retention in treatment as average number of days in treatment. Compliance as % of missing clinic visits and as withdrawal symptoms (scores). Use of primary substance of abuse as % of opiate positive urine samples and as average daily amount of supplemental methadone received.
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Katz 2004

Methods	Allocation: randomised controlled trial; Blinding not possible and blinding of outcome assessor unclear
Participants	211 indigent opiate abusers; mean age (1)35.7 (2)36.5 years; male (1)40% (2)37%; African American (1)62% (2)74%, Caucasian (1)32% (2)25%, Other (1)6% (2)1%; Mean education years (1)11.3 (2)11.4; Employed (1)19.3% (2)26.9%; Married (1)19.8% (2)15.1%, Single (1)80.2% (2)84.9%
Interventions	For all 0.3 mg/day intramuscular buprenorphine administered for 4 days; in addition all patients who were still enrolled on Friday received a 7 day clonidine patch to wear during the following week, group counselling was held on a daily basis (1) Contingent n. 109, vouchers $100 if urine tested negative for both opiates and cocaine on Friday; (2) Non contingent n.102, vouchers delivered independent of their urine test results

Katz 2004 (*Continued*)

Outcomes	Use of opioids	
Notes		
Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

McCaul 1984

Methods	Allocation: randomised controlled trial; Randomization: method not reported. Blindness: single blind. Groups similar for all but 3 of 36 variables.	
Participants	102 opiate dependent. (1)35 (2)32 (3)35. Results on 92: (1)31, (2)29, (3)32.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. Ex C: Need for medical or psychiatric hospitalisation at the time of admission, plan for an imminent move from the Philadelphia area.	
Interventions	For all MMT, 60 to 90 mg/day. (1) Enhanced Methadone Services, on site medical, psychiatric, employment and family therapies services. (2) Standard Methadone Services, counseling sessions 1 per week. (3) 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 participants 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	Results on 92 participants who completed at least 2 weeks of the protocol and who were contacted at 24 weeks.	
Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Rawson 1983

Methods	Randomised controlled trial. Allocation: The allocation in the groups done using a random numbers table. Groups similar for demographic and drug use variables.
Participants	50 heroin dependents, (1)25 (2)25. Average age 30; 66% men; mean use of heroin 8.8 years, mean number of previous detoxification treatments 4.
Interventions	For all methadone detoxification, 35 mg on day 1 tapered to zero on day 21. (1) Counseling Treatment, mandatory psychotherapeutic counseling session on the second dosing day. Subsequent non mandatory sessions were scheduled during the second and the third weeks of treatment. (2) Control. Duration 21 days, follow-up at 6 months.
Outcomes	Retention in treatment as no. completed, no. of mean days in treatment, no. of drop-outs. Use of primary substance of abuse as no. of participants with morphine negative samples. Compliance as no. visits attended while in treatment. Results at follow-up as no. of participants transferred to MMT, no. in continued treatment for 6 months, no. re-addicted and no. lost
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Robles 2002

Methods	Allocation: randomised controlled trial; Randomization: method not reported but it seems that those who recruited participants were aware of the assignment schedule to ensure that participants in both groups received vouchers in equal amounts and temporal distribution. No differences between groups.
Participants	48 opiate dependent, age between 18-65 years, eligible for MMT according to FDA guidelines, reported intravenous opiate use during the past 30 days. (1)26, (2)22. Mean age 40.7; 64.5% men; 48% White; 41.6%; 19% employed part time; 31% employed full time; 50% unemployed; 66% HIV positive; 66% reporting needle sharing; 66% reporting use of condom. Ex cr: pregnant women, current major psychiatric disorders other than drug abuse, unstable serious medical illness.
Interventions	For all: Methadone detoxification after maintenance treatment. During weeks 1-4 MMT then randomisation, MMT continue during weeks 5-10 then methadone detoxification during weeks 11-23. In the weeks 24-26 no medication. (1) Contingency management, methadone mean dose 76.4, patients could obtain vouchers 3 times a week by providing opiate urine specimens. Upon providing the first opiate free urine specimen, participants received a voucher of $2.50, thereafter the value of the voucher increased by $1.50 with every consecutive opiate free urine to a maximum of $40. A maximum of $2232 could be earned. (2) Control, methadone mean dose 70.3, patients did not receive vouchers. Duration: 26 weeks

