TREATMENTS OF SUBSTANCE USE DISORDERS
THE SYSTEMATIC REVIEWS OF THE COCHRANE DRUGS AND ALCOHOL GROUP (CDAG)
Laura Amato, Marina Davoli, Simona Vecchi, Carlo A Perucci

Updated March 2005

THE COCHRANE COLLABORATION

The Cochrane Collaboration, launched in 1992, is a global cooperative organization aimed to produce, update and disseminate systematic reviews of the effect of health care interventions. Reviews are timely updated and the results are disseminated to clinicians, decision-makers, patients.

THE SISTEMATIC REVIEWS

The principal objective of systematic reviews is to develop an information:
• Evidence based
• Easily accessible
• Internationally developed
• Clinically relevant
• Updated
They are useful because size and availability of data are huge and increasing, access to results of research is sometime random, quality of research is heterogeneous and many studies are too small (low statistical power)
They can take into account not only the random variability between different Randomised Controlled Trials (RCT) which are the most powerful research design to evaluate the effectiveness of health care, but also the etherogeneity (temporal, geografic, population, setting…), the different experimental conditions and the quality of RCTs.
They allow to judge:
–Whether there are sufficient evidences of effectiveness of the intervention
–Whether it is necessary to conduct further studies for the evaluation of a treatment and which aspects should be considered

THE COCHRANE REVIEW GROUP ON DRUG AND ALCOHOL

The Cochrane Group on Drug and Alcohol founded in the 1998, has the editorial base in Rome at the Department of Epidemiology of ASL RM E. As part of the Cochrane collaboration, the group is aimed to produce, update and disseminate systematic reviews of trials on the prevention, treatment and rehabilitation of the problematic use of drugs and alcohol.
Different interventions are offered for prevention, treatment and rehabilitation of substance abuse. The choice is often guided by common sense, intuition, experience or ideology and not always by evidence. Clinicians and policy makers need accessible, up to date, objective evidence regarding the effectiveness of interventions.
Our systematic reviews are based on all Randomised Controlled Trials and Controlled Clinical Trials that describe an active intervention (including prevention, treatment and rehabilitation) aimed at reducing the potential for harm or the actual harm directly related to the use of different dependence producing substances.
The group created and maintains a specialised register of trials on the evaluation of effectiveness of treatments. As of December 2004 it contains 6195 trials (2817 RCT, 1389 CCT, 1989 other study design)
The references are systematically searched on the electronic databases (MEDLINE, EMBASE, PsychInfo). The full text article are obtained and coded (3039 articles till now).

As of September 2004 the group published 26 reviews, 17 review protocols

THE EDITORIAL PROCESS OF A SYSTEMATIC REVIEW

The systematic reviews are the result of a complex process :
–Formulate a proper question
–Comprehensive data search
–Objective selection and data extraction
–Critical evaluation of primary studies
They provide a priori definition of objectives, search strategy, inclusion criteria, data collection procedures and means of data analysis.
All the process is peer reviewed.
Once a review has been completed it is expected the Reviewer will update the review regularly. The Reviewer is asked to review the literature on a regular basis; at least once a year. In cases where new evidence is available the review should be updated. However, in the case where no new evidence exists the date of last update will still be modified to reflect the date of this process.
The Trial Search Coordinator perform the search strategy on the group's specialised register quarterly and forwards the results to the reviewer.
In case of significant changes the peer review process is carried out. The judgement is up to the Coordinating Editor.

WHERE YOU CAN FIND THE PUBLISHED REVIEWS

The Cochrane reviews are published on the Cocrane Library
How to subscribe the Cochrane Library :
Please contact:
Sarah Stevens, Cochrane Library Customer
Services Advisor, John Wiley & Sons Ltd, 1 Oldlands
Way, Bognor Regis, West Sussex, PO22 9SA, UK.
Tel. +44 (0)1243 843355 Fax. +44 (0) 1243 843232
E-mail sasteven@wiley.co.uk

Abstracts of the reviews on MEDLINE and on
http://www.cochrane.org/cochrane/revabstr/mainindex.htm;
Abstracts in Italian on www.ossfad.iss.it dell'Osservatorio fumo, droga e alcool dell'Istituto Superiore di Sanità

REVIEWS AND PROTOCOLS PUBLISHED BY THE COCHRANE GROUP ON DRUG AND ALCOHOL

(Cochrane Library, issue 3.2004)

WHAT'S NEW

NEW REVIEWS

- Faggiano F, Vigna-Taglianti FD, Versino E, Zambon A, Borraccino A, Lemma P School-based prevention for illicit drugs' use
- Day E, Ison J, Strang J Inpatient versus other settings for detoxification for opioid dependence
- McCarthy G, Myers B, Siegfried N Treatment for Methaqualone dependence in adults

NEW PROTOCOLS

- Gates S, Foxcroft D, Smith LA Auricular acupuncture for cocaine dependence
- McQueen J, Allan L, Mains D Brief interventions for heavy alcohol users admitted to general hospital wards
- Perry AE, Ali RL, Coulton S, Glanville JM, Godfrey C, Lunn J, McDougall C, Neale ZJ Interventions for drug-using offenders in the courts, secure establishments and the community.
- Denis C, Fatseas M, Lavie E, Auriacombe M Pharmacological interventions for benzodiazepine dependence management among benzodiazepine users in outpatient settings
- Gillman MA, Lichtigfeld FJ, Young TN Psychotropic analgesic nitrous oxide for alcoholic withdrawal states

REVIEWS SUBSTANTIALLY UPDATED

- Ferri M, Davoli M, Perucci CA Heroin maintenance for chronic heroin dependents

Reviews

Opiate: Management of withdrawal

1. Opioid antagonists with minimal sedation for opioid withdrawal
2. Buprenorphine for the management of opioid withdrawal
3. Alpha 2 adrenergic agonists for the management of opioid withdrawal
4. Opioid antagonists under heavy sedation or anaesthesia for opioid withdrawal
5. Methadone at tapered doses for the management of opioid withdrawal

Opiate: Maintenance treatment

6. Naltrexone maintenance treatment for opioid dependence
7. LAAM maintenance versus methadone maintenance for heroin dependence
8. Methadone maintenance versus no opioid replacement therapy for opioid dependence
9. Buprenorphine maintenance vs placebo or methadone maintenance for opioid dependence
10. Heroin maintenance for chronic heroin addicts
11. Methadone maintenance at different dosages for opioid dependence
12. Substitution treatment of injecting opioid users for prevention of HIV infection

Opiate: Psychosocial Treatments

13. Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification
14. Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence
15. Psychosocial treatment for opiate abuse and dependence

Opiate: Other

16. Inpatient versus other settings for detoxification for opioid dependence

Alcohol

17. Opioid antagonists for alcohol dependence
18. Primary prevention for alcohol misuse in young people

Cocaine

19. Carbamazepine for cocaine dependence
20. Antidepressant for cocaine dependence
21. Dopamine agonists for cocaine dependence

Amphetamine

22. Treatment for amphetamine abuse and dependence
23. Treatment for amphetamine psychosis disorder
24. Treatment for amphetamine

Other Drugs

25. Treatment for Methaqualone dependence in adults

Poly drugs

26. School-based prevention for illicit drugs' use

Protocols

1. Acamprosate for alcohol dependence alcol
2. Acupunture for opioid dependence
3. Auricular acupuncture for cocaine dependence
4. Anticonvulsants for the management of alcohol withdrawal
5. Benzodiazepines for alcohol withdrawal
6. Brief interventions for excessive drinkers in primary care health settings
7. Brief interventions for heavy alcohol users in general medical wards
8. Disulfiram for alcohol dependence
9. Interventions for drug-using offenders in the courts, secure establishments and the community.
10. Interventions for prevention of drug use by young people delivered in non-school settings.
11. Neuroelectric stimulation for the management of opioid withdrawal
12. Pharmacological interventions for benzodiazepine dependence management among benzodiazepine users in outpatient settings
13. Psychosocial interventions for alcohol use disorders
14. Psychosocial treatments for psychostimulants dependence
15. Parenting programs for preventing tobacco, alcohol and drug abuse in children under 18
16. Psychotropic analgesic nitrous oxide for alcoholic withdrawal states
17. 12-step type programmes and Alcoholics Anonymous for alcohol dependence

OPIATE: MANAGEMENT OF WITHDRAWAL

[1] OPIOID ANTAGONISTS WITH MINIMAL SEDATION FOR OPIOID WITHDRAWAL

Gowing L., Ali R., White J. Date first publication issue 2, 2000,; Date of the last substantial update issue 2, 2002

Background Managed withdrawal (detoxification) is necessary prior to drug-free treatment. It may also represent the end point of long-term opioid replacement treatment such as methadone maintenance.

Objectives To assess the effectiveness of interventions involving opioid antagonists to induce withdrawal, in combination with medication to ameliorate symptoms but with minimal sedation.

Selection criteria Randomised or quasi-randomised controlled clinical trials or prospective controlled cohort studies that compared antagonist-induced (conscious) withdrawal with other approaches to modify the signs and symptoms of withdrawal in opioid-dependent participants.

Main results Ten studies (5 randomised and 5 non-randomised controlled trials), involving 770 participants, met the inclusion criteria for the review. Treatment regimes using opioid antagonists to induce withdrawal, with minimal sedation, varied in a number of aspects preventing description of a "standard" approach.

Antagonist-induced withdrawal is associated with similar or less overall severity than withdrawal managed primarily with an alpha2 adrenergic agonist. This is probably because of earlier resolution of withdrawal. Peak severity is likely to be higher with antagonist-induced withdrawal and require the use of additional adjunct medications. Withdrawal from methadone may be more severe than withdrawal from heroin, but data are limited.
Antagonist-induced withdrawal appears to be associated with somewhat higher rates of completion of withdrawal and achievement of maintenance doses of naltrexone but there were insufficient data for statistical analyses. The benefit of higher rates of completion of withdrawal is lessened by apparently low rates of retention in subsequent naltrexone maintenance treatment.
Reviewers' conclusions The use of opioid antagonists combined with alpha2 adrenergic agonists is feasible and probably increases the likelihood of transfer to naltrexone compared to withdrawal managed primarily with an adrenergic agonist.
A high level of monitoring and support is desirable for several hours following administration of opioid antagonists because of the possibility of vomiting, diarrhoea and delirium.
Further research is required to confirm the relative effectiveness of antagonist-induced regimes, as well as variables influencing the severity of withdrawal, adverse effects, the most effective antagonist-based treatment regime, and approaches that might increase retention in subsequent naltrexone maintenance treatment.

[2] BUPRENORPHINE FOR THE MANAGEMENT OF OPIOID WITHDRAWAL

Gowing L, Ali R, White J. Date first publication issue 3, 2000; **Date of the last substantial update issue 4, 2004**

Background Managed withdrawal (detoxification) is a necessary step prior to drug-free treatment. It may also represent the end point of long-term opioid replacement treatment such as methadone maintenance. The availability of managed withdrawal is essential to an effective treatment system.
Objectives To assess the effectiveness of interventions involving the use of buprenorphine to manage the acute phase of opioid withdrawal.
Selection criteria Randomised or quasi-randomised controlled clinical trials or prospective controlled cohort studies that compared different buprenorphine regimes, or that compared buprenorphine with another form of treatment (or placebo) to modify the signs and symptoms of withdrawal in participants who were primarily opioid dependent.
Main results Thirteen studies (10 RCTs), involving 744 participants, met the criteria for inclusion in the review. Seven studies compared buprenorphine with clonidine; 3 compared buprenorphine with methadone; 1 compared buprenorphine with oxazepam; 2 compared rapid and slow rates of tapering buprenorphine dose; 1 compared 3 different starting doses of buprenorphine.
For groups treated with buprenorphine, withdrawal severity was less than that in groups treated with clonidine; peak severity was similar to those treated with methadone, but withdrawal symptoms may resolve more quickly with buprenorphine. Withdrawal is probably more severe when doses are tapered rapidly following a period of maintenance treatment.
Buprenorphine is associated with fewer adverse effects than clonidine, and completion of withdrawal is significantly more likely with buprenorphine. Buprenorphine and methadone in reducing doses are probably similar in terms of rates of completion of withdrawal, but the evidence is limited. Completion of withdrawal following buprenorphine maintenance treatment may be more likely when doses are reduced gradually.
Reviewers' conclusions Buprenorphine is more effective than clonidine, and of similar effectiveness to methadone, for the management of opioid withdrawal. Many aspects of treatment protocol and relative effectiveness need to be investigated further in order to determine the most effective way of using buprenorphine to manage opioid withdrawal.

[3] ALPHA2 ADRENERGIC AGONISTS FOR THE MANAGEMENT OF OPIOID WITHDRAWAL

Gowing L., Farrell M., Ali R., White J. Date first publication issue 1, 2001; Date of the last substantial update issue 4, 2004

Background Withdrawal (detoxification) is necessary prior to drug-free treatment. It may also represent the end point of long-term treatment such as methadone maintenance. The availability of managed withdrawal is essential to an effective treatment system.
Objectives To assess the effectiveness of interventions involving the use of alpha2 adrenergic agonists (clonidine, lofexidine, guanfacine) to manage opioid withdrawal in terms of withdrawal signs and symptoms, completion of treatment and adverse effects.
Selection criteria Controlled trials comparing alpha2 adrenergic agonists with reducing doses of methadone, symptomatic medications or placebo, or comparing different alpha2 adrenergic agonists to modify the signs and symptoms of withdrawal in participants who were primarily opioid dependent.
Main results Twenty-two studies, involving 1709 participants, were included. Eighteen were randomised controlled trials; for the remaining studies allocation was by participant choice in two, one used alternate allocation and in one the method of allocation was unclear. Twelve studies compared a treatment regime based on an alpha2 adrenergic agonist with one based on reducing doses of methadone. Diversity in study design, assessment and reporting of outcomes limited the extent of quantitative analysis.
For the comparison of alpha2 adrenergic agonist regimes with reducing doses of methadone, there were insufficient data for statistical analysis, but withdrawal intensity appears similar to, or marginally greater with alpha2 adrenergic agonists, while signs and symptoms of withdrawal occur and resolve earlier in treatment. Participants stay in treatment longer with methadone. No significant difference was detected in rates of completion of withdrawal with adrenergic agonists compared to reducing doses of methadone, or clonidine compared to lofexidine. Clonidine is associated with more adverse effects (low blood pressure, dizziness, dry mouth, lack of energy) than reducing doses of methadone. Lofexidine does not reduce blood pressure to the same extent as clonidine, but is otherwise similar to clonidine.
Reviewers' conclusions No significant difference in efficacy was detected for treatment regimes based on the alpha2 adrenergic agonists clonidine and lofexidine, and those based on reducing doses of methadone over a period of around 10 days, for the management of withdrawal from heroin or methadone. Participants stay in treatment longer with methadone regimes and experience less adverse effects. The lower incidence of hypotension makes lofexidine more suited to use in outpatient settings than clonidine. There are insufficient data available to support a conclusion on the efficacy of other alpha2 adrenergic agonists.

[4] OPIOID ANTAGONISTS UNDER HEAVY SEDATION OR ANAESTHESIA FOR OPIOID WITHDRAWAL
Gowing L., Ali R., White J. Date first publication issue 1, 2001; Date of the last substantial update issue 1, 2002

Background Withdrawal (detoxification) is necessary prior to drug-free treatment. It may also represent the end point of long-term opioid replacement treatment such as methadone maintenance. The availability of managed withdrawal is essential to an effective treatment system.
Objectives To assess the effectiveness of interventions involving the administration of opioid antagonists to induce opioid withdrawal with concomitant heavy sedation or anaesthesia.
Selection criteria Randomised or quasi-randomised controlled trials that compared the administration of opioid antagonists under heavy sedation or anaesthesia with another form of treatment.
Main results As yet, no studies have been published comparing treatment regimes involving the administration of opioid antagonists under heavy sedation or anaesthesia with other approaches to detoxification. Treatment regimes for the studies considered for this review varied in the opioid antagonist used, the dose and mode of administration, the anaesthetic agent, duration of anaesthesia and adjunct medications employed. More detailed monitoring of withdrawal is required before any conclusions can be drawn as to what comprises a typical pattern of withdrawal and what factors might influence the pattern. There is only very limited information on referral to ongoing treatment, and relapse to opioid use. Together with the lack of adequate comparisons, this

makes it impossible to draw any conclusions about the long-term effectiveness, or the cost-effectiveness, of withdrawal induced by opioid antagonists under heavy sedation or anaesthesia.
Reviewers' conclusions Considerably more research evidence will be needed before any conclusions can be drawn regarding the effectiveness of managing withdrawal by administration of opioid antagonists under heavy sedation or anaesthesia. The risk of vomiting during sedation, respiratory depression and cardiac irregularities point to the approach being limited to facilities equipped for intubation, assisted ventilation and a high level of monitoring, and with the capacity to respond to adverse events that might occur. The approach must be regarded as experimental with both risks and benefits remaining uncertain.

