



EMCDDA PAPERS

How can contingency management support treatment for substance use disorders? A systematic review

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Abstract: Contingency management (CM) is a general behavioural intervention technique used in the treatment of drug dependence to systematically arrange consequences and it is designed to weaken drug use and strengthen abstinence.

The main elements of CM interventions are behavioural reinforcers and monitoring, which aim to promote social reintegration by sustaining compliance, abstinence and/or attendance at work.

We performed a systematic review of studies on the effectiveness of CM alongside pharmacological treatment of dependence.

We included 38 studies on opioid users ($n = 20$), cocaine users in methadone therapy ($n = 14$), cocaine users ($n = 3$) and methamphetamine users ($n = 1$). We found that CM was useful for reducing drug use among cocaine users and opioid users in substitution treatment for reducing and abstaining from cocaine use. In opioid detoxification, CM increased retention in

treatment and improved abstinence. In terms of the cost-effectiveness of CM, the evidence is not strong enough to recommend its systematic implementation.

We included three studies on the economic analysis with evidence for cost-effectiveness analysis: one review (based upon nine published studies) and two additional studies. The review confirms that evidence for cost-effectiveness has limited generalisability beyond original research.

Our limited analysis shows that CM is a feasible and promising adjunct to treatment interventions for drug users.

Keywords **treatment of drug use**
contingency management
systematic review

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Background

Description of the interventions

Contingency management (CM) is a general behavioural intervention technique used in the treatment of drug dependence that aims to alter drug use by systematically arranging consequences; this technique is designed to weaken drug use and strengthen abstinence (Griffith et al., 2000).

CM is one key element of a broader behavioural approach belonging to the theory of operant conditioning (West, 2013). Operant conditioning assumes that individuals are conditioned by the consequences of their behaviour. Pleasant consequences reinforce some behaviours and punishment discourages them. This model originates from the experiments of Burrhus Frederic Skinner (1938) on learning processes in animals, in which he noticed that behaviours that are not reinforced are easily abandoned.

Various techniques are derived from operant conditioning theory, including techniques to shape the behaviour of pupils in the classroom (Altman and Linton, 1971), psychiatric hospital inpatients (in particular through the *token economy* system (Ayllon and Azrin, 1968)) and drug users (Weaver et al., 2014).

In drug addiction studies, operant conditioning theory has implications for the explanation of the development of addiction and for the strategies used to prevent it and to promote recovery (West, 2013).

The main elements of CM interventions are targeted contingency, behavioural reinforcers and monitoring. The ultimate goal of CM is to promote social reintegration by sustaining compliance, abstinence and/or attendance at

work. Reinforcers are benefits, which can be cash, vouchers, prizes or other kinds of perceived privileges, such as taking home doses of methadone (Higgins et al., 2004; Petry, 2000; Stitzer and Petry, 2006). The patient will gain or lose reinforcers according to whether he/she can consistently and regularly achieve the expected outcomes or not. The duration of the CM intervention can vary. For example, we found that descriptions of interventions ranged from 8 weeks (Petry, 2000) to 52 weeks (Silverman et al., 2004). CM has been used in many types of addictive behaviour. It has been extensively used in different substance use disorders, such as problematic use of marijuana (Stanger et al., 2009), opioids (Chopra et al., 2009) and cocaine (Barry et al., 2009; Silverman et al., 2004), as well as in nicotine dependence (Yi et al., 2008), methamphetamine use disorders (Roll et al., 2006), alcohol dependence (Petry, 2000) and polydrug abuse (Silverman et al., 2002).

For the treatment of substance use disorders, CM is provided, for example, in detoxification clinics, psychosocial counselling services and methadone maintenance programmes (Stitzer and Petry, 2006).

CM approaches, whereby rewards (e.g. cash, vouchers, prizes or other privileges such as therapy delivered at home) are contingent on successfully performing a particular activity (e.g. getting a job, providing a substance-negative urine sample, participating in a screening) (Figure 1) showed some promising results for substance-dependent patients in the USA. Their application might raise particular ethical concerns in the EU (EMCDDA, 2012); nevertheless, the UK National Institute for Health and Care Excellence (NICE) (Table 1) recommends that CM should be applied and assessed in routine clinical practice in the UK, identifying specific targets for application, such as increasing patients' compliance with testing for infectious diseases (Weaver et al., 2014).

FIGURE 1

Targets and possible use of contingency management along the treatment journey

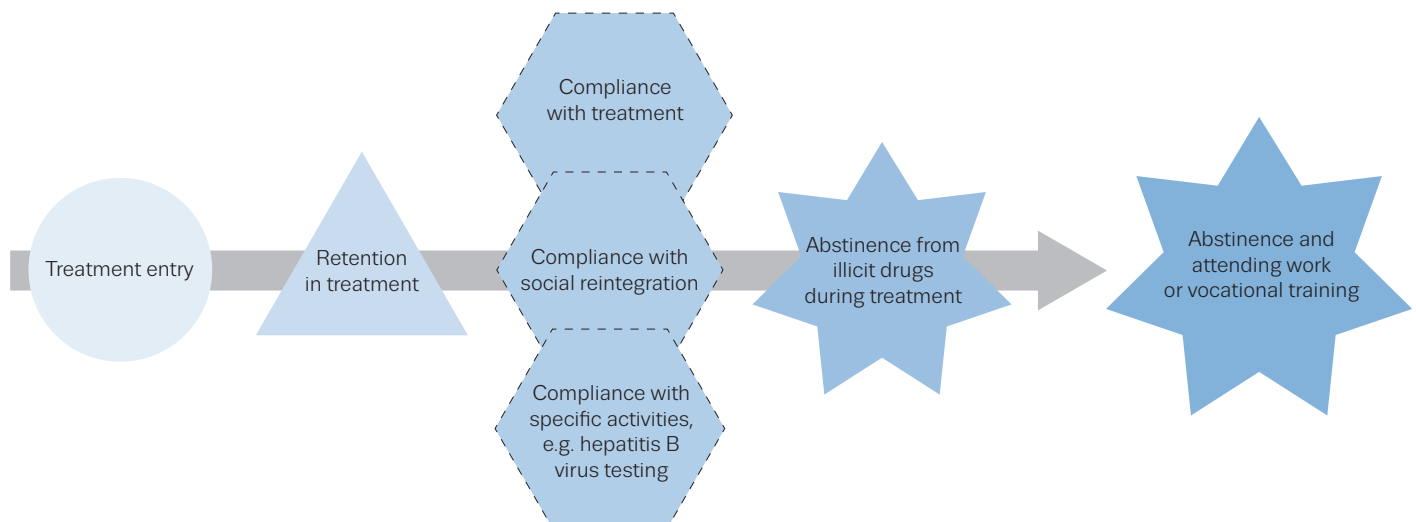


TABLE 1

Examples of resources used to deliver and implement contingency management interventions

Country	Resource	Website
International	WHO 'Guidelines for identification and management of substance use and substance use disorders in pregnancy' (mentions CM)	http://www.who.int/substance_abuse/publications/pregnancy_guidelines/en/ (date of publication: 2014)
UK	The Public Health England website has a collection of resources to implement CM	http://www.nta.nhs.uk/CM%20Page.aspx (accessed November 2015)
UK	NICE Guideline No 120, 'Psychosis with substance misuse' (mentions CM)	https://www.nice.org.uk/guidance/cg120 (date of publication: 2011)
USA	'Medication-assisted treatment for opioid addiction in opioid treatment programs' (mentions CM)	http://store.samhsa.gov/shin/content/SMA12-4214/SMA12-4214.pdf (date of last edition 2014)

How the interventions may work

It has been noted that 'reinforcement processes play a central role in the genesis, maintenance, and recovery from substance use disorders' (Higgins et al., 2004). CM is supposed to interfere with the drug-related reinforcement cycle by introducing a competitive source of rewarding (Higgins et al., 2004; Stitzer and Petry, 2006). When the reinforcement power of the incentives prevails over the effect of the abused drugs, human behaviour consequently should change. During the process of continuous rehabilitation, CM interventions help to decrease the sensitivity of drug users to substance-related environments (Stitzer and Petry, 2006).

Why is this review important?

Many studies (including systematic reviews and meta-analyses) have been published on the use of CM for substance use disorders (Barry et al., 2009; Benishek et al., 2014; Chopra et al., 2009; Farronato et al., 2013; Griffith et al., 2000; Prendergast et al., 2006; Petry, 2000; Petry and Simcic, 2002; Petry et al., 2010; Schierenberg et al., 2012), with a focus on the effectiveness of the CM application and generalisation.

Several Cochrane systematic reviews have assessed the efficacy of psychosocial interventions, which also include CM for substance use disorders (Amato et al., 2011a,b; Denis et al., 2013; Knapp et al., 2007; Lui et al., 2008; Mayet et al., 2014). However, these reviews included studies on a specific substance of abuse and dependence, assessing the effects of CM in combination with other psychosocial interventions.

A protocol of a Cochrane review has been published on this topic, but results are not yet available (Pan et al., 2012).

CM can be a suitable intervention to support the social reintegration of patients; nevertheless, a comprehensive review of the available studies is needed to enable decision-making. This review should also consider the economic aspect to determine if CM would add sufficient value to justify its costs.

Objectives

The objectives of this review are:

- to assess the effectiveness of the CM approach in combination with substitution treatment or detoxification for drug-dependent people by assessing whether or not there is an increase in the retention of patients in treatment, in patients achieving abstinence or reducing their use of substances, in patients' participation in screening programmes for the detection of human immunodeficiency virus (HIV) and hepatitis B and C virus infection, and in patients' participation in hepatitis B virus vaccination programmes;
- to provide an updated synthesis of the studies on the costs and cost-effectiveness of CM interventions for drug users.

Methods**Inclusion criteria****Types of studies**

We included published articles with the objective of evaluating the effectiveness of CM in treating drug use addiction that were based on randomised clinical trials and quasi randomised controlled trials and studies that looked at the costs associated with implementing these CM interventions.

