TREATMENTS OF SUBSTANCE USE DISORDERS
THE SYSTEMATIC REVIEWS OF THE COCHRANE DRUGS AND ALCOHOL GROUP (CDAG)
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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 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 heterogeneity (temporal, geographic, 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 6596 trials (3115 RCT, 1415 CCT, 2066 other study design)
The references are systematically searched on the electronic databases (MEDLINE, EMBASE, and PsychInfo). The full text articles are obtained and coded (3446 articles till now).

As of March 2006 the group published 31 reviews, 15 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 performs 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.

Methodological Quality of the studies

The components of the quality of experimental studies can be summarised as follows:
- randomisation, i.e. the fact that the treatment/s is/are assigned by chance;
- allocation concealment, in relation to the unawareness of the researcher on the next assignment, to avoid selection bias;
- blinding of those providing and receiving the intervention after the allocation, to avoid performance bias for providers and to avoid contamination, systematic differences in compliance, systematic differences in the placebo effect and detection bias for patients;
- recording how many patients were lost to follow up in each group and for each outcome measure to estimate the attrition bias;
- blinding of the outcome assessor to avoid detection bias.

The methodological quality of the included studies of the reviews published by our Group is assessed following the criteria suggested by the Cochrane Collaboration. These criteria are based on the allocation concealment and are the following (A=highest quality):

A. adequate allocation concealment; any procedure ensuring adequate concealment of allocation, such as: central randomization(e.g. allocation by a central office unaware of subject characteristics), pre-numbered or coded identical bottles or containers which are administered serially to participants, drug prepared by the pharmacy, serially numbered, opaque, sealed envelopes, on-site computer system combined with allocations kept in a locked unreadable; computer file that can be accessed only after the characteristics of an enrolled participant have been entered or other description that contained elements convincing of concealment;
B. unclear allocation concealment; when the authors either did not report an allocation concealment approach at all or report an approach that did not fall in the category A or C.
C. inadequate allocation concealment; Any procedure not assuring adequate concealment of allocations such as: alternation or reference to case numbers dates of birth, day of the week. Any procedure that is entirely transparent before allocation, such as an open list of random numbers or other description that contained elements convincing of not concealment

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

(Cochrane Library, issue 3.2005)

WHAT'S NEW

NEW PROTOCOLS

- Taixiang W, Bo L, Feng L, Wei-na J. Traditional chinese medicine for opioid withdrawal syndrome
- Terplan M, Grimes D. Psychosocial interventions for pregnant women in outpatient illicit drug treatment programs compared to other interventions

REVIEWS SUBSTANTIALLY UPDATED

- Gowing L, Ali R, White J. Buprenorphine for the management of opioid withdrawal
- Gowing L, Ali R, White J. Opioid antagonists under heavy sedation or anaesthesia for the management of opioid withdrawal

Reviews

OPIATE: DETOXIFICATION INTERVENTIONS

1. Methadone at tapered doses for the management of opioid withdrawal
2. Buprenorphine for the management of opioid withdrawal
3. Alpha 2 adrenergic agonists for the management of opioid withdrawal
4. Opioid antagonists with minimal sedation for opioid withdrawal
5. Opioid antagonists under heavy sedation or anaesthesia for opioid withdrawal
6. Psychosocial and pharmacological treatments versus pharmacological treatments for opioid detoxification
7. Inpatient versus outpatient detoxification for opioid dependence

OPIATE: MAINTENANCE INTERVENTIONS

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9. Methadone maintenance at different dosages for opioid dependence
10. Substitution treatment of injecting opioid users for prevention of HIV infection
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15. Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence
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ALCOHOL:

17. Primary prevention for alcohol misuse in young people
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19. Anticonvulsants for the management of alcohol withdrawal
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COCAINE:

21. Carbamazepine for cocaine dependence
22. Antidepressant for cocaine dependence
23. Dopamine agonists for cocaine dependence
24. Auricular acupuncture for cocaine dependence

AMPHETAMINE:

25. Treatment for amphetamine abuse and dependence
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27. Treatment for amphetamine withdrawal

POLYDRUG:

28. School based prevention for illicit drug's use
29. Intervention for prevention of drug use by young people delivered in non-school settings
30. Therapeutic communities for substance related disorder

OTHER DRUGS: PHARMACOLOGICAL INTERVENTIONS

31. Treatment for Methaqualone dependence in adults

Protocols

1. Acamprosate for alcohol dependence alcohol
2. Acupunture for opioid dependence
3. Brief interventions for excessive drinkers in primary care health settings
4. Brief interventions for heavy alcohol users in general medical wards
5. Disulfiram for alcohol dependence
6. Interventions for drug-using offenders in the courts, secure establishments and the community
7. Neuroelectric stimulation for the management of opioid withdrawal
8. Parenting programs for preventing tobacco, alcohol and drug abuse in children under 18
9. Pharmacological interventions for benzodiazepine dependence management among benzodiazepine users in outpatient settings
10. Psychosocial interventions for alcohol use disorders
11. Psychosocial treatments for psychostimulants dependence
12. Psychosocial interventions for pregnant women in outpatient illicit drug treatment programs compared to other interventions
13. Psychotherapeutic interventions for cannabis abuse and/or dependence in outpatient settings
14. Psychotropic analgesic nitrous oxide for alcoholic withdrawal states
15. Selective serotonin reuptake inhibitors for alcohol use disorders
16. Traditional Chinese medicine for opioid withdrawal syndrome
17. 12-step type programmes and Alcoholics Anonymous for alcohol dependence