[5] METHADONE AT TAPERED DOSES FOR THE MANAGEMENT OF OPIOID WITHDRAWAL
Amato L, Davoli M, Ferri M, Ali R. Date first publication issue 1, 2002; Date of the last substantial update issue 3, 2003

Background Despite widespread use in many countries of tapered methadone for detoxification from opiate dependence, the evidence of efficacy to prevent relapse and promote lifestyle change has not been systematically evaluated.
Objectives To determine whether tapered methadone is effective to manage withdrawal from opioids.
Selection criteria All randomised controlled trials which focus on the use of tapered methadone (length of treatment max 30 days) versus all other pharmacological detoxification treatments, placebo and different modalities of methadone detoxification programs for the treatment of opiate withdrawal. Trials including patients with additional diagnoses such as benzodiazepine dependence were also eligible.
Main results 20 studies were included in the review, with 1357 people randomised. 10 studies compared methadone with adrenergic agonists, 7 studies compared different modalities of methadone detoxification, 2 studies compared methadone with other opioid agonists, 1 study compared methadone with chlordiazepoxide one with placebo.
The conclusions of the 10 studies that compared methadone with adrenergic agonists showed no substantial clinical difference of the two treatments in terms of retention in treatment, degree of discomfort and detoxification success rates.
The conclusions of the 6 studies that compare different methadone reduction schedules, showed that different types of methadone withdrawal schedule produce different responses in terms of time course of withdrawal, the severity of withdrawal response and possibly in terms of subsequent engagement with treatment.
Regarding the studies that compare methadone with other opioid agonists, in Sorensen 1982 methadyl acetate performed similarly to methadone on most process and outcome measures, while in Tennant 1975, methadone reduced severity of withdrawal and had fewer drop-outs than did a propoxyphene group.
In Drummond 1989, using chlordiazepoxide vs methadone, the results suggest that the two drugs had similar results in terms of overall effectiveness.
San 1992 compared methadone with placebo and found more severe withdrawal and more drop outs in the placebo group.
The results indicate that tapered methadone and other medications used in the included studies are effective in the treatment of the heroin withdrawal syndrome, although symptoms experienced by subjects differed according to the medication used and the program adopted. It seems that regardless of which medication is selected for heroin detoxification, the rates of subsequent heroin abstinence are about equal. This suggests that the medications are similar in terms of overall effectiveness. Improvements were achieved when other services such as counseling and other supporting services were offered contemporaneously with detoxification.
Reviewers' conclusions Data from literature are hardly comparable; programs vary widely with regard to duration, design and treatment objectives, impairing the application of meta-analysis. Results of many outcomes could not be summarised because they were presented either in graphical form or provided only statistical tests and p-values. For most studies standard deviation for continuous variables were not provided. The studies included in this review confirm that slow

tapering with temporary substitution of long acting opioids, accompanied by medical supervision and ancillary medications can reduce withdrawal severity. Nevertheless the majority of patients relapsed to heroin use. However this cannot be considered a goal for a detoxification as heroin dependence is a chronic, relapsing disorder and the goal of detoxification should be to remove or reduce dependence on heroin in a controlled and human fashion and not a treatment for heroin dependence.

OPIATE: MAINTENANCE TREATMENT

[6] NALTREXONE MAINTENANCE TREATMENT FOR OPIOID DEPENDENCE.

Kirchmayer U., Davoli M., Verster A. Date first publication issue 1, 1999; Date of the last substantial update issue 2, 2003

Background Despite widespread use of naltrexone maintenance in many countries for more than a decade, the evidence of its effects has not yet been systematically evaluated.
Objectives To evaluate the effects of naltrexone maintenance treatment in preventing relapse in opioid addicts after detoxification.
Selection criteria All controlled studies of naltrexone; treatment of heroin addicts after detoxification.
Main results Eleven studies met the criteria for inclusion in this review, even if not all of them were randomised. The methodological quality of the included studies varied, but was generally poor. Meta-analysis could be performed to a very low degree only, because the studies and their outcome measures were very heterogeneous. A statistically significant reduction of (re-)incarcerations was found for patients treated with naltrexone and behaviour therapy in respect to those treated with behaviour therapy only. The other outcomes considered in the meta-analysis did not yield any significant results. Final conclusions on whether naltrexone treatment may be considered effective in maintenance therapy cannot be drawn from the clinical trials available so far.
Reviewers' conclusions The available trials do not allow a final evaluation of naltrexone maintenance treatment yet. A trend in favour of treatment with naltrexone was observed for certain target groups (particularly people who are highly motivated), as has been previously described in the literature.

[7] LAAM MAINTENANCE VERSUS METHADONE MAINTENANCE FOR HEROIN DEPENDENCE

Clark N, Lintzeris N, Gijsbers A, Whelan G, Dunlop A, Ritter A, Ling W. Date first publication issue 2, 2002,

Background LAAM and methadone are both full mu opiate agonists and have been shown to reduce dependence on heroin when given continuously under supervised dosing conditions. LAAM has a long duration of action requiring dosing every two or three days compared to methadone which requires daily dosing. LAAM is not as widely available internationally as methadone, and may be withdrawn from the market following ten cases of life-threatening cardiac arrhythmias and an association with QT prolongation.
Objectives To compare the efficacy and acceptability of LAAM maintenance with methadone maintenance in the treatment of heroin dependence.
Selection criteria All randomised controlled trials, controlled clinical trials and controlled prospective studies comparing LAAM and methadone maintenance for the treatment of heroin dependence and measuring outcomes of efficacy or acceptability were included.
Main results Eighteen studies, (15 RCTs, 3 Controlled prospective studies) met the inclusion criteria for the review. Three were excluded from the meta-analysis due to lack of data on retention, heroin use or mortality. Cessation of allocated medication (11 studies, 1473 participants) was greater with LAAM than with methadone, (RR 1.36, 95%CI 1.07-1.73, p=0.001, NNT=7.7 (or 8)). Non-abstinence was less with LAAM (5 studies, 983 participants; RR 0.81, 95%CI 0.72-0.91, p=0.0003, NNT=9.1 (or 10)). In 10 studies (1441 participants) there were 6 deaths from a range of causes, 5 in participants assigned to LAAM (RR 2.28 (95%CI 0.59-8.9, p=0.2). other relevant

outcomes, such as quality of life and criminal activity could not be analysed because of lack of information in the primary studies.
Reviewers' conclusions LAAM appears more effective than methadone at reducing heroin use. More LAAM patients than methadone ceased their allocated medication during the studies, but many transferred to methadone and so the significance of this is unclear. There was no difference in safety observed, although there was not enough evidence to comment on uncommon adverse events.

[8] METHADONE MAINTENANCE VERSUS NO OPIOID REPLACEMENT THERAPY FOR OPIOID DEPENDENCE
Mattick RP, Breen C, Kimber J, Davoli M. Date first publication issue 4, 2002; Date of the last substantial update issue 2, 2003

Background Methadone maintenance was the first widely used form of opioid replacement therapy developed to treat heroin dependence, and it remains the best-researched treatment for this problem. Despite the widespread use of methadone in maintenance treatment for opioid dependence in many countries, it is a controversial treatment whose effectiveness has been disputed.
Objectives To evaluate the effects of methadone maintenance treatment (MMT) compared with treatments that did not involve opioid replacement therapy (i.e., detoxification, offer of drug-free rehabilitation, placebo medication, wait-list controls) for opioid dependence.
Selection criteria All randomised controlled clinical trials of methadone maintenance therapy compared with either placebo maintenance or other non-pharmacological therapy for the treatment of opioid dependence.
Main results Six studies met the criteria for inclusion in this review, all were randomised clinical trials, two were double-blind. There were a total number of 954 participants. The method of concealment of allocation was inadequate in one study, not clearly described in four studies, but adequate in a sixth study. Based on the meta-analysis, methadone appeared statistically significantly more effective than non-pharmacological approaches in retaining patient in treatment (3 RCTs, RR=3.05; 95%CI: 1.75-5.35) and in the suppression of heroin use (3 RCTs, RR=0.32; 95%CI: 0.23-0.44), but not statistically in criminal activity (3 RCTs, RR=0.39; 95%CI: 0.12-1.25).
Reviewers' conclusions Methadone is an effective maintenance therapy intervention for the treatment of heroin dependence as it retains patients in treatment and decreases heroin use better than treatments that do not utilise opioid replacement therapy. It does not show a statistically significant superior effect on criminal activity.

[9] BUPRENORPHINE MAINTENANCE VS PLACEBO OR METHADONE MAINTENANCE FOR OPIOID DEPENDENCE
Mattick RP, Kimber J, Breen C, Davoli M. Date first publication issue 4, 2002; Date of the last substantial update issue 3, 2003

Background Buprenorphine has recently been reported to be an alternative to methadone and LAAM for maintenance treatment of opioid dependent individuals, differing results are reported concerning its relative effectiveness indicating the need for an integrative review.
Objectives To evaluate the effects of buprenorphine maintenance against placebo and methadone maintenance in retaining patients in treatment and in suppressing illicit drug use.
Selection criteria Randomised clinical trials of buprenorphine maintenance compared with either placebo or methadone maintenance for opioid dependence.
Main results Thirteen studies met the inclusion criteria, all were randomised clinical trials, all but one were double-blind. The method of concealment of allocation was not clearly described in 11 of the studies, otherwise methodological quality was good. Buprenorphine given in flexible doses appeared statistically significantly less effective than methadone in retaining patient in treatment (RR= 0.82; 95% CI: 0.69-0.96). Low dose buprenorphine is not superior to low dose methadone. High dose buprenorphine does not retain more patients than low dose methadone, but may suppress heroin use better. There was no advantage for high dose buprenorphine over high dose methadone in retention (RR=0.79; 95% CI:0.62-1.01), and high dose buprenorphine was inferior in

suppression of heroin use. Buprenorphine was statistically significantly superior to placebo medication in retention of patients in treatment at low doses (RR=1.24; 95% CI: 1.06-1.45), high doses (RR=1.21; 95% CI: 1.02-1.44), and very high doses (RR=1.52; 95% CI: 1.23-1.88). However, only high and very high dose buprenorphine suppressed heroin use significantly above placebo.

Reviewers' conclusions Buprenorphine is an effective intervention for use in the maintenance treatment of heroin dependence, but it is not more effective than methadone at adequate dosages.

[10] HEROIN MAINTENANCE FOR CHRONIC HEROIN ADDICTS

Ferri M, Davoli M, Perucci CA Date first publication issue 3, 2003**; Date of the last substantial update issue 2, 2005**

Background Dependent heroin users are characterised by the persistence of use in spite of the difficulties they experience with health, law, social achievements and personal relationships. The present review will consider maintenance treatment in which the patients enter programs of pharmacological administration tailored to achieve patient stabilisation. Many medications have been used for this purpose such as: Methadone, Buprenorphine and LAAM. The present review will focus on maintenance treatment through the prescription of heroin.

Objectives To assess the efficacy and acceptability of heroin maintenance versus methadone or other substitution treatments for opioid dependence, in retaining patients in treatment; reducing the use of illicit substances and improving health and social functioning.

Selection criteria Randomised controlled trials of heroin (alone or combined with methadone) maintenance treatment compared with any other pharmacological treatments for heroin dependents.

Main results 2400 references were obtained and 20 studies were eligible, 4 met the inclusion criteria for a total of 577 patients. The studies included could not be analysed cumulatively because of heterogeneity of interventions and outcomes considered. Two studies compared injected heroin to oral methadone for 1 year (270 patients) but considered different outcomes; one study compared injected heroin and methadone to oral methadone for 6 months (51 patients); and one compared inhaled heroin and methadone to oral methadone for 1 year (235 patients). Retention in treatment: in two studies there was no statistical difference between groups; one study (N=96) had a RR=2.82 (95% CI 1.70-4.68) in favour of heroin; one study (N=235) had a RR 0.79 (95%CI 0.68-0.90) in favour of methadone. Relapse to illegal heroin use, based on self report: in one study the proportion of people still using heroin were 64% in the heroin group, 59% methadone group; in the other study the RR was 0.33 (95%CI 0.15-0.72) in favour of heroin. The remaining studies did not provide the data. Criminal offence: one of the two studies which provided details about this showed the potential of heroin prescription in reducing the risk of being charged RR 0.32 (95% CI 0.14-0.78). Social functioning: the two studies reporting this outcome did not show statistical difference between intervention groups. The two most recent studies considered criminal offence and social functioning as part of a multidomain outcome measure and showed higher improvement among those treated with heroin plus methadone over those on methadone only.

Reviewers' conclusions No definitive conclusions about the overall effectiveness of heroin prescription is possible because of non-comparability of the experimental studies available to be included in this review. Results favouring heroin treatment come from studies conducted in countries where the treatment system is comprehensive and easy accessible Methadone Maintenance Treatment at effective dosages is available. In those studies heroin prescription was addressed to patients who had failed previous methadone treatments.

[11] METHADONE MAINTENANCE AT DIFFERENT DOSAGES FOR OPIOID DEPENDENCE

Faggiano F, Vigna-Taglianti F, Versino E, Lemma P CA Date first publication issue 3, 2003

Background Methadone maintenance treatment (MMT) is a long term opiod replacement therapy, recognised as effective in the management of opiod dependence. Even if MMT at high dosage is

recommended as therapy for reducing illicit opioid use and promoting longer retention in treatment, at present day "the organisation and regulation of the methadone maintenance treatment varies widely".

Objectives To evaluate the efficacy of different dosages of MMT for opioid dependence in modifying health and social outcomes and in promoting patients' familial, occupational and relational functioning.

Selection criteria Randomised Controlled Trials (RCT) and Controlled Prospective Studies (CPS) evaluating methadone maintenance at different dosages in the management of opioid dependence were included in the review. Non-randomised trials were included when proper adjustment for confounding factors was performed at the analysis stage.

Main results 22 studies were excluded from the review. 21 studies were included; of them, 11 were RCTs with 2279 people randomised and 10 were CPSs with 3715 people followed-up.
Outcomes: Retention rate - RCTs: High vs low doses at shorter follow-ups: RR=1.36 [1.13,1.63], and at longer ones: RR=1.62 [0.95,2.77].
Opioid use (self reported), times/w - RCTs: high vs low doses WMD= -2.00 [-4.77,0.77] high vs middle doses WMD= -1.89[-3.43, -0.35]
Opioid abstinence, (urine based) at >3-4 w - RCTs: high vs low ones: RR=1.59 [1.16,2.18] high vs middle doses RR=1.51[0.63,3.61]
Cocaine abstinence (urine based) at >3-4 w - RCTs: high vs low doses RR=1.81 [1.15,2.85]
Overdose mortality - CPSs: high dose vs low dose at 6 years follow up: RR=0.29 [0.02-5.34] high dose vs middle dose at 6 years follow up: RR=0.38 [0.02-9.34] middle dose vs low dose at 6 years follow up: RR=0.57 [0.06-5.06]

Reviewers' conclusions Methadone dosages ranging from 60 to 100 mg/day are more effective than lower dosages in retaining patients and in reducing use of heroin and cocaine during treatment. To find the optimal dose is a clinical ability, but clinician must consider these conclusions in treatment strategies.

[12] SUBSTITUTION TREATMENT OF INJECTING OPIOID USERS FOR PREVENTION OF HIV INFECTION

Gowing L., Farrell M, Bornemann R, Ali R., White J. Date first publication issue 4, 2004

Background Injecting drug users are vulnerable to infection with HIV and other blood borne viruses as a result of collective use of injecting equipment as well as sexual behaviour.

Objectives To assess the effect of oral substitution treatment for opioid dependent injecting drug users on rates of HIV infections, and high risk behaviours.

Selection criteria Studies were required to consider the incidence of risk behaviours, or the incidence of HIV infection related to substitution treatment of opioid dependence. All types of original studies were considered.

Main results Twenty-eight studies, involving 7900 participants, were included. The majority were not randomised controlled studies. Issues of confounding and bias are discussed. The studies varied in several aspects limiting the extent of quantitative analysis.

Reviewers' conclusions Oral substitution treatment for opioid-dependent injecting drug users is associated with statistically significant reductions in illicit opioid use, injecting use and sharing of injecting equipment. It is also associated with reductions in the proportion of injecting drug users reporting multiple sex partners or exchanges of sex for drugs or money, but has little effect on condom use. It appears that the reductions in risk behaviours related to drug use do translate into reductions in cases of HIV infection. The lack of data from randomised controlled studies limits the strength of the evidence presented in this review. However, these findings add to the stronger evidence of effectiveness of substitution treatment on drug use, and treatment retention outcomes shown by other systematic reviews. On this basis, the provision of substitution treatment for opioid dependence in countries with emerging HIV and injecting drug use problems as well as in countries with established populations of injecting drug users should be supported.

OPIATE: PSYCHOSOCIAL TREATMENTS

[13] PSYCHOSOCIAL AND PHARMACOLOGICAL TREATMENTS VERSUS PHARMACOLOGICAL TREATMENTS FOR OPIOID DETOXIFICATION

Amato L, Minozi S, Davoli M, Vecchi S, Ferri M, Mayet S Date first publication issue 4, 2004

Background Different pharmacological approaches aimed at opioid detoxification are effective. Nevertheless a majority of patients relapse to heroin use, and relapse to re-addiction is a substantial problem in the rehabilitation of dependent heroin users. Some studies have suggested that the sorts of symptoms which are most distressing to addicts during detoxification are psychological symptoms 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.
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.
Main results The searching process resulted in the identification of 77 different studies: 8 studies met inclusion criteria. These studies considered 5 different psychosocial interventions and 2 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 RR 1.68 (95% CI 1.11-2.55), results at follow-up RR 2.43 (95% CI 1.61-3.66), and compliance RR 0.48 (95% CI 0.38-0.59). In respect of the use of heroin during the treatment, the differences were not statistically significant but favoured the combined treatments.
Reviewers' conclusions Psychosocial treatments offered in addition to pharmacological detoxification treatments are effective in terms of completion of treatment, 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.

