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Review

Cochrane systematic reviews in the field of addiction: What's there and what should be☆

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ABSTRACT

The Cochrane Drugs and Alcohol Group aims to produce, update, and disseminate systematic reviews on the prevention, treatment, and rehabilitation of problematic drug and alcohol use. The objective of the present paper was to summarize the main characteristics of the published systematic reviews in the field of drug and alcohol dependence, in terms of the topics covered, methods used to produce the reviews, and available evidence. By January 2010, the Group had published 52 reviews with 694 primary studies included out of 2059 studies considered for inclusion. Of these publications, 44% were published in 12 journals, including Drug and Alcohol Dependence (11%) with the highest number of publications, and 68% were conducted in North America. The majority of included studies (90%) were randomized controlled trials. Evaluating their methodological quality, we found that allocation concealment methods were not properly described in the majority of studies (18% adequate, 73% unclear, 9% inadequate). The percentage of interventions shown to be beneficial varied according to the substance considered: 42% for opioids, 37% for alcohol, 14% for psychostimulants, 7% for polydrugs, and 33% for prevention. Furthermore, 75% of the reviews provided specific information on further research needs. Cochrane reviews provide information on the most effective treatments, particularly in the area of opioid and alcohol dependence, and help clarify areas for further research.

Contents

☆ A list of references for the 52 Cochrane reviews used in this paper (as noted in Table 2 of this paper) can be found in the supplementary materials by accessing the online version of this paper.

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1. Introduction

According to the World Health Organization, the prevalence of alcohol dependence in the European Union is estimated to be between 3.8% (Germany) and 12.2% (Poland) of the adult population, whereas the prevalence is estimated to be 7.7% and 9.3% in the United States and Canada, respectively (WHO, 2005). The most recent figures for illicit drug use indicate that the prevalence of opioid abuse among persons 15–64 years of age is approximately 0.5% in most Western countries (i.e. EU, USA, Canada, and Australia) (UNODC World Drug Report, 2009). The prevalence of cocaine abuse is estimated to be roughly 1% in the EU and Australia, but over 2% in Canada and approximately 3% in the US. The prevalence of amphetamine abuse is generally lower than 1%, but cannabis use rates are over 10% in several European countries, Canada, the US, and Australia (UNODC World Drug Report, 2009).

Substance use disorders are associated with a wide range of serious health, social, and economic complications. The health status of alcohol and drug users is generally affected by their pattern of consumption (de Alba et al., 2004) and, consequently, their life expectancy is often significantly lower than that of the general population (Price et al., 2001; Sørensen et al., 2005; Wahren et al., 1997), with a great impact on the mortality of young adults (Bargagli et al., 2006). People who abuse drugs are less likely to be working (Ettner et al., 1997), and alcohol dependence is associated with premature retirement due to health (Romelsjo et al., 2004). Housing, relationship, and judicial problems are also well documented among people who are substance dependent. Drug and alcohol dependence incurs high costs due to multiple hospitalizations and treatment episodes (Rehm et al., 2007).

Different interventions are offered for the prevention and treatment of substance use and dependence. The choice is often guided by common sense, intuition, experience, beliefs, or ideology and not always by evidence. Clinicians and policy makers need accessible, up-to-date, objective evidence regarding the effectiveness of different interventions. The aim of this paper is to review and report on the state of the production of Cochrane systematic reviews in the area of drug and alcohol dependence in terms of available evidence.

The Cochrane approach attempts to control for variable quality and provide a robust, even if sometimes limited, commentary on tightly defined interventions. Reviews are the result of a complex process that includes: formulating a proper question, comprehensively searching studies, objectively selecting and extracting data, critically evaluating primary studies, and synthesizing and updating results. In the last few years, grading the quality of the evidence has been added to this process. Several studies have evaluated the quality of systematic reviews and consistently found a better quality for Cochrane versus non-Cochrane reviews (Delaney et al., 2007; Jadad et al., 2000; Jørgensen et al., 2008; Moher et al., 2007; Moja et al., 2005; Olsen et al., 2001; Tricco et al., 2009).