OPIATE: MANAGEMENT OF WITHDRAWAL

[1] 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, 2005

Background Despite widespread use in many countries the evidence of tapered methadone's efficacy in managing opioid withdrawal has not been systematically evaluated.
Objectives To evaluate the effectiveness of tapered methadone compared with other detoxification treatments and placebo in managing opioid withdrawal on completion of detoxification and relapse rate.
Search Strategy Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 1, 2005), MEDLINE (January 1966 to December 2004), EMBASE (January 1988 to December 2004), PsycINFO (January 1985 to December 2004), and reference lists of articles. We also contacted manufacturers and researchers in the field.
Selection criteria All randomised controlled trials which focus on the use of tapered methadone versus all other pharmacological detoxification treatments or placebo for the treatment of opiate withdrawal.
Main results Sixteen trials involving 1187 people were included. Comparing methadone versus any other pharmacological treatment we observed no clinical difference between the two treatments in terms of completion of treatment, relative risk (RR) 1.12 (95% CI 0.94 to 1.34) and results at follow-up RR 1.17 (95% CI 0.72 to 1.92). It was impossible to pool data for the other outcomes but the results of the studies did not show significant differences between the considered treatments. These results were confirmed also when we considered the single comparisons: methadone with: adrenergic agonists (11 studies), other opioid agonists (4 studies), chlordiazepoxide (1 study). Comparing methadone with placebo (1 study) more severe withdrawal and more drop outs were found in the placebo group.
The results indicate that the medications used in the included studies are similar in terms of overall effectiveness, although symptoms experienced by participants differed according to the medication used and the program adopted.
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. 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.

[2] Substantially updated 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 2, 2006**

Background Managed withdrawal 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.
Objectives To assess the effectiveness of interventions involving the use of buprenorphine to manage opioid withdrawal, for withdrawal signs and symptoms, completion of withdrawal and adverse effects.
Search Strategy Cochrane Central Register of Controlled Trials (The Cochrane Library, including the Cochrane Drugs and Alcohol Group trials register, Issue 3, 2005), MEDLINE (January 1966 to August 2005), EMBASE (January 1985 to August 2005), PsycINFO (1967 to August 2005), CINAHL(1982 to July 2005) and reference lists of articles.
Selection criteria Experimental interventions involved the use of buprenorphine to modify the signs and symptoms of withdrawal in participants who were primarily opioid dependent. Comparison interventions involved reducing doses of methadone, alpha2 adrenergic agonists, symptomatic medications or placebo, or different buprenorphine-based regimes.
Main results Eighteen studies (14 randomised controlled trials), involving 1356 participants, were included. Ten studies compared buprenorphine with clonidine; four compared buprenorphine with

methadone; one compared buprenorphine with oxazepam; three compared different rates of buprenorphine dose reduction; two compared different starting doses of buprenorphine. (Two studies included more than one comparison.) Relative to clonidine, buprenorphine is more effective in ameliorating the symptoms of withdrawal, patients treated with buprenorphine stay in treatment for longer, particularly in an outpatient setting SMD 0.82 (95% CI 0.57 to 1.06), and are more likely to complete withdrawal treatment RR 1.73 (95% CI 1.21 to 2.47). At the same time there is no significant difference in the incidence of adverse effects, but drop-out due to adverse effects may be more likely with clonidine. Severity of withdrawal is similar for withdrawal managed with buprenorphine and withdrawal managed with methadone, but withdrawal symptoms may resolve more quickly with buprenorphine. There is a trend towards completion of withdrawal treatment being more likely with buprenorphine relative to methadone RR 1.30 (95% CI 0.97 to 1.73).
Reviewers' conclusions Buprenorphine is more effective than clonidine for the management of opioid withdrawal. There appears to be no significant difference between buprenorphine and methadone in terms of completion of treatment, but withdrawal symptoms may resolve more quickly with buprenorphine.

[3] ALPHA$_2$ 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 alpha$_2$ adrenergic agonists (clonidine, lofexidine, guanfacine) to manage opioid withdrawal in terms of withdrawal signs and symptoms, completion of treatment and adverse effects.
Search Strategy Drugs and Alcohol Group trials register (October 2003), Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 3, 2003), MEDLINE (January 1966 to September 2004), EMBASE (January 1985 to September 2004), PsycINFO (September 2004), Australian Medical Index (October 2003) and reference lists of the articles. We also contacted manufacturers in the field.
Selection criteria Controlled trials comparing alpha$_2$ adrenergic agonists with reducing doses of methadone, symptomatic medications or placebo, or comparing different alpha$_2$ 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 alpha$_2$ 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 alpha$_2$ 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 alpha$_2$ 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 alpha$_2$ 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 alpha$_2$ adrenergic agonists.