Robles 2002 (*Continued*)

Outcomes	Retention in treatment as no. retained. Use of primary substance of abuse as % of opiate negative urine samples, % of repeated opiate negative specimens. Severity of dependence as average number of intravenous drug injection per week. Compliance as withdrawal symptoms (scores of Visual Analog Scale) as no. lost.
Notes	

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Yandoli 2002

Methods	Allocation: randomised controlled trial; Randomization: method not reported but it seems that those who recruited participants were aware of the assignment schedule in order to put participants cohabiting in the same group. Blinding: open label. No differences between groups
Participants	119 opiate dependent, age over 18, use of opiate more than 6 months, agree to be seen with their partner or family if required. (1)41 (2)38 (3)40. Average age 28; 63% men; 80% living with a partner, of those 53% with a drug using partner, 14% living with the family of origin, 6% living alone; 27% employed full time, 20% employed part time 53% unemployed; 59% had criminal convictions, 18% refused to answer, 23% never charged with criminal offence. Ex C: History of psychiatric treatments, currently dependent on alcohol
Interventions	For all methadone detoxification. (1) Family Therapy, methadone in a strict reduction regime non negotiable reducing daily dose 5 mg every 2 weeks plus 16 session of 1 hour every 2 weeks and then monthly. (2) Standard Clinic, methadone in a flexible reduction regime , which sometimes included continuing on a stable dose or occasionally increasing the dose temporarily on the basis of expressed needs of the clients. The course of the treatment was open-ended. Plus supportive counseling combined with information and advice on managing the drug problem. (3) Low Contact, methadone as (1) plus clients were seen monthly for a standardized 30 min interview for up 12 months. Results at follow-up 6 and 12 months.
Outcomes	Results at follow-up as % of participants followed at 6 and 12 months, no. of heroin-free, occasional use, regular use, in prison or unavailable, mortality rates as no. of deaths.
Notes	

Risk of bias

Item	Authors' judgement	Description

Yandoli 2002 (*Continued*)

Allocation concealment?	No	C - Inadequate

Footnotes
BDT: Buprenorphine Detoxification Treatment
COPES: Community Oriented Program Environment Scale
DSM-III-R: Diagnostic and Statistical Manual of Mental Disorders, American Psychiatric Association Washington DC
Ex C: Exclusion Criteria
FDA: Food and Drug Administration
HIV: Human Immunodeficency Virus
MMT: Methadone Maintenance Treatment

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

Baer 1999	Excluded as the study design was not in the inclusion criteria: review article.
Ball 2004	Excluded as type of intervention not in the inclusion criteria: no pharmacological treatment associated with psychosocial
Barnett 2006	Excluded as type of outcomes not in the inclusion criteria: no separate data for detoxification and maintenance pharmacological interventions
Booth 1996	Excluded as the study design was not in the inclusion criteria: prospective study
Brooner 1998	Excluded as the study design was not in the inclusion criteria: experimental prospective study.
Carpenter 2006	Excluded as type of intervention not in the inclusion criteria: no group with pharmacological treatment alone
Carroll 2001	Excluded because the type of pharmacological intervention (naltrexone) not in the inclusion criteria
Chappel 1999	Excluded as the study design was not in the inclusion criteria of the review: review article
Conrod 2000	Excluded as the type of participants was not in the inclusion criteria: females between 30 and 50 years of age and dependent on or abusing alcohol, a prescription drug or both.
Curtis 1998	Excluded as the study design and the type of participants was not in the inclusion criteria of the review: prospective intervention study; participants were patients discharged from an inpatient psychiatric service, excluded only those whose Axis I diagnosis was substance abuse or organic mental disorder and who stayed in the hospital less than 7 days.