We performed a search limited to the four journals that represent the principal source of articles in the field of drug addiction from January 2006 to March 2010 and found only 11 non-Cochrane reviews, versus 52 published in the Cochrane Library.

2. Methods

The Cochrane Drugs and Alcohol Group (CDAG), as part of the Cochrane Collaboration, aims to produce, update, and disseminate systematic reviews of trials on the prevention, treatment, and rehabilitation of problematic drug and alcohol use. CDAG was founded in 1998 and has an editorial base in Rome (Davoli and Ferri, 2000; further information available at http://www.cdag.cochrane.org).

A total of 185 authors have published with the CDAG: 92 from the European Union, 28 from Australia, 22 from Asia, 21 from North America, 10 from South America, 7 from South Africa, and 5 from the Middle East. The systematic reviews published by CDAG are based on randomized controlled trials (RCTs) 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 inclusion of other study designs is considered in limited circumstances (Amato et al., 2010). The publication of Cochrane reviews follows an editorial process, peer-reviewed from the protocol stage onwards, with regular updates every 2 years according to the criteria of the Cochrane Collaboration (Higgins and Green, 2008).

In this paper, we summarize the main characteristics of the published systematic reviews, in terms of the topics covered, methods used to produce the reviews, and available evidence.

3. Results

3.1. Topics covered by the reviews

By January 2010, the CDAG published 52 reviews (see Reference list of reviews) covering pharmacological and psychosocial treatments of opioid (20 reviews), alcohol (10 reviews), cocaine and other psychostimulant (11 reviews), polydrug (4 reviews), and cannabis, benzodiazepine, and metaqualone (1 review each) abuse or dependence. The effectiveness of preventive interventions across different substances was considered in four reviews.

3.2. Comprehensive search strategy to identify studies to be included in systematic reviews

The convincing evidence for the presence of several types of reporting bias demonstrates the need to comprehensively search for studies that meet the eligibility criteria for a Cochrane review. In fact, the comprehensiveness of the search affects both the validity of the review findings and the precision of the effect estimate (Clarke and Chalmers, 1998; Hopewell et al., 2009; Sterne et al., 2008). Reporting bias arises when the dissemination of research findings is influenced by the nature and direction of results. A recent review (Hopewell et al., 2009) examining the time to publication for clinical trial results, found that about half of all trials are published, and that those with positive results were published, on average, approximately 2–3 years earlier than trials with null or negative results. More recent evidence suggests that abstracts presented at the College on Problems of Drug Dependence (CPDD) conference that show negative or null results have half the likelihood of being subsequently published than those with positive findings (Vecchi et al., 2009). (The College on Problems of Drug Dependence is the longest standing group in the US

addressing problems of drug misuse. Its annual scientific meeting serves as a forum that brings together basic and clinical scientists.)

Therefore, 'positive' results that indicate an intervention works are more likely to be published, more likely to be published rapidly, more likely to be published in English, more likely to be published more than once, more likely to be published in high impact journals, and, related to the last point, more likely to be cited by others.

Cochrane reviews entail an explicit transparent search strategy to find both published or unpublished trials (Higgins and Green, 2008); for this purpose, CDAG created and maintains a specialized register of trials on the evaluation of treatment effectiveness. The studies are systematically searched in the electronic databases (MEDLINE, EMBASE, CINAHL), conference proceedings from the main conferences held in the addiction field, and trial registers of ongoing trials. We found that the process of systematically searching the literature identifies 15% of published studies that would have not been found through a non-systematic search. As of January 2010, the register contained 6971 references to studies.

3.3. Sources of studies included in the published reviews

A total of 694 studies were included in the 52 published reviews; 91% of them were found in electronic databases and the remaining 9% were conference proceedings, sections or books, thesis dissertations, or unpublished trials found looking through major conference proceedings, reference lists of retrieved studies and by contacting the authors of included studies. Although MEDLINE represents the major electronic source of included studies, roughly 15% of included studies came from other electronic sources, EMBASE and CINAHL.

Forty-seven percent of the 694 studies included were published in 12 journals, the remaining studies were published in 163 different journals (Table 1).