[4] 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 1, 2006

Background Managed withdrawal is necessary prior to drug-free treatment. It may also represent the end point of long-term opioid replacement treatment.

Objectives To assess the effectiveness of opioid antagonists in combination with minimal sedation to induce withdrawal, in terms of intensity of withdrawal, adverse effects and completion of treatment.

Search Strategy Cochrane Central Register of Controlled Trials (The Cochrane Library, Issue 3, 2005, which includes the Cochrane Drugs and Alcohol Group register), MEDLINE (January 1966 to August 2005), EMBASE (January 1985 to August 2005), PsycINFO (1967 to August 2005), CINAHL (1982 to July 2005) and reference lists of articles.

Selection criteria Experimental interventions involved the use of opioid antagonists in combination with minimal sedation to manage withdrawal in opioid-dependent participants compared with other approaches or different opioid antagonist regime..

Main results Nine studies (5 randomised controlled trials), involving 775 participants, met the inclusion criteria for the review.

Withdrawal induced by opioid antagonists in combination with an adrenergic agonist is more intense than withdrawal managed with clonidine or lofexidine alone, but the overall severity is less. Limited data showed that antagonist-induced withdrawal may be more severe when the last opioid used was methadone rather than heroin or another short-acting opioid. Delirium may occur following the first dose of opioid antagonist, particularly with higher doses (> 25mg naltrexone).

The studies included suggest there is no significant difference in rates of completion of treatment for withdrawal induced by opioid antagonists, in combination with an adrenergic agonist, compared with adrenergic agonist alone.

Reviewers' conclusions The use of opioid antagonists combined with alpha2 adrenergic agonists is a feasible approach to the management of opioid withdrawal. However, it is unclear whether this approach reduces the duration of withdrawal or facilitates transfer to naltrexone treatment to a greater extent than 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.

[5] Substantially updated 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 2, 2006**

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, in terms of withdrawal signs and symptoms, completion of treatment and adverse effects.

Search Strategy Drugs and Alcohol Group register (October 2003), Cochrane Central Register of Controlled Trials (The Cochrane Library, Issue 4, 2004), Medline (January 1966 to January 2005),

Embase (January 1985 to January 2005), PsycINFO (1967 to January 2005), and Cinahl (1982 to December 2004) and reference lists of studies.

Selection criteria Controlled trials comparing antagonist-induced withdrawal under heavy sedation or anaesthesia with another form of treatment, or a different regime of anaesthesia-based antagonist-induced withdrawal.

Main results Six studies (five randomised controlled trials) involving 834 participants met the inclusion criteria for the review.

Antagonist-induced withdrawal is more intense but less prolonged than withdrawal managed with reducing doses of methadone, and doses of naltrexone sufficient for blockade of opioid effects can be established significantly more quickly with antagonist-induced withdrawal than withdrawal managed with clonidine and symptomatic medications. The level of sedation does not affect the intensity and duration of withdrawal, although the duration of anaesthesia may influence withdrawal severity. There is a significantly greater risk of adverse events with heavy, compared to light, sedation RR 3.21 (95% CI 1.13 to 9.12) and probably also other forms of detoxification.

Reviewers' conclusions Heavy sedation compared to light sedation does not confer additional benefits in terms of less severe withdrawal or increased rates of commencement on naltrexone maintenance treatment. Given that the adverse events are potentially life-threatening, the value of antagonist-induced withdrawal under heavy sedation or anaesthesia is not supported. The high cost of anaesthesia-based approaches, both in monetary terms and use of scarce intensive care resources, suggest that this form of treatment should not be pursued.

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

Amato L, Minozzi 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.

Search Strategy Cochrane Drugs and Alcohol Group trials register (14 April 2003). Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library Issue 3, 2003), MEDLINE (January 1966 to April 2003); EMBASE (January 1980 to April 2003); PsycINFO (1985 to April 2003) and reference list of articles.

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

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.

[7] 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.
Search Strategy Cochrane Central Register of Controlled Trials (CENTRAL - The Cochrane Library Issue 3, 2004); MEDLINE (January 1966-March 2004); EMBASE (January 1988-March 2004); PsycInfo (January 1967-March 2004); CINAHL (January 1982-March 2004). In addition the Current Contents, Biological Abstracts, Science Citation Index and Social Sciences Index were searched.
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.