(*Continued*)

Czuchry 2000	Excluded as the type of participants and the intervention was not in the inclusion criteria: Participants were probationers drug dependent (any drug) and the two treatments compared were both psychosocial without pharmacological intervention.
Dawe 1993	Excluded as the type of interventions were not in the inclusion criteria: after detoxification, participants were randomised in four groups all without pharmacological interventions.
Donovan 2001	Excluded as the type of participants and of interventions were not in the inclusion criteria: Participants were substance abusers (any drug), the experimental intervention was "attrition prevention" compared to standard care while awaiting treatment admission.
Fals-Stewart 1996	Excluded as the type of participants not in the inclusion criteria: substances abusers (any drug).
Fiorentine 1999	Excluded as the design not in the inclusion criteria: review article.
Fiorentine 2000	Excluded as the design was not in the inclusion criteria: review article.
Galanter 2004	Excluded as the intervention was not in the inclusion criteria: comparison between network therapy without drugs and buprenorphine without psychosocial
Gibson 2003	Excluded as type of intervention not in the inclusion criteria: no psychosocial treatment
Greenwald 2005	Excluded as type of intervention not in the inclusion criteria: the study evaluate the efficacy of fentanyl compared with naltrexone
Griffith 2000	Excluded as the study design not in the inclusion criteria: overview
Gruber 2000	Excluded as the type of participants and intervention was not in the inclusion criteria: participants were inner city opiate abusers discharged from detoxification unit; the interventions were (1) reinforcement-based intensive outpatient treatment and (2) community treatment resources, none with pharmacological plus psychosocial programs.
Haro 2006	Excluded as type of outcomes not in the inclusion criteria: knowledge about drugs, satisfaction and motivation were the outcomes considered but no data were provided
Havens 2007	Excluded as type of intervention not in the inclusion criteria: strengths-based case management compared with passive referral
Hawton 1987	Excluded as the type of participants not in the inclusion criteria: participants were overdose patients.
Humphreys 1999	Excluded as the study design not in the inclusion criteria: review article.
James 2004	Excluded as type of intervention not in the inclusion criteria: no pharmacological treatment considered

(*Continued*)

Joe 2001	Excluded as the study design not in the inclusion criteria: cohort study
Jones 2005	Excluded as type of intervention not in the inclusion criteria: no pharmacological treatment considered
Katz 2007	Excluded as type of intervention not in the inclusion criteria: no pharmacological treatment considered
McCusker 1995	Excluded as the type of intervention not in the inclusion criteria: comparison of two drug free programs in short or long version.
McGlynn 1993	Excluded as the study design and the participants not in the inclusion criteria: research demonstration project and the participants were dually diagnosed homeless
Moos 1999	Excluded as the study design and the type of participants not in the inclusion criteria: cohort study and participants were substance abusers (any drug).
Moos 2001	Excluded as the study design and the type of participants not in the inclusion criteria: participants were substance abusers (any drug).
Moos 2003	Excluded as the study design not in the inclusion criteria: review article.
Morgenstern 2001	Excluded as the type of participants and intervention not in the inclusion criteria: participants were substance dependent (any drug) and intervention was a comparisons between high standardization cognitive behavioural treatment, low standardization cognitive behavioural treatment, and treatment as usual.
Nurco 1995	Excluded as type of outcomes reported not in the inclusion criteria: the outcomes were responses on interview containing15 agree/disagree questions tapping orientations to locus-of-control beliefs about drug misuse.
Ouimette 1998	Excluded as the study design not in the inclusion criteria: review article
Page 1982	Excluded as the type of participants not in the inclusion criteria: participants were drug dependent (any drug).
Platt 1991	Excluded as the study design not in the inclusion criteria: review article
Prendergast 2006	Excluded as the study design not in the inclusion criteria: review
Rawson 1979	Excluded because the type of intervention not in the inclusion criteria;: pharmacological intervention with naltrexone
Reilly 1995	Excluded as the design not in the inclusion criteria: clinical not controlled study.
Romijn 1990	Excluded as the study design not in the inclusion criteria: evaluation study.
Saunders 1995	Excluded as the type of intervention not in the inclusion criteria: brief motivational intervention compared to a control group (education package), no information available on pharmacological intervention.