3.4. Study selection

The 52 reviews published by the Group considered 2059 trials for inclusion, of which only 694 (34%), with a total of 230,666 participants, satisfied the quality criteria for inclusion (Table 2). Although the inclusion criteria can vary between reviews and be attributed, in part, to the sensitivity of the search strategy, the proportion of studies that satisfy the criteria is low overall. Despite the considerable number of trials carried out on the treatment of addiction, our findings seem to confirm that only a few of them contribute to the cumulative knowledge on the effectiveness of interventions (Chalmers, 1998).

In the reviews published by the Group, only 10% were not RCTs. These studies were included in some of the reviews considering maintenance treatments for opioid dependence, and the reasons for inclusion were that they considered long-term outcomes, such as mortality, that are difficult to analyze in RCTs due to power limitations. The other non-RCT studies were included in three reviews on preventive interventions in which non-RCTs often represent the only available source of evidence. Results from these studies are considered in a separate analysis or for commentary purposes.

3.5. Assessment of quality

The extent to which a Cochrane review can draw conclusions about the effects of an intervention depends on whether the data and results from the included studies are valid. In particular, a meta-analysis of invalid studies may produce misleading results, yielding a narrow confidence interval around the wrong intervention effect estimate. Therefore, the evaluation of the validity of the included studies is an essential component of a Cochrane review and should influence its analysis, interpretation, and conclusions. Many studies have shown an association between poor study quality and the overestimation of effect (Egger et al., 1997, 2003; Hopewell, 2004; Hopewell et al., 2007; Villar et al., 1997).

Systematic reviews should evaluate and take into account the internal validity (i.e. the extent to which systematic errors or bias are avoided) of each trial included, but also the applicability and generalizability or external validity (i.e. whether the results of a trial can be reasonably applied to a definable group of patients in a particular setting in routine practice) (Dekkers et al., 2009).

3.5.1. Internal validity. The Cochrane Collaboration's recommended tool for assessing the risk of bias (Higgins and Green, 2008) in the included studies considers four domains: random sequence generation, allocation concealment, blinding (of those providing and receiving the intervention), and incomplete outcome data. Among these four domains, the allocation concealment, is historically the most frequently assessed. It implies any procedure ensuring adequate concealment of allocation, thus preventing any foreknowledge of the forthcoming allocations. As far as allocation concealment is considered, methods were not properly described in the majority of studies: 18% of the included studies reported adequate allocation concealment, in 73% allocation concealment was unclear, and in 9% it was inadequate. The proportion of included trials with documented adequate allocation concealment is lower than in other Cochrane reviews (i.e. fertility regulation, pregnancy and child birth, and health) (Helmerrhorst et al., 2006). This proportion, however, has improved over time, from 14% to 24%, for trials published before and after 1998, when the CONSORT statement on how to report the results of randomized studies was published (Moher et al., 1998).

3.5.2. External validity. The main threat to external validity comes from the clinical setting, particularly the social and cultural context in which the studies were conducted, and this is particularly true in the field of addiction, where these contexts can actively affect the overall treatment outcome. Context factors might pertain to the host organization in which an intervention is offered, such as the expertise, experience, and morale of the staff expected to carry out the intervention, the competing priorities for the staff's attention, and the local resources.

Primary studies included in these reviews were conducted in North America (68%), Europe (22%), Australia/New Zealand (5%), Asia (3%), the Middle East (1%), and South Africa (1%). The distribution, however, was heterogeneous across substances of abuse; for example, studies conducted in North America varied from 93% each for psychostimulants and polydrug abuse to 45% and 56% for alcohol and opioid dependence, respectively (Table 1).