OPIATE: MAINTENANCE TREATMENT

[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.
Search Strategy All the following databases up to 2001 Cochrane Drugs and Alcohol Review Group Register, the Cochrane Controlled Trials Register, MEDLINE, EMBASE, Current Contents, Psychlit, CORK [www. state.vt.su/adap/cork], Alcohol and Drug Council of Australia (ADCA) [www.adca.org.au], Australian Drug Foundation (ADF-VIC) [www.adf.org.au], Centre for Education and Information on Drugs and Alcohol (CEIDA) [www.ceida.net.au], Australian Bibliographic Network (ABN), and Library of Congress databases, available NIDA monographs and the College on Problems of Drug Dependence Inc. proceedings, the reference lists of all identified studies and

published reviews; authors of identified RCTs were asked about other published or unpublished relevant RCTs.

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 to 5.35) and in the suppression of heroin use: 3 RCTs, RR 0.32; (95% CI 0.23 to 0.44), but not statistically in criminal activity: 3 RCTs, RR 0.39 (95%CI 0.12 to 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] METHADONE MAINTENANCE AT DIFFERENT DOSAGES FOR OPIOID DEPENDENCE

Faggiano F, Vigna-Taglianti F, Versino E, Lemma. 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.

Search Strategy MEDLINE (OVID 1966-2001), EMBASE (1988-2001), ERIC (1988-2001), Psychinfo (1947-2001), Cochrane Controlled Trials Register (CCTR) (1947-2001), Register of the Cochrane Drug and Alcohol Group (CDAG) (1947-2001). The CDAG search strategy was applied together with a specific MESH strategy. Further studies were searched through letters to the authors and check of references.

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 versus low doses at shorter follow-ups: RR=1.36 (95% CI 1.13 to 1.63), and at longer ones: RR=1.62 (95% CI 0.95 to 2.77).

Opioid use (self reported), times/w - RCTs: high versus low doses WMD= -2.00 (95% CI -4.77 to 0.77) high versus middle doses WMD= -1.89(95% CI -3.43 to 0.35)

Opioid abstinence, (urine based) at >3-4 w - RCTs: high versus low ones: RR=1.59 (95%CI 1.16 to 2.18] high versus middle doses RR=1.51 (95% CI 0.63 to 3.61)

Cocaine abstinence (urine based) at >3-4 w - RCTs: high versus low doses RR=1.81 (95% CI 1.15 to 2.85)

Overdose mortality - CPSs: high dose versus low dose at 6 years follow up: RR=0.29 (95% I0.02-5.34) high dose versus middle dose at 6 years follow up: RR=0.38 (95% CI 0.02 to 9.34) middle dose versus low dose at 6 years follow up: RR=0.57 (95% CI 0.06 to 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.

[10] 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.
Search Strategy Cochrane Drugs and Alcohol Group trials register, Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, PsycINFO, CINAHL, and NLM Gateway from their date of commencement to July 2003. We also searched reference lists of articles, reviews and conference abstracts
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.

[11] BUPRENORPHINE MAINTENANCE VERSUS 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.
Search Strategy The following databases up to 2001, inclusive: Cochrane Drugs and Alcohol Review Group Register, the Cochrane Controlled Trials Register, MEDLINE, EMBASE, Current Contents, Psychlit, CORK [www. state.vt.su/adap/cork], Alcohol and Drug Council of Australia (ADCA) [www.adca.org.au], Australian Drug Foundation (ADF -VIC) [www.adf.org.au], Centre for Education and Information on Drugs and Alcohol (CEIDA) [www.ceida.net.au], Australian Bibliographic Network (ABN), Library of Congress databases, available NIDA monographs, the College on Problems of Drug Dependence Inc. proceedings, the reference lists of all identified studies and published reviews. Authors of identified RCT's were asked about any other published or unpublished relevant RCT.
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 to 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 to 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 to 1.45), high doses RR 1.21 (95% CI 1.02 to 1.44), and very high doses RR 1.52 (95% CI 1.23 to 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.

[12] 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.

Search Strategy MEDLINE (January 1966 - August 2000), PsycINFO (1887 - August 2000), EMBASE (January 1985 - August 2000), and Cochrane Controlled Trials Register (Issue 2 2000). We hand searched NIDA monographs until August 2000 and reference lists of articles. The specialised register of trials of the Cochrane Group on Drugs and Alcohol was searched until February 2003.

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 to 1.73). Non-abstinence was less with LAAM, 5 studies, 983 participants, RR 0.81 (95% CI 0.72 to 0.91). 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 to 8.9). 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.

[13] 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.

Search Strategy Cochrane Central Register of Trials (The Cochrane Library Issue 1, 2005; MEDLINE (1966 to 2005), EMBASE (1980 to 2005) and CINAHL until 2005 (on OVID). There was no language or publication year restriction. We also contacted researchers in the field.

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 to 4.68) in favour of heroin; one study (N=235) had a RR 0.79 (95% CI 0.68 to 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 to 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 to 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 multi-domain 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 are 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.

[14] ORAL NALTREXONE MAINTENANCE TREATMENT FOR OPIOID DEPENDENCE

Minozzi S, Amato L, Vecchi S, Davoli M, Kirchmayer U, Verster A. Date first publication issue 1, 1999; Date of the last substantial update issue 1, 2006

Background Research on the clinical application of oral naltrexone agrees on several things. From a pharmacological perspective, naltrexone works. From an applied perspective, however, this medication is not used since the medication compliance and the retention rates are very poor.