A particular CM intervention used for treating drug use can be considered economically efficient if its monetary benefits exceed its monetary costs. The most succinct measure of economic efficiency is the cost-benefit ratio, which is a measure of the benefit derived from the investment of a single monetary unit. Cost-effectiveness studies provide the cost information of an option in monetary terms and the outcomes in non-monetary terms. The most usual outcome measure used in cost-effectiveness studies on the treatment of drug use addictions is reductions in use or abstinence. Treatment retention, treatment compliance and mental health status are also considered, as secondary outcomes.

We excluded non-empirical articles; specifically narrative literature reviews and commentaries were excluded.

Types of participants

Adult (≥ 18 years old) individuals that were dependent (according to DSM-IV (the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders) or ICD 10 (the 10th edition of the International Statistical Classification of Diseases and Related Health Problems)) on any illicit substance (opioids, cocaine, amphetamine/methamphetamines, marijuana) or patients with polysubstance dependence were included; patients with tobacco and/or alcohol dependence only were excluded.

Types of interventions

The experimental intervention was CM in combination with any pharmacological treatment (opioid substitution treatment (OST), detoxification). The control intervention was any pharmacological treatment without CM.

Types of outcomes

The primary outcomes were patients' retention in treatment, use of the main substance of abuse (based on self-reported data and urine analysis or other biochemical markers), monetary units, cost–benefit ratios, cost-effectiveness ratios, incremental cost-effectiveness ratios (ICERs) and acceptability curves.

The secondary outcomes were the use of other substances (based on self-reported data and urine analysis or other biochemical markers), relapse prevention, participation in screening programmes for HIV, hepatitis B and C virus infections, overall mortality and overdoses.

Search strategy

Electronic searches for the identification of studies

We searched the following electronic databases when looking for studies about the effectiveness of CM:

- Cochrane Drugs and Alcohol Group's specialised register of trials (September 1998 to September 2014);
- Cochrane Central Register of Controlled Trials (CENTRAL; The Cochrane Library, September 2014);
- PubMed (January 1966 to September 2014);
- EMBASE (embase.com) (January 1974 to September 2014);

- CINAHL (EbscoHOST) (1982 to September 2014);
- ISI Web of Science (September 2005 to September 2014).

We searched these databases using MeSH and free-text terms relating to substance use disorders and CM. We combined the PubMed search with the Cochrane Highly Sensitive Search Strategy for identifying randomised trials in MEDLINE: sensitivity maximising version (2008 revision) (Lefebvre et al., 2011). Detailed search strategies were developed for each database used, accounting for differences in controlled vocabulary and syntax rules. The detailed search strategies are shown in Annex 1.

We searched the following electronic databases when looking for studies on costs and cost efficiency:

- Cochrane Drugs and Alcohol Group's specialised register of trials;
- Cochrane Central Register of Controlled Trials (CENTRAL; The Cochrane Library, most recent issue);
- MEDLINE (2000 onwards);
- PubMed;
- British Library 'on demand';
- EconLit;
- NHS Economic Evaluation Database;
- ResearchGate.

We searched these databases using MeSH and free-text terms relating to substance use disorders and CM. Detailed search strategies were developed for each database used, accounting for differences in controlled vocabulary and syntax rules. Since the structure of costs changes considerably over time, it was considered of limited relevance to look for articles published before 2000. We also searched reference lists, but of previously identified materials.

Searching other resources

We searched:

- the reference lists of all relevant papers to identify further studies;
- some of the main electronic sources of ongoing trials (including the World Health Organization (WHO) International Clinical Trials Registry Platform (www.who.int/ictrp) and; the UK Clinical Trials Gateway (<https://www.ukctg.nihr.ac.uk/>);
- conference proceedings that were likely to contain trials relevant to the review (e.g. of the College on Problems of Drug Dependence (CPDD));
- national focal points for drug research (e.g. the National Institute of Drug Abuse (NIDA) and the National Drug and Alcohol Research Centre (NDARC)).

Authors of included studies and experts in the field in various countries were contacted to find out if they knew of any other published or unpublished controlled trials. No language restrictions were applied.

Data collection and analysis

Selection of studies

Two authors independently screened titles and abstracts of studies obtained by the search strategy and agreed on the preliminary selection. The full-text version of each potentially relevant study located in the search was obtained and assessed for inclusion independently by two authors. In the case of disagreement, a third author was consulted.

Data extraction and management

Data were extracted independently by two authors. Any disagreement was discussed and solved by consensus.

Assessment of the risk of bias in included studies

The assessment of the risk of bias for randomised controlled trials and controlled clinical trials in this review was performed by two authors independently using the criteria recommended by the Cochrane Handbook (Higgins et al., 2011).

Data synthesis

We planned to combine the results of studies in a meta-analysis, provided the interventions and outcomes were comparable, using a random effect model. The random effect model considers heterogeneity (differences) among included trials. However, the included studies were not comparable and did not provide sufficient details to be pooled in a meta-analysis. We therefore limited the analysis to counting the number of studies with statistically significant results for each outcome considered.

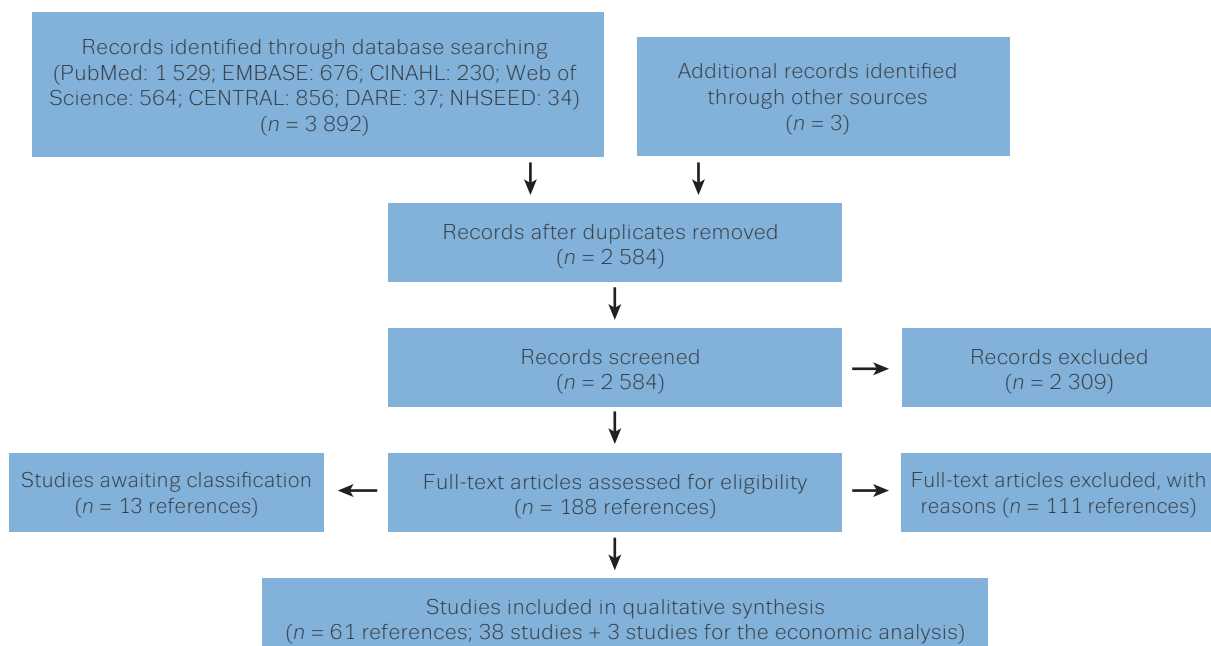
Measures of treatment costs

A particular intervention could be considered economically efficient if its monetary benefits exceed its monetary costs. Unit costs, cost–benefit ratios, cost-effectiveness ratios, ICERs and acceptability curves were used to evaluate costs and the relative cost-effectiveness of interventions.

There are currently no agreed-upon methods for pooling combined estimates of cost-effectiveness (e.g. ICERs, cost–utility ratios, cost–benefit ratios), extracted from multiple economic evaluations, using meta-analysis or other quantitative synthesis methods. However, if estimates measure costs in a common metric, these can be pooled using a meta-analysis. However, extreme caution is required and, prior to any decision to pool estimates using a meta-analysis, particular attention should be given to whether or not the metric in question has equivalent meaning across studies.

FIGURE 2

Flow chart of study assessment and selection



Economic evaluation tools for health interventions

The pursuit of efficiency in the healthcare sector requires that priority be given to those treatments that provide the greatest benefits per unit of cost. Different approaches have been used to assess the benefits and costs of health interventions. Here, some of the methods used to compare costs with benefits of health interventions are described.

Cost-benefit analysis is a method of comparing the costs and the (money-valued) benefits of various courses of action. It entails systematic comparisons of all the relevant costs and benefits of the proposed alternative schemes, with a view to determining (a) which scheme, or size of scheme, or combination of schemes, maximises the difference between the benefits and the costs, or (b) the magnitude of the benefit that can result from schemes having various costs.

Cost-effectiveness analysis is a method of comparing the opportunity cost of various courses of action that have the same benefit or comparing alternatives. Benefits are normally quantified as health outcomes and measured, for instance, in natural units such as life years saved or improvements in functional status (e.g. blood pressure). This approach is used when benefits are difficult to value monetarily. It has similarities with cost–benefit analysis, but the benefits, instead of being expressed in monetary terms or as several non-commensurable benefits, are expressed in terms of a homogeneous index of health results achieved, for instance measured in terms of related deaths. Therefore, as cost and benefits are measured in non-comparable units, their ratios provide a yardstick of the relative efficiency of alternative interventions. A major limitation of a cost-effectiveness analysis is its inability to compare interventions with different natural effects.

Cost-utility analysis is an adaption of cost-effectiveness analysis that measures benefits using a utility-based measure such as quality-adjusted life years (QALYs). QALYs provide a common currency for measuring the extent of health gains that result from healthcare interventions. The health gain is measured by the number of years of life that would be added by each intervention (life expectancy) and the quality of life that each person assesses that each healthcare intervention provides. NICE defines the QALY as a ‘measure of a person’s length of life, weighted by a valuation of their health-related quality of life’.