In order to grade the quality of the evidence, the Grading of Recommendation, Assessment, Development, and Evaluation Working Group (GRADE) developed a system for grading the quality of evidence (GRADE Working Group, 2004; Guyatt et al., 2008a,b; Schünemann et al., 2006) which takes into account issues not only related to internal validity but also to external validity such as directness of results. The most recent Cochrane systematic reviews may contain a summary of findings table in which the quality of the included studies, valuated using the GRADE methodology, is incorporated to formulate a judgment of the overall quality of available evidence (Higgins and Green, 2008). The "Summary of findings' tables present the main findings of a review in a transparent and simple tabular format. In particular, they provide key information concerning the quality of evidence, the magnitude of effect of the interventions examined, and the sum of available data on the main outcomes. In the GRADE system, evidence is classified as "high" (further research is very unlikely to change confidence in the estimate of effect), "moderate" (further research is likely to have an

Table 1
Journals in which the 694 studies included in the Cochrane Drugs and Alcohol Systematic Reviews were published, January 2010.

	Journal	No. of studies published	% of studies published
1	Drug and Alcohol Dependence	75	11
2	Archives of General Psychiatry	36	5
3	Addiction	34	5
4	Journal of Substance Abuse Treatment	32	5
5	Journal of Consulting and Clinical Psychology	25	4
6	Alcoholism, Clinical and Experimental Research	18	3
7	JAMA	17	2
8	Journal of Studies on Alcohol	16	2
9	NIDA Research Monograph	16	2
10	The American Journal on Addictions	14	2
11	Addictive Behaviours	13	2
12	American Journal of Drug and Alcohol Abuse	13	2
	Total	309	44.5

The remaining 385 studies (55.5%) were published in 163 different journals.

important impact on confidence in the estimate of effect and may change the estimate), "low" (further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate), or "very low" (any estimate of effect is very uncertain). This methodology has been introduced routinely in Cochrane systematic reviews since 2008.

In the reviews in which this method was applied, the majority of the results were rated as moderate or low quality, meaning that further research may change or is likely to change the estimates.

Finally, systematic reviews could be improved in the future by improving the applicability of the results in clinical practice. Most of the methodological research efforts in the field of systematic reviews, particularly the work by the Cochrane Collaboration, have focused on the evaluation of internal validity. The results of these efforts emphasize a better consideration of internal validity in systematic reviews performed by the Cochrane Collaboration (Moher et al., 1999; Moja et al., 2005). However, evaluating the applicability of results is of similar importance. A recent article (Ahmad et al., 2010) assessed the methods and reporting of information on the applicability of trial results in systematic reviews and found that the applicability is poorly reported or taken into account. In order to ameliorate the applicability of results, in the future, authors must identify which applicability items are important (according to the type of treatment evaluated) and should be collected and reported.

3.6. Synthesis of results

The synthesis of results, when appropriate, can be done using the statistical methods of meta-analysis. A quantitative summary of results was possible in more than two-thirds of the published reviews (39/52). The most frequent reason for not pooling results is the high heterogeneity across studies (11 reviews), whereas an absence of studies or only one study being retrieved is another reason for not performing a meta-analysis (three reviews and two reviews, respectively).

3.7. Implication for practice

To measure the available evidence for each intervention evaluated in the systematic reviews, we used the classification suggested by Clinical Evidence (Enkin et al., 1998): "beneficial", effectiveness has been demonstrated by clear evidence from systematic reviews, RCTs, or the best alternative source of information, and the expectation of harm is small compared to the benefits; "likely to be beneficial", effectiveness is less well established than for those considered beneficial; "tradeoff between benefits and harm", clinicians and patients should weigh the beneficial and harmful effects according to individual circumstances and priorities; "unknown effectiveness", there is currently insufficient data or data of inadequate quality; "unlikely to be beneficial", a lack of effectiveness is less well established than for those considered as likely to be ineffective or harmful; and "likely to be ineffective or harmful", ineffectiveness or associated harm has been demonstrated by clear evidence.

In the reviews, the same intervention can often be compared with placebo or another intervention. For our purposes, we considered each comparison separately. The operative criteria used to apply the Clinical Evidence classification to the comparisons evaluated in the reviews published by our Group are as follows:

1. beneficial: all or majority of outcomes have significant positive results
2. likely to be beneficial: at least one outcome with significant positive results

Table 2
Studies included and excluded in the Cochrane Drugs and Alcohol Systematic Reviews and Country of origin of Included studies, January 2010.