Objectives To evaluate the effects of naltrexone maintenance treatment versus placebo or other treatments in preventing relapse in opioid addicts after detoxification.

Search Strategy Cochrane Drugs and Alcohol Group Register of Trials (January 2005), Cochrane Central Register of Controlled Trials (CENTRAL - The Cochrane Library Issue 1, 2005), MEDLINE (1973-first year of naltrexone use in humans- January 2005), EMBASE (1974- January 2005), PsycINFO (OVID-January 1985 to January 2004). We inspected reference lists of relevant articles and we contacted pharmaceutical producers of naltrexone, authors and other Cochrane review groups.

Selection criteria All randomised and controlled clinical trials which focus on the use of naltrexone maintenance treatment versus placebo, or other treatments to reach sustained abstinence from opiate drugs

Main results Ten studies, 696 participants, met the criteria for inclusion in this review. Only two studies described an adequate allocation concealment. The results show that naltrexone maintenance therapy alone or associated with psychosocial therapy is more efficacious that placebo alone or associated with psychosocial therapy in limiting the use of heroin during the treatment RR 0,72 (95% CI 0.58 to 0.90). If we consider only the studies comparing naltrexone with placebo, the difference do not reach the statistical significance, RR 0.79 (95% CI 0.59 to 1.06). With respect to the number of participants re incarcerated during the study period, the naltrexone associated with psychosocial therapy is more effective than the psychosocial treatment alone; RR 0.50 (95% CI 0.27 to 0.91).

No statistically significant benefit was shown in terms of retention in treatment, side effects or relapse results at follow-up for any of the considered comparisons.

Reviewers' conclusions Unfortunately the studies did not provide an objective evaluation of naltrexone treatment in the field of opioid dependence. The conclusions are also limited due to the heterogeneity of the trials both in the interventions and in the assessment of outcomes.

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

Amato L, Minozzi 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.

Search Strategy Cochrane Drugs and Alcohol Group's trials register (14 April 2003), the Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 3, 2003), MEDLINE (January 1966 to April 2003), EMBASE (January 1980 to April 2003), PsycINFO (January 1985 to April 2003) and reference lists of articles.

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 to 0.91); no statistically significant additional benefit was shown in terms of retention in treatment RR 0.94 (95% CI 0.85 to 1.02); and results at follow-up RR 0.90 (95% CI 0.76 to 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.

[16] 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.

Search Strategy Cochrane drugs and Alcohol Group Register of Trials (21 January 2004); Cochrane Central Register of Controlled Trials (CENTRAL-The Cochrane Library, Issue 1, 2004); MEDLINE (1966-2003), LILACS (1982-2003), EMBASE (1980-2003), PsycINFO (1872-2003). In addition reference searching, personal communication, conference abstracts, unpublished trials, book chapters on treatment of opioid dependence.

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.

ALCOHOL:

[17] 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.
Search Strategy Project CORK, BIDS, PSYCLIT, ERIC, ASSIA, MEDLINE, FAMILY-RESOURCES-DATABASE, HEALTH-PERIODICALS-DATABASE, EMBASE, BIDS, Dissertation-Abstracts, SIGLE, DRUG-INFO, SOMED, Social-Work-Abstracts, National-Clearinghouse-on-Alcohol-and-Drug-Information, Mental-Health-Abstracts, DRUG-database, ETOH (all searched Feb-June 2002).
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.

[18] 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.
Search Strategy Cochrane Group on Drugs and Alcohol (September 2003); Cochrane Controlled Trials Register (Cochrane Library 2001, issue 4), MEDLINE (1966-October 2001), EMBASE (1980-December 2001), CINHAL (1982 -December 2001). Du Pont Pharmaceutical and Ivax Corporation were contacted for information regarding unpublished trials. The reference lists of the obtained papers were examined.
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, e.g., 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.

[19] ANTICONVULSANTS FOR ALCOHOL WITHDRAWAL

Polycarpou A, Papanikolaou P, Ioannidis JPA, Contopoulos-Ioannidis DG. Date first publication issue 3, 2005

Background Alcohol withdrawal syndrome is a cluster of symptoms that occurs in alcohol-dependent people after cessation or reduction in alcohol use. This systematic review focuses on the evidence of anticonvulsants' use in the treatment of alcohol withdrawal symptoms.

Objectives To evaluate the effectiveness and safety of anticonvulsants in the treatment of alcohol withdrawal.

Search Strategy Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 3, 2004); MEDLINE (1966 to October 2004); EMBASE (1988 to October 2004) and EU-PSI PSI-Tri database with no language and publication restrictions and references of articles.

Selection criteria All randomized controlled trials examining the effectiveness, safety and overall risk-benefit of an anticonvulsant in comparison with a placebo or other pharmacological treatment or another anticonvulsant were considered.