(*Continued*)

Schinka 1998	Excluded as the type of participants not in the inclusion criteria: participants were substance dependent (any drug)
Secades Villa 2004	Excluded as type of intervention not in the inclusion criteria: no pharmacological treatment
Stanton 1997	Excluded as the study design not in the inclusion criteria: overview.
Stecher 1994	Excluded as the type of participants and intervention not in the inclusion criteria: participants were double diagnosed homeless and two residential programs were compared.
Zimmermann 2006	Excluded as type of intervention not in the inclusion criteria: no information on pharmacological treatment

DATA AND ANALYSES

Comparison 1. Any Psychosocial plus any Pharmacological detoxification Intervention versus any Pharmacological alone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Completion of treatment	5	184	Risk Ratio (M-H, Fixed, 95% CI)	1.68 [1.11, 2.55]
2 Use of primary substance	4	320	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.71, 0.93]
3 Number of subjects abstinent at follow-up	3	208	Risk Ratio (M-H, Fixed, 95% CI)	2.43 [1.61, 3.66]

Comparison 2. Any Psychosocial Intervention plus MDT versus MDT alone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Completion of treatment	4	145	Risk Ratio (M-H, Fixed, 95% CI)	1.48 [0.93, 2.35]
2 Use of primary substance	2	70	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.44, 1.07]
3 Number of subjects abstinent at follow-up	2	169	Risk Ratio (M-H, Fixed, 95% CI)	2.46 [1.61, 3.76]
4 Compliance as clinic absences during the treatment	3	1138	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.38, 0.59]

Comparison 3. Contingency Management Approaches plus MDT versus MDT alone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Completion of treatment	3	95	Risk Ratio (M-H, Fixed, 95% CI)	1.51 [0.93, 2.46]
2 Compliance as clinical absences during the treatment	2	196	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.15, 0.56]

Comparison 4. Contingency Management Approaches plus BDT versus BDT alone

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Use of primary substance	2	250	Risk Ratio (M-H, Random, 95% CI)	0.85 [0.74, 0.97]

Analysis 1.1. Comparison 1 Any Psychosocial plus any Pharmacological detoxification Intervention versus any Pharmachological alone, Outcome 1 Completion of treatment.

Review: Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification

Comparison: 1 Any Psychosocial plus any Pharmacological detoxification Intervention versus any Pharmachological alone

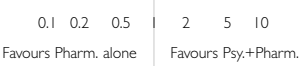
Outcome: 1 Completion of treatment

Study or subgroup	Any Psych.+any Pharm n/N	Pharmach. alone n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Bickel 1997	10/19	4/20		17.2 %	2.63 [0.99, 6.98]
Higgins 1984	5/9	6/18		17.7 %	1.67 [0.69, 4.00]
McCaul 1984	7/10	2/10		8.8 %	3.50 [0.95, 12.90]
Rawson 1983	4/25	3/25		13.2 %	1.33 [0.33, 5.36]
Robles 2002	11/26	9/22		43.1 %	1.03 [0.53, 2.03]
Total (95% CI)	**89**	**95**		**100.0 %**	**1.68 [1.11, 2.55]**

Total events: 37 (Any Psych.+any Pharm), 24 (Pharmach. alone)

Heterogeneity: $Chi^2 = 4.13$, df = 4 (P = 0.39); $I^2 = 3\%$

Test for overall effect: Z = 2.43 (P = 0.015)



Analysis 1.2. Comparison 1 Any Psychosocial plus any Pharmacological detoxification Intervention versus any Pharmachological alone, Outcome 2 Use of primary substance.