The **incremental cost-effectiveness ratio (ICER)** is the ratio between the difference in cost between one therapeutic and another and their difference in benefits:

$$\text{ICER} = (C1 - C2) / (E1 - E2)$$

where C1 and E1 are the cost and effect, respectively, of the intervention or treatment group and where C2 and E2 are the cost and effect, respectively, of the control group. Costs are usually described in monetary units, while benefits or the effect on health status are frequently measured in terms of QALYs.

The best-known institution that has adopted the ‘incremental cost-effectiveness ratio’ evaluation criteria is NICE, UK.

Sources: Appleby, 2016; Culyer, 2005; National Institute for Health and Care Excellence, 2007.

Results

Results of the bibliographic search

After removing duplicates, a total of 2 584 records were retrieved; 275 titles were judged as potentially relevant (Figure 2). They were grouped according to their types of participants as follows: opioid-dependent patients, cocaine-dependent patients, patients dependent on opioids and/or cocaine, cannabis-dependent patients, stimulant-dependent patients and polysubstance-abusing or -dependent patients. Given the huge number of potentially relevant records identified, we acquired the full-text version of 185 records for more detailed evaluation and inclusion in our review, including those on opioid-dependent patients, cocaine-dependent patients, patients dependent on both opioids and cocaine, cannabis-dependent patients and stimulant-dependent patients; we did not consider the studies on polysubstance-abusing patients, which will be analysed in a further review.

Results are presented separately for the five types of participants considered. Details of studies are available in Annex 1.

Cannabis-dependent patients

The full-text versions of 12 articles related to seven studies were acquired; all were excluded because none of them assessed the effectiveness of the CM approach in addition to a substitution or detoxification pharmacological treatment compared with pharmacological treatment alone (i.e. the inclusion criteria); the effectiveness of CM without pharmacological interventions has been studied in a previous publication (EMCDDA, 2015). See the references of the excluded studies on cannabis-dependent patients.

Stimulant-dependent patients

The full-text versions of 16 articles were acquired and one study (two articles) was included (Huber et al., 2001; Shoptaw et al., 2006), which included 229 methamphetamine-abusing or -dependent patients randomised to receive sertraline plus CM ($n = 61$), sertraline only ($n = 59$), matching placebo plus CM ($n = 54$) or matching placebo only ($n = 55$). The CM intervention was given to patients with negative urine for methamphetamine metabolites. A voucher was given to patients in the CM intervention for their initial metabolite-free sample, which was worth USD 2.50, and this increased in value by USD 1.25 for each consecutive metabolite-free sample. Each third consecutive metabolite-free sample earned a USD 10.00 bonus voucher. This study was conducted in the USA.

Effect of interventions

This study did not report data on patients' retention in treatment, but patients in the CM intervention used less methamphetamine.

Cocaine-dependent patients

The full-text versions of 50 articles were acquired. Only three studies (five articles) were included (Jones et al., 2001, 2004; Schmitz et al., 2006, 2008, 2009), which, in total, enrolled 447 patients who met the criteria for cocaine dependence (Jones et al., 2004; Schmitz et al., 2008, 2009). Patients included in the Schmitz et al. (2009) study were also dependent on alcohol; the mean age in this study was 37 years and 76 % of the participants were male.

Jones et al. (2004) assessed the efficacy of tryptophan compared with placebo, both with and without CM. Schmitz et al. (2008) assessed the efficacy of levodopa compared with placebo, with or without CM or cognitive behavioural therapy (CBT), and Schmitz et al. (2009) assessed the efficacy of naltrexone compared with placebo, with or without CM.

The CM intervention was the same in all of the studies: patients were rewarded for having urine sample negative for cocaine metabolites. The voucher for the initial metabolite-free sample was worth USD 2.50 and increased in value by USD 1.25 for each consecutive metabolite-free sample. Each third consecutive metabolite-free sample earned a USD 10.00 bonus voucher.

All three studies were conducted in the USA.

Effect of interventions

All of the studies assessed patients' retention in treatment. None of the studies found significant differences between groups.

All of the studies assessed the mean percentages of urine positive or negative for cocaine metabolites; two of the three studies reported statistically significant results in favour of CM.

All the studies assessed continuous abstinence; two of the three studies reported statistically significant results in favour of CM.

Patients dependent on cocaine and opioids

The full-text versions of 41 articles were acquired after being judged to be potentially relevant, and 14 studies (23 articles) were included (Jones et al., 2001; Kosten et al., 2003; Oliveto et al., 2005; Petry and Martin, 2002; Petry et al., 2005,

Poling et al., 2006; Rawson et al., 2002; Rowan-Szal et al., 2005; Silverman et al., 2004, 2007a,b; Umbricht et al., 2014; Winstanley et al., 2011). Three studies were classified as awaiting classification because only conference proceedings with incomplete information were retrieved. In total, the 14 included studies enrolled 1 550 patients who met criteria for both cocaine and opioid dependence.

All the studies assessed the effectiveness of CM in addition to standard care (methadone maintenance plus counselling in all but two studies: in Kosten et al. (2003), buprenorphine maintenance was provided and, in Oliveto et al. (2005), LAAM maintenance at doses of 30 mg and 100 mg were provided). Four studies also assessed the efficacy of the addition of a pharmacological treatment: desipramine in Kosten et al. (2003), bupropione in Poling et al. (2006), topiramate in Umbricht et al. (2014) and fluoxetine in Winstanley et al. (2011). Two studies also assessed the effectiveness of two different amounts of monetary reinforcement (Petry et al., 2007, 2014).

CM intervention differed among studies: in five studies, the CM was based on negative results in urine for cocaine alone (Petry et al., 2007; Rowan-Szal and Simpson, 2003; Silverman et al., 2007 a, b; Umbricht et al., 2014; Winstanley et al., 2011); in four studies it was based on negative results in urine for cocaine and opioids (Kosten et al., 2003; Oliveto et al., 2005; Petry and Martin, 2002; Poling et al., 2006); in one study it was based on negative results in urine for cocaine and alcohol (Petry et al., 2014); and, in Silverman et al. (2004), the CM of taking home methadone was based on negative results in urine for cocaine and opioids, whereas vouchers were based on negative results in urine for cocaine alone. In three studies (Jones et al., 2001; Petry et al., 2005; Rowan-Szal et al., 2005), the CM was based on negative results in urine for cocaine and attending a counselling session or achieving other individualised treatment goals. All but one study (Silverman et al., 2007a,b) gave vouchers or prizes with monetary values; in only one arm of the Silverman et al. (2004) study was the premium CM the taking home of methadone. In Silverman et al. (2007 a,b), the premium CM consisted in the possibility of continuing to work and earn money, while the control group had access to the therapeutic workplace irrespective of urine analysis results.

All of the studies were conducted in the USA.

Effect of interventions

All but two studies (Petry et al., 2014; Rowan-Szal et al., 2005) assessed patients' retention in treatment. Only 1 out of these 12 studies found a significant difference in favour of CM. Winstanley et al. (2011) reported that significantly more patients dropped out from the fluoxetine without CM group compared with the other three groups.

All but one study (Petry et al., 2007) assessed the mean percentages of positive or negative results in the urine for cocaine metabolites. Of these, 10 out of 13 studies reported statistically significant results in favour of CM. In Petry et al. (2014), the results were statistically significant for the group with higher monetary reinforcement only. Eight studies assessed continuous abstinence. All of these reported statistically significant results in favour of CM.

Eight studies assessed the mean percentages of positive or negative results in the urine for opioid metabolites. Two of these reported statistically significant results in favour of CM. Two studies assessed continuous abstinence, both of which reported statistically significant results in favour of CM.

Opioid-dependent patients

The full-text versions of 63 articles were acquired after being judged to be potentially relevant. Of these, 20 studies (31 articles) were included (Bickel et al., 1997, 2008; Carroll et al., 2001, 2002; Chawarski et al., 2008; Chen et al., 2013; Chutuape et al., 1999, 2001; DeFulio et al., 2012; Dunn et al., 2013–14 (reported as one study); Everly et al., 2011; Higgins et al., 1986; Hser et al., 2011; Jiang et al., 2012; McCaul et al., 1984; Neufeld et al., 2008; Nunes et al., 2006; Preston et al., 1999, 2000; Stitzer et al., 1992). Seven studies were classified as awaiting classification because only conference proceedings with incomplete information were retrieved.

In total, the 20 included studies enrolled 1 676 patients who met criteria for opioid dependence. The mean age of these studies was 36.5 years and 73.2 % of participants were male; one study (Chawarski et al., 2008) did not report the mean age or sex distribution of the participants.

Three types of pharmacological intervention were provided in the studies. Three studies assessed the efficacy of CM in addition to detoxification treatment (Bickel et al., 1997; Higgins et al., 1986; McCaul et al., 1984), 10 studies assessed CM in addition to maintenance or agonist substitution treatment (Bickel et al., 2008; Chawarski et al., 2008; Chen et al., 2013; Chutuape et al., 1999, 2001; Hser et al., 2011; Jiang et al., 2012; Neufeld et al., 2008; Preston et al., 2000; Stitzer et al., 1992) and seven assessed CM in addition to naltrexone treatment in already detoxified patients (Carroll et al., 2001, 2002; DeFulio et al., 2012; Dunn et al., 2013–14; Everly et al., 2011; Nunes et al., 2006; Preston et al., 1999).

The CM intervention differed among the studies. In the three studies on detoxification treatment, CM included assessment of negative results in the urine for opioid. In the 10 studies on maintenance or agonist treatment, CM was based on the assessment of negative results in the urine for cocaine and opioids in three studies (Bickel et al., 2008; Chutuape et al.,

1999, 2001); on negative results in the urine for opioids in two studies (Chawarski et al., 2008; Preston et al., 2000); on negative results in the urine for opioids, cocaine and benzodiazepines in one study (Stitzer et al., 1992); on negative results in the urine for opioids plus methadone ingestion in three studies (Chen et al., 2013; Hser et al., 2011; Jiang et al., 2012); and on negative results in the urine for any illicit drug and attending a counselling session in one study (Neufeld et al., 2008). In the seven studies on naltrexone treatment, CM was based on negative results in the urine for opioids plus naltrexone ingestion in one study (Carroll et al., 2001); on negative results in the urine for opioids, cocaine and benzodiazepines plus naltrexone ingestion in two studies (Carroll et al., 2002; Nunes et al., 2006); and on naltrexone ingestion alone in four studies (DeFulio et al., 2012; Dunn et al., 2013–14; Everly et al., 2011; Preston et al., 1999).