[14] PSYCHOSOCIAL COMBINED WITH AGONIST MAINTENANCE TREATMENTS VERSUS AGONIST MAINTENANCE TREATMENTS ALONE FOR TREATMENT OF OPIOID DEPENDENCE

Amato L, Minozi S, Davoli M, Vecchi S, Ferri M, Mayet S Date first publication issue 4, 2004

Background Methadone maintenance at proper doses is effective in retaining patients in treatment and suppressing heroin use. Questions remain regarding the efficacy of the psychosocial services that are offered by most maintenance programs.
Objectives To evaluate the effectiveness of any psychosocial plus any agonist maintenance treatment versus any agonist treatment alone for opiate dependence in retaining patients in treatment, reducing the use of substances and improving health and social status.
Selection criteria RCTs which focus on any psychosocial plus any agonist compared to any agonist maintenance intervention for opiate dependence. People aged less than 18 and pregnant women were excluded. Psychosocial in combination with antagonist maintenance treatment are excluded too.
Main results The searching process resulted in the identification of 77 different studies: 12 studies met the inclusion criteria. These studies considered 8 different psychosocial interventions and 1 pharmacological treatment: Methadone Maintenance (MMT). The results show additional benefit in adding any psychosocial treatment to standard methadone maintenance treatment in relation to

the use of heroin during the treatment RR 0.69 (95% CI 0.53-0.91); no statistically significant additional benefit was shown in terms of retention in treatment RR 0.94 (95% CI 0.85-1.02); and results at follow-up RR 0.90 (95% CI 0.76-1.07).
Reviewers' conclusions The present evidence suggests that adding any psychosocial support to Standard MMT significantly improves the non-use of heroin during treatment. Retention in treatment and results at follow-up are also improved, although this finding did not achieve statistical significance. Insufficient evidence is available on other possible relevant outcomes such as Psychiatric symptoms/psychological distress, Quality of life.
Limitations to this review are imposed by the heterogeneity of the trials both in the interventions and the assessment of outcomes. Results of studies were sometimes in disagreement and because of lack of detailed information no meta analysis could be performed to analyse the results related to the outcomes more often reported as positive results in the single studies. Duration of the studies was also too short to analyse other relevant outcomes such as mortality. In order to study the possible added value of any psychosocial treatment over an already effective treatment such as standard MMT, only big multi site studies could be considered which define experimental interventions and outcomes in the most standardized way as possible.

[15] Psychosocial treatment for opiate abuse and dependence

Mayet S, Farrell M, Ferri M, Amato, L, Davoli, M, Date first publication issue 1, 2005

Background: Substance dependence is a major social and public health problem; therefore it is a priority to develop effective treatments. The treatment of opioid dependence is complex. Previous Cochrane reviews have explored the efficacy of pharmacotherapy for opiate dependence. This current review focuses on the role of psychosocial interventions alone for the treatment of opiate dependence. There are many different psychosocial interventions offered to opiate addicts, which are widely spread. There is some evidence for the effectiveness of psychosocial interventions, but no systematic review has even been carried out.
Objectives: To assess the efficacy and acceptability of psychosocial interventions alone for treating opiate use disorders.
Selection criteria: The inclusion criteria for all randomised-controlled trials were that they should focus on psychosocial interventions alone for treating opioid use disorders.
Main results: Five studies fit the study criteria. These analysed Contingency Management, Brief Reinforcement Based Intensive Outpatient Therapy coupled with Contingency Management, Cue Exposure therapy, Alternative Program for Methadone Maintenance Treatment Program Drop-outs (MMTP) and Enhanced Outreach-Counselling Program. All the treatments were studied against the control (standard) treatment; therefore it was not possible to identify which type of psychosocial therapy was most effective.The main findings were that both Enhanced Outreach Counselling and Brief Reinforcement Based Intensive Outpatient Therapy coupled with Contingency Management had significantly better outcomes than standard therapy within treatment. This was regarding relapse to opioid use, re-enrolment in treatment and retention in treatment. At 1-month and 3-month follow up the effects of Reinforcement Based Intensive Outpatient Therapy were not sustained. There was no further follow up of the Enhanced Outreach Counselling group. The Alternative Program for MMTP Drop-outs and the behavioural therapies of Cue Exposure and Contingency Management alone were no better than the control (standard) therapy. As the studies were heterogeneous, it was not possible to pool the results and perform a meta-analysis.
Reviewers' conclusions: The available evidence has low numbers and is heterogeneous. At present psychosocial treatments alone are not adequately proved treatment modalities or superior to any other type of treatment.
It is important to develop a better evidence base for psychosocial interventions to assist in future rationale planning of opioid use drug treatment services. Large-scale randomised trials are required with longer follow up stating methods of randomisation, allocation concealment and blinding. Where possible this should include intention to treat analysis, with power calculations performed prior to the trial. These studies can be designed and delivered to provide usable data for better understanding of this important component of intervention in the field of dependence.

OPIATE: OTHER

[16] NEW INPATIENT VERSUS OTHER SETTINGS FOR DETOXIFICATION FOR OPIOID DEPENDENCE

Day E, Ison J, Strang J. **Date first publication issue 2, 2005**

Background There are a complex range of variables that can influence the course and subjective severity of opioid withdrawal. There is a growing evidence for the effectiveness of a range of medically-supported detoxification strategies, but little attention has been paid to the influence of the setting in which the process takes place.

Objectives To evaluate the effectiveness of any inpatient opioid detoxification programme when compared with all other time-limited detoxification programmes on the level of completion of detoxification, the intensity and duration of withdrawal symptoms, the nature and incidence of adverse effects, the level of engagement in further treatment post-detoxification, and the rates of relapse post-detoxification.

Selection criteria Randomised controlled clinical trials comparing inpatient opioid detoxification (any drug or psychosocial therapy) with other time-limited detoxification programmes (including residential units that are not staffed 24 hours per day, day-care facilities where the patient is not resident for 24 hours per day, and outpatient or ambulatory programmes, and using any drug or psychosocial therapy).

Main results Only one study met the inclusion criteria. This did not explicitly report the number of participants in each group that successfully completed the detoxification process, but the published data allowed us to deduce that 7 out of 10 (70%) in the inpatient detoxification group were opioid-free on discharge, compared with 11 out of 30 (37%) in the outpatient group. There was very limited data about the other outcomes of interest.

Reviewers' conclusions This review demonstrates that there is no good available research to guide the clinician about the outcomes or cost-effectiveness of inpatient or outpatient approaches to opioid detoxification.

ALCOHOL

[17] OPIOID ANTAGONISTS FOR ALCOHOL DEPENDENCE

Srisurapanont M, Jarusuraisin N. Kittiratanapaiboon P. Date first publication issue 3, 2000; Date of the last substantial update issue 1, 2005

Background Opioid antagonists can decrease alcohol consumption in animals. Their harms and benefits have been examined in many clinical trials.

Objectives To determine the effectiveness of opioid antagonists in attenuating or preventing the recommencement of alcohol consumption in patients with alcohol dependence in comparison to placebo, other medications and psychosocial treatments. In addition, discontinuation rate, death, patient satisfaction, functioning, health-related quality of life and economic outcomes were also evaluated.

Selection criteria All relevant randomised controlled trials (RCTs) were included. Participants were people with alcohol dependence. Naltrexone (NTX), nalmefene (NMF) and other opioid antagonists with/without other biological or psychosocial treatments were examined. Two primary outcomes were number of participants with relapses (including those who return to heavy drinking) and number of participants who return to drinking. Other outcomes of interest were time to first drink, percentage or number of drinking days, number of standard drinks, craving, percentage or number of days or episodes of heavy drinking, amount of alcohol consumed, discontinuation rate, patient satisfaction, impaired function, health-related quality of life, economic and death.

Main results The review included 29 RCTs presented in 36 articles. Except two RCTs of nalmefene, all others investigated NTX. In comparison to placebo, a short-term treatment of NTX significantly decreased the relapse [RR (95% CI) = 0.64 (0.51 to 0.82)] and was likely to decrease the return to drinking [RR (95% CI) = 0.87 (0.76 to 1.00). In the respect of acceptability, NTX treatment significantly diminished treatment withdrawal [RR (95% CI) = 0.82 (0.70 to 0.97). While a medium-term treatment of NTX gave no benefit in the respect of relapse prevention, it was found

to be beneficial on two of four secondary outcomes by increasing time to first drink and diminishing craving. A medium-term treatment of NTX was superior to acamprosate in reducing relapses, standard drinks and craving. NTX plus an intensive psychosocial treatment (PST) was not superior to NTX plus a simple PST on any primary and secondary short-term outcomes. For a medium-term treatment, NTX plus an intensive PST was superior to NTX plus a simple PST in increasing time to first drink and decreasing craving.
Reviewers' conclusions The review findings support that short-term treatment of NTX decreases the chance of alcohol relapses for 36% (number-needed-to-treat or NNT = 7) and likely to reduce the chance of returning to drinking for 13% (NNT = 12). In comparison to placebo group, NTX treatment can lower the risk of treatment withdrawal in alcohol-dependent patients for 28% (NNT = 13). Some major limitations of the available evidence include short study duration in many trials, small sample sizes in most trials and lack of data on psychosocial benefits. In conclusion, NTX should be accepted as a short-term treatment for alcoholism. Strategies to improve adherence to NTX treatment, eg, PSTs and management of adverse effects, should be concomitantly given. We have not yet known so far how long alcohol-dependent patients who respond to NTX treatment should continue their treatment. Due to too little evidence, NMF should have no role for the treatment of alcohol dependence.

[18] PRIMARY PREVENTION FOR ALCOHOL MISURE IN YOUNG PEOPLE

Foxcroft DR, Ireland D, Lister-Sharp DJ, Lowe G, Breen R. Date first publication issue 3, 2002;

Background Alcohol misuse is a cause of concern for health services, policy makers, prevention workers, the criminal justice system, youth workers, teachers and parents.
Objectives 1. To identify and summarize rigorous evaluations of psychosocial and educational interventions aimed at the primary prevention of alcohol misuse by young people. 2. To assess the effectiveness of primary prevention interventions over the longer-term (> 3 years).
Selection criteria 1. randomised controlled and non-randomised controlled and interrupted time series designs. 2. educational and psychosocial primary prevention interventions for young people up to 25 years old. 3. alcohol-specific or generic (drugs; lifestyle) interventions providing alcohol outcomes reported. 4. alcohol outcomes: alcohol use, age of alcohol initiation, drinking 5+ drinks on any one occasion, drunkeness, alcohol related violence, alcohol related crime, alcohol related risky behaviour.
Selection criteria 1. randomised controlled and non-randomised controlled and interrupted time series designs. 2. educational and psychosocial primary prevention interventions for young people up to 25 years old. 3. alcohol-specific or generic (drugs; lifestyle) interventions providing alcohol outcomes reported. 4. alcohol outcomes: alcohol use, age of alcohol initiation, drinking 5+ drinks on any one occasion, drunkeness, alcohol related violence, alcohol related crime, alcohol related risky behaviour.

Main results 20 of the 56 studies included showed evidence of ineffectiveness. No firm conclusions about the effectiveness of prevention interventions in the short- and medium-term were possible. Over the longer-term, the Strengthening Families Program (SFP) showed promise as an effective prevention intervention. The Number Needed to Treat (NNT) for the SFP over 4 years for three alcohol initiation behaviours (alcohol use, alcohol use without permission and first drunkeness) was 9 (for all three behaviours). One study also highlighted the potential value of culturally focused skills training over the longer-term (NNT=17 over three-and-a-half years for 4+ drinks in the last week).
Reviewers' conclusions: Research into important outcome variables needs to be undertaken. 2. Methodology of evaluations needs to be improved. 3. The Strengthening Families Programme needs to be evaluated on a larger scale and in different settings. 4. Culturally-focused interventions require further development and rigorous evaluation. 5. An international register of alcohol and drug misuse prevention interventions should be established and criteria agreed for rating prevention intervention in terms of safety, efficacy and effectiveness.

COCAINE

[19] CARBAMAZEPINE FOR COCAINE DEPENDENCE
Lima AR, Lima MS, Soares BGO, Farrell M. Date first publication issue 2, 2000; Date of the last substantial update issue 2, 2002

Background Cocaine dependence has become a substantial public health problem, developing a significant number of medical, psychological and social problems, including the spread of infectious diseases (e.g. AIDS, hepatitis and tuberculosis), crime, violence and neonatal drug exposure. Although there is no consensus regarding how to treat cocaine dependence, effective pharmacotherapy has a potentially major role to play as part of a broader treatment milieu. The anti-convulsant carbamazepine, a tricyclic medication that is widely used to treat a variety of neurological and psychiatric disorders, has also been used for treatment of cocaine dependence, although its effectiveness has not been established.
Objectives To determine whether carbamazepine (CBZ) is effective for the treatment of cocaine dependence.
Selection criteria The inclusion criteria for all randomised controlled trials were that they should focus on the use of carbamazepine drugs versus placebo on the treatment of cocaine dependence. Trials including patients with additional diagnosis such as opiate dependence were also eligible.
Main results 5 studies were included in the review, with 455 people randomised. No differences were found regarding positive urine sample for cocaine metabolites. Scores on Spielberg State Anxiety Inventory slightly favoured carbamazepine, but didn't reach statistical significance. Dropouts were high in both groups up to 70% in the placebo group. Less dropout occurred in the carbamazepine group (RR 0.87 95%CI 0.71-1.06). When no retention in treatment was due to side effects no differences were found. The number of participants presenting at least one side effect, reported in Kranzler (Kranzler 1995), was higher in the carbamazepine group (RR 4.33 95% CI 1.45-12.91).
Reviewers' conclusions There is no current evidence supporting the clinical use of CBZ in the treatment of cocaine dependence. Larger randomised investigation must be considered taking into account that these time-consuming efforts should be reserved for medications showing more relevant and promising evidence.

[20] ANTIDEPRESSANT FOR COCAINE DEPENDENCE
Lima MS, Reisser AAP, Soares BGO, Farrell M. Date first publication issue 4, 2001; Date of the last substantial update issue 2, 2003

Background Cocaine dependence is a common and serious condition, which has become a substantial public health problem. The past decade has witnessed a sustained search for an effective pharmacotherapeutic agent for the treatment of cocaine dependence. While

administration of cocaine acutely increases intercellular dopamine, serotonin, and norepinephrine levels by blocking their presynaptic reuptake, chronic cocaine abuse leads to down-regulation of monoamine systems. Post-cocaine use depression and cocaine craving may be linked to this down-regulation. Antidepressant pharmacotherapy, by augmenting monoamine levels, may alleviate cocaine abstinence symptomatology, as well as relieving dysphoria and associated craving by general antidepressant action.

Objectives To conduct a systematic review of all RCTs on the use of antidepressants for treating cocaine dependence.

Selection criteria The inclusion criteria for all randomised controlled trials were that they should focus on the use of antidepressants on the treatment of cocaine dependence. Trials including patients with additional diagnosis such as opiate dependence were also eligible.

Main results 18 studies were included in the review, with 1177 people randomised. Positive urine sample for cocaine metabolites was the main efficacy outcome, with no significant results obtained regardless of the type of antidepressant. Compared to other drugs, desipramine performed better but showing just a non significant trend with heterogeneity present as revealed by the chi-square test (8.6, df=3; p=0.04). One single trial showed imipramine performed better than placebo in terms of clinical response according to patient's self-report. A similar rate of patients remaining in treatment was found for both patients taking desipramine or placebo. Results from one single trial suggest fluoxetine patients on SSRIs are less likely to dropout. Similar results were obtained for trials where patients had additional diagnosis of opioid dependence and/or were in methadone maintenance treatment.

Reviewers' conclusions There is no current evidence supporting the clinical use of antidepressants in the treatment of cocaine dependence. Given the high rate of dropouts in this population, clinicians may consider adding psychotherapeutic supportive measures aiming to keep patients in treatment.

[21] DOPAMINE AGONISTS FOR COCAINE DEPENDENCE

Soares BGO, Lima MS, Reisser AAP, Farrell M. Date first publication issue 4, 2001; Date of the last substantial update issue 2, 2003

Background Cocaine dependence is a common and serious condition, which has become nowadays a substantial public health problem. There is a wide and well documented range of consequences associated to chronic use of this drug, such as medical, psychological and social problems, including the spread of infectious diseases (e.g. AIDS, hepatitis and tuberculosis), crime, violence and neonatal drug exposure.

Therapeutic management of the cocaine addicts includes an initial period of abstinence from the drug. During this phase the subjects may experience, besides the intense craving for cocaine, symptoms such as depression, fatigue, irritability, anorexia, and sleep disturbances. It was demonstrated that the acute use of cocaine may enhance dopamine transmission and chronically it decreases dopamine concentrations in the brain. Pharmacological treatment that affects dopamine could theoretically reduce these symptoms and contribute to a more successful therapeutic approach.

Objectives To evaluate the efficacy and acceptability of dopamine agonists for treating cocaine dependence.

Selection criteria The inclusion criteria for all randomised controlled trials were that they should focus on the use of dopamine agonists on the treatment of cocaine dependence.

Main results Seventeen studies were included, with 1224 participants randomised. Amantadine, bromocriptine, and pergolide were the drugs evaluated. The main outcomes evaluated were positive urine sample for cocaine metabolites, for efficacy, and retention in treatment, as an acceptability measure. There were no significant differences between interventions, and in trials where participants had primary cocaine dependence or had additional diagnosis of opioid dependence and/or were in methadone maintenance treatment.

Reviewers' conclusions Current evidence does not support the clinical use of dopamine agonists in the treatment of cocaine dependence. Given the high rate of dropouts in this population, clinicians may consider adding other supportive measures aiming to keep patients in treatment.

AMPHETAMINE

[22] TREATMENT FOR AMPHETAMINE ABUSE AND DEPENDENCE

Srisurapanont M, Jarusuraisin N, Kittiratanapaiboon P Date first publication issue 4, 2001

Background The ease of synthesis from inexpensive and readily available chemicals makes possible the wide spread of amphetamine dependence and abuse. Amphetamine use is of concern because it causes a variety of devastating health consequences, including physical and neurological disorders due to amphetamines, amphetamine-induced mental disorders, health consequences of amphetamine use and social consequences of amphetamine use.
Objectives To search and determine risks, benefits and costs of a variety of treatments for amphetamine dependence or abuse.
Selection criteria All relevant randomised controlled trials (RCTs) and clinical controlled trials (CCTs) were included. Participants were people with amphetamine dependence or abuse, diagnosed by any set of criteria. Any kinds of biological and psychological treatment both alone and combined were examined. A variety of outcomes, for example, number of treatment responders, score changes, were considered.
Main results Fluoxetine, amlodipine, imipramine and desipramine have been investigated in four randomised-controlled trials. In comparison to placebo, short-term treatment of fluoxetine (40 mg/day) significantly decreased craving. In comparison to imipramine 10 mg/day, medium-term treatment of imipramine 150 mg/day significantly increased the duration of adherence to treatment. All four drugs had no benefits on a variety of outcomes, including amphetamine use.
Reviewers' conclusions The evidence about the treatment for amphetamine dependence and abuse is very limited. It shows that fluoxetine, amlodipine, imipramine and desipramine have very limited benefits for amphetamine dependence and abuse. Fluoxetine may decrease craving in short-term treatment. Imipramine may increase duration of adherence to treatment in medium-term treatment. Apart from these, no other benefits, in particular proximal benefits, can be found. This limited evidence suggests that no treatment has been demonstrated to be effective for the treatment of amphetamine dependence and abuse.Although there is a large number of people with amphetamine dependence and abuse worldwide, very few controlled trials in this issue have been conducted. As the previous treatment trials show no promising result, other treatments, both biological and psychosocial, should be further investigated. However, the results of neurotoxic studies of amphetamines are also crucial for the study designs appropriate for further treatment studies for amphetamine dependence and abuse.