Substance of abuse	No. of reviews	Total studies considered	No. of included studies (%)	No. of excluded studies	No. of participants	Asia	Australia	Europe	Middle East	North America	South Africa
Alcohol	10	479	176 (37%)	303	24733	2%	5%	44%	0	45%	4%
Opioid	20	828	239 (29%)	597	36511	5%	7%	28%	4%	56%	0
Psychostimulants	11	252	115 (46%)	137	9971	3%	3%	1%	0	93%	0
Cannabis	1	39	6 (15%)	33	1297	17%	0	0	83%	0	0
Benzodiazepines	1	40	8 (20%)	27	494	0	50%	0	50%	0	0
Metaqualone	1	0	0	0	0	0	0	0	0	0	0
Poly drugs	4	148	44 (30%)	104	19712	0	5%	2%	0	93%	0
Prevention	4	279	112 (40%)	167	1385557	1%	4%	4%	0	91%	0
Total[a]	52	2059[a]	694[a] (34%)	1368	230666[a]	3%	5%	22%	1%	68%	1%

[a] Six studies included and in common between opiate, psychostimulants, alcohol or poly drugs were counted once.

Table 3
Interventions and comparisons proved to be beneficial or likely to be beneficial, in the published reviews, January 2010.

Substance of abuse considered	Outcomes and measure of the effect (CI 95%)
Alcohol	
Naltrexone versus placebo	Discontinuation rate RR 0.82 (0.70, 0.97); number of participants who return to heavy drinking RR 0.64 (0.51, 0.82)
Benzodiazepines versus placebo	Alcohol withdrawal seizures RR 0.16 (0.04, 0.69)
Anticonvulsants + other versus other	Life-threatening side effects RR 0.12 (0.03, 0.44)
GHB versus diazepam for withdrawal	CIWA-Ar scores for tremor SMD −0.85 (da −1.30 a −0.40) and agitation SMD −0.54 (da −0.97 a −0.11)
GHB versus naltrexone for maintaining abstinence	Number of subjects abstinent RR 2.59 (da 1.35 a 4.98)
Brief intervention versus control in primary care:	Quantity of drinking (g/week) WMD −41.40 (−57.30, −25.50); Binge drinkers RD −0.15 (−0.21, −0.08); Loss to follow up RD 0.04 (0.01, 0.07)
Brief intervention versus control in general hospital wards	Mean alcohol consumption/week change scores from baseline at 1 year follow up WMD −0.18 (−0.33, −0.03)
Opioid maintenance treatments	
Methadone maintenance treatment (MMT) versus no MMT	Retention in treatment old studies RR 3.05 (1.75, 5.35); retention in treatment new studies RR 4.44 (3.26, 6.04); morphine positive urines or hair analysis RR 0.66 (0.56, 0.78)
MMT 60–109 mg versus 40–59 mg day	Retention at 27–40 weeks RR 1.23 (1.05, 1.45)
MMT 60–109 mg versus 1–39 mg day	Retention at 17–26 weeks RR 1.36 (1.13, 1.63); use of opiate (abstinent >3–4 weeks) RR 1.59 (1.16, 2.18); use of cocaine (abstinent >3–4 weeks) RR 1.81 (1.15, 2.85)
MMT high dose versus middle	Leaving treatment (follow up 12–24 months) RR 0.68 (0.51, 0.89)
MMT middle dose versus low	Leaving treatment (follow up 12–24 months) RR 0.57 (0.48, 0.67)
MMT high dose versus low	Leaving treatment (follow up 12–24 months) RR 0.35 (0.27, 0.45)
Low dose buprenorphine versus placebo	Retention in treatment RR 1.50 (1.19, 1.88)
Medium dose buprenorphine versus placebo	Retention in treatment RR 1.74 (1.06, 2.87); morphine positive urines SMD −0.28 (−0.47, −0.10)
High dose buprenorphine versus placebo	Retention in treatment RR 1.74 (1.02, 2.96); morphine positive urines SMD −1.23 (−1.95, −0.51)
Comparison before and after substitution treatment to prevent HIV infection	Proportion reporting injecting use RR 0.45 (0.35, 0.59); overall risk assessment RR 0.74 (0.68, 0.81)
Naltrexone versus placebo	Use of heroin RR 0,72 (0.58, 0.90)
Any psychosocial plus pharmacological versus pharmacological standard	Abstinent at follow up RR 1.15 (1.01, 1.32)
Any behavioural plus pharmacological versus pharmacological standard	Continuous week of abstinence SMD +1.91 (+0.20, +3.62)
Opioid treatments aimed at detoxification	
Methadone versus placebo	Completion of treatment RR 1.95 (1.25, 8.91)