In addition, the type of premium earned differed greatly among the studies. In the three studies on detoxification, it consisted in a monetary voucher (Bickel et al., 1997), a methadone dose increase (Higgins et al., 1986) or the taking home of methadone (McCaul et al., 1984). In the 10 studies on maintenance or agonist treatment, it consisted of the taking home of methadone in five studies (Chawarski et al., 2008; Chutuape et al., 1999, 2001; Neufeld et al., 2008; Stitzer et al., 1992), the remaining being monetary vouchers. In the Chinese study (Chen et al., 2013) the monetary voucher had to be spent on paying for treatment. In the seven studies on naltrexone, it consisted of monetary vouchers in four studies (Carroll et al., 2001, 2002; Nunes et al., 2006; Preston et al., 1999) and permission to attend the therapeutic workplace and earning money in three studies (DeFulio et al., 2012; Dunn et al., 2013–14; Everly et al., 2011).

Three studies were conducted in China, one was conducted in Malaysia and all of the others were conducted in the USA. For a detailed description of the studies' characteristics and results, see the tables of included studies in Annex 1.

Effect of interventions

Regarding the retention of patients in treatment:

- Of the studies on maintenance or agonist treatment (of which eight assessed retention in treatment), only three found a significant difference in favour of CM.
- Of the studies on detoxification treatment, all three assessed retention in treatment, and two found a significant difference in favour of CM.
- Of the studies on naltrexone treatment, all seven assessed retention in treatment, and five found a significant difference in favour of CM.

Regarding patients' use of opioids:

- Of the studies on maintenance or agonist treatment: seven studies assessed the mean percentages of positive or negative results in the urine for opioid metabolites and three of these reported statistically significant results in favour of CM; four studies assessed continuous abstinence and three of these reported statistically significant results in favour of CM.
- Of the studies on detoxification treatment: two studies assessed the mean percentages of positive or negative results in the urine for opioid metabolites and one of these reported statistically significant results in favour of CM; three studies assessed continuous abstinence and two of these reported statistically significant results in favour of CM.
- Of the studies on naltrexone treatment: seven assessed the mean percentages of positive or negative results in the urine for opioid metabolites and one of these reported statistically significant results in favour of CM; two studies assessed continuous abstinence and one of these reported statistically significant results in favour of CM.

Regarding patients' use of cocaine:

- Of the studies on maintenance or agonist treatment: three studies assessed the mean percentages of positive or negative results in the urine for cocaine metabolites; none found a significant effect in favour of CM; none assessed continuous abstinence.
- Of the studies on detoxification treatment, none assessed the patients' use of cocaine.
- Of the studies on naltrexone treatment: six studies assessed the mean percentages of positive or negative results in the urine for opioid metabolites and one of these reported statistically significant results in favour of CM; none assessed continuous abstinence.

Regarding patients' use of opioids and cocaine:

- Of the studies on maintenance or agonist treatment: two studies assessed the mean percentages of positive or negative results in the urine for cocaine metabolites and one of these found a significant effect in favour of CM; three studies assessed continuous abstinence and two of these found a significant effect in favour of CM.
- Of the studies on detoxification treatment, none assessed patients' use of opioids and cocaine.
- Of the studies on naltrexone treatment, none assessed patients' use of opioids and cocaine.

TABLE 2

Quick guide to results

Participants	Intervention	Number of studies	Comparison	Quick guide	Outcomes
Methamphetamine use	CM (voucher of USD 2.50 for drug-free urine) + sertraline	1 study, <i>n</i> = 229	Matching placebo	+	Retention in treatment (<i>n</i> = 1/1)
				+	Methamphetamine use (<i>n</i> = 1/1)
Cocaine dependence	CM (voucher of USD 2.50 for drug-free urine)	3 studies, <i>n</i> = 447	Tryptophan or placebo	–	Retention in treatment (<i>n</i> = 0/3)
			Levodopa with placebo and CBT	++	Reduction of drug use and abstinence (<i>n</i> = 2/3)
Cocaine and opioid dependence	CM (vouchers with monetary prizes or taking home dosages) + methadone	14 studies, <i>n</i> = 1 550	Standard care (methadone + counselling and some pharmacological interventions)	–	Retention in treatment (<i>n</i> = 1/12)
				++	Use of cocaine (<i>n</i> = 10/13)
				++	Continuous cocaine abstinence (<i>n</i> = 8/8)
				–	Use of opioids (<i>n</i> = 2/8)
				+	Continuous opioids abstinence (<i>n</i> = 2/2)
Opioid dependence	CM (vouchers with monetary prizes) + opioid detoxification	3 studies, <i>n</i> = 98	Opioid detoxification only	++	Retention in treatment (<i>n</i> = 2/3)
				+	Use of opioids (<i>n</i> = 1/2)
				++	Continuous opioids abstinence (<i>n</i> = 2/3)
	CM (vouchers with monetary prizes) + naltrexone	7 studies, <i>n</i> = 431	Naltrexone only	+	Retention in treatment (<i>n</i> = 5/7)
				–	Use of opioids (<i>n</i> = 1/7)
				–	Continuous opioids abstinence (<i>n</i> = 1/2)
				–	Use of cocaine (<i>n</i> = 1/6)
	CM (vouchers with monetary prizes) + OST with methadone or buprenorphine	10 studies, <i>n</i> = 1 177	OST only or with counselling	–	Retention in treatment (<i>n</i> = 3/8)
				–	Use of opioids (<i>n</i> = 3/7)
				++	Continuous opioids abstinence (<i>n</i> = 3/4)
				–	Use of cocaine (<i>n</i> = 0/3)
				–	Use of opioids and cocaine (<i>n</i> = 1/2)
				++	Continuous opioids and cocaine abstinence (<i>n</i> = 2/3)

Notes:

- ++ positive effect on outcome in the majority of studies
- + positive effect on outcome but with study limitations (i.e. two or fewer studies)
- no positive effect on outcome.

In the outcome column, the number of studies is shown in brackets (*n* = studies with positive results/total number of studies measuring the outcome).

Economic evaluations of contingency management

In systematic surveys of clinicians and programme directors, the most frequently cited obstacle to implementing CM in clinical practice was the relatively high cost of rewards/incentives. Other considerations, such as ethical issues (e.g. paying drug users to do the right thing), practical considerations including the limited use of frequent urine screens to verify abstinence by many clinical programmes and limited knowledge to apply CM, were also frequently mentioned as barriers for a wider adoption of this approach (Carroll, 2014).

A question often raised is about the benefit of this approach to others in view of the costs of implementation. However, the number of studies analysing the costs of CM is relatively low. This section will describe the evidence on the economic evaluations of CM, in particularly trying to answer the following

question: what are the costs and benefits of applying CM as an adjunctive treatment to standard care of drug use, compared with alternative therapies?

In January 2015, Shearer et al. (2015) performed a systematic literature review on economic evaluations of CM in relation to the treatment of illicit drug use. The inclusion criteria for evaluations were that (i) CM was applied as an adjunctive treatment to illicit drug users; (ii) the CM intervention was analysed by comparing it with treatment as usual (TAU) or other interventions, or different types or schedules of CM interventions were analysed; (iii) CM was evaluated based on any clinical outcomes; (iv) it was a full economic evaluation (defined as the comparison of differences in both the costs and the consequences of alternative interventions); and (v) the study was published between 1982 and 2013, inclusive. The main methodological procedures that have been identified as necessary to perform systematic reviews of cost–benefit

analyses were respected (National Institute for Health and Care Excellence, 2014; Drummond et al., 2005).

Shearer et al. (2015) concluded that, in all studies in which CM was adjunctive, treatment was more effective but also more costly. In addition, the authors stated that the evidence on cost-effectiveness was limited because these economic analyses were not generalisable. The studies that were included had small sample sizes and were conducted only in the USA. On the other hand, the authors stressed that a proper economic evaluation of this type of intervention should have taken into account more than simply the cost of treatment. In fact, CM may have an impact on various behaviours of the patients, including criminal activity, with consequent effects on costs of the judicial system. Shearer and colleagues stated that evidence of cost-effectiveness of CM, including criminal justice savings, would be an essential in supporting policy responses.

In this regard, the current literature survey identified two additional studies, not included in Shearer et al. (2015), which estimated the costs and benefits in relation to criminal dissuasion and activity. McCollister et al. (2009) and Sheidow et al. (2012) estimated the costs of criminal activity, of criminal systems (family courts and drug courts) and of different types of treatment for adolescents in the USA, using CM as one of the adjunctive treatments possible. They measured the impacts on adolescent substance use and criminal behaviours and estimated the costs and benefits of different alternatives. However, these two studies seem to have been based on the same small sample, sharing part of the research team ⁽¹⁾. These studies differed in the methods applied to estimate cost-effectiveness. While the first applied a multivariate analysis to evaluate effects, the second deducted the average cost-effectiveness ratios (ACER) of alternatives. Both concluded that CM was the most costly alternative. While McCollister et al. (2009) concluded that the cost-effectiveness of CM was not statistically significantly different from the use of other evidence-based treatments, Sheidow et al. (2012) concluded that the use of CM as an adjunctive treatment was efficient for reducing all the outcomes of interest and the most cost-effective in reducing polydrug use, alcohol use and heavy alcohol use. However, again, these studies suffer from a lack of external validity and their conclusions cannot be generalised to other contexts, as recognised by their authors.

Consequently, these studies support the conclusion of Shearer et al. (2015) that the evidence for cost-effectiveness is not yet strong enough to come to any firm conclusion to support the implementation of what may be a promising strategy of drug treatment programmes.

Discussion

Contingency management is applied for a variety of interventions and settings and the overall results show that CM often helps to keep people in treatment, and it provides overall positive findings with opioid and cocaine addicts, but this is less clear for other substances. Furthermore, even though evidence is not yet strong enough to be fully conclusive, it seems to suggest that adding CM to other treatment approaches increases costs but can be a promising strategy overall if economic effects are considered (see Table 3 for main results).