Main results Forty-eight studies, involving 3610 people were included. Despite the considerable number of randomized controlled trials, there was a variety of outcomes and of different rating scales that led to a limited quantitative synthesis of data. For the anticonvulsant versus placebo comparison, therapeutic success tended to be more common among the anticonvulsant-treated patients RR 1.32 (95% CI 0.92 to 1.91), and anticonvulsant tended to show a protective benefit against seizures RR 0.57 (95% CI 0.27 to 1.19), but no effect reached formal statistical significance. For the anticonvulsant versus other drug comparison, CIWA-Ar score showed non-significant differences for the anticonvulsants compared to the other drugs at the end of treatment (weighted mean difference (WMD) -0.73 (95% CI -1.76 to 0.31). For the subgroup analysis of carbamazepine versus benzodiazepine, a statistically significant protective effect was found for the anticonvulsant WMD -1.04 (95% CI -1.89 to -0.20), but this was based on only 260 randomized participants. There was a non-significant decreased incidence of seizures RR 0.50 (95% CI 0.18 to

1.34) favouring the patients that were treated with anticonvulsants than other drugs, and side-effects tended to be less common in the anticonvulsant-group RR 0.56 (95% CI 0.31 to 1.02).
Reviewers' conclusions It is not possible to draw definite conclusions about the effectiveness and safety of anticonvulsants in alcohol withdrawal, because of the heterogeneity of the trials both in interventions and the assessment of outcomes. The extremely small mortality rate in all these studies is reassuring, but data on other safety outcomes are sparse and fragmented.

[20] BENZODIAZEPINES FOR ALCOHOL WITHDRAWAL
Ntais C, Pakos E, Kyzas P, Ioannidis JPA Date first publication issue 3, 2005

Background Alcohol withdrawal syndrome is a cluster of symptoms that occurs in alcohol-dependent people after cessation or reduction in alcohol use. This systematic review focuses on the evidence of benzodiazepines' use in the treatment of alcohol withdrawal symptoms.
Objectives To evaluate the effectiveness and safety of benzodiazepines in the treatment of alcohol withdrawal.
Search Strategy Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 4, 2004), MEDLINE (1966 to October 2004) and EU-PSI PSI-Tri database with no language and publication restrictions. We also screened references of retrieved articles.
Selection criteria All randomized controlled trials examining the effectiveness and safety of a benzodiazepine in comparison with a placebo or other pharmacological intervention or other benzodiazepine were considered.
Main results Fifty-seven trials, with a total of 4,051 people were included. Despite the considerable number of randomized controlled trials, there was a very large variety of outcomes and of different rating scales and relatively limited quantitative synthesis of data was feasible. Benzodiazepines offered a large benefit against alcohol withdrawal seizures compared to placebo RR 0.16 (95% CI 0.04 to 0.69). Benzodiazepines had similar success rates as other drugs RR 1.00 (95% CI 0.83 to 1.21) or anticonvulsants in particular RR 0.88 (95% CI 0.60 to 1.30) and offered a significant benefit for seizure control against non-anticonvulsants RR 0.23 (95% CI 0.07 to 0.75), but not against anticonvulsants RR 1.99 (95% CI 0.46 to 8.65). Changes in Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) scores at the end of treatment were similar with benzodiazepines versus other drugs, although some small studies showed isolated significant differences for other, less commonly, used scales. Data on other comparisons were very limited, thus making quantitative synthesis for various outcomes not very informative.
Reviewers' conclusions Benzodiazepines are effective against alcohol withdrawal symptoms, in particular seizures, when compared to placebo. It is not possible to draw definite conclusions about the relative effectiveness and safety of benzodiazepines against other drugs in alcohol withdrawal, because of the large heterogeneity of the trials both in interventions and assessment of outcomes but the available data do not show prominent differences between benzodiazepines and other drugs in success rates.

COCAINE:

[21] 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.
Search Strategy Cochrane Controlled Trials Register (Cochrane Library issue 1, 1999), MEDLINE (f1966 - October 1997), EMBASE (1980 - October 1997), PsycLIT (1974 - July 1997), Biological Abstracts and LILACS (1982 - 1997); scan of reference list of relevant articles; personal communication; conference abstracts; unpublished trials from pharmaceutical industry; book chapters on treatment of cocaine dependence. The specialised register of trials of Cochrane Group on Drugs and Alcohol until February 2003.
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. Fewer dropouts occurred in the carbamazepine group RR 0.87 (95% CI 0.71 to 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 to 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.

[22] 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.
Search Strategy Cochrane Controlled Trials Register (Cochrane Library, issue 4, 2000), MEDLINE (1966 - 2000), EMBASE (1980 - 2000), LILACS (1982 - 2000), PsycLIT (1974 - 2000), Biological Abstracts (1982 t- 2000). Reference searching; personal communication; conference abstracts; unpublished trials from pharmaceutical industry; book chapters on treatment of 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.