Buprenorphine versus clonidine	Completion of treatment RR 1.64 (1.31, 2.06); mean days in treatment SMD 0.92 (0.57, 1.27); mean overall withdrawal score SMD −0.59 (−0.79, −0.39)
Adrenergic agonists versus placebo	Completion of treatment RR 1.90 (1.28, 2.81)
Any psychosocial + any pharmacological versus pharmacological alone	Completion of treatment RR 1.68 (1.11, 2.55); use of opiate RR 0.82 (0.71, 0.93); abstinent at follow up RR 2.43 (1.61, 3.66)
Any psychosocial + methadone versus methadone alone	Abstinent at follow up RR 2.46 (1.61, 3.76); compliance (no. of absences) RR 0.48 (0.38, 0.59)
Contingency management + methadone versus methadone alone	Compliance (no. of absences) RR 0.29 (0.15, 0.56)
Contingency management + buprenorphine versus buprenorphine alone	Use of opiate RR 0.47 (0.25, 0.86)
Psychostimulants: cocaine	
Risperidone versus placebo	Dropout RR 0.77 (0.61, 0.98)
Disulfiram versus no pharmacological treatment	Use of cocaine as weeks of continuous abstinence) MD 2.10 (0.69, 3.51) and as number of subjects with 3 or more weeks of continuous abstinence RR 1.88 (1.09, 3.23)
CBT + contingency versus CBT + bonus	Use of cocaine (at least 5 consecutive weeks) RR 0.51 (0.36, 0.71)
Psycho stimulants: amphetamines	
Any pharmacological versus placebo for withdrawal syndrome	Discontinuation rate RR 0.52 (0.29, 0.94); global state WMD −0.27 (−0.54, −0.01)
Amineptine versus placebo for withdrawal syndrome	Discontinuation rate RR 0.22 (0.07, 0.70); average score in global state WMD −0.54 (−0.82, −0.26)
Poly abuse	
Interventions for drug using offenders in the Courts: drug testing & sanctions versus routine	Arrests at 90 days OR 1.33 (1.04, 1.70)
Prevention	
Interventions in school setting: Skills versus usual curricula	Decision making skills SMD +0.78 (+0.46, +1.09); self-esteem SMD +0.22 (+0.03, +0.40); cannabis use RR 0.82 (0.73, 0.92)
Interventions in school setting: Affective versus usual curricula	Drug knowledge SMD +1.88 (+1.27, +2.50); decision making skills SMD +1.35 (+0.79, +1.91)
Interventions in school setting: Affective versus knowledge	Drug knowledge SMD +0.60 (+0.18, +1.03); decision making skills SMD +1.22 (+0.33, +2.12)
Interventions in school setting: Knowledge versus usual curricula	Drug knowledge WMD +0.91 (+0.42, +1.39)
To reduce alcohol misuse in University or College students: social norms web feedback versus control	Alcohol related problems up to 3 months SMD −0.31 (−0.59, −0.02); peak blood alcohol content up to 3 months SMD −0.77 (−1.25, −0.28); drinking frequency up to 3 months SMD −0.38 (−0.63, −0.13); quantity of drinking up to 3 months SMD −0.29 (−0.50, −0.09); drinking norms up to 3 months SMD −0.75 (−0.98, −0.52); alcohol related problems 4–16 months SMD −0.26 (−0.45, −0.07); drinking frequency 4–16 months SMD −0.31 (−0.49, −0.13); drinking norms 4–16 months SMD −0.59 (−1.02, −0.17); quantity of drinking gender specific SMD −0.45 (−0.86, −0.05); drinking norms gender specific SMD −0.95 (−1.33, −0.57)
To reduce alcohol misuse in University or College students: social norms mailed feedback versus control	Quantity of drinking gender specific SMD −0.51 (−0.92, −0.09)
To reduce alcohol misuse in University or College students: social norms individual face to face feedback versus control	Drinking frequency up to 3 months SMD −0.39 (−0.66, −0.12); binge drinking up to 3 months SMD −0.25 (−0.49, −0.02); alcohol related problems 4–16 months SMD −024 (−0.42, −0.07); drinking frequency 4–16 months SMD −0.26 (−0.26, −0.08)
To reduce alcohol misuse in University or College students: social norms group face to face feedback versus control	Quantity of drinking up to 3 months SMD −0.32 (−0.63, −0.02); binge drinking up to 3 months SMD −0.38 (−0.62, −0.14)