The CM approach has been studied under very different conditions and settings. The participants enrolled in the studies we analysed had problems related to stimulants, cocaine, opioids, and cocaine and opioids, or polysubstance problems. The CM approach was used as a stand-alone intervention, as an adjunct to other psychosocial interventions or in combination with pharmacological therapy. Pharmacological treatments also varied, both in the objective (detoxification or maintenance) and in the type of drug used. Finally, CM approaches also varied, both in the types of behaviour reinforced (drug abstinence in the majority of studies, but also attending psychosocial therapy groups or compliance with the pharmacological treatment) and in the type of reward. Most of the trials used monetary premium, but some used the

TABLE 3
Description of main results

Participants	Intervention	Summary of results
Methamphetamine use	CM (voucher of USD 2.50 for drug-free urine) + sertraline	Results come from only one study, but they indicate that CM helps to decrease methamphetamine use and improves retention in treatment
Cocaine dependence	CM (voucher of USD 2.50 for drug-free urine)	Positive effect of CM in reducing cocaine use but not in retaining people in treatment
Cocaine and opioid dependence	CM (vouchers with monetary prizes or taking home dosages) + methadone	CM not effective in increasing retention but very positive effect in reducing cocaine use and increasing continuous abstinence. Results for opioid use are contrasting
Opioid dependence	CM (vouchers with monetary prizes) + opioid detoxification	Significant effect of CM in retaining patients in treatment as well as in decreasing opioid use and increasing continuous abstinence
	CM (vouchers with monetary prizes) + naltrexone	Some positive effects of CM in retaining patients in treatment but no evidence of effect on use of opioids or cocaine
	CM (vouchers with monetary prizes) + OST with methadone or buprenorphine	Positive effects only for continuous opioids and cocaine abstinence, but no effect in decreasing use or retaining people in treatment

⁽¹⁾ Although the corresponding author common to both studies was contacted, no reply was received.

possibility of taking home prescribed pharmaceuticals or the possibility of continuing to attend the therapeutic workplace.

The cost-effectiveness analysis benefited from a recent systematic literature survey, from which conclusions were drawn based on nine selected articles. These articles concerned the USA; focused mostly on drug addiction, including stimulants, opioids and cannabis; and included CM that rewarded abstinence or abstinence and treatment attendance, or adherence to anti-retroviral medication in HIV-positive methadone maintenance patients. All studies made economic evaluations based on data from randomised controlled trials, performing cost-effectiveness analysis or cost analysis from the perspective of the payers only. CM tended to make treatment more effective but also more costly. The authors complemented this analysis with two papers that assessed cost-effectiveness including judicial interventions costs, treatment costs and the decline in crime rates as additional outcomes. Again, the review suggests that CM makes treatment more expensive but conclusions depend upon the method used to assess cost-effectiveness. If the method used to evaluate the dominance of CM over alternatives was a multivariate analysis, the cost-effectiveness of CM is not significantly different from other strategies; if dominance is appraised with ACER, then treatment is significantly cost-effective (on average). However, ACERs can be misleading for informing choices between interventions (Drummond et al., 2005). In addition, the applicability of these studies is limited by external validity considerations, which prevent these conclusions from being applied to other frameworks.

Quality of the evidence

Overall, the retrieved studies had a low quality of reporting. The vast majority of the studies did not report information about random sequence generation for randomisation, and allocation of patients to groups was concealed. None of the studies was double blinded because it was not possible to blind participants and providers to the kind of intervention assessed. None of the trials reported information about blinding of the outcome assessor, but the outcomes considered were objective in all of the trials (retention in treatment and use of substances assessed by urine analysis); therefore, the risk of detection bias was judged to be low. Of all of the studies, 34 % were judged to be at high risk of attrition bias for the outcome substance of use because an intention-to-treat analysis was not done and the rate of drop out was greater than 30 %. Only five studies (13 %) did not report results about retention in treatment and were judged to be at high risk of selective reporting.

The quality of the evidence on the cost-effectiveness of CM varies. However, a minority of studies do not indicate the costing year, which prevents data from being revalued and, therefore, makes comparisons across studies difficult. Samples were also frequently small. Most studies did in fact take the

'service provider' perspective of costs, but frequently did not explicitly state their analytical perspective.

Limitations in the review process

The major limitation of our review is the fact that it was not possible to perform a meta-analysis of the results of primary studies and, thus, the necessity to base our conclusions on the number of studies with statistically significant results. This is because of the poor quality of reporting of the primary studies, which, in many cases, did not report the raw data but only the results of the statistical analysis in terms of the *p*-value or the results of regression analysis. Furthermore, the studies used different ways of measuring the outcomes of interest, making between-study comparisons difficult. For example, some studies looked for positive results in urine analysis and others looked for negative results, and continuous abstinence was measured over different time periods, with some studies counting the mean number of days or weeks of continuous abstinence while others counted the number of subjects achieving a predefined period of continuous abstinence.

We did not assess the risk of publication bias with a funnel plot, which is a graph that represents the risk that studies with negative results are underreported. Nevertheless, as the search strategy was comprehensive – including systematic inspection of websites of conference proceedings and bibliographic searches of many databases (without date and language restrictions) and the inspection of the reference lists of retrieved studies and already published systematic reviews – we consider that the probability is small that relevant studies on this topic have been missed, but the possibility that some unpublished studies have not been retrieved cannot be ruled out.

Conclusions

Although limited, the present analysis shows that CM is a feasible and promising adjunct to treatment interventions for drug users.

Contingency management has been studied alongside various types of interventions provided in different settings. Overall, the study results show that CM can help keep people in treatment, and promote a reduction of opioid and cocaine problems in patients in opioid substitution treatment. Data on patients with other substance-related problems are less available for this analysis. The provision of CM as an adjunct to other treatment approaches increases costs but, even though evidence is not yet strong enough to conclude on cost-effectiveness, it seems to suggest that CM is a promising strategy overall if the economic effects are considered in the long term.

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Annex 1

Characteristics of included studies and results

Stimulant-dependent patients (n = 1)

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Shoptaw et al. (2006), USA	229 patients who met criteria for methamphetamine abuse or dependence (DSM-IV diagnostic criteria) Mean age: 33.3 years Male: 61.5 %	(1) Sertraline + CM (n = 61) (2) Sertraline only (n = 59) (3) Matching placebo + CM (n = 54) (4) Matching placebo only (n = 55)	CM based on negative urine result for methamphetamine metabolites. The voucher for the initial metabolite-free sample was worth USD 2.50 and increased in value by USD 1.25 for each consecutive metabolite-free sample. Each third consecutive metabolite-free sample earned a USD 10.00 bonus voucher	Treatment retention Methamphetamine use (urine analysis) – subjects with at least 3 weeks of consecutive abstinence	3.5 months	Retention: results presented only in a figure. Sertraline-only participants were retained in treatment for significantly less time than participants in all other treatment conditions ($\chi^2 (3) = 8.40, p < 0.05$) Methamphetamine use: at least 3 weeks of consecutive abstinence: sertraline + CM: 42.6 % placebo + CM: 51.9 % sertraline only: 25.4 % placebo only: 41.8 % ($p = 0.035$) Sertraline vs. placebo: 34.2 % vs. 46.8 % ($p = 0.052$) CM vs. no CM: 47 % vs. 33.3 % ($p = 0.036$)

Cocaine-dependent patients (n = 3)

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Jones et al. (2004), USA	199 cocaine-dependent patients (DSM-IV diagnostic criteria) Mean age: 36 years Male: 56 %	(1) Tryptophan + CM (n = 45) (2) Tryptophan no CM (n = 56) (3) Placebo + CM (n = 58) (4) Placebo no CM (n = 40)	CM voucher based on negative urine results for cocaine metabolites. Patients earned a USD 2.50 voucher for their first cocaine-negative urine sample, and vouchers for subsequent consecutive cocaine-negative samples increased by USD 1.50. Patients earned a USD 10.00 bonus for every three consecutive cocaine-negative urine samples. Control voucher: earnings not contingent upon sample results	Treatment retention Cocaine use (urine analysis) – as (i) % of positive urine results and (ii) mean days of continuous cocaine abstinence	4 months	Retention: results presented only in a figure No significant differences in cocaine use (urine analysis): (i) % of cocaine-positive results (missing values counted as positive) tryptophan + CM: 32.4 % tryptophan no CM: 38.1 % placebo + CM: 24.5 % placebo no CM: 35.6 % Main effect for voucher conditions ($p < 0.05$): (ii) Days of continuous cocaine abstinence (missing values counted as positive) tryptophan + CM: 20.2 tryptophan no CM: 13.9 placebo + CM: 21.8 placebo no CM: 14 Main effect for voucher conditions ($p < 0.05$):

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Schmitz et al. (2009), USA	87 cocaine- and alcohol-dependent patients (DSM-IV diagnostic criteria) Mean age: 34.4 years Male: 87.3 %	(1) Naltrexone + CM (n = 20) (2) Placebo + CM (n = 14) (3) Naltrexone no CM (n = 20) (4) Placebo no CM (n = 27)	CM voucher based on negative urine results for cocaine metabolites. Patients earned a USD 2.50 voucher for their first cocaine-negative urine sample, and vouchers for subsequent consecutive cocaine-negative samples increased by USD 1.25. Patients earned a USD 10.00 bonus for every three consecutive cocaine-negative urine samples	Treatment retention Cocaine use (urine analysis) – as % of positive urine results	3 months	Retention: data not reported. No significant differences between groups Cocaine use (urine analysis): data not reported. The probability of having a cocaine-positive urine sample did not change over time as a function of medication, therapy or their interaction
Schmitz et al. (2008), USA	161 cocaine-dependent patients (DSM-IV diagnostic criteria) Mean age: 41 years Male: 85.7 %	(1) Levodopa (n = 25) (2) Levodopa + CBT (n = 28) (3) Levodopa + CBT + CM (n = 23) (4) Placebo + CBT + CM (n = 27) (5) Placebo + CBT (n = 31) (6) Placebo (n = 27)	CM voucher based on negative urine results for cocaine metabolites. Patients earned a USD 2.50 voucher for their first cocaine-negative urine sample, and vouchers for subsequent consecutive cocaine-negative samples increased by USD 1.25. Patients earned a USD 10.00 bonus for every three consecutive cocaine-negative urine samples	Treatment retention Cocaine use (urine analysis) – as (i) % of positive urine results and (ii) number of consecutive negative urine results	3 months	Retention: data not reported. No significant differences between groups Cocaine use (urine analysis): (i) % of cocaine-positive results (results for each group presented only in a figure) any levodopa: 61.6 % any placebo: 79.1 % ($p < 0.05$); any CBT: 84 % any CM: 59 % ($p < 0.05$); levodopa + CM: 40 % placebo + CM: 77 % levodopa + CM vs. any other ($p < 0.05$) (ii) Mean number of consecutive negative urine results any levodopa: 5.2 any placebo: 1.5 ($p < 0.05$); any CBT: 5.2 any CM: 1.3 ($p < 0.05$); levodopa + CM vs. any other ($p < 0.05$)