[23] TREATMENT FOR AMPHETAMINE PSYCHOSIS DISORDER

Srisurapanont M, Kittiratanapaiboon P. Jarusuraisin N. Date first publication issue 4, 2001

Background During the phase of chronic, high-dose consumption of amphetamines, many amphetamine users may have the experience of paranoia and hallucination. It has long been believed that dopamine antagonists, such as chlorpromazine, haloperidol, and thioridazine, are effective for the treatment of amphetamine psychosis.
Objectives To search and determine risks, benefits, and costs of a variety treatments for amphetamine psychosis.
Selection criteria All relevant randomised controlled trials (RCTs) and clinical trials (CCTs) were included. Participants were people with amphetamine psychosis, diagnosed by any set of criteria. Any kinds of biological and psychological treatments both alone and combined were examined. A variety of outcomes, for example, number of treatment responders, score changes, were considered.
Main results The comprehensive searches found no controlled trials of treatment for amphetamine psychosis meeting the criteria for considering studies.
Reviewers' conclusions The evidence about the treatment for amphetamine psychosis is very limited. To our knowledge, no controlled trials of treatment for amphetamine psychosis have been carried out. The results of two studies in amphetamine users show that agitation and some

psychotic symptoms may be abated within an hour after antipsychotic injection. Whether this limited evidence can be applied for amphetamine psychotic patients is not yet known. The risks and benefits of giving an antipsychotic injection should be further investigated in amphetamine psychotic patients. Medications that have been used for the treatment of acute exacerbation of schizophrenia should be studied in amphetamine psychotic patients. The medications that may be of interest are conventional antipsychotics, newer antipsychotics and benzodiazepines. However, naturalistic studies of amphetamine psychotic symptoms and course are also crucial for the development of study designs appropriate for further treatment studies of amphetamine psychosis.

[24] TREATMENT FOR AMPHETAMINE WITHDRAWAL

Srisurapanont M, Kittiratanapaiboon P. Jarusuraisin N. Date first publication issue 4, 2001

Background Amphetamine withdrawal has been less studied although it is a common problem with a prevalent rate of 87% among amphetamine users. Its symptoms, in particular intense craving, may be a critical factor leading to relapse of amphetamine use. In clinical practice, treatment for cocaine withdrawal has been recommended for the management of amphetamine withdrawal although the pharmacodynamic and pharmacokinetic properties of these two substances are not the same.

Objectives To search and determine risks, benefits, and costs of a variety of treatments for the management of amphetamine withdrawal.

Selection criteria All relevant randomised controlled trials (RCTs) and controlled clinical trials (CCTs) were included. Participants were people with amphetamine withdrawal, diagnosed by any set of criteria. Any kinds of biological and psychological treatments both alone and combined were examined. A variety of outcomes, for example, number of treatment responders, score changes, were considered.

Main results The results of two studies have shown some benefits of amineptine in the treatment of amphetamine withdrawal. Those benefits can be seen in the respects of discontinuation rate and global state, as measured by Clinical Global Impression Scale. However, no direct benefit of amineptine on amphetamine withdrawal symptoms or craving was shown.

Reviewers' conclusions The evidence about the treatment for amphetamine withdrawal is very limited. Amineptine has limited benefits on some amphetamine withdrawal symptoms. Due to a number of reports of amineptine abuse, it has been withdrawn from the market for a few years. At present, no available treatment has been demonstrated to be effective in the treatment of amphetamine withdrawal. The medications that should be considered for further treatment studies may be those with the propensities to increase dopamine, norepinephrine and/or serotonin acitivities of the brain. Naturalistic studies of amphetamine withdrawal symptoms and course are also crucial for the development of study designs appropriate for further treatment studies of amphetamine withdrawal.

OTHER DRUGS

[25] *NEW* TREATMENT FOR METHAQUALONE DEPENDENCE IN ADULTS

McCarthy G, Myers B, Siegfried N **Date first publication issue 2, 2005**

Background Methaqualone is a potent quinazoline, a class of sedative-hypnotics, that has a high potential for abuse. While the oral use of methaqualone (Quaalude, Mandrax) has waned in western countries since the mid-late 1980's, the practice of smoking methaqualone is a serious public health problem in South Africa, other parts of Africa and India. In the context of diminishing resources devoted to substance abuse treatment in regions affected by methaqualone abuse, it would be desirable to base treatment on the best evidence available. This review aimed to provide health care workers, policy-makers and consumers with the necessary information to make decisions regarding effective treatment of this highly dependence-producing drug.

Objectives To compare the effectiveness of any type of pharmacological or behavioural treatment administered in either an in-patient or out-patient setting compared with either a placebo or no treatment or a waiting list, or with another form of treatment administered in either an in- or out-patient setting.
Selection criteria All randomised controlled trials and quasi-randomised trials of the effectiveness of treatment programmes (in- or out-patient) for methaqualone dependence and abuse were considered for inclusion in this review.
Main results No studies were found that met the inclusion criteria.
Reviewers' conclusions To date, no randomized controlled trials appear to have been conducted. Consequently, the effectiveness of inpatient versus outpatient treatment, psychosocial treatment versus no treatment, and pharmacological treatments versus placebo for methaqualone abuse or dependence has yet to be established.

POLY DRUGS

[26] NEW SCHOOL-BASED PREVENTION FOR ILLICIT DRUGS' USE

Faggiano F, Vigna-Taglianti FD, Versino E, Zambon A, Borraccino A, Lemma P. **Date first publication issue 2, 2005**

Background Drug addiction is a chronic, relapsing disease. Primary interventions should be aimed to reduce first use, or prevent the transition from experimental use to addiction. School is the appropriate setting for preventive interventions.
Objectives To evaluate the effectiveness of school-based interventions in improving knowledge, developing skills, promoting change, and preventing or reducing drug use versus usual curricular activities or a different school-based intervention .
Selection criteria RCTs, CCTs or Controlled Prospective Studies (CPS) evaluating school-based interventions designed to prevent substance use.
Main results 32 studies (29 RCTs and 3 CPSs) were included. 28 were conducted in the USA; most were focused on 6th-7th grade students, and based on post-test assessment.
RCTs
(1) Knowledge vs usual curricula
Knowledge focused programs improve drug knowledge (SMD=0.91; 95% CI: 0.42, 1.39).
(2) Skills vs usual curricula
Skills based interventions increase drug knowledge (WMD=2.60; 95% CI: 1.17-4.03), decision making skills (SMD=0.78; CI95%: 0.46-1.09), self-esteem (SMD=0.22; CI95%: 0.03-0.40), peer pressure resistance (RR=2.05; CI95%: 1.24-3.42), drug use (RR=0.81; CI95%: 0.64, 1.02), marijuana use (RR=0.82; CI95%: 0.73, 0.92) and hard drug use (RR=0.45; CI95%: 0.24-0.85).
(3) Skills vs knowledge
No differences are evident.
(4) Skills vs affective
Skills-based interventions are only better than affective ones in self-efficacy (WMD=1.90; CI95%: 0.25, 3.55).
(5) Affective vs usual curricula
Affective interventions improve drug knowledge (SMD=1.88; CI95%: 1.27, 2.50) and decision making skills (SMD=1.35; CI95%: 0.79, 1.9).
(6) Affective vs knowledge
Affective interventions improve drug knowledge (SMD=0.60; CI95%: 0.18,1.03), and decision making skills (SMD=1.22; CI95%: 0.33, 2.12).
Results from CPSs
No statistically significant results emerge from CPSs.
Reviewers' conclusions Skills based programs appear to be effective in deterring early-stage drug use. The replication of results with well designed, long term randomised trials, and the evaluation of single components of intervention (peer, parents, booster sessions) are the priorities for research. All new studies should control for cluster effect.

References of the included studies

N.B. The number in square brackets are referred to the review in which the study is included

1. Abbott PJ, Moore BA, Weller SB, Delaney HD. AIDS risk behavior in opioid dependent patients treated with community reinforcement approach and relationships with psychiatric disorders. Journal of Addictive Diseases. 1998; 17(4): 33-48 [12]
2. Abbott PJ, Weller SB, Delaney HD, Moore BA. Community reinforcement approach in the treatment of opiate addicts. American Journal of Drug and Alcohol Abuse 1998;24(1):17-30. [14]
3. Abrahms J L. A Cognitive-behavioural versus nondirective group treatment program for opioid addicted persons: an adjunct to methadone maintenance.. The International Journal of Addictions 1979;14(4):503-511. [14]
4. Ahmadi J, Ahmadi N. A double blind, placebo-controlled study of naltrexone in the treatment of alcohol dependence. German Journal of Psychiatry 2002;5:85-9. [17]
5. Allison K, Siver G, Dignam C. Effects on students of teacher training in use of a drug education curriculum. Journal of Drug Education 1990;20:31-46. [18]
6. Alterman AI, Droba M, Antelo RE, Cornish JW, Sweeney KK, Parikh GA, O'Brien CP. Amantadine may facilitate detoxification of cocaine abusers. Drug and Alcohol Dependence 1992;31:19-29. [21]
7. Amass L, Bickel WK, Higgins ST, Hughes JR. A preliminary investigation of outcome following gradual or rapid buprenorphine detoxification. Journal of Addictive Diseases 1994;13(3):33-45.RT:Journal article [2]
8. Anton RF, Moak DH, Latham PK, Waid LR, Malcolm RJ, Dias JK, Roberts JS. Posttreatment results of combining naltrexone with cognitive-behavior therapy for the treatment of alcoholism. Journal of Clinical Psychopharmacology 2001;21(1):72-7. [17]
9. Arndt IO, Dorozynsky L, Woody GE, McLellan AT, O'Brien CP. Desipramine treatment of cocaine dependence in methadone-maintained patients. Archives of General Psychiatry. Archives of General Psychiatry 1992;49:888-893. [20]
10. Avants SK, Margolin A, Kosten TR, Rounsaville BJ, Schottenfeld RS. When is less treatment better? The role of social anxiety in matching methadone patients to psychosocial treatments. Journal of Consulting & Clinical Psychology. 1998; 66(6):924-931 [12]
11. Bagnall G. Alcohol Education for 13 year olds - Does it Work? Results from a controlled Evaluation. British Journal of Addiction 1990;85:89-96. [18]
12. Baker A, Kochan N, Dixon J, Wodak A, Heather N. HIV risk-taking behaviour among injecting drug users currently, previously and never enrolled in methadone treatment. Addiction. 1995; 90(4):545-554 [12]
13. Baldwin S. Alcohol Education and Young Offenders: Medium and short-term effectiveness of education programmes. Berlin: Springer-Verlag, 1990. [18]
14. Balldin J, Berglund M, Borg S, Mansson M, Bendtsen P, Franck J, Gustafsson L, Halldin J, Nilsson LH, Stolt G, Willander A. A 6-month controlled naltrexone study: combined effect with cognitive behavioral therapy in outpatient treatment of alcohol dependence. Alcoholism: Cinical and Experimental Research 2003;27:1142-9. [17]
15. Batki SL, Moon J, Bradley M, Hersh D, Smolar S, Mengis M, Delucchi K, Sexe D, Bennett S, Lefkowitz E, Chu W, Morello L, Jacob III P, Jones RT. Fluoxetine in methamphetamine dependence -- a controlled trial: preliminary analysis. In: Harris LS, editor(s). Problems of drug dependence 1999: Proceedings of the 61st annual scientific meeting of the College on Problems of Drug Dependence, Inc (NIDA Research Monograph, 180, NIH Pub. No. 00-4737). Washington, DC: U.S. Government Printing Office, 2000:235. [22]

16. Batki SL, Moon J, Delucchi K, Hersh D, Bradley M, Aguillon-Doms C, Mendelson J, Jones RT, Panganiban T, Everhart T, Mengis M, Smolar S, Helmke H, Jacob III P. Amlodipine treatment of methamphetamine dependence, a controlled outpatient trial: preliminary analysis. Personal communication with Dr. Steven L Batki. [22]

17. Batki SL, Sorensen JL, Gibson DR, Maude-Griffin P. HIV-infected i.v. drug users in methadone treatment: outcome and psychological correlates - a preliminary report. NIDA Research Monograph. 1989, 95: 405-406 [12]

18. Batki SL, Washburn AM, Delucchi K, Jones RT. A controlled trial of fluoxetine in crack cocaine dependence. Drug and Alcohol Dependence 1996;41:137-142. [20]

19. Bearn J, Bennett J, Martin T, Gossop M, Strang J. The impact of naloxone/lofexidine combination treatment on the opiate withdrawal syndrome. Addiction Biology 2001;6(2):147-156. [1]

20. Bearn J, Gossop M, Strang J. Accelerated lofexidine treatment regimen compared with conventional lofexidine and methadone treatment for in-patient opiate detoxification. Drug & Alcohol Dependence 1998;50:227-232. [3] [5]

21. Bearn J, Gossop M, Strang J. Randomised double-blind comparison of lofexidine and methadone in the in-patient treatment of opiate withdrawal. Drug & Alcohol Dependence 1996;43(1-2):87-91. [3] [5]

22. Beaulieu MA, Jason LA. A drug abuse prevention program aimed at teaching seventh grade students problem solving strategies. Children and Youth Services Review 1988;10:131-149. [18]

23. Benos VJ. Clonidin beim opiatentzugssyndrom [Clonidine in opiate withdrawal syndrome]. Fortschritte der Medizin 1985;103(42):991-995. [3]

24. Bernstein E, Woodal WG. Changing perceptions of riskiness in drinking, drugs and driving: an emergency department-based alcohol and substance abuse prevention program. Ann Emergency Med 1987;16(12):1350-4. [26]

25. Bertschy G, Bryois C, Bondolfi G, Velardi A, Budry P, Dascal D et al. The association carbamazepine-mianserin in opiate withdrawal: a double blind pilot study versus clonidine. Pharmacological Research 1997;35(5):451-456. [3]

26. Beswick T, Best D, Rees S, Bearn J, Gossop M, Strang J. Major disruptions of sleep during treatment of the opiate withdrawal syndrome: differences between methadone and lofexidine detoxification treatments. Addiction Biology 2003;8:49-57. [3]

27. Bickel WK, Amass L, Higgins ST, Badger GJ, Esch RA.. Effects of adding behavioral treatment to opioid detoxification with buprenorphine.. Journal of Consulting and Clinical Psychology 1997;65(5):803-810. [13]

28. Botvin GJ et al. A cognitive behavioral approach to substance abuse prevention. Addictive Behaviors 1984;9:137-147. [18]

29. Botvin GJ, Baker E, Dusenbury L, Tortu S et al. Preventing adolescent drug abuse through a multimodal cognitive behavioral approach: Results of a 3 year study. Journal of Consulting and Clinical Psychology 1990;58:437-446. [18]

30. Botvin GJ, Baker E, Dusennbury L, Tortu S, Botvin EM. Preventing adolescent drug abuse through a multimodal cognitive-behavioral approach: results of a 3-year study. J Consulting Clin Psychology 1990;58(4):437-46. [26]

31. Botvin GJ, Baker E, Renick NL, Filazzola AD, Botvin EM. A cognitive-behavioral approach to substance abuse prevention. Addictive Behaviors 1984;9:137-47. [26]

32. Botvin GJ, Epstein JA, Baker E, Diaz T, Ifill-Williams M. School-based drug abuse prevention with inner-city minority youth. Journal of Child and Adolescent Substance Abuse 1997;6(1):5-19. [26]

33. Botvin GJ, Griffin KW, Diaz T, Ifill-Williams M. Drug abuse prevention among minority adolescents: posttest and one-year follow-up of a school-based preventive intervention. Prev science 2001;2(1):1-13. [26]

34. Botvin GJ, Schinke SP, Epstein JA, Diaz T, Botvin EM. Effectiveness of culturally focused and generic skills training approaches to alcohol and drug abuse prevention among minority adolescents: two-year follow-up results. Psychology of Addictive Behaviours 1995;9:183-194. [18]

35. Botvin GJ, Schinke SP, Epstein JA, Diaz T. Effectiveness of culturally focused and generic skills training approaches to alcohol and drug abuse prevention among minority youths. Psychology Addictive Behaviors 1994;8(2):116-27. [26]

36. Brahen LS, Capone T, Wiechert V, Desiderio D. Naltrexone and cyclazocine. A controlled treatment study. Archives of General Psychiatry 1977;34(10):1181-4. [6]

37. Brahen LS, Capone T, Wojak JC. The double-blind crossover trial design: How good is it for psychoactive drugs? American Journal of Drug and Alcohol Abuse 1979;6(2):189-96. [6]

38. Bremberg S, Arborelius E. Effects on adolescent alcohol-consumption of a school-based student-centered health counseling programme. Scandinavian Journal of Social Medicine 1994;22:113-119. [18]

39. Brewer LC. Social skills training as a deterrent to entry level drug experimentation among 15-year-old adolescents. Unpublished Ph.D. Dissertation, University of Pennsylvania 1991. [18]

40. Britton BM. The privatization of methadone maintenance; changes in risk behavior associated with cost related detoxification. Addiction Research. 1994; 2(2):171-181 [12]

41. Brooner R, Kidorf M, King V, Beilenson P, Svikis D, Vlahov D. Drug abuse treatment success among needle exchange participants. Public Health Reports. 1998; 113:129-139 [12]