Review: Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification

Comparison: 1 Any Psychosocial plus any Pharmacological detoxification Intervention versus any Pharmachological alone

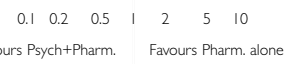
Outcome: 2 Use of primary substance

Study or subgroup	Any Psych.+any Pharm n/N	Any Pharmacological n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Bickel 1997	15/19	18/20		13.8 %	0.88 [0.67, 1.15]
Katz 2004	75/109	84/102		68.4 %	0.84 [0.72, 0.98]
McCaul 1984	5/10	10/10		8.3 %	0.52 [0.29, 0.96]
Rawson 1983	10/25	12/25		9.5 %	0.83 [0.44, 1.56]
Total (95% CI)	**163**	**157**		**100.0 %**	**0.82 [0.71, 0.93]**

Total events: 105 (Any Psych.+any Pharm), 124 (Any Pharmachological)

Heterogeneity: $Chi^2 = 2.43$, df = 3 (P = 0.49); $I^2 = 0.0\%$

Test for overall effect: Z = 2.96 (P = 0.0031)



Analysis 1.3. Comparison 1 Any Psychosocial plus any Pharmacological detoxification Intervention versus any Pharmachological alone, Outcome 3 Number of subjects abstinent at follow-up.

Review: Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification

Comparison: 1 Any Psychosocial plus any Pharmacological detoxification Intervention versus any Pharmachological alone

Outcome: 3 Number of subjects abstinent at follow-up

Study or subgroup	Any Psych+Any Pharm n/N	Any Pharmacological n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Bickel 1997	4/19	2/20		10.2 %	2.11 [0.43, 10.19]
Rawson 1983	8/25	4/25		21.0 %	2.00 [0.69, 5.80]
Yandoli 2002	26/41	19/78		68.8 %	2.60 [1.65, 4.10]
Total (95% CI)	**85**	**123**		**100.0 %**	**2.43 [1.61, 3.66]**

Total events: 38 (Any Psych+Any Pharm), 25 (Any Pharmacological)

Heterogeneity: $Chi^2 = 0.25$, df = 2 (P = 0.88); $I^2 = 0.0\%$

Test for overall effect: Z = 4.23 (P = 0.000024)

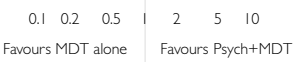
Analysis 2.1. Comparison 2 Any Psychosocial Intervention plus MDT versus MDT alone, Outcome 1 Completion of treatment.

Review: Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification

Comparison: 2 Any Psychosocial Intervention plus MDT versus MDT alone

Outcome: 1 Completion of treatment

Study or subgroup	Any Psychosocial+MDT n/N	MDT alone n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Higgins 1984	5/9	6/18		21.3 %	1.67 [0.69, 4.00]
McCaul 1984	7/10	2/10		10.7 %	3.50 [0.95, 12.90]
Rawson 1983	4/25	3/25		16.0 %	1.33 [0.33, 5.36]
Robles 2002	11/26	9/22		52.0 %	1.03 [0.53, 2.03]
Total (95% CI)	**70**	**75**		**100.0 %**	**1.48 [0.93, 2.35]**
Total events: 27 (Any Psychosocial+MDT), 20 (MDT alone)					
Heterogeneity: Chi^2 = 2.85, df = 3 (P = 0.41); I^2 =0.0%					
Test for overall effect: Z = 1.66 (P = 0.098)					



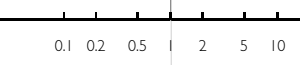
Analysis 2.2. Comparison 2 Any Psychosocial Intervention plus MDT versus MDT alone, Outcome 2 Use of primary substance.

Review: Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification

Comparison: 2 Any Psychosocial Intervention plus MDT versus MDT alone

Outcome: 2 Use of primary substance

Study or subgroup	Any Psychosocial+MDT n/N	MDT alone n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
McCaul 1984	5/10	10/10		46.7 %	0.52 [0.29, 0.96]
Rawson 1983	10/25	12/25		53.3 %	0.83 [0.44, 1.56]
Total (95% CI)	**35**	**35**		**100.0 %**	**0.69 [0.44, 1.07]**
Total events: 15 (Any Psychosocial+MDT), 22 (MDT alone)					
Heterogeneity: Chi^2 = 1.14, df = 1 (P = 0.29); I^2 =12%					
Test for overall effect: Z = 1.64 (P = 0.10)					



Analysis 2.3. Comparison 2 Any Psychosocial Intervention plus MDT versus MDT alone, Outcome 3 Number of subjects abstinent at follow-up.