RR = relative risk; RD = risk difference; SMD = standard mean difference; WMD = weighted mean difference; MD = mean difference. The confidence interval (CI) was of 95%.

3. tradeoff between benefits and harm: mixed (positive and negative) results
4. unknown effectiveness: no meta-analysis
5. unlikely to be beneficial: no significant result
6. likely to be ineffective or harmful: at least one outcome with significant negative results or a clear excess of side effects (qualitatively reported or RR > 2).

Based on these criteria, for the 142 comparative interventions considered, 41 (29%) were beneficial or likely to be beneficial for at least one of the outcomes considered in the review, 3 (2%) were a tradeoff between benefits and harms, 45 (32%) had unknown effectiveness, 46 (32%) were unlikely to be beneficial, and 7 (5%) were likely to be ineffective or harmful. These proportions varied according to the type of substance of abuse studied; for example, the interventions that were found to be beneficial or likely to be beneficial were 37% for alcohol, 42% for opioids, 17% for psychostimulants, 7% for polydrugs, and 33% for prevention.

Table 3 lists the interventions that were found to be beneficial or likely to be beneficial according to the type of substance abuse considered in the published reviews and the outcomes for which the various measures of the effect were significant in favor of the treatment considered.

These results should be considered cautiously, remembering that they referred only to interventions, comparisons, and outcomes considered in the studies included in the reviews, and we are aware that the evidence presented is not thorough and definitive. Furthermore, the assessment of the methodological quality of included studies showed relevant weaknesses in the information available to judge their quality. Also, the results have come mostly from RCTs evaluating the efficacy in a specific research setting and not the effectiveness in the clinical practice, this point can be taken into consideration when judging the overall quality of the evidence.

Nevertheless, the results of the reviews can represent a useful and valuable source of material to inform clinical practice. Furthermore, the availability of systematic reviews that provide evidence of effectiveness might represent a valuable source of material to be used in the process of producing national guidelines by reducing the need for many different countries to repeat the same reviews with a substantial duplication of work and waste resources. In recent years, Cochrane systematic reviews have been used extensively in the process of developing guidelines by international and national organizations (WHO, 2009; NICE, 2006; Australian National Drug Strategy, 2006; Prodigy, 2005).

The purpose of Cochrane reviews is to facilitate healthcare decision making by patients and the general public, clinicians, administrators, and policy makers. A clear statement of findings, a considered discussion, and a clear presentation of the authors' conclusions are important parts of the review. In particular, the following issues can help people make better informed decisions and increase the usability of Cochrane reviews: information on all important outcomes, including adverse outcomes; the quality of the evidence for each of these outcomes as it applies to specific populations and specific interventions; and clarification of the manner in which particular values and preferences may bear on the balance of the benefits, harms, burden, and costs of the intervention.

3.8. Implication for research

One of the aims of an international collaboration among a group of researchers is to promote valid evidence and shape future research in directions where specific questions that arise from the systematic collation of existing work informs future research directions. The need for further research can be divided into two broad categories: the need for further systematic reviews and the need for further primary research.