42. Buntwal N, Bearn J, Gossop M, Strang J. Naltrexone and lofexidine combination treatment compared with conventional lofexidine treatment for in-patient opiate detoxification. Drug & Alcohol Dependence 2000;59:183-188. [1]

43. Camacho LM, Bartholomew NG, Joe GW, Cloud MA, Simpson DD. Gender, cocaine and during-treatment HIV risk reduction among injection opioid users in methadone maintenance. Drug & Alcohol Dependence. 1996;41(1):1-7 [12]

44. Cami J, De Torres S, San L, Sole A, Guerra D, Ugena B. Efficacy of clonidine and of methadone in the rapid detoxification of patients dependent on heroin. Clinical Pharmacology and Therapeutics 1985;38(3):336-41. [3] [5]

45. Campbell JL, Thomas HM, Gabrielli W, Liskow BI, Powell BJ. Impact of Desipramine or Carbamazepine on patient retention in outpatient cocaine treatment: preliminary findings. Journal of Addictive Diseases 1994;13(4):191-199. [19] [20]

46. Caplan M, Weissberg RP, Grober JS, Sivo P, et al. Social competence promotion with inner city and suburban young adolescents: Effects on social adjustment and alcohol use. Journal of Consulting and Clinical Psychology 1992;60:56-63. [18]

47. Caplehorn JRM, Bell J. Methadone dosage and retention of patients in maintenance treatment. Med J Australia 1993;159:640. [11]

48. Caplehorn JRM, Dalton MSYN, Cluff MC, Petrenas AM. Retention in methadone maintenance and heroin addicts' risk of death. Addiction 1994;89:203-207. [11]

49. Caplehorn JRM, Irwig L, Saunders JB. Physicians' attitudes and retention of patients in their methadone maintenance programs. Subst Use Misuse 1996;31(6):663-677. [11]

50. Carnwath T, Hardman J. Randomised double-blind comparison of lofexidine and clonidine in the out-patient treatment of opiate withdrawal. Drug & Alcohol Dependence 1998;50(3):251-254. [3]

51. Carroll K, Ziedonis D, O'Malley S, McCance-Katz E, Gordon L, Rounsaville B. Pharmacologic intervention for alcohol- and cocaine-abusing individuals: a pilot study of disulfiram vs. naltrexone. The American Journal on Addictions 1993;2(1):77-9. [17]

52. Carroll Km, Rounsaville BJ, Gordon LT, Nich C, Jatlow P, Bisighini RM, Gawin FH. Psychotherapy and Pharmacotherapy for Ambulatory Cocaine Abusers. Archives of General Psychiatry 1994;51:177-187. [20]

53. Chatham LR, Hiller ML, Rowan-Szal GA, Joe GW, Simpson DD. Gender differences at admission and follow-up in a sample of methadone maintenance clients. Substance Use & Misuse. 1999; 34(8):1137-1165 [12]

54. Cheskin LJ, Fudala PJ, Johnson RE. A controlled comparison of buprenorphine and clonidine for acute detoxification from opioids. Drug & Alcohol Dependence 1994;36(2):115-121. [2]

55. Chick J, Anton R, Checinski K, Croop R, Drummond DC, Farmer R, Labriola D, Marshall J, Moncrieff J, Morgan MY, Peters T, Ritson B. A multicentre, randomized, double-blind, placebo-controlled trial of naltrexone in the treatment of alcohol dependence or abuse. Alcohol and Alcoholism 2000;35(6):587-93. [17]

56. Clayton RR, Cattarello A, Walden KP. Sensation seeking as a potential mediating variable for school based prevention intervention: A two year follow-up of DARE. Health Commun. 1991;3:229-239. [18] [26]

57. Cook R, Lawrence H, Morse C, Roehl J. An evaluaion of the alternatives approach to drug abuse prevention. International Journal of the Addictions 1984;19:767-787. [18] [26]

58. Corbin SKT, Jones RT, Schulman RS. Drug refusal behavior: the relative efficacy of skill-based treatment. J Pediatric Psychology 1993;18(6):769-84. [26]

59. Cornish JW, Manny I, Fudala PJ, Neal S, Poole SA, Volpicelli P, O'Brien CP. Carbamazepine treatment for cocaine dependence. Drug and Alcohol Dependence 1995;38:221-227. [19]

60. Cornish JW, Metzger D, Woody GE, Wilson D, McLellan AT, Vandergrift B, O´Brien CP. Naltrexone pharmacotherapy for opioid dependent federal probationers. Journal of Substance Abuse Treatment 1997;14(6):529-34. [6]

61. Covi L, Hess JM, Kreiter NA, Haertzen CA. Effects of Combined Fluoxetine and Counseling in the Outpatient Treatment of Cocaine Abusers. American Journal of Drug and Alcohol Abuse 1995;21(3):327-344. [20]

62. Curran S, Savage C. Patients response to naltrexone: issues of acceptance, treatment effects, and frequency of administration. NIDA Research Monograph Series 1976;9:67-69. [6]

63. Dawe S & Gray J A. Craving and drug reward: a comparison of methadone and clonidine in detoxifying opiate addicts. Drug and Alcohol Dependence 1995;39(3):207-12. [5]

64. Dawe S, Pwoell J, Richards D, Gossop M, Marks I, Strang J, Gray JA. Does post-withdrawal cue exposure improve outcome in opiate addiction? A controlled trial. Addiction 1993;88:1233-1245. [15]

65. Del Rio M, Mino A, Perneger TV. Predictors of patient retention in a newly established methadone maintenance treatment programme. Addiction 1997;92(10):1353-1360. [11]

66. Dent CW, Sussman S, Stacy AW. Project Towards No Drug Abuse: generalizability to a general high school sample. Prev Med 2001;32:514-20. [26]

67. Dielman TE, Shope JT, Butchart AT, Campanelli PC. Preventing of adolescent alcohol misuse: An elementary school programme. Journal of Pediatric Psychology 1986;11:259-282. [18]

68. D'Ippoliti D, Davoli M, Perucci CA, Pasqualini F, Bargagli AM. Retention in treatment of heroin users in Italy: the role of treatment type and of methadone maintenance dosage. Drug and Alcohol Dependence. 1998;52:167-171. [11]

69. Dolan KA, Shearer J, MacDonald M, Mattick RP, Hall W & Wodak AD. A randomised controlled trial of methadone maintenance treatment versus wait list control in an Australian prison system. Drug & Alcohol Dependence. 2003; 72:59-65 [12]

70. Dole V, Robinson J, Orraca J, Towns E, Searcy P, Caine E. Methadone treatment of randomly selected criminal addicts. New England Journal of Medicine 1969;280:1372-1375. [8]

71. Drummond D C, Turkington D, Rahman M Z, Mullin P J, Jackson P. Chlordiazepoxide vs. Methadone in opiate withdrawal: a preliminary double blind trial. Drug and Alcohol Dependence 1989;23(1):63-71. [5]

72. Durrant LH. A multicomponent approach to prevention of adolescent substance abuse. Unpublished Ph.D. Dissertation, University of Utah 1986. [18]

73. Duryea EJ, Okwumabua JO. Effects of a preventive alcohol education programme after three years.. Journal of Drug Education 1988;18:23-31. [18]

74. Ehrman RN, Robbins SJ, Cornish JW, Childress AR, O'Brien CP. Failure of rtanserin to block cocaine cue reactivity in humans. Drug and Alcohol Dependence 1996;42:167-174. [20]

75. Eiler K, Schaefer MR, Salstrom D, Lowery R. Double-blind comparison of bromocriptine and placebo in cocaine withdrawal. Am J Drug Alcohol Abuse 1995;21:65-79. [21]

76. Ellickson PL, Bell RM, Harrison ER. Changing adolescent propensities to use drugs: Results from Project ALERT. Health Education Quarterly 1993;20:227-242. [18]

77. Ellickson PL, Bell RM. Drug prevention in junior high: a multi-site longitudinal test. Science 1990;247:1299-305. [26]

78. Ellickson PL, McCaffrey DF, Ghosh-Dastidar B, Longshore DL. New inroads in preventing adolescent drug use: results from a large scale trial of project ALERT in middle schools. Adolescent Health 2003;93(11):1830-6. [26]

79. Finch E, Groves I, Feinmann C, Farmer R. A low threshold methadone stabilisation programme - Description and first stage evaluation. Addiction Research. 1995; 3(1):63-71 [12]

80. Fingerhood MI, Thompson MR, Jasinski DR. A comparison of clonidine and buprenorphine in the outpatient treatment of opiate withdrawal. Substance Abuse 2001;22(3):193-199. [2]

81. Fischer G, Gombas W, Eder H, Jagsch R, Peternell A, Stuehlinger G, Pezawas L, Aschauer H, Kasper S. Buprenorphine versus methadone maintenance for the treatment of opioid dependence. Addiction 1999;94:1337-1347. [9]

82. Freedman RR, Czertko G. A comparison of thrice weekly LAAM and daily methadone in employed heroin addicts. Drug & Alcohol Dependence 1981;8(3):215-22. [7]

83. Fulwiler R L, Hargreaves W A, Bortman R A. Detoxification from heroin using self vs physician regulation of methadone dose. International Journal of the Addiction 1979;14(2):289-98. [5]

84. Furr-Holden CDM, Ialongo NS, Anthony JC, Petras H, Kellam SG. Developmentally inspired drug prevention: middle school outcomes in a school-based randomized prevention trial. Drug Alcohol Dependence 2004;73:149-58. [26]

85. Galarza NJ, Ramirez DD, Guzman F, Caballero JA, Martinez AJ. The use of natlrexone to treat ambulatory patients with alcohol dependence. Boletin Asociacion Medica de Puerto Rico 1997;89(10-11-12):157-60. [17]

86. Galloway GP, Newmeyer J, Knapp T, Stalcup SA, Smith D. A controlled trial of imipramine for the treatment of methamphetamine dependence. Journal of Substance Abuse Treatment 1996;13(6):493-7. [22]

87. Gastpar M, Bonnet U, Boning J, MannK, Schmidt LG, Soyka M, Wetterling T, Kielstein V, Labriola D, Croop R. Lack of efficacy of naltrexone in the prevention of alcohol relapse: results from a German multicenter study. Journal of Clinical Psychopharmacology 2002;22:592-8. [17]

88. Gaughwin M, Solomon P, Ali R. Correlates of retention on the South Australian Methadone Program 1981-91. Austr NZ J Public Health 1998;22(7):771-776. [11]

89. Gawin FH, Kleber HD, Byck R, Rounsaville BJ, Kosten TR, Jatlow PI, Morgan C. Desipramine Facilitation of Inicial Cocaine Abstinence. Archives of General Psychiatry. Archives of General Psychiatry 1989;46:117-121. [20]

90. Gerra G, Marcato A, Caccavari R, Fontanesi B, Delsignore R, Fertonani G, et al. Clonidine and opiate receptor antagonists in the treatment of heroin addiction. Journal of Substance Abuse Treatment 1995;12(1):35-41. [1] [3]

91. Gerra G, Zaimovic A, Giusti F, Di Gennaro C, Zambelli U, Gardini S, Delsignore R. Lofexidine versus clonidine in rapid opiate detoxification. Journal of Substance Abuse Treatment 2001;21(1):11-17. [1]

92. Gerra G, Zaimovic A, Rustichelli P, Fontanesi B, Zambelli U, Timpano M, et al. Rapid opiate detoxification in outpatient treatment: Relationship with naltrexone compliance. Journal of Substance Abuse Treatment 2000;18(1):185-191. [1] [3] [5]

93. Giannini AJ, Loiselle RH, Giannini MC. Space-Based Abstinence: Alleviation of Withdrawal Symptoms in Combinative Cocaine-Phencyclidine Abuse. Clinical Toxicology. Clinical Toxicology 1987;25(6):493-500. [20]

94. Giannini J, Malone DA, Giannini MC, Price W, Loiselle RH. Treatment of depression in chronic cocaine and phencyclidine abuse with desipramine. Journal of Clinical Pharmacology 1986;26:211-214. [20]

95. Giannini JA, Folts JD, Feather NJ, Sullivan SB. Bromocriptine and Amantadine in Cocaine Detoxification. Psychiatry Research 1989;29:11-16. [21]

96. Gilchrist LD, Schinke SP, Trimble JE, Cvetkovich GET. Skills enhancement to prevent substance abuse among American Indian adolescents. International Journal of the Addictions 1987;22:869-879. [18]

97. Gliksman L, Douglas RR, Smythe C. The impact of a high school alcohol education programme utilizing a live theatrical performance: A comparative study. Journal of Drug Education 1983;13:229-248. [18]

98. Goldberg L, MacKinnon DP, Elliot DL, Moe EL, Clarke G, Cheong J. The Adolescents Training and Learning to Avoid Steroids Program. Arch Pediatr Adolesc Med 2000;154:332-338. [18]

99. Goldstein A, Judson B. Three critical issues in the management of methadone programs: Critical Issue 3: Can the community be protected against the hazards of take-home methadone. In: Bourne P, editor(s). Addiction. New York: Academic Press, 1974:140-148. [7]

100. Goldstein A, Judson BA. Efficacy and side effects of three widely different methadone doses. Proc Natl Conf Methadone Treat 1973;(1):21-44. [11]

101. Goldstein MF, Deren S, Kang SY, Des Jarlais DC, Magura S. Evaluation of an alternative program for MMTP drop-outs: impact on treatment re-entry. Drug and Alcohol Dependence 2002;66:181-7. [15]

102. Goodstadt MS, Sheppard MA. Three approaches to alcohol education. Journal of Studies on Alcohol 1983;44:362-380. [18]

103. Gossop M, Marsden J, Stewart D, Rolfe A. Patterns of improvement after methadone treatment: 1 year follow-up results from the National Treatment Outcome Research Study (NTORS). Drug & Alcohol Dependence. 2000; 60:275-286 [12]

104. Gossop M, Marsden J, Stewart D, Treacy S. Outcomes after methadone maintenance and methadone reduction treatments: two-year follow-up results from the National Treatment Outcome Research Study. Drug Alcohol Dependence 2001;62:255-264. [11]

105. Green L, Gossop M. Effects of information on the opiate withdrawal syndrome. British Journal of Addiction 1988;83(3):305-309. [5]

106. Grella CE, Anglin D, Rawson R, Crowley R, Hasson A. What happens when a demonstration project ends. Consequences for a clinic and its clients. Journal of Substance Abuse Treatment. 1996; 13(3):249-256 [12]

107. Grevert P, Masover B, Goldstein A. Failure of methadone and levomethadyl acetate (levo-alpha-acetylmethadol, LAAM) maintenance to affect memory. Archives of General Psychiatry 1977;34(7):849-53. [7]

108. Grevert P, Masover B, Goldstein A. Failure of methadone and levomethadyl acetate (levo-alpha-acetylmethadol, LAAM) maintenance to affect memory. Archives of General Psychiatry 1977;34(7):849-53. [7]

109. Grey C, Osborn E, Reznikoff M. Psychosocial factors in outcome in two opiate addiction treatments. Journal of Clinical Psychology 1986;42(1):185-9. [6]

110. Gruber K, Chutuape M A, Stitzer M L. Reinforcement-based intensive outpatient treatment for inner city opiate abusers: a short-term evaluation. Drug and Alcohol Dependence 2000;57:211-223. [15]

111. Guardia J, Caso C, Arias F, Gual A, Sanahuja J, Ramirez M, Mengual I, Gonzalvo B, Segura L, Trujols J, Casas M. A double-blind, placebo-controlled study of naltrexone in the treatment of alcohol-dependence disorder: results from a multicenter clinical trial. Alcoholism: Clinical and Experimental Research 2002;26:1381-7. [17]

112. Gunne L, Gronbladh L. The Swedish methadone maintenance program: A controlled study. Drug and Alcohol Dependence 1981;7:249-256. [8]

113. Gupta AK, Jha BK. Clonidine in heroin withdrawal syndrome: A controlled study in India. British Journal of Addiction 1988;83(9):1079-1084. [3]

114. Halikas JA, Crosby RD, Pearson VL, Graves NM. A randomized double-blind stuidy of carbamazepine in the treatment of cocaine abuse. Clin Pharmacol Ther 1997;62:89-105. [19]

115. Hall SM, Bass A, Hargreaves W A, Loeb P. Contingency management and information feedback in outpatient heroin detoxification. Behaviour Therapy 1979;10:443-451. [5] [13]

116. Hall SM, Tunis S, Triffleman E, Banys P, Clark HW, Tusel D, Stewart P, Presti D. Continuity of Care and Desipramine in Primary Cocaine Abusers. The Journal of Nervous and Mental Disease. The Journal of Nervous and Mental Disease 1994;182:570-575. [20]

117. Handelsman L, Limpitlaw L, Williams D, Schmeidler J, Paris P, Stimmel B. Amantadine does not reduce cocaine-dependent methadone maintenance patients. Drug and alcohol Dependence. Drug and alcohol Dependence 1995;39:173-180. [21]

118. Handelsman L, Rosenblum A, Palij M, Magura S, Foote J, Lovejoy M, Stimmel B. Bromocriptine for Cocaine Dependence - A Controlled Clinical Trial. The american Journal on Addictions 1997;6:54-64. [21]

119. Hansen WB, Anderson Johnson C, Flay BR, Graham JW, Sobel J. Affective and social influences approaches to the prevention of multiple substance abuse among seventh grade students: results from project SMART. Preventive Medicine 1988;17:135-54. [26]

120. Hansen WB, Graham JW. Preventing alcohol, marijuana and cigarette use among adolescents: peer pressure resistance training versus establishing conservative norms. Prev Med 1991;20:414-30. [26]

121. Hansen WB, Graham JW. Preventing alcohol, marijuana, and cigarette use among adolescents: Peer pressure resistance training versus establishing conservative norms. Prev. Med 1991;20:414-430. [18]