Patients dependent on both cocaine and opioids ($n = 14$)

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Jones et al. (2001), USA	80 pregnant methadone-maintained women meeting DSM-III-R criteria for opioid dependence and cocaine dependence Mean age: 28 years	(1) ST + CM ($n = 44$) (2) ST (MMT in residential treatment for 1 week + 1 week of intensive outpatient) ($n = 36$)	CM voucher based on attending full-day treatment and providing a cocaine-negative urine sample. The vouchers had monetary values and could be exchanged for merchandise and services purchased by research staff. Initially, the monetary value of the voucher was USD 5 for day 1, with increases of USD 5/ day for each consecutive day that the target behaviour was met. By treatment day 14, participants could earn up to USD 70 for that day	Treatment retention Cocaine and opioid use (urine analysis) – as (i) % of cocaine- and opioid-positive results and (ii) number of consecutive opioid- and cocaine-free urine samples	2 weeks	Retention: ST + CM: 41/44 (93.2 %) ST: 34/36 (94.4 %) Cocaine use (urine analysis): (i) % of cocaine-positive results (data not shown), results in favour of CM ($p < 0.05$) Opioid use (urine analysis): (i) % of opioid-positive results (data not shown) results in favour of CM ($p < 0.05$) (ii) Mean number of consecutive opioid- and cocaine-free urine samples ST + CM: 4.2 ST: 3.9 ($p = ns$)
Kosten et al. (2003), USA	160 opioid- and cocaine-dependent patients (DSM-IV diagnostic criteria) Mean age: 36.5 years Male: 65.6 %	(1) Buprenorphine + desipramine (DES) + CM ($n = 40$) (2) Buprenorphine + DES no CM ($n = 40$) (3) Buprenorphine + placebo (PBO) + CM ($n = 40$) (4) Buprenorphine + PBO no CM ($n = 40$)	CM voucher based on negative urine results for cocaine and opioid metabolites. The first negative urine result was worth USD 3, increasing by USD 1 for every consecutive negative urine result and reset back to USD 3 if urine result was positive	Treatment retention Cocaine and opioid use (urine analysis) – as (i) weekly mean proportion of negative urine results and (ii) average number of weeks of continuous abstinence	3 months	Retention: data not reported. No significant differences between groups Cocaine use (urine analysis): (i) Weekly mean proportion of negative urine results DES + CM: 60 % DES no CM: 36 % PBO + CM: 37 % PBO no CM: 49 % DES + CM vs. other three ($p = 0.05$) Opioid and/or cocaine use: DES + CM: 50 % DES no CM: 29 % PBO + CM: 25 % PBO no CM: 29 % DES + CM vs. other three ($p = 0.05$) Opioid use: DES + CM: 65 % DES no CM: 54 % PBO + CM: 49 % PBO no CM: 43 % DES + CM vs. other three ($p = 0.01$) (ii) Average number of weeks of continuous abstinence Cocaine use: DES + CM: 3.7 DES no CM: 1.9 PBO + CM: 1.8 PBO no CM: 2.4 DES + CM vs. other three ($p = 0.05$) Opioid and/or cocaine use: DES + CM: 3.0 DES no CM: 1.6 PBO + CM: 1.2 PBO no CM: 1.2 DES + CM vs. other three ($p = 0.02$)

Author (Year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Oliveto et al. (2005), USA	140 cocaine-dependent methadone patients (DSM-IV diagnostic criteria) Mean age: 36.5 years Male: 74.3 %	(1) LAAM 30 mg + CM (n = 35) (2) LAAM 100 mg + CM (n = 35) (3) LAAM 30 mg no CM (n = 35) (4) LAAM 100 mg no CM (n = 35)	CM based on negative urine results for cocaine and opioids. Patients earned USD 3 or first negative urine result. Each consecutive, drug-free urine sample thereafter increased in monetary value by USD 1. Patients who remained abstinent during the entire 12-week trial were able to earn goods and services worth a maximum of USD 738. For the yoked group (control group), each patient was yoked to a person in the CM group, such that the yoked person earned vouchers based on the person in the CM group's performance	Treatment retention Cocaine and opioid use (urine analysis) – as median % of negative urine results	3 months	Retention: data shown in figure. No significant differences between groups Cocaine use (urine analysis) as median % of negative urine results: (1) LAAM 30 mg + CM: 39.6 % (2) LAAM 100 mg + CM: 51 % (3) LAAM 30 mg no CM: 37.5 % (4) LAAM 100 mg no CM: 33.7 % LAAM 100 mg + CM had significantly more negative urine results than all the other groups ($p < 0.0001$) Opioid use (urine analysis) as median % of negative urine results: (1) LAAM 30 mg + CM: 29.8 % (2) LAAM 100 mg + CM: 52 % (3) LAAM 30 mg no CM: 40.6 % (4) LAAM 100 mg no CM: 51 % Any LAAM 100 mg vs. any LAAM 30 mg ($p < 0.0001$)
Petry and Martin (2002), USA	42 cocaine-dependent methadone patients (DSM-IV diagnostic criteria) Mean age: 38.5 years Male: 29 %	(1) ST + CM (n = 19) (2) ST (methadone + counselling) (n = 23)	CM based on negative urine results for cocaine and opioids. CM patients earned the opportunity to draw from a bowl and win prizes ranging from USD 1 to USD 100 in value for submitting samples negative for cocaine and opioids	Treatment retention Cocaine and opioid use (urine analysis) – as % of negative urine samples	3 months	Retention: ST + CM: 1/19 ST: 2/23 ($p = ns$) Cocaine use (urine analysis) as % of negative urine samples: Data not reported; no significant difference Opioid use (urine analysis) as % of negative urine samples: Data not reported; no significant difference
Petry et al. (2005), USA	77 cocaine-dependent methadone patients (DSM-IV diagnostic criteria) Mean age: 39.5 years Male: 27 %	(1) ST + CM (n = 40) (2) ST (methadone + counselling) (n = 37)	CM based on negative urine results for cocaine and for attending group sessions. Prizes ranging from USD 1 to USD 100	Treatment retention Cocaine and opioid use (urine analysis – as (i) % of negative urine samples and (ii) mean duration of continuous abstinence	3 months	Retention: ST + CM: 5/40 ST: 6/37 ($p = ns$) Cocaine use (urine analysis): (i) % of negative urine samples ST + CM: 34.6 % ST: 16.8 % ($p < 0.001$) (ii) Mean duration of continuous abstinence ST + CM: 2.9 weeks ST: 0.8 weeks ($p < 0.05$) Opioid use (urine analysis): (i) % of negative urine samples ST + CM: 69.3 % ST: 72.3 % ($p = ns$)

Author (Year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Petry et al. (2007), USA	74 cocaine-dependent methadone patients (DSM-IV diagnostic criteria) Mean age: 41.6 years Male: 43.7 %	(1) ST + USD 300 prize CM ($n = 30$) (2) ST + USD 585 voucher CM ($n = 27$) (3) ST (methadone + counselling) ($n = 19$)	CM based on negative urine result for cocaine. USD 300 prize CM: average expected prize earnings were about USD 300 USD 585 voucher CM: expected maximum of about USD 585 in vouchers	Treatment retention Cocaine and opioid use (urine analysis – as (i) median % negative urine results, (ii) median number of weeks of continuous abstinence and (iii) number of subjects with continuous abstinence	3 months	Retention: data not reported. No significant differences between groups Cocaine use (urine analysis): (i) Median % of negative urine results ST + USD 300 prize CM: 67.4 % ST + USD 585 voucher CM: 56.6 % ST: 4.2 % ($p < 0.05$) (ii) Median number of weeks of continuous abstinence 12 weeks ST + USD 300 prize CM: 6 ST + USD 585 voucher CM: 6 ST: 0 CM vs. ST ($p < 0.05$) (iii) Number of subjects with continuous abstinence ST + USD 300 prize CM: 8/28 (28.6 %) ST + USD 585 voucher CM: 8/27 (29.6 %) ST: 0/19 CM vs. ST ($p < 0.05$) Opioid use: (i) Median % of negative urine results No significant difference between groups
Petry et al. (2014), USA	240 cocaine-dependent methadone patients (DSM-IV diagnostic criteria) Mean age: 40.3 years Male: 50 %	(1) ST + USD 300 prize CM ($n = 58$) (2) ST + USD 900 prize CM ($n = 62$) (3) ST + USD 900 voucher CM ($n = 63$) (4) ST (methadone + counselling) ($n = 57$)	CM based on negative urine result for cocaine and alcohol. USD 300 prize CM: average expected prize earnings were about USD 300 USD 900 prize CM: average expected prize earnings were about USD 900 USD 900 voucher CM: expected maximum of about USD 900 in vouchers	Cocaine and alcohol use (urine analysis) – as (i) % of cocaine- and alcohol-negative results and (ii) longest duration of abstinence (weeks)	3 months	Cocaine and alcohol use (urine analysis): (i) % of cocaine- and alcohol-negative results (mean, SD): ST + USD 300 prize CM: 55.5 (39.1) ST + USD 900 prize CM: 55.1 (41.6) ST + USD 900 voucher CM: 59.1 (38.4) ST: 36.0 (39.5) None of the CM conditions differed from one another. The two USD 900 conditions differed significantly from ST ($p < 0.05$) conditions, while the USD 300 prize condition did not. (ii) Longest duration of abstinence (weeks): ST + USD 300 prize CM: 3.1 (4.0) ST + USD 900 prize CM: 3.7 (4.0) ST + USD 900 voucher CM: 3.4 (3.7) ST: 1.7 (2.7) Any CM vs. ST ($p < 0.05$)