Cochrane reviews include a section on the implication for research in which the authors provide suggestions on how to improve the quality or respond to gaps in primary research. In an effort to summarize these implications, a scale was developed by Clarke et al. (2007), and the results show that, regarding our reviews, 74% report specific types of interventions and outcomes that should be prioritized in future studies, 5% concluded that no more research was needed, and 21% did not make any recommendations regarding future research.

Our findings suggest that there is substantial room for improvement in the area of primary research, both in terms of the quality of reporting and the quality of conduct. The quality of reporting has improved in recent years; the use of the CONSORT statement has had an effect among general journals (Moher et al., 2001), but more effort is required by specialist journals to incorporate CONSORT, considering that roughly 50% of the studies included in our reviews were published in only ten journals, out of which five have adopted CONSORT guidelines.

To obtain results that permit a cumulative synthesis and, above all, have results of high quality that can allow clinical choices, the new studies should enroll a large number of participants (at least 400) and consider a few important outcomes related to the efficacy, safety, and acceptability of the considered interventions. Furthermore, for some outcomes usually assessed with scales, such as withdrawal syndrome, consistency in rating continuous outcomes on the same scales should also be achieved in order to obtain comparable information from all relevant studies. Moreover, comparative effectiveness studies and studies that assess the effectiveness of preventive public health campaigns are needed.

3.9. Updating the results

Systematic reviews that are not maintained may become out of date or misleading, thus the availability of updated summaries of evidence is relevant; a previous study (Shojania et al., 2007) showed that the median duration of survival of a systematic review, free of new relevant studies requiring updating, is 5.5 years since publication, though this time was shorter in some cases: only 4/52 of our reviews were outdated more than 5 years.

4. Conclusions and future developments

Considering the drug and alcohol field, Cochrane systematic reviews seem to meet their primary aim, providing independent reviews of evidence on the effectiveness of treatments and identifying underlying areas of uncertainty. The reviews also identify a wide range of interventions unlikely to be beneficial, and even likely to be ineffective or harmful. Eventually, Cochrane reviews provide useful results to guide clinicians in choosing treatment and assist in the process of developing evidence-based guidelines, particularly in the area of opioid dependence and alcoholism.

Even though Cochrane systematic reviews are a valuable resource for those who have to produce clinical guidelines, they should also be considered as a tool to inform the research agenda in terms of setting priorities, identifying areas of uncertainty, and promoting multicenter high quality studies addressing questions that contribute to progressing knowledge on the effectiveness and safety of treatment and, consequently, meet the needs of patients, their care givers, and policy makers.

Cochrane reviews seem to have, on average, better methodological quality than other systematic reviews (Jørgensen et al., 2008; NICE, 2006); the costs of maintaining such a high quality standard might discourage some authors from attempting to conduct a Cochrane review. However, there is an added value in publishing them, particularly, an impact factor as been recently assigned to the Cochrane Database of Systematic Reviews, which, since 2010,

moved from quarterly to monthly publication. In 2009, the Collaboration launched a new feature, Cochrane Journal Club, a free, online instrument to introduce recent Cochrane reviews. Finally, support for new authors, such as training materials and learning resources, are freely available.

While judging quality is relatively easy, evaluating relevance of systematic reviews is more challenging. Same authors have criticized the Cochrane Library for publishing irrelevant reviews (Lang et al., 2007; Mandel et al., 2006; Pagliaro et al., 2010). A recent strategic review of the Cochrane Collaboration (http://ccreview.wikispaces.com) has established a strategy to prioritize Systematic Reviews .In the future, our efforts will concentrate on prioritizing the publication of reviews that are likely to generate considerable interest in the international public health community, have the potential to change policy or treatments, and are of public interest. Updating the existing relevant reviews is another challenge as well.

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Contributors

Laura Amato and Marina Davoli wrote the first draft of the manuscript. All the authors contributed to and have approved the final manuscript.

Conflict of interest

All authors declare that they have no conflict of interest pertaining to the manuscript.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.drugalcdep.2010.08.003.

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