122. Hansen WB, Johnson CA, Flay BR, Graham JW, Sobel J. Affective and social influences approaches to the prevention of multiple substance abuse among seventh grade students: Results from project SMART. Preventive Medicine 1988;17:135-154. [18]

123. Harmon MA. Reducing the risk of drug involvement among early adolescents: An evaluation of Drug Abuse Resistance Education (DARE). Evaluation Review 1993;17:221-239. [18]

124. Hartnoll RL. Evaluation of heroin maintenance in controlled trial. Archives of General Psychiatry 1980;37:877-884. [10]

125. Hecht ML, Corman SR, Miller-Rassulo M.. An evaluation of the Drug Resistance Project: a comparision of film versus live performance media. Health Communication 1993;5(2):75-88. [26]

126. Heinala P, Alho H, Kiianmaa K, Lonnqvist J, Kuoppasalmi K, Sinclair JD. Targeted use of naltrexone withour prior detoxification in the treatment of alcohol dependence: a factorial double-blind placebo-controlled trial. Journal of Clinical Psychopharmacology 2001;21(3):287-92. [17]

127. Hersh D, Van Kirk JR, Kranzler HR. Naltrexone treatment of comorbid alcohol and cocaine use disorders. Psychopharmacology 1998;139:44-52. [17]

128. Higgins ST, Stitzer ML, Bigelow GE, Liebson IA.. Contingent Methadone dose increases as a method for reducing illicit opiate use in detoxification patients.. NIDA Research Monograph 1984;55:178-183. [13]

129. Higgins ST, Stitzer ML, Bigelow GE, Liebson IA.. Contingent methadone delivery: effects on illicit opiate use. Drug and Alcohol Dependence 1986;17:3111-3122. [13]

130. Holder HD (Ed). A community prevention Trial To Reduce Alcohol-Involved Trauma. Addiction 1997;92(Supplement 2):(whole issue). [18]

131. Hollister LE. Clinical evaluation of naltrexone treatment of opiate-dependent individuals. Report of the National Research Council Committee on Clinical Evaluation of Narcotic Antagonists. Archives of General Psychiatry 1978;35(3):335-40. [6]

132. Hopkins RH, Mauss AL, Kearney KA, Weisheit RA. Comprehensive Evaluation of a model alcohol education curriculum. Journal of Studies on Alcohol 1988;49:38-50. [18]

133. Howells C, Allen S, Gupta J, Stillwell G, Marsden J, Farrell M. Prison based detoxification for opioid dependence: A randomised double blind controlled trial of lofexidine and methadone. Drug & Alcohol Dependence 2002;67(2):169-176. [3] [5]

134. Huang X, Huang X, Peng H, Mai G. Placebo-controlled trial of naltrexone in outpatient treatment of alcohol dependence. Chinese Mental Health Journal 2002;16:302-3. [17]

135. Hurry J, McGurk H. An evaluation of a primary prevention programme for schools. Addiction Research 1997;5(1):23-38. [26]

136. Iguchi MY, Belding MA, Morral AR, Lamb RJ, Husband SD. Reinforcing operants other than abstinence in drug abuse treatment: an effective alternative for reducing drug use. Journal of Consulting and Clinical Psychology 1997;65(3):421-428. [14]

137. Iguchi MY. Drug abuse treatment as HIV prevention: changes in social drug use patterns might also reduce risk. Journal of Addictive Diseases. 1998; 17(4):9-18 [12]

138. Irwin S, Blachly PH, Marks J, Carlson E, Loewen J, Reade N. The behavioral, cognitive and physiologic effects of long-term methadone and methadyl treatment. 1973 [proceedings]. NIDA Research Monograph 1976;8:66-7. [7]

139. Janiri L, Mannelli P, Persico AM, Serretti A, Tempesta E. Opiate detoxification of methadone maintenance patients using lefetamine, clonidine and buprenorphine. Drug & Alcohol Dependence 1994;36(2):139-145. [2]

140. Jenkins SW, Warfield NA, Blaine JD, Cornish J, Ling W, Rosen MI, Urschel H, Wesson D, Ziedonis D. A Pilot Trial of Gepirone vs. Placebo in the Treatment of Cocaine Dependency. Psychopharmacology Bulletin 1992;28(1):21-26. [20]

141. Jiang Zuo-ning et al. Rapid detoxification with clonidine for heroin addiction. A comparative study on its efficacy vs methadone. Chinese Journal of Neurology and Psychiatry 1993;26(1):10-13. [3] [5]

142. Jittiwutikan J, Srisurapanont M, Jarusuraisin N. Amineptine in the treatment of amphetamine withdrawal: a placebo-controlled, randomised, double-blind study. Journal of the Medical Association of Thailand 1997;80(9):587-91. [24]

143. Johnson BA, Ait Daoud N, Prihoda TJ. Combining ondansetron and naltrexone effectively treats biologically predisposed alcoholics: from hypotheses to preliminary clinical evidence. Alcoholism, Clinical and Experimental Research 2000;24(5):737-42. [17]

144. Johnson R, Jaffe J, Fudala P. A controlled trial of buprenorphine treatment for opioid dependence. JAMA 1992;267:2750-2755. [9]

145. Johnson RE, Chatupe MA, Strain E, Walsh S, Stitzer ML, Bigelow GE. A comparison of levomethadyl acetate, buprenorphine, and methadone for opioid dependence. New England Journal of Medicine 2000;343:1290-7. [7] [11]

146. Johnson RE, Chutuape MA, Strain, EC, Walsh SL, Stitzer ML, Begelow GE. First Randomized Controlled Trial (RCT) of Methadone (M), Levomethadyl Acetate (LAAM) and Buprenorphine (BUP) in Opioid Dependence Treatment. Clinical Pharmacology & Therapuetics 1999;65(2). [9]

147. Johnson RE, Eissenberg T, Stitzer M, Strain E, Liebson I, Bigelow G.. A placebo controlled trial of buprenorphine as a treatment for opioid dependence. Drug and Alcohol Dependence 1995;40:17-25. [9]

148. Johnson RE, Jaffe JH, Fudala PJ. A controlled trial of buprenorphine treatment for opioid dependence. JAMA 1992;267(20):2750-55. [11]

149. Jones RT, Corbin SKT, Sheehy L, Bruce S. Substance refusal: more than "Just Say No". J Child Adolescent Substance Abuse 1995;4(2):1-26. [26]

150. Jones RT, McDonald DW, Fiore MF, Arrington T, Randall J. A primary preventive approach to children's drug refusal behavior: the impact of Rehearsal-Plus. J Pediatric Psychology 1990;15(2):211-23. [26]

151. Kahn A, Mumford JP, Rogers GA, Beckford H. Double-blind study of lofexidine and clonidine in the detoxification of opiate addicts in hospital. Drug & Alcohol Dependence 10-1-1997;44(1):57-61. [3]

152. Kampman K, Volpicelli, Alterman A, Cornish J, Weinrieb R, Epperson L, Sparkman T, O'Brien CP. Amantadiene in the early treatment of cocaine dependence: a double-blind, placebo-controlled trial. Drug and Alcohol Dependence 1996;41:25-33. [21]

153. Karp-Gelernter E, Savage C, McCabe OL. Evaluation of clinic attendance schedules for LAAM and methadone: A controlled study. International Journal of the Addictions 1982;17(5):805-813. [7]

154. Katz EC, Chutuape MA, Jones HE, Stitzer ML,. Voucher Reinforcement for Heroin and Cocaine Abstinence inan Outpatient Drug-Free Program. Experimental and Clinical Psychopharmacology 2002;10(2):136-143. [15]

155. Khatami M, Woody G, O' Brien C, Mintz J. Biofeedback treatment of narcotic addiction: a double blind study. Drug and Alcohol Dependence 1982;9:111-117. [14]

156. Kiefer F, Jahn H, Tarnaske T, Helwig H, Briken P, Holzbach R, Kampf P, Stracke R, Baehr M, Naber D, Wiedemann K. Comparin and combing naltrexone and acamprosate in relapse prevention of alcoholism. Archives of General Psychiatry 2003;60:92-9. [17]

157. Kienbaum P, Scherbaum N, Thurauf N, Michel MC, Gastpar M, Peters J. Acute detoxification of opioid-addicted patients with naloxone during propofol or methohexital anesthesia: a comparison of withdrawal symptoms, neuroendocrine, metabolic, and cardiovascular patterns. Critical Care Medicine 2000;28(4):969-976. [4]

158. Kim S, McLeod JH, Shantzis C. An outcome evaluation of refusal skills program as a drug abuse prevention strategy. J Drug Education 1989;19(4):363-71. [26]

159. King VL, Kidorf MS, Stoller KB, Brooner RK. Influence of psychiatric comorbidity on HIV risk behaviors: changes during drug abuse treatment. Journal of Addictive Diseases. 2000, 19(4):65-83 [12]

160. Kleber H D, Riordan C E, Rounsaville B, Kosten T, Charney D, Gaspari J, Hogan I, O'Connor C. Clonidine in outpatient detoxification from methadone maintenance. Archives of General Psychiatry 1985;42(4):391-4. [3] [5]

161. Klepp KI, Kelder SH, Perry CL. Alcohol And Marijuana Use Among Adolescents: Long-Term Outcomes Of The Class of 1989 Study. Annals of Behavioural Medicine 1995;17(1):19-24. [18]

162. Knox PC, Donovan DM. Using naltrexone in inpatient alcoholism treatment. Journal of Psychoactive Drugs 1999;31(4):373-88. [17]

163. Kolar AF, Brown BS, Weddington WW, Haertzen CC, Michaelson BS, Jaffe JH. Treatment of Cocaine Dependence in Methadone Maintenance Clients: A Pilot Study Comparing the Efficacy of Desipramine and Amantadine. The International Journal of the Addictions. The International Journal of the Addictions 1992;27(7):849-868. [20] [21]

164. Kosten T, Schottenfeld R, Ziedonis D, Falcioni J. Buprenorphine versus methadone maintenance for opioid dependence. J Nerv Ment Dis 1993;181:358-364. [9] [11]

165. Kosten TR, Morgan CM, FalcioneJ, Schottenfeld RS. Pharmacotherapy for Cocaine-Abusing Methadone-Maintened Patients Using Amantadine or Desipramine. Archives of General Psychiatry 1992;49:894-898. [20] [21]

166. Kosten TR, Schottenfeld R, Ziedonis D, Falcioni J. Buprenorphine versus methadone maintenance for opioid dependence. J Nervous Mental Disease 1993;181(6):358-364. [9] [11]

167. Kranzler HR, Bauer LO, Hersh D, Klinghoffer V. Carbamazepine treatment of cocaine dependence: a placebo-controlled trial. Drug and Alcohol Dependence 1995;38:203-211. [19]

168. Kranzler HR, Bauer LO. Bromocriptine and cocaine reactivity in cocaine-dependent patients. British Journal of Addiction 1992;87:1537-1548. [21]

169. Kranzler HR, Modesto Lowe V, Van Kirk J. Naltrexone vs Nefazodone for treatment of alcohol dependence: a placebo-controlled trial. Neuropsychopharmacology 2000;22(5):493-503. [17]

170. Krystal JH, Cramer JA, Krol WF, Kirk GF, Rosenheck RA for the Veterans Affairs Naltrexone Cooperative Study 425 Gruop. Naltrexone in the treatment of alcohol dependence. New England Journal of Medicine 2001;345(24):1734-1739. [17]

171. Kwiatkowski CF, Booth RE. Methadone maintenance as HIV risk reduction with street-recruited injecting drug users. Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology. 2001; 26(5):483-489 [12]

172. Ladewig D. Naltrexone - an effective aid in the psychosocial rehabilitation process of former opiate dependent patients. Therapeutische Umschau 1990;47(3):247-50. [6]

173. Lal B, Singh G. Experiences of a methadone detoxification programme for opium addicts. Drug Alcohol Dependence 1976;1(6):391-8. [5]

174. Landabaso MA, Iraurgi I, Sanz J, Calle R, Ruiz de Apodaka J, Jimenez-Lerma JM, Gutierrez-Fraile M. Naltrexone in the treatment of alcoholism: two-year follow up results. European Journal of Psychiatry 1999;13(2):97-105. [17]

175. Latt NC, Jurd S, Houseman J, Wutzke SE. Naltrexone in alcohol dependence: a randomised controlled trial of effectiveness in a standard clinical setting. MJA 2002;176:530-4. [17]

176. Lee A, Tan S, Lim D, Winslow RM, Wong KE, Allen J, Hall W, Parker G. Naltrexone in the treatment of male alcoholics-an effectiveness study in Singapore. Drug and Alcohol Review 2001;20:193-9. [17]

177. Lehmann WX. The use of 1-alpha-acetyl-methadol (LAAM) as compared to methadone in the maintenance and detoxification of young heroin addicts. 1973 [proceedings]. NIDA Research Monograph 1976;8:82-3. [7]

178. Lerner A, Sigal M, Bacalu A, Shiff R, Burganski I, Gelkopf M. A naltrexone double-blind placebo controlled study in Israel. Israel Journal of Psychiatry and Related Sciences 1992;29(1):36-43. [6]

179. Li M, Chen K, Mo Z. Use of qigong therapy in the detoxification of heroin addicts. Alternative Therapies in Health & Medicine 2002;8(1):50-59. [3]

180. Lin S-K, Strang J, Su L-W, Tsai C-J, Hu W-H. Double-blind randomised controlled trial of lofexidine versus clonidine in the treatment of heroin withdrawal. Drug & Alcohol Dependence 1997;48(2):127-133. [3]

181. Ling W, Charuvastra C, Collins J, Batki S, Brown L, Kintaudi P, Wesson D, McNicholas L, Tusel D, Malkerneker U, Renner J, Santos E, Casadonte P, Fye C, Stine S, Wang R, Segal D.. Buprenorphine maintenance treatment of opiate dependence: a multicenter, randomized clinical trial. Addiction 1998;93:475-486. [9]

182. Ling W, Charuvastra C, Kaim SC, Klett CJ. Methadyl acetate and methadone as maintenance treatments for heroin addicts. A veterans administration cooperative study. Archives of General Psychiatry 1976;33(6):709-20. [7] [11]

183. Ling W, Klett CJ, Gillis RD. A cooperative clinical study of methadyl acetate. I. Three-times-a-week regimen. Archives of General Psychiatry 1978;35(3):345-53. [7]

184. Ling W, Wesson D, Charuvastra C, Klett J. A controlled trial comparing buprenorphine and methadone maintenance in opioid dependence. Archives of General Psychiatry 1996;53:401-407. [9] [11]

185. Lintzeris N, Bell J, Bammer G, Jolley DJ, Rushworth L. A randomized controlled trial of buprenorphine in the management of short-term ambulatory heroin withdrawal. Addiction 2002;97(11):1395-1404. [2]

186. Liu ZM, Cai ZJ, Wang XP, Ge Y, Li CM. Rapid detoxification of heroin dependence by buprenorphine. Acta Pharmacologica Sinica 1997;18(2):112-114. [2]

187. Loveland-Cherry CJ, Thomson-Ross L, Kaufman SR. Effects of a Home-Based Family Intervention on Adolescent Alcohol Use and Misuse. Journal of Studies on Alcohol / Supplement 1999;13:94-102. [18]

188. Maddux JF, Desmond DP. Outcomes of methadone maintenance 1 year after admission. Journal of Drug Issues. 1997; 27(2):225-238 [12]

189. Maddux JF, Prihoda TJ, Vogtsberger KN. The relationship of methadone dose and other variables to outcomes of methadone maintenance. Am J Addictions 1997;6(3):246-255. [11]

190. Magura S, Kang S, Shapiro JL. Outcomes of intensive AIDS education for male adolescent drug users in jail. Journal of Adolescent Health 1994;15:457-463. [18]

191. Magura S, Siddiqi Q, Freeman RC, Lipton DS. Changes in cocaine use after entry to methadone treatment. Journal of Addictive Diseases. 1991; 10(4):31-45 [12]

192. Malcom R, Kajdasz DK, Herron J, Anton RF, Brady KT. Double-blind, placebo-controlled outpatient trial of pergolide for cocaine dependence. Drug and Alcohol Dependence 2000; 60:161-168. [21]

193. Malcom R, Phillips JD, Brady KT, Roberts JR. A comparison of pergolide and bromocriptine in the initial rehabilitation of cocaine dependence. The American Journal on Addictions 1994; 3(2):144-150. [21]

194. Malhotra A, Basu D, Chintalapudi M, Mattoo SK, Varma VK. Clonidine versus withdrawal using an opioid in in-patient opioid detoxification. European Addiction Research 1997;3:146-149. [3]

195. Malvin JH, Moskovitz JM, Schaps E, Schaeffer GA. Evaluation of two school-based alternatives programs. J Alcohol Drug Education 1985;30(3):98-108. [26]

196. Marcovici M, CP OB, McLellan AT, Kacian J. A clinical, controlled study of l-alpha-acetylmethadol in the treatment of narcotic addiction. American Journal of Psychiatry 1981;138(2):234-6. [7]

197. Margolin A, Avants SK, Warburton LA, Hawkins KA, Shi J. A randomized clinical trial of a manual-guided risk reduction intervention for HIV-positive injection drug users. Health Psychology. 2003; 22(2):223-228 [12]

198. Margolin A, Kosten TR, Avants SK, Wilkins J, Ling W, Beckson M, Arndt IO, Cornish J, Ascher JA, Li SH, Bridge P. A multicenter trial of bupropion for cocaine dependence in methadone-maintained patients. Drug and Alcohol Dependence 1995;40:125-131. [20]

199. Marlatt GA, Baer JS, Kivlahan DR, Dimeff LA, Larimer ME, Quigley LA, Somers JM, Williams E. Screening and Brief Intervention for High-Risk College Student Drinkers: Results From a 2-Year Follow-Up Assessment. Journal of Consulting and Clinical Psychology 1998;66((4)):604-615. [18]

200. Mason BJ, Ritvo EC, Morgan RO, Salvato FR, Goldberg G, Welch B, Mantero-Atienza E. A double-blind, placebo-controlled pilot study to evaluate the efficacy and safety of oral nalmefene HCl for alcohol dependence. Alcoholism: Clinical and Experimental Research 1994;18(5):1162-7. [17]