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Poling et al. (2006), USA	106 cocaine-dependent methadone patients (DSM-IV diagnostic criteria) Mean age: 34.6 years Male: 70 %	(1) ST (methadone + counselling) + bupropion + CM (n = 27) (2) ST + placebo + CM (n = 25) (3) ST + bupropion no CM (n = 77) (4) ST + placebo no CM (n = 71)	CM based on negative urine results for cocaine and opioids. Each negative urine sample resulted in a monetary-based voucher that increased in value for consecutive drug-free urine samples during weeks 1 to 13. Completion of abstinence-related activities also resulted in a voucher. The voucher control groups received vouchers for submitting urine samples, regardless of results	Treatment retention Cocaine and opioid use (urine analysis) – as (i) proportion of positive urine samples and (ii) mean number of consecutive weeks of abstinence	6 months	Retention: data not reported. No significant differences between groups Cocaine use (urine analysis): (i) Proportion of positive urine samples: data shown in figure In the bupropion + CM group, the proportion of cocaine-positive samples significantly decreased during weeks 3 to 13 ($p = 0.001$) relative to week 3 and remained low during weeks 14 to 25. In the placebo + CM group, cocaine use significantly increased during weeks 3 to 13 ($p = 0.001$) relative to week 3, but then significantly decreased relative to the initial slope during weeks 14 to 25 ($p = 0.001$). The no CM groups showed no significant improvement in cocaine use. (i) Mean number of consecutive weeks of abstinence ST + bupropion + CM: 6.7 ST + placebo + CM: 4.3 ST + bupropion no CM: 4.5 ST + placebo no CM: 3.0 ST + bupropion + CM vs. any other ($p < 0.01$) Opioid use (urine analysis): (i) Proportion of positive urine samples: data not reported. No significant differences between groups (ii) Mean number of consecutive weeks of abstinence ST + bupropion + CM: 5.7 ST + placebo + CM: 4.6 ST + bupropion no CM: 5.5 ST + placebo no CM: 3.4 ST + placebo + CM vs. ST + placebo no CM ($p < 0.05$)
Rawson et al. (2002), USA	120 cocaine-dependent methadone patients (DSM-IV diagnostic criteria) Mean age: 42 years Male: 53.5 %	(1) ST + CM (n = 30) (2) ST (methadone + counselling) (n = 30)	CM based on negative urine results for cocaine. Voucher started at a value of USD 2.50 and increased in value by USD 1.25 for each further negative urine result up to USD 20	Treatment retention Cocaine use (urine analysis) – as (i) mean % of negative urine samples and (ii) number of subjects with 3 weeks' continuous abstinence	4 months	Retention: data shown in figure. No significant differences between groups Cocaine use (urine analysis): (i) Mean % of negative urine samples ST + CM: 60 % ST: 23 % ($p < 0.05$) (ii) Number of subjects with 3 weeks' continuous abstinence ST + CM: 63 % ST: 27 % ($p < 0.05$)

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Rowan-Szal et al. (2005), USA	61 cocaine-dependent methadone patients (DSM-IV diagnostic criteria) Mean age: 33 years Male: 62.7 %	(1) ST + cocaine-specific counselling module (COCA) (n = 16) (2) ST + CM (n = 13) (3) ST + COCA + CM (n = 17) (4) ST (methadone + counselling) (n = 15)	CM based on negative urine results for cocaine, attending counselling sessions and completing tasks related to individualised treatment goals developed with their counsellor. Each counselling session attendance earned one star, cocaine-negative urine samples earned two stars and clients earned eight bonus stars if they attended all weekly counselling sessions during the intervention. In addition, meeting specific goal-related tasks negotiated between the client and counsellor earned a maximum of 10 stars. Within the protocol, clients could earn a maximum of 50 stars during the 8-week intervention (for a total prize value of about USD 25)	Cocaine use (urine analysis) – as (i) mean % of positive urine samples and (ii) number of subjects with 6 weeks' continuous abstinence	2 months	Cocaine use (urine analysis): (i) Mean % of positive urine samples: data not shown. CM clients had significantly lower rates of cocaine positive urine samples than those in the no CM conditions ($p < 0.01$). (ii) Number of subjects with 6 weeks' continuous abstinence Any CM: 44 % Any no CM: 19 % ($p < 0.05$)

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Silverman et al. (2004), USA	78 cocaine-dependent methadone patients (DSM-IV diagnostic criteria) Mean age: 39 years Male: 55 %	(1) ST + take-home methadone CM ($n = 26$) (2) ST + take-home methadone CM + monetary CM vouchers ($n = 26$) (3) ST ($n = 26$)	Take-home methadone CM based on negative urine results for cocaine and opioids. Vouchers contingent on negative urine results for cocaine. Vouchers began at USD 2.50 and increased by USD 1.25 to a maximum of USD 40.00 for every consecutive cocaine-negative urine result. A USD 10.00 bonus given for three consecutive cocaine-negative urine samples until a maximum of USD 40.00	Treatment retention Cocaine and opioid use (urine analysis) – as (i) mean % of negative urine samples and (ii) longest duration of abstinence (weeks)	13 months	Retention: ST: 54 % ST + take-home methadone CM: 62 % ST + take-home methadone CM + monetary CM vouchers: 73 % ($p = ns$) Cocaine use (urine analysis): (i) Mean % of negative urine samples: data shown in figure ST + take-home methadone CM + monetary CM vouchers vs. other two groups ($p < 0.05$) (ii) Longest duration of abstinence (weeks) ST + take-home methadone CM: 7.1 (95 % CI: 3.7–10.5) ST + take-home methadone CM + monetary CM vouchers: 20.2 (95 % CI: 13.5–26.9) ST: 2.3 (95 % CI: 0.4–4.3) ST + take-home methadone + CM vs. ST and ST + take-home methadone + CM vs. take-home alone ($p < 0.001$) Opioid use (urine analysis): (i) Mean % of negative urine samples: data shown in figure ST + take-home methadone CM + monetary CM vouchers vs. other two groups ($p < 0.05$) (ii) Longest duration of abstinence (weeks) ST + take-home methadone CM: 9.2 (95 % CI: 5.2–13.2) ST + take-home methadone CM + monetary CM vouchers: 21 (95 % CI: 14.5–27.3) ST: 4.8 (95 % CI: 2.6–7.0) ST + take-home methadone + CM vs. ST and ST + take-home methadone + CM vs. take-home alone ($p < 0.001$)
Silverman et al. (2007), USA	56 cocaine-dependent methadone patients (DSM-IV diagnostic criteria) Mean age: 45.7 years Male: not reported	(1) ST + CM workplace ($n = 28$) (2) ST (methadone + counselling) + workplace no CM ($n = 28$)	CM based on negative urine results for cocaine. CM group must provide urine samples showing cocaine abstinence three a week to work and maintain maximum pay. No CM group could work independent of their urinalysis results	Cocaine and opioid use (urine analysis) – as mean % of negative urine samples	6 months	Cocaine use (urine analysis) as mean % of positive urine samples: (1) ST + CM workplace: 28.7 % (2) ST (methadone + counselling) + workplace no CM: 10.2 % ($p = 0.004$) Opioid use (urine analysis) as mean % of positive urine samples: (1) ST (methadone + counselling) + workplace no CM: 47.8 % (2) ST + CM workplace: 42.5 % ($p = ns$)

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Umbricht et al. (2014), USA	171 cocaine-dependent methadone patients (DSM-IV diagnostic criteria) Mean age: 42 years Male: 52 %	(1) ST (methadone + counselling) + topiramate + CM (n = 40) (2) ST + placebo + CM (n = 39) (3) ST + topiramate no CM (n = 45) (4) ST + placebo no CM (n = 47)	CM based on negative urine results for cocaine. The first cocaine-negative urine sample earned a USD 2.50 voucher. The voucher value increased by USD 1.50 for each subsequent cocaine-negative urine sample. A bonus of USD 10.00 was awarded for every three consecutive cocaine-negative urine samples	Treatment retention Cocaine use (urine analysis) – as mean % of negative urine samples	3 months	Retention: (1) ST + topiramate + CM: 68 % (2) ST + placebo + CM: 69 % (3) ST + topiramate no CM: 58 % (4) ST + placebo no CM: 70 % (p = ns) Cocaine use (urine analysis) as mean % of negative urine samples: (1) ST + topiramate + CM: 45 % (2) ST + placebo + CM: 54 % (3) ST + topiramate no CM: 43 % (4) ST + placebo no CM: 47 % (p = ns)
Winstanley et al. (2011), USA	145 cocaine-dependent methadone patients (DSM-IV diagnostic criteria) Mean age: 38.5 years Male: 54.6 %	(1) ST (methadone + counselling) + fluoxetine + CM (n = 35) (2) ST + placebo + CM (n = 33) (3) ST + fluoxetine no CM (n = 38) (4) ST + placebo no CM (n = 39)	CM based on negative urine results for cocaine. The first cocaine-negative urine sample earned a USD 2.50 voucher. The voucher value increased by USD 1.50 for each subsequent cocaine-negative urine sample. A bonus of USD 10.00 was awarded for every three consecutive cocaine-negative urine samples	Treatment retention Cocaine use (urine analysis) – operationalised as a dichotomous variable of use versus no use based on positive urine toxicology testing (obtained thrice weekly)	8 months	Retention: data shown in figure. Significantly more patients drop out from fluoxetine no CM than the other three groups (p < 0.01) Cocaine use (urine analysis): data not shown. Subjects in the placebo + CM group were significantly (p < 0.05) less likely to use cocaine (76 %) than the placebo no CM group. Subjects in either the fluoxetine no CM or fluoxetine + CM group were less likely to use cocaine (18 %, p = 0.66; 33 %, p = 0.40, respectively) than the placebo no CM group

MMT, methadone maintenance treatment; ns, not significant; ST, standard treatment.