[23] 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.
Search Strategy Cochrane Library, EMBASE, MEDLINE, PsycLIT, Biological Abstracts and LILACS; reference searching; personal communication; conference abstracts; unpublished trials from pharmaceutical industry; book chapters on treatment of cocaine dependence, was performed in December of 2002. The specialised register of trials of the Cochrane Group on Drugs and Alcohol was searched until February 2003.
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.

[24] AURICULAR ACUPUNCTURE FOR COCAINE DEPENDENCE

Gates S, Smith LA, Foxcroft DR. Date first publication issue 1, 2006

Background Auricular acupuncture (insertion of acupuncture into a number, usually five, of specific points in the ear) is a widely-used treatment for cocaine dependence.
Objectives To determine whether auricular acupuncture is an effective treatment for cocaine dependence, and to investigate whether its effectiveness is influenced by the treatment regimen.
Search Strategy Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 3, 2004); MEDLINE (January 1966 to October 2004) , EMBASE (January 1988 to October 2004); PsycInfo (1985 to October 2004); CINAHL (1982 to October 2004); SIGLE (1980 to October 2004) and reference lists of articles.

Selection criteria Randomised controlled trials comparing a therapeutic regimen of auricular acupuncture with sham acupuncture or no treatment for reduction of cocaine use in cocaine dependents.
Main results Seven studies with a total of 1,433 participants were included. All were of generally low methodological quality. No differences between acupuncture and sham acupuncture were found for attrition RR 1.05 (95% CI 0.89 to 1.23) or acupuncture and no acupuncture: RR 1.06 (95% CI 0.90 to 1.26) neither for any measure of cocaine or other drug use. However, the number of participants included in meta-analyses was low, and power was limited. Moderate benefit or harm is not ruled out by these results. Methodological limitations of the included studies may have also made the results open to bias.
Reviewers' conclusions There is currently no evidence that auricular acupuncture is effective for the treatment of cocaine dependence. The evidence is not of high quality and is inconclusive. Further randomised trials of auricular acupuncture may be justified.

AMPHETAMINE:

[25] TREATMENT FOR AMPHETAMINE DEPENDENCE AND ABUSE
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.
Search Strategy The specialised register of trials of the Cochrane Group on Drugs and Alcohol (until February 2003), MEDLINE (1966-December 2000), EMBASE (1980-February 2001), CINAHL (1982-January 2001), Cochrane Controlled Trials Register (Cochrane Library 2000 issue 4). References of obtained articles were searched.
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.

[26] TREATMENT FOR AMPHETAMINE PSYCHOSIS
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 variety treatments for amphetamine psychosis.
Search Strategy MEDLINE (1966-2000), EMBASE (1980-2000), CINAHL (1982- January 2001) and Cochrane Controlled Trials Register (Cochrane Library 2000 issue 4) were undertaken. References to the articles obtained by any means were searched. the specialised register of trials of the Cochrane Group on Drugs and Alcohol was searched until February 2003.
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.

[27] 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.
Search Strategy MEDLINE (1966 - December 2000), EMBASE (1980 - February 2001), CINAHL (1982 - January 2001), Cochrane Controlled Trials Register (Cochrane Library 2000 issue 4). References of the obtained articles. The specialised register of trials of the Cochrane Group on Drugs and Alcohol until February 2003.
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 activities 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.

POLY DRUGS

[28] 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.
Search Strategy Cochrane Drug and Alcohol Group trial register (February 2004), the Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 2, 2004), MEDLINE (1966 to February 2004) , EMBASE (1988 to February 2004), and other databases. We also contacted researchers in the field and checked reference lists of articles.
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 versus usual curricula
Knowledge focused programs improve drug knowledge SMD 0.91 (95% CI 0.42 to 1.39).
(2) Skills versus usual curricula
Skills based interventions increase drug knowledge WMD 2.60 (95% CI 1.17 to 4.03), decision making skills SMD 0.78 (95% CI 0.46 to 1.09), self-esteem SMD 0.22 (95% CI 0.03 to 0.40), peer pressure resistance RR 2.05 (95% CI 1.24 to3.42), drug use RR 0.81 (95% CI 0.64 to 1.02), marijuana use RR 0.82 (95% CI 0.73 to 0.92) and hard drug use RR 0.45 (95% CI 0.24 to 0.85).
(3) Skills versus knowledge
No differences are evident.
(4) Skills versus affective
Skills-based interventions are only better than affective ones in self-efficacy WMD 1.90 (95% CI 0.25 to 3.55).
(5) Affective versus usual curricula
Affective interventions improve drug knowledge SMD 1.88 (95% CI 1.27 to 2.50) and decision making skills SMD 1.35 (95% CI 0.79 to 1.9).
(6) Affective versus knowledge
Affective interventions improve drug knowledge SMD 0.60 (95% CI 0.18 to 1.03), and decision making skills SMD 1.22 (95% CI 0.33 to 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.