201. Mason BJ, Salvato FR, Williams LD, Ritvo EC, Cutler RB. A double-blind, placebo-controlled study of oral nalmefene for alcohol dependence. Archives of General Psychiatry 1999;56:719-24. [17]

202. Mattick RP, Ali R, White J, O'Brien S, Wolk S, Danz, C.. Buprenorphine versus methadone maintenance therapy: a randomised double-blind trial with 405 opioid-dependent patients. Addiction 2003;98:441-452. [9]

203. Mc Lellan AT, Arndt IO, Metzger DS, Woody GE, O' Brien CP. The effects of psychosocial services in substance abuse treatment. JAMA 1993;269(15):1953-1959. [14]

204. McBride N, Midford R, Farringdon F, Phillips M.. Early results from a school alcohol harm minimizaiton study: the School Health and Alcohol Harm Reduction Project. Addiction 2000;95((7)):1021-1042. [18]

205. McCaul ME, Stitzer ML, Bigelow GE, Liebson IA.. Contingency management interventions: effects on treatment outcome during methadone detoxification. Journal of Applied Behaviour Analysis 1984;17(1):35-43. [13]

206. McElroy SL, Weiss RD, Mendelson JH, Teoh SK, McAfee B, Mello NK. Desipramine treatment for relapse prevention in cocaine dependence. National Institute on Drug Abuse Research Monograph Series 1989;95:57-63. [20]

207. Meandzija B, O'Connor PG, Fitzgerald B, Rounsaville BJ, Kosten TR. HIV infection and cocaine use in methadone maintained and untreated intravenous drug users. Drug & Alcohol Dependence. 1994; 36(2):109-113 [12]

208. Mello NK, Mendelson JH, Kuehnle JC, Sellers MS. Operant analysis of human heroin self-administration and the effects of naltrexone. The Journal of Pharmacology and Experimental Therapeutics 1981;216(1):45-54. [6]

209. Metzger DS, Woody GE, McLellan AT, O'Brien CP, Druley P, Navaline H et al. Human immunodeficiency virus seroconversion among intravenous drug users in- and out-of-treatment: an 18-month prospective follow-up. Journal of Acquired Immune Deficiency Syndromes. 1993; 6(9):1049-1056 [12]

210. Milby JB, Garrett C, English C, Fritschi O, Clarke C. Take-home methadone: contingency effects on drug-seeking and productivity of narcotic addicts. Addictive Behaviours 1978;3:215-230. [14]

211. Monti PM, Spirito A, Myers M, Colby SZ, Barnett NP, Rohsenow DJ, Woolard R, Lewander W. Brief Intervention for harm Reduction With Alcohol-Positive Adolescents in a Hospital Emergency Department. Journal of Consulting and Clinical Psychology 1999;67((6)):989-994. [18]

212. Montoya ID, Levin FR, Fudala PJ, Gorelick DA. Double-blind comparison of carbamazepine and placebo for treatment of cocaine dependence. Drug and Alcohol Dependence 1995;38:213-219. [19]

213. Morris PLP, Hopwood M, Whelan G, Gardiner J, Drummond E. Naltrexone for alcohol dependence: a randomized controlled trial. Addiction 2001;96:1565-1573. [17]

214. Moscovitz H, Brookof D, Nelson L. A Randomized Trial of Bromocriptine for Cocaine Users Presenting to the Emergency Department. Journal of General Internal Medicine 1993;8:1-4. [21]

215. Moskowitz JM, Malvin JH, Schaeffer GA, Schaps E. An experimental evaluation of a drug education course. Journal of Drug Education 1984;14:9-22. [18] [26]

216. Moss AR, Vranizan K, Gorter R, Bacchetti P, Watters J, Osmond D. HIV seroconversion in intravenous drug users in San Francisco, 1985-1990. AIDS. 1994; 8(2):223-231 [12]

217. Newman IM, Anderson CS, Farrell KA. Role rehearsal and efficacy: Two 15 month evaluations of a ninth grade alsohol education programme. Journal of Drug Education 1992;22:55-67. [18]

218. Newman R, Whitehill W. Double-blind comparison of methadone and placebo maintenance treatments of narcotic addicts in Hong Kong. Lancet 1979;September 8:485-488. [8]

219. Nigam AK, Ray R, Tripathi BM. Buprenorphine in opiate withdrawal: a comparison with clonidine. Journal of Substance Abuse Treatment 1993;10(4):391-394. [2]

220. Nunes EV, McGrath PJ, Quitkin FM, Ocepek-Welikson K, Stewart JW, Koening T, Wager S, Klein DF. Imipramine treatment of cocaine abuse: possible boundaries of efficacy. Drug and Alcohol Dependence 1995;39:185-195. [20]

221. O'Brien CP, Childress AR, Arndt IO, McLellan AT, Woody GE, Maany I. Pharmacological and behavioral treatments of cocaine dependence: controlled studies. Journal of Clinical Psychiatry 1988;49 suppl.:17-22. [20]

222. O'Connor PG, Carroll KM, Shi JM, Schottenfeld RS, Kosten TR, Rounsaville BJ. Three methods of opioid detoxification in a primary care setting. A randomized trial. Annals of Internal Medicine 1997;127(7):526-530. [1] [2]

223. O'Connor PG, Waugh ME, Carroll KM, Rounsaville BJ, Diakogiannis IA, Schottenfeld RS. Primary care-based ambulatory opioid detoxification: the results of a clinical trial. Journal of General Internal Medicine 1995;10(5):255-260. [1]

224. Oliveto A, Kosten TR, Shottenfeld R, Falcioni J, Ziedonis D. Desipramine, amantadine, or fluoxetine in buprenorphine-maintained cocaine users. Journal of Substance Abuse Treatment 1995 Nov-Dec; 12(6):423-428. [21]

225. O'Malley SS, Jaffe AJ, Chang G, Schottenfeld RS, Meyer RE, Rounsaville B. Naltrexone and coping skills therapy for alcohol dependence: a controlled study. Archives of General Psychiatry 1992;49:881-7. [17]

226. O'Malley SS, Rounsaville BJ, Farren C, Namkoong K, Wu R, Robinson J, O'Connor PG. Initial and maintenance naltrexone treatment for alcohol dependence using primary care vs specialty care. Archives of Internal Medicine 2003;163:1695-1704. [17]

227. Oslin D, Liberto JG, O'Brien J, Krois S, Norbeck J. Naltrexone as an adjunctive treatment for older patients with alcohol dependence. The American Journal of Geriatric Psychiatry 1997a;5(4):324-32. [17]

228. Palinkas LA, Atkins CJ, Miller C, Ferreira D. Social Skills Training for Drug Prevention in High-Risk Female Adolescents. Preventive Medicine 1996;25:692-701. [18]

229. Pani P, Maremmani I, Pirastu R, Tagliamonte A, Gessa G.. Buprenorphine: a controlled trial in the treatment of opioid dependence.. Drug and Alcohol Dependence 2000;60:39-50. [9]

230. Pentz MA, Dwyer JH, MacKinnon DP, Flay BR, Hansen WB, Wang EYI et al. A mulicommunity trial for primary prevention of adolescent drug abuse: effects on drug use prevalence. JAMA, The Journal of the American Medical Association 1989;261:3259-3266. [18]

231. Perez de los Cobos J, Duro P, Trujols J, Tejero A, Batle F, Ribalta E, Casas M. Methadone tapering plus amantadine to detoxify heroin dependent inpatients with or without an active cocaine use disorder: two randomised controlled trials. Drug and Alcohol Dependence 2001; 63:187-195. [21]

232. Perneger TV, Giner F, del Rio M, Mino A. Randomised trial of heroin maintenance programme for addicts who fail in conventional drug treatments. British Medical Journal 1998;317(7150):13-18. [10]

233. Perry CL, Grant M. Comparing peer-led to teacher-led youth alcohol education in four countries. (Australia, Chile, Norway and Swaziland.). Alcohol Health & Research World 1988;12:322-326. [18]

234. Perry CL, Williams CL, Veblen-Mortenson S, Toomey TL, Komro KA, Anstine PS, McGovern PG, Finnegan JR, Forster JL, Wagenaar AC, Wolfson M. Project Northland: Outcomes of a Communitywide

Alcohol Use Prevention program during Early Adolescence. American Journal of Public Health 1996;86(7):956-965. [18]

235. Petitjean S, Stohler R, Deglon J, Livoti S, Waldvogel D, Uehlinger C, Ladewig D. Double blind randomized trial of buprenorphine and methadone in opiate dependence.. Drug and Alcohol Dependence 2001;62:97-104. [9]

236. Petitjean S, von Bardeleben U, Weber M, Ladewig D. Buprenorphine versus methadone in opiate detoxification: preliminary results. In: Drug & Alcohol Dependence. Vol. 66. 2002:S138. [2]

237. Pozzi G, Conte G, De Risio S. Combined use of trazodone-naltrexone versus clonidine-naltrexone in rapid withdrawal from methadone treatment. A comparative inpatient study. Drug & Alcohol Dependence 2000;59(3):287-294. [1]

238. Preston KL, Umbricht A, Epstein DH. Methadone dose increase and abstinence reinforcement for treatment of continued heroin use during methadone maintenance. Arch Gen Psychiatry 2000;57:395-404. [11] [14]

239. Rawson R A, Mann A J, Tennant F S Jr, Clabough D. Efficacy of psychotherapeutic counselling during 21-day ambulatory heroin detoxification. NIDA Research Monograph 1983;43:43310-4. [5] [13]

240. Rawson RA, Glazer M, Callahan EJ, Liberman RP. Naltrexone and behaviour therapy for heroin addiction. NIDA Research Monograph Series 1979;25:26-43. [6]

241. Resnick RB, Washton AM, Garwood J, Perzel J. LAAM instead of take-home methadone. NIDA Research Monograph 1982;41:473-5. [7]

242. Rhoades HM, Creson D, Ronith E, Schmitz J, Grabowski J. Retention, HIV risk, and illicit drug use during treatment: methadone dose and visit frequency. Am J Public Health 1998;88(1):34-39. [11]

243. Ringwalt C, Ennett ST, Holt KD. An outcome evaluation of project DARE.. Health Education Research 1991;6:327-337. [18] [26]

244. Ritter A, Lintzeris N, Kutin J, Bammer G, Clark N, Panjari M, Harris A, Godspodarevskaja E. LAAM Implementation Trial. Melbourne, Australia: Turning Point Alcohol & Drug Centre, 2001. [7]

245. Robles E, Stitzer M, Strain EC, Bigelow GE, Silverman K. 2002;65:179-189.. Voucher-based reinforcement of opiate abstinence during methadone detoxification. Drug and Alcohol Dependence 2002;65:179-189. [13]

246. Rosenbaum DP, Flewelling R, Bailey S, Ringwalt C, Wilkinson D. "Cops in the Classroom": A longitudinal evaluation of Drug Abuse Resistance Education. Journal of research in Crime and Delinquency 1994;31:1-31. [18]

247. Rosenbaum DP, Hanson GS. Assessing the effects of school-based drug education: a six-year multilevel analysis of project DARE. J Research Crime Delinquency 1998;35(4):381-412. [26]

248. Ross C, Richard L, Potvin L. One year outcome evaluation of an alcohol and drug abuse prevention program in a Quebec high school. Revue Canadienne Santè Publique 1998;89(3):166-70. [26]

249. Rounsaville BJ, Glazer W, Wilber CH, Weissman MM, Kleber HD. Short-term interpersonal psychotherapy in methadone-maintained opiate addicts. Archives of General Psychiatry 1983;40(6):629-636. [14]

250. Rubio G, Jimenez-Arriero MA, Ponce G, Palomo T. Naltrexone versus acamprosate: one year follow-up of alcohol dependence treatment. Alcohol & Alcoholism 2001;36(5):419-425. [17]

251. Rubio G, Manzanares J, Lopez-Munoz F, Alamo C, Ponce G, Jimenez-Arriero MA, Palomo T. Naltrexone improves outcome of a controlled drinking program. Journal of Substance Abuse Treatment 2002;23:361-6. [17]

252. San L, Camì J, Fernandez T, Olle J M, Peri J M, Torrens M. Assessment and management of opioid withdrawal symptoms in buprenorphine-dependent subjects. British Journal of Addiction 1992;87(1):55-62. [5]

253. San L, Camì J, Peri J, Mata R, Porta M. Efficacy of clonidine, guanfacine and methadone in the rapid detoxification of heroin addicts: a controlled clinical trial. British Journal of Addiction 1990;85(1):141-7. [3] [5]

254. San L, Fernández T, Camí J, Gossop M. Efficacy of methadone versus methadone and guanfacine in the detoxification of heroin-addicted patients. Journal of Substance AbuseTreatment 1994;11(5):463-469. [3] [5]

255. San L, Pomarol G, Peri JM, Olle JM, Cami J. Follow-up after a six-month maintenance period on naltrexone versus placebo in heroin addicts. British Journal of Addiction 1991;86(8):983-90. [6]

256. Savage C, Karp EG, Curran SF, Hanlon TE, McCabe OL. Methadone/LAAM maintenance: a comparison study. Comprehensive Psychiatry 1976;17(3):415-24. [7]

257. Scaggs LS. A substance abuse awareness prevention program: knowledge, attitudes and behaviours. Unpublished Ph.D. Dissertation, Ohio State University 1985. [18]

258. Schinke SP, Tepavac L, Cole KC. Preventing Substance Use Among Native American Youth: Three-Year Results. Addictive Behaviours 2000;25((3)):387-397. [18]

259. Schneider U, Paetzold W, Eronat V, Huber TJ, Seifert J, Wiese B, Emrich HM. Buprenorphine and carbamazepine as a treatment for detoxification of opiate addicts with multiple drug misuse: a pilot study. Addiction Biology 2000;5:65-69. [2]

260. Schottenfeld R, Pakes J, Oliveto A, Ziedonis D, Kosten T. Buprenorphine vs methadone maintenance treatment for concurrent opioid dependence and cocaine abuse. Arch Gen Psychiatry 1997;54(8):713-20. [9] [11]

261. Sees KL, Delucchi KL, Masson C, Rosen A, Clark HW, Robillard H et al. Methadone maintenance vs 180-day psychosocially enriched detoxification for treatment of opioid dependence: a randomized controlled trial. JAMA. 2000; 283(10):1303-1310 [12]

262. Seifert J, Metzner C, Paetzold W, Borsutzky M, Passie T, Rollnik J et al. Detoxification of opiate addicts with multiple drug abuse: a comparison of buprenorphine vs. methadone. Pharmacopsychiatry 2002;35(5):159-164. [2]

263. Senay E, Jaffe J, diMenza S, Renault P. A 48-week study of methadone, methadyl acetate, and minimal services. In: Opiate Addiction: Origins and Treatment. New York: W.H. Winston & Sons, 1974. [7]

264. Senay E, Tennant FS, Washton AM. [Boehringer Ingelheim GmbH report number U85-0844]. Boehringer Ingelheim Pty Ltd 1983. [3]

265. Senay EC, Dorus W, Renault PF. Methadyl acetate and methadone. An open comparison. JAMA 1977;237(2):138-42. [7]

266. Seoane A, Carrasco G, Cabré L, Puiggrós A, Hernández E, Álvarez M et al. Efficacy and safety of two new methods of rapid intravenous detoxification in heroin addicts previously treated without success. British Journal of Psychiatry 1997;171:340-345. [4]

267. Serpelloni G, Carrieri MP, Rezza G, Morganti S, Gomma M, Binkin N. Methadone treatment as a determinant of HIV risk reduction among injecting drug users: a nested case-control study. AIDS Care. 1994; 6(2):215-220 [12]

268. Sexter J, Sullivan AP, Wepner SF, Denmark R. Substance abuse: assessment of the outcomes of activities and activity clusters in school-based prevention. Int J Addictions 1984;19(1):79-92. [26]

269. Sheehan M, Schonfeld C, Ballard R, Schofield F, Najman J, Siskind V. A Three Year Outcome Evaluation of a Theory Based Drink Driving Education Program. Journal of Drug Education 1996;26(3):295-312. [18]

270. Shope JT, Copeland LA, Maharg R, Dielman TE. Effectiveness of a High School Alcohol Misuse Prevention Program. Alcoholism: Clinical and Experimental Research 1996;20((5)):791-798. [18]

271. Shope JT, Copeland LA, Marcoux BC, Kamp ME. Effectiveness of a School-Based Substance Abuse Prevention Program. Journal of Drug Education 1996;26((4)):323-337. [18]

272. Shoptaw S, Kintaudi PC, Charuvastra C, Ling W. A screening trial of amantadine as a medication for cocaine dependence. Alcohol and Drug Dependence 2002; 66:217-224. [21]

273. Shufman EN, Porat S, Witzum E, Gandacu C, Bar-Hamburger R, Ginath Y. The efficacy of naltrexone in preventing reabuse of heroin after detoxification. Biological Psychiatry 1994;35(12):935-45. [6]

274. Sigelman CK, Bridges LJ, Leach DB, Mack KL, Rinehart CS, Sorongon AG, Brewster AB, Wirtz PW. The efficacy of an education program to teach children a scientific theory of how drugs affect behavior. Applied Developmental Psychology 2003;24:573-93. [26]

275. Simpson DD, Joe GW, Rowan-Szal G, Greener J. Client engagement and change during drug abuse treatment. Journal of Substance Abuse. 1995; 7(1):117-134 [12]

276. Snow DL, Tebes JK, Arthur MW, Tapasak RC. Two-year follow-up of a social-cognitive intervention to prevent substance use. J Drug Education 1992;22(2):101-14. [26]

277. Sorensen J L, Hargreaves W A , Weinberg J A. Withdrawal from heroin in three or six weeks. Comparison of methadyl acetate and methadone. Archives of General Psychiatry 1982;39(2):167-71. [5]