Review: Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification

Comparison: 2 Any Psychosocial Intervention plus MDT versus MDT alone

Outcome: 3 Number of subjects abstinent at follow-up

Study or subgroup	Any Psychosocial+MDT n/N	MDT alone n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Rawson 1983	8/25	4/25		23.4 %	2.00 [0.69, 5.80]
Yandoli 2002	26/41	19/78		76.6 %	2.60 [1.65, 4.10]
Total (95% CI)	**66**	**103**		**100.0 %**	**2.46 [1.61, 3.76]**
Total events: 34 (Any Psychosocial+MDT), 23 (MDT alone)					
Heterogeneity: Chi^2 = 0.20, df = 1 (P = 0.65); I^2 =0.0%					
Test for overall effect: Z = 4.18 (P = 0.000030)					

Analysis 2.4. Comparison 2 Any Psychosocial Intervention plus MDT versus MDT alone, Outcome 4 Compliance as clinic absences during the treatment.

Review: Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification

Comparison: 2 Any Psychosocial Intervention plus MDT versus MDT alone

Outcome: 4 Compliance as clinic absences during the treatment

Study or subgroup	Any Psychosocial+MDT n/N	MDT alone n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Higgins 1984	5/49	20/49		10.0 %	0.25 [0.10, 0.61]
Higgins 1986	5/49	14/49		7.0 %	0.36 [0.14, 0.92]
Rawson 1983	83/460	169/482		82.9 %	0.51 [0.41, 0.65]
Total (95% CI)	**558**	**580**		**100.0 %**	**0.48 [0.38, 0.59]**
Total events: 93 (Any Psychosocial+MDT), 203 (MDT alone)					
Heterogeneity: Chi^2 = 2.78, df = 2 (P = 0.25); I^2 =28%					
Test for overall effect: Z = 6.72 (P < 0.00001)					

Analysis 3.1. Comparison 3 Contingency Management Approaches plus MDT versus MDT alone, Outcome 1 Completion of treatment.

Review: Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification

Comparison: 3 Contingency Management Approaches plus MDT versus MDT alone

Outcome: 1 Completion of treatment

Study or subgroup	Contingency+MDT n/N	MDT alone n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Higgins 1984	5/9	6/18		25.4 %	1.67 [0.69, 4.00]
McCaul 1984	7/10	2/10		12.7 %	3.50 [0.95, 12.90]
Robles 2002	11/26	9/22		61.9 %	1.03 [0.53, 2.03]
Total (95% CI)	**45**	**50**		**100.0 %**	**1.51 [0.93, 2.46]**
Total events: 23 (Contingency+MDT), 17 (MDT alone)					
Heterogeneity: Chi^2 = 2.86, df = 2 (P = 0.24); I^2 =30%					
Test for overall effect: Z = 1.65 (P = 0.099)					

Analysis 3.2. Comparison 3 Contingency Management Approaches plus MDT versus MDT alone, Outcome 2 Compliance as clinical absences during the treatment.

Review: Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification

Comparison: 3 Contingency Management Approaches plus MDT versus MDT alone

Outcome: 2 Compliance as clinical absences during the treatment

Study or subgroup	Contingency+MDT n/N	MDT alone n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Higgins 1984	5/49	20/49		58.8 %	0.25 [0.10, 0.61]
Higgins 1986	5/49	14/49		41.2 %	0.36 [0.14, 0.92]
Total (95% CI)	**98**	**98**		**100.0 %**	**0.29 [0.15, 0.56]**
Total events: 10 (Contingency+MDT), 34 (MDT alone)					
Heterogeneity: Chi^2 = 0.29, df = 1 (P = 0.59); I^2 =0.0%					
Test for overall effect: Z = 3.71 (P = 0.00021)					

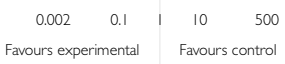
Analysis 4.1. Comparison 4 Contingency Management Approaches plus BDT versus BDT alone, Outcome 1 Use of primary substance.