[29] INTERVENTIONS FOR PREVENTION OF DRUG USE BY YOUNG PEOPLE DELIVERED IN NON-SCHOOL SETTINGS

Gates S, McCambridge J, Smith LA, Foxcroft DR. Date first publication issue 1, 2006

Background Interventions intended to prevent or reduce use of drugs by young people may be delivered in schools or in other settings. This review aims to summarise the current literature about the effectiveness of interventions delivered in non schools settings.

Objectives (1) To summarise the current evidence about the effectiveness of interventions delivered in non-school settings intended to prevent or reduce drug use by young people under 25; (2) To investigate whether interventions' effects are modified by the type and setting of the intervention, and the age of young people targeted; (3) To identify areas where more research is needed.

Search Strategy Cochrane Central Register of Controlled Trials (CENTRAL - The Cochrane Library Issue 4, 2004), MEDLINE (1966 to 2004), EMBASE (1980 to 2004), PsycInfo (1972 to 2004), SIGLE (1980 to 2004), CINAHL (1982 to 2004) and ASSIA (1987 to 2004) and reference lists of articles.

Selection criteria Randomised trials that evaluated an intervention targeting drug use by young people less than 25 years of age, delivered in a non-school setting, compared with no intervention or another intervention that reported substantive outcomes relevant to the review.

Main results Seventeen studies, 9 cluster randomised studies, with 253 clusters, 8 individually randomised studies with 1230 participants, evaluating four types of intervention: motivational interviewing or brief intervention, education or skills training, family interventions and multi-component community interventions. Many studies had methodological drawbacks, especially high levels of loss to follow-up. There were too few studies for firm conclusions. One study of motivational interviewing suggested that this intervention was beneficial on cannabis use. Three family interventions (Focus on Families, Iowa Strengthening Families Program and Preparing for the Drug-Free Years), each evaluated in only one study, suggested that they may be beneficial in preventing cannabis use. The studies of multi component community interventions did not find any strong effects on drug use outcomes, and the two studies of education and skills training did not find any differences between the intervention and control groups.

Reviewers' conclusions There is a lack of evidence of effectiveness of the included interventions. Motivational interviewing and some family interventions may have some benefit. Cost-effectiveness has not yet been addressed in any studies, and further research is needed to determine whether any of these interventions can be recommended.

[30] THERAPEUTIC COMMUNITIES FOR SUBSTANCE RELATED DISORDER

Smith LA, Gates S, Foxcroft D. Date first publication issue 1, 2006

Background Therapeutic communities (TCs) are a popular treatment for the rehabilitation of drug users in the USA and Europe.

Objectives To determine the effectiveness of TC versus other treatments for substance dependents, and to investigate whether effectiveness is modified by client or treatment characteristics.

Search Strategy Cochrane Central Register of Controlled Trials (The Cochrane Library Issue 2, 2005); MEDLINE, EMBASE, Psycinfo, CINAHL, SIGLE from their inception to March 2004 and reference lists of articles.

Selection criteria Randomised controlled trials comparing TC with other treatments, no treatment or another TC.

Main results Seven studies were included. Differences between studies precluded any pooling of data, results are summarised for each trial individually: TC versus community residence: no significant differences for treatment completion; Residential versus day TC: attrition (first two weeks), and abstinence rates at six months significantly lower in the residential treatment group; Standard TC versus enhanced abbreviated TC: number of employed higher in standard TC RR 0.78 (95% CI 0.63 to 0.96). Three months versus six months programme within modified TC, and six months versus 12 months programme within standard TC: completion rate higher in the three months programme and retention rate (40 days) significantly greater with the 12 months than 6

months programme.
Two trials evaluated TCs within a prison setting: one reported significantly fewer re incarcerated 12 months after release from prison in the TC group compared with no treatment, RR 0.68 (95% CI 0.57 to 0.81). In the other, people treated in prison with TC compared with Mental Health Treatment Programmes showed significantly fewer re incarcerations RR 0.28 (95% CI 0.13 to 0.63), criminal activity RR 0.69 (95% CI 0.52 to 0.93) and alcohol and drug offences RR 0.62 (95% CI 0.43 to 0.90) 12 months after release from prison.
Reviewers' conclusions There is little evidence that TCs offer significant benefits in comparison with other residential treatment, or that one type of TC is better than another. Prison TC may be better than prison on it's own or Mental Health Treatment Programmes to prevent re-offending post-release for in-mates. However, methodological limitations of the studies may have introduced bias and firm conclusions cannot be drawn due to limitations of the existing evidence.

OTHER DRUGS

[31] 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.
Search Strategy Cochrane Drugs and Alcohol Group' Register of Trials (February 2004); Cochrane Central Register of Controlled Trials (CENTRAL-The Cochrane Library, Issue 2, 2004); MEDLINE (OVID - January 1966 to February 2004), PsycInfo (OVID - January 1967 to February 2004). Relevant conference proceedings and reference lists of relevant articles were hand-searched. Broad internet searches were conducted and contact made with experts in the field.
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.

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

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