278. Sos I, Kiss N, Csorba J, Gerevich J. A tizanidin hatekonysaga heroinfuggo betegek akut megvonasi tuneteinek kezeleseben [Tizanidine in the treatment of acute withdrawal symptoms in heroin dependent patients]. Orvosi Hetilap 2000;141(15):783-786. [3]

279. Spoth RL, Lopez Reyes M, Redmond C, Shin C. Assessing a public Health Approach to Delay Onset and Progression of Adolescent Substance Use: Latent Transition and Log-Linear Analyses of Longitudinal Family Preventive Intervention Outcomes. Journal of Consulting and Clinical Psychology 1999;67((5)):619-630. [18]

280. Spoth RL, Redmond C, Trudeau L, Shin C. Longitudinal Substance Initiation Outcomes for a Universal Preventive Intervention Combining Family and School Programs. Psychology of Addictive Behaviours (in press). [18]

281. Srisurapanont M, Jarusuraisin N, Jittiwutikan J. Amphetamine withdrawal: II. A placebo-controlled, randomised, double-blind study of amineptine treatment. Australian and New Zealand Journal of Psychiatry 1999;33:94-98. [24]

282. St Pierre TL, Kaltreider DL, Mark MM, Aikin KJ. Drug prevention in a community setting: A longitudinal study of the relative effectiveness of a three year primary prevention programme in Boys & Girls Clubs across the nation. American Journal of Community Psychology 1992;20:673-706. [18]

283. Stark K, Mueller R, Bienzle U, Guggenmoos-Holzmann I. Methadone maintenance treatment and HIV risk-taking behaviour among injecting drug users in Berlin. Journal of Epidemiology & Community Health. 1996; 50(5):534-537 [12]

284. Stitzer ML, Iguchi MY, Felch LJ. Contingent take-home incentive: effects on drug use of methadone maintenance patients. Journal of Consulting and Clinical Psychology 1992;60(6):927-934. [14]

285. Strain E, Stitzer M, Liebson I, Bigelow G. Buprenorphine versus methadone in the treatment of opioid dependent cocaine users. Psychopharmocology 1994;116(4):401-6. [9]

286. Strain E, Stitzer M, Liebson I, Bigelow G. Comparison of buprenorphine and methadone in the treatment of opioid dependence. Am J Psychiatry 1994;151(7):1025-1030. [9]

287. Strain EC, Bigelow GE, Liebson IA, Stitzer ML. Moderate- vs high-dose methadone in the treatment of opioid dependence: a randomized trial. JAMA 1999;281(11):1000-1005. [11]

288. Strain EC, Stitzer ML, Liebson IA, Bigelow GE. Dose-response effects of methadone in the treatment of opioid dependence. Annals of Internal Medicine 1993;119:23-27. [8] [11]

289. Strang J, Gossop M. Comparison of linear versus inverse exponential methadone reduction curves in the detoxification of opiate addicts. Addiction Behaviors 1990;15(6):541-547. [5]

290. Strang J, Marsden J, Cummins M, Farrell M, Finch E, Gossop M et al. Randomized trial of supervised injectable versus oral methadone maintenance: report of feasibility and 6-month outcome. Addiction. 2000; 95(11):1631-1645 [12]

291. Sussman S, Dent CW, Craig S, Ritt-Olsen A, McCuller WJ. Development and immediate impact of a self-instruction curriculum for an adolescent indicated drug abuse prevention trial. J Drug Education 2002;32(2):121-37. [26]

292. Sussman S, Dent CW, Stacy AW, Craig S. One-Year Outcomes of Project Towards No Drug Abuse. Preventive Medicine 1998;27:632-642. [18] [26]

293. Tennant FS Jr ;Sagherian AA. Double-blind comparison of amantadine and bromocriptine for ambulatory withdrawal from cocaine dependence. Archives of Internal Medicine 1987;147(1):109-12. [21]

294. Tennant FS Jr, Russel B A., Casas S K, Bleick R N. Heroin detoxification. A comparison of propoxyphene and methadone. JAMA 1975;232(10):1019-23. [5]

295. Tennant FS, Tarver AL. Double-blind comparison of desipramine and placebo in withdrawal from cocaine dependence. NIDA Research Monograph Series 1985;55:159-163. [20]

296. Tennant RS Jr, Tarver A, Pumphrey E, Seecof R. Double-blind comparison of desipramine and placebo for treatment of phencyclidine or amphetamine dependence. NIDA Research Monograph 1986;67:310-7. [22]

297. Thiede H, Hagan H, Murrill CS. Methadone treatment and HIV and hepatitis B and C risk reduction among injectors in the Seattle area. Journal of Urban Health. 2000; 77(3):331-345 [12]

298. Thornton PI, Igleheart HC, Silverman LH. Subliminal stimulation of symbiotic fantasies as an aid in the treatment of drug abusers. The International Journal of Addictions 1987;22(8):751-765. [14]

299. Torrens M, Castillo C, Pérez-Solà V. Retention in a low-threshold methadone maintenance program. Drug and Alcohol Dependence 1996;41:55-59. [11]

300. Triffleman E, Deluchi K, Tunis S, Banys P, Hall S. Desipramine in the treatment of ¨crack¨cocaine dependence Preliminary results. National Institute on Drug Abuse Research Monograph Series 1992;132:317. [20]

301. Umbricht A, Hoover DR, Tucker MJ, Leslie JM, Chaisson RE, Preston KL. Opioid detoxification with buprenorphine, clonidine, or methadone in hospitalized heroin-dependent patients with HIV infection. Drug & Alcohol Dependence 2003;69:263-272. [2]

302. Umbricht A, Montoya ID, Hoover DR, Demuth KL, Chiang CT, Preston KL. Naltrexone shortened opioid detoxification with buprenorphine. Drug and Alcohol Dependence 1-10-1999;56(3):181-190. [1]

303. Valentine J, Griffith J, Ruthazer R, Gottlieb B, Keel S. Strengthening causal inference in adolescent drug prevention studies: methods and findings from a controlled study of the Urban Youth Connection Program. Drugs and Society 1998;12(1/2):127-45. [26]

304. Van Ameijden EJC, Langendam MW, Coutinho RA. Dose-effect relationship between overdose mortality and prescribed methadone dosage in low-threshold maintenance programs. Addictive Behaviors 1999;24(4):559-563. [11]

305. van den Brink W, Hendriks Vincent M, van Ree Jan M. Medical co-prescription of heroin to chronic, treatment-resistant methadone patients in the netherlands. Journal of Drug Issues 1999;29(3):587-606. [10]

306. van den Brink W, Hendriks VM, Blanken P, Koeter WJ, van Zwieten BJ, van Ree JM. Medical prescription of heroin to treatment resistant heroin addicts: two randomised controlled trials. BMJ 2003;327:310-6. [10]

307. Vanichseni S, Wongsuwan B, The Staff of BMA Narcotics Clinic No.6, Choopanya K, Wongpanich K.. A controlled trial of methadone in a population of intravenous drug users in Bangkok:implications for prevention of HIV. International Journal of the Addictions 1991;26(12):1313-1320. [8]

308. Vining E, Kosten TR, Kleber HD. Clinical utility of rapid clonidine naltrexone detoxification for opioid abusers. British Journal of Addiction 1988;83(5):567-575. [1]

309. Volpicelli Jr, Alterman AI, Hayashida M, O'Brien CP. Naltrexone in the treatment of alcohol dependence. Archives of General Psychiatry 1992;49:876-80. [17]

310. Volpicelli JR, Rhines K, Rhines JS, Volpicelli LA, Alterman AI, O'Brien CP. Naltrexone and alcohol dependence. Archives of General Psychiatry 1997;54:737-42. [17]

311. Wagenaar AC,Murray DM, Gehan JP, Wolfson M, Forster JL, Toomey TL, Perry CL, Jones-Webb R. Communities Mobilizing for Change on Alcohol: Outcomes froma Randomized Community Trial. Journal of Studies on Alcohol 2000;61:85-94. [18]

312. Wang RI, Young LD. Double-blind controlled detoxification from buprenorphine. NIDA Research Monograph 1996;162:114. [2]

313. Washton A M, Resnick R B. Clonidine versus methadone for opiate detoxification. Lancet 13-12-1980;2(8207):1297. [3] [5]

314. Weddington WW, Brown BS, Haertzen CA, Hess JM, Mahaffey JR, Kolar AF, Jaffe JH. Comparison of Amantadine Combined with Psychotherapy for Treatment of Cocaine Dependence. American Journal on Drug and Alcohol Abuse 1991;17:137-152. [20] [21]

315. Werch CE, Anzalone DM, Brokiewicz LM, Felker J, Carlson JM, Castellon-Vogel EA. An Intervention for Preventing Alcohol Use Among Inner-city Middle School Students. Archives of Family Medicine 1996;5((3)):146-152. [18]

316. Werch CE, Carlson JM, Pappas DM, DiClemente CC. Brief Nurse Consultations for Preventing Alcohol Use Among Urban Youth. Journal of School Health 1996;66((9)):335-338. [18]

317. Werch CE, Carlson JM, Pappas DM, Edgemon P, Di Clemente CC. Effects of a Brief Alcohol Preventive Intervetion for Youth Attending School Sports Physical Examinations. Substance Use and Misuse 2000;35((3)):421-432. [18]

318. Werch CE, Pappas DM, Carlson JM, Diclemente CC. Short and Long Term Effects of a Pilot Prevention Program to Reduce Alcohol Consumption. Substance Use and Misuse 1998;33((11)):2303-2321. [18]

319. Werch CE, Pappas DM, Carlson JM, Edgemon P, Sinder JA, DiClemente CC. Evaluation of a Brief Alcohol Prevention Program for Urban School Youth. American Journal of Health Behaviour 2000;24((2)):120-131. [18]

320. Werch CE, Young M, Clark M, Garrett C, Hooks S, Kersten C. Effects of a take-home drug prevention program on drug-related communication and beliefs of parents and children. J School Health 1991;61(8):346-50. [26]

321. White JM, Danz C, Kneebone J, La Vincente S, Newcombe D, Ali R. Relationship between LAAM-methadone preference and treatment outcomes. Submitted for publication. [7]

322. Wilhelmson BU, Laberg JC, Klepp K. Evaluation of two Student and Teacher involved Alcohol Prevention Programmes. Addiction 1994;89:1157-1165. [18]

323. Williams AB, McNelly EA, Williams AE, D'Aquila RT. Methadone maintenance treatment and HIV type 1 seroconversion among injecting drug users. AIDS Care. 1992; 4(1):35-41 [12]

324. Williams AF, DiCocco LM, Unterberger H. Philosophy and Evaluation of an Alcohol Education Programme. Quarterly Journal of Studies on Alcohol 1968 1968;29:685-702. [18]

325. Wilson BK, Elms RR, Thomson CP. Outpatient versus hospital methadone detoxification: An experimental comparison. International Journal of the Addictions 1975;10(1):13-21. [16]

326. Woody GE, Luborsky L, McLellan AT, O' Brien CP, Beck AT, Blaine J, Herman I, Hole A. Psychotherapy for opiate addicts. Does it help? Archives of General Psychiatry 1983;40(6):639-645. [14]

327. Woody GE, McLellan AT, Luborsky L, O' Brien CP. Psychotherapy in community methadone programs: a validation study. American Journal of Psychiatry 1995;152(9):1302-1308. [14]

328. Yancovitz S, Des Jarlais D, Peskoe Peyser N, Drew E, Friedman P, Trigg H, Robinson J. A randomized trial of an interim methadone maintenance clinic. Am J of Pub Health 1991;81:1185 - 1191. [8]

329. Yandoli D, Eisler I, Robbins C, Mulleady G, Dare C.. A comparative study of family therapy in the treatment of opiate users in a London drug clinic.. The Association for Family Therapy and Systemic Practice 2002;24:402-422. [13]

330. ZaisD A, McLellan T, Alterman A, Cnaan R. Efficacy of Enhanced Outreach Counseling to Reenroll High-Risk Drug Users 1 Year After Discharge From Treatment. American Journal Of Psychiatry 1996;153(8):1095-1096. [15]

331. Zaks A, Fink M, Freedman AM. Levomethadyl in maintenance treatment of opiate dependence. JAMA 1972;220(6):811-813. [7]

References for reviews and protocols:

- Alderson P, Green S, Higgins JPT, editors, Cochrane Reviewers' Handbook 4.2.2 [updated March 2004]. In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons, Ltd.

References of published Reviews:

- Gowing L, Ali R, White J. Opioid antagonists with minimal sedation for opioid withdrawal. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [1]

- Gowing L, Ali R, White J, Buprenorphine for the management of opioid withdrawal (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [2]

- Gowing L, Farrell M, Ali R, White J. Alpha2 adrenergic agonists for the management of opioid withdrawal. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [3]

- Gowing L, Ali R, White J, Opioid antagonists under heavy sedation or anaesthesia for the management of opioid withdrawal. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [4]

- Amato L, Davoli M, Ferri M, Ali R. Methadone at tapered doses for the management of opioid withdrawal (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [5]

- Kirchmayer U, Davoli M, Verster A. Naltrexone maintenance treatment for opioid dependence. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [6]

- Clark N, Lintzeris N, Gijsbers A, Whelan G, Ritter A, Dunlop A. LAAM maintenance vs methadone maintenance for heroin dependence. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [7]

- Mattick RP, Breen C, Kimber J. Davoli M. Methadone maintenance versus no opioid replacement therapy for opioid dependence. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [8]

- Mattick RP, Kimber J, Breen C. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [9]

- Ferri M, Davoli M, Perucci CA. Heroin maintenance for chronic heroin dependent. (Cochrane Review). In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd. [10]

- Faggiano F, Vigna-Taglianti F, Versino E, Lemma P. Methadone maintenance at different dosages for opioid dependence. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [11]

- Gowing L., Farrell M, Bornemann R, Ali R., White J. Substitution treatment of injecting opioid users for prevention of HIV infection (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [12]

- Amato L, Minozzi S, Davoli M, Ferri M, Vecchi S, Mayet S.. Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [13]

- Amato L, Minozi S, Davoli M, Vecchi S, Ferri M, Mayet S. Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [14]

- Mayet S, Farrell M, Ferri M, Amato L, Davoli M.. Psychosocial treatment for opiate abuse and dependence (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [15]

- Day E, Ison J, Strang J Inpatient versus other settings for detoxification for opioid dependence. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [16]

- Srisurapanont M, Jarusuraisin N. Opioid antagonists for alcohol dependence. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [17]

- Foxcroft DR, Lister-Sharp DJ, Lowe G, Breen R, Ireland D. Primary prevention of alcohol misuse in young people. (Cochrane Review) In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [18]

- Lima AR, Lima MS, Soares BGO, Farrell M. Carbamazepine for cocaine dependence. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [19]

- Lima MS, Reisser AAP, Soares BGO, Farrell M. Antidepressants for cocaine dependence. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [20]

- Soares BGO, Lima MS, Reisser AAP, Farrell M. Dopamine agonists for cocaine dependence. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [21]

- Srisurapanont M, Jarusuraisin N, Kittirattanapaiboon P. Treatment for amphetamine abuse and dependence. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [22]

- Srisurapanont M, Kittiratanapaiboon P, Jarusuraisin N. Treatment for amphetamine psychosis disorder. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [23]

- Srisurapanont M, Jarusuraisin N, Kittirattanapaiboon P. Treatment for amphetamine withdrawal. (Cochrane Review). In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [24]

- McCarthy G, Myers B Treatment for Mandrax (combination of methaqualone, cannabis and tobacco) dependence in adults. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [25]

- Faggiano F, Lemma P, Borraccino A, Angius P, Ippolito R, Versino E. School-based prevention for illicit drugs' use. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 2, 2005. Chichester, UK: John Wiley & Sons Ltd. [26]

References of published Protocols

- Auriacombe M, Pascale F, Notz N Neuroelectric stimulation for the management of opioid withdrawal. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- Denis C, Fatséas M, Lavie E, Auriacombe M. Pharmacological interventions for benzodiazepine dependence management among benzodiazepine users in outpatient settings. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- Ferri M, Amato L, Davoli M 12-step type programmes and Alcoholics Anonymous for alcohol dependence. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- Fox G C, Loughlin P, Cook CCH Acamprosate for alcohol dependence. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- Fox G C, Loughlin P, Cook CCH Disulfiram for alcohol dependence. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- Gates S, Foxcroft D, Smith LA. Auricular acupuncture for cocaine dependence. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- Gillman MA, Lichtigfeld FJ, Young TN. Psychotropic analgesic nitrous oxide for alcoholic withdrawal states. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- Kaner E, Campbell C, Pienaar ED, Heather N, Schlesinger C, Saunders J. Brief interventions for excessive drinkers in primary care health settings. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- Lima MS, Soares BGO, Farrel M Psychosocial interventions for alcohol use disorders. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- McCambridge J, Gates S, Smith LA, Foxcroft DR. Interventions for prevention of drug use by young people delivered in non-school settings. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- McQueen J, Allan L, Mains D, Grey J. Brief interventions for heavy alcohol users admitted to general hospital wards. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- Ntais C, Pakos E, Panayiotis K, Ioannidis JPA Benzodiazepines for alcohol withdrawal. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- Perry AE, Ali RL, Coulton S, Glanville JM, Godfrey C, Lunn J, McDougall C, Neale ZJ. Interventions for drug-using offenders in the courts, secure establishments and the community. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- Petrie J, Bunn F, Byrne G Parenting programs for preventing tobacco, alcohol and drug abuse in children under 18. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- Polycarpou A, Papanikolaou P, Contopoulos-Ioannidis DG, Ioannidis JPA. Anticonvulsants for the management of alcohol withdrawal. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- Soares BGO, Lima MS, Farrell M Psychosocial treatments for psychostimulants dependence. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.

- Ying LI, Jing Li, Man Jia Zhu, Fan Rong Liang Acupuncture for opioid dependence. Protocol for a Cochrane Review. In: The Cochrane Library, Issue 1, 2005. Chichester, UK: John Wiley & Sons Ltd.