Review: Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification

Comparison: 4 Contingency Management Approaches plus BDT versus BDT alone

Outcome: 1 Use of primary substance

Study or subgroup	Psychosocial+BDT n/N	BDT alone n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Bickel 1997	15/19	18/20		24.2 %	0.88 [0.67, 1.15]
Katz 2004	75/109	84/102		75.8 %	0.84 [0.72, 0.98]
Total (95% CI)	**128**	**122**		**100.0 %**	**0.85 [0.74, 0.97]**
Total events: 90 (Psychosocial+BDT), 102 (BDT alone)					
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.09$, df = 1 (P = 0.76); $I^2 = 0.0\%$					
Test for overall effect: Z = 2.44 (P = 0.015)					



APPENDICES

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

Diagnosis=opioid or opiate* or heroin

Appendix 2. CENTRAL search strategy

1. Substance-Related Disorders:mesh
2. ((opioid or opiate*) next (abuse* or addict* or dependen*)):TI,AB
3. #1 or #2
4. (opiat* or opioid* or heroin* or narcoti*):TI,AB
5. HEROIN:mesh
6. #4 or #5
7. PSYCHOTHERAPY:MESH
8. psychother*:TI,AB
9. psychosocial:TI, AB
10. (social next/2 skill*):TI,AB
11. (coping next/2 skill):TI,AB
12. Counseling:TI,AB
13. (behavi* next/2 therap*):TI,AB
14. Reinforcement (Psychology):MESH
15. (contingent next 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 #2

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 Techniques"[Mesh]
31. "stress management"
32. case management [mesh]
33. (Therapeutic 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. "Random Allocation"[Mesh]
37. "Double-Blind Method"[Mesh]
38. "Single-Blind Method"[Mesh]
39. ("Clinical Trial "[Publication Type] OR "Clinical Trials as Topic"[Mesh])

40. (clinical and trial)
41. ((singl* or doubl* or trebl* or tripl*) and (blind* or mask*))
42. Placebos [Mesh]
43. placebo*[TIAB]
44. random*[TIAB]
45. Research Design [Mesh]
46. #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45
47. #4 AND #8 AND #34
48. #47 AND #47
49. #48 limit to humans

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 blinde procedure/exp
37. single blinde 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. Substance Use Disorders [MH]
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. methadone or methadone[MH]
7. heroin or heroin[MH]
8. #5 OR #6 OR #7
9. random*
10. (clin* and trial*)
11. (singl* or doubl* or tripl* or trebl*) and (mask* or blind*)
12. crossover*
13. allocate*
14. assign*
15. ((random*) and (allocate* or assign*))
16. Random Assignment [MH]
17. Clinical Trials [MH]
18. #9 OR #10 #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17
19. #4 AND #8 AND #18

((drug or substance) and (addict* or dependen* or abuse*or disorder*))
((opioid* or opiate*) and (abuse* or addict* or dependen*))
#1 OR #2 OR #3
(opioid* or opiate*)
methadone or methadone[MH]
heroin or heroin[MH]
#5 OR #6 OR #7
random*
(clin* and trial*)
(singl* or doubl* or tripl* or trebl*) and (mask* or blind*)
crossover*
allocate*
assign*
((random*) and (allocate* or assign*))
Random Assignment [MH]
Clinical Trials [MH]
#9 OR #10 #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17
#4 AND #8 AND #18

WHAT'S NEW

Last assessed as up-to-date: 8 April 2008.

7 April 2009	Amended	minor editorial changes
1 December 2008	Amended	changed odds ratio in risk ratio in comparison 4.1
20 October 2008	Amended	Contact details amended

HISTORY

Protocol first published: Issue 2, 2003

Review first published: Issue 4, 2004

22 April 2008	Amended	minimal changes
9 April 2008	New citation required and conclusions have changed	new search, new trials, change to conclusion
26 July 2004	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Laura Amato and Simona Vecchi inspected the search hits by reading the titles and the abstracts. Laura Amato and Silvia Minozzi wrote the review and Marina Davoli supervised; Marica Ferri and Soraya Mayet commented on the draft.

DECLARATIONS OF INTEREST

None

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INDEX TERMS

Medical Subject Headings (MeSH)

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

MeSH check words

Humans