Opioid-dependent patients (n = 20)

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Bickel et al. (1997), USA	39 opioid-dependent patients (DSM-IV diagnostic criteria) Mean age: 34.1 years Male: 63 %	Detoxification treatment (1) Buprenorphine dose reduction + CM (n = 19) (2) Buprenorphine dose reduction (n = 20)	CM based on negative urine results for opioids. The first negative urine sample earned 29 points at USD 1.25 per point or a USD 3.63 voucher. The voucher value increased by one point for each subsequent negative urine sample. A bonus of USD 5.00 was awarded for every three consecutive negative urine samples until the maximum of USD 658.38 for abstinence continued for 23 weeks	Treatment retention Opioid use (urine analysis) – as number of patients with continuous abstinence Other substance use	5 months	Retention: (1) Buprenorphine + CM: 53 % (2) Buprenorphine: 20 % (p = 0.03) Opioid use (urine analysis) as number of patients with continuous abstinence 12 weeks (1) Buprenorphine + CM: 26 % (2) Buprenorphine: 5 % (p = 0.06) 16 weeks (1) Buprenorphine + CM: 11 % (2) Buprenorphine: 0 % (p = ns) Other substance use: No significant difference between groups

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Bickel et al. (2008), USA	135 opioid-dependent patients (DSM-IV diagnostic criteria) Mean age: 28.5 years Male: 55.6 %	Maintenance treatment (1) Buprenorphine + computer-assisted community reinforcement approach (CRA) + CM (n = 45) (2) Buprenorphine + therapist-delivered CRA + CM (n = 45) (3) Buprenorphine + counselling (n = 45)	CM based on negative urine results for opioids and cocaine. Each voucher point was worth USD 0.25. The first negative sample was worth 29 points or USD 7.25. Vouchers increased by one point with each consecutive negative sample. In addition, a USD 10.00 bonus was earned for a week of negative samples. Continuous abstinence throughout the 23-week maintenance phase resulted in voucher earnings of USD 1 316.75.	Treatment retention Opioid and cocaine use (urine analysis) – as average weeks of continuous abstinence; missed urine samples were considered positive	5 months	Retention: (1) Buprenorphine + computer-assisted CRA + CM: 62 % (2) Buprenorphine + therapist-delivered CRA + CM: 53 % (3) Buprenorphine: 58 % (p = ns) Opioid and cocaine use (urine analysis) as average weeks of continuous abstinence (1) Buprenorphine + computer-assisted CRA + CM: 7.78 (2) Buprenorphine + therapist-delivered CRA + CM: 7.98 (3) Buprenorphine: 4.69 Any CM vs. no CM (p = 0.05)
Carroll et al. (2001), USA	79 opioid-dependent detoxified patients (DSM-IV diagnostic criteria) Mean age: 32.5 years Male: 77 %	Naltrexone maintenance treatment (1) Naltrexone + CM (n = 35) (2) Naltrexone (n = 44)	CM based on negative urine results for opioids and naltrexone ingestion. For negative urine samples for opioids and naltrexone ingestion, the subject earned the equivalent of USD 0.80. Vouchers increased by USD 0.40 with each consecutive negative sample. Continuous abstinence and naltrexone ingestion throughout the 12-week study period resulted in voucher earnings of USD 561	Treatment retention Opioid use (urine analysis) – as (i) mean number of negative urine samples and (ii) maximum number of days' continuous abstinence Cocaine use (urine analysis) – as (i) number of negative urine samples and (ii) maximum number of days' continuous abstinence	3 months	Retention: (1) Naltrexone: 25.6 % (2) Naltrexone + CM: 45.9 % (p = 0.05) Opioid use (urine analysis): (i) Mean number of negative urine samples (1) Naltrexone + CM: 18.9 (p = 0.05) (2) Naltrexone: 13.5 (ii) Maximum number of days' continuous abstinence (1) Naltrexone + CM: 49.1 (p = 0.05) (2) Naltrexone: 37.7 Cocaine use (urine analysis): (i) Mean number of negative urine samples (1) Naltrexone + CM: 16 (p = ns) (2) Naltrexone: 12.2 (ii) Maximum number of days' continuous abstinence (1) Naltrexone + CM: 45 (p = ns) (2) Naltrexone: 37.1

Author (Year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Carroll et al. (2002), USA	55 opioid-dependent detoxified patients (DSM-IV diagnostic criteria) Mean age: 33.8 years Male: 81 %	Naltrexone maintenance treatment (1) Naltrexone + low-value CM (n = 17) (2) Naltrexone + high-value CM (n = 20) (3) Naltrexone (n = 18)	CM based on negative urine results for opioids, cocaine and benzodiazepines and naltrexone ingestion. Low value: for the first negative urine sample and naltrexone ingestion, the subject earned the equivalent of USD 0.80. Vouchers increased by USD 0.40 with each consecutive negative sample. Continuous abstinence and naltrexone ingestion throughout the 12-week study period resulted in voucher earnings of USD 561. High value: the same as above but they earned USD 20 for the first negative urine sample and naltrexone ingestion and earned up to USD 1.152 throughout the 12-week study period	Treatment retention Opioid use (urine analysis) – as (i) mean % of positive urine samples and (ii) maximum number of days' continuous abstinence Cocaine use (urine analysis) – as (i) mean % of positive urine samples and (ii) maximum number of days' continuous abstinence	3 months	Retention: Weeks in treatment (1) Naltrexone + low-value CM: 8.9 (2) Naltrexone + high-value CM: 7.3 (3) Naltrexone: 6.2 (p = ns) Opioid use (urine analysis): Results for subjects before drop out (i) Mean % of positive urine samples (1) Naltrexone + low-value CM: 7 % (2) Naltrexone + high-value CM: 16 % (3) Naltrexone: 0 % Any CM vs. control (p = ns) (ii) Maximum number of days' continuous abstinence (1) Naltrexone + low-value CM: 6.05 (2) Naltrexone + high-value CM: 54.3 (3) Naltrexone: 40.5 (p = ns) ITT analysis: results not reported; frequency of opioid use less in the CM combined (p < 0.001) Cocaine use (urine analysis): Results for subjects before drop out (i) Mean % of positive urine samples (1) Naltrexone + low-value CM: 11 % (2) Naltrexone + high-value CM: 12 % (3) Naltrexone: 16 % (p = ns) (ii) Maximum number of days' continuous abstinence (1) Naltrexone + low-value CM: 54.6 (2) Naltrexone + high-value CM: 47.2 (3) Naltrexone: 36 (p = ns) ITT analysis: results not reported
Chawarski et al. (2008), Malaysia	24 opioid-dependent detoxified patients (DSM-IV diagnostic criteria) Mean age: not reported Male: not reported	Maintenance treatment (1) Buprenorphine + CM (n = 12) (2) Buprenorphine (n = 12)	CM based on negative urine samples for opioids. Participants with two successive opioid-negative tests were provided three or four daily take-home doses. Participants with three successive opioid-negative tests were provided six take-home doses	Treatment retention Opioid use (urine analysis) – as (i) proportion of negative urine samples and (ii) maximum consecutive weeks abstinent	2 months	Retention: (1) Buprenorphine + CM: 100 % (2) Buprenorphine: 92 % (p = ns) Opioid use (urine analysis): (i) Proportion of negative urine samples (1) Buprenorphine + CM: 87 % (2) Buprenorphine: 69 % (p = 0.04) (ii) Maximum consecutive weeks abstinent (1) Buprenorphine + CM: 10.3 % (2) Buprenorphine: 7.8 % (p < 0.05)

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Chen et al. (2013), China	246 opioid-dependent patients (ICD-10 diagnostic criteria) Mean age: 38.1 years Male: 92.3 %	Maintenance treatment (1) MMT + CM (n = 126) (2) MMT (n = 120)	CM based on negative urine results for opioids and methadone ingestion. Participants had the opportunity to draw for prizes once per week. The prizes were vouchers that could be redeemed only to pay for treatment (according to the national guidelines, each participant is required to pay 10 Yuan (USD 1.6) per day for MMT). The prize container contained 500 balls with 50.0 % yielding no prize, 41.8 % yielding prizes worth 5 Yuan (USD 0.8), 8.0 % worth 10 Yuan (USD 1.6) and 0.2 % worth 100 Yuan (USD 16). Participants earned one draw for each negative urine test. In the first week, a participant who attended 7 consecutive days of MMT was eligible to earn one draw for attendance. The number of draws that the participant was eligible to earn continued to increase to 12 in the 12th week, as long as the participant had uninterrupted attendance. In total, participants could earn up to 84 draws if they visited the MMT clinic for 84 days and submitted six negative urine specimens	Treatment retention Opioid use (urine analysis) – as proportion of negative urine samples	3 months	Retention: (1) MMT + CM: 81.7 % (2) MMT: 67.5 % ($p = 0.01$) Opioid use (urine analysis) as proportion of negative urine samples (1) MMT + CM: 68.3 % (2) MMT: 57.6 % ($p = 0.001$)

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Chutuape et al. (1999), USA	29 opioid-dependent patients (DSM-IV diagnostic criteria) Mean age: 40.7 years Male: 83.4 %	Maintenance treatment (1) MMT CM take home daily ($n = 11$) (2) MMT CM take home weekly ($n = 10$) (3) MMT no take home ($n = 8$)	CM based on negative urine results for opioids and cocaine. Take home daily: subjects earned one take home for each urine sample submitted that was free of both opioids and cocaine. Take home weekly: subjects assigned to the weekly protocol earned their first take home after submitting three consecutive opioid- and cocaine-free urine samples. Thereafter, they could continue earning one take home for each opioid- and cocaine-free urine sample submitted. For both groups, take-home privileges were revoked, however, as soon as the subject submitted a urine sample positive for opioids or cocaine	Opioid and/or cocaine use (urine analysis) – as (i) decrease in proportion of positive urine samples and (ii) mean number of consecutive drug-free samples	4 months	Opioid and/or cocaine use (urine analysis): (i) Decrease in proportion of positive urine samples for opioids and/or cocaine (1) MMT CM take home daily: 14 % (2) MMT CM take home weekly: 18 % (3) MMT no take home: 2 % Any CM vs. no CM ($p = ns$) (ii) Mean number of consecutive drug-free samples (1) MMT CM take home daily: 4 (2) MMT CM take home weekly: 6.4 (3) MMT no take home: 1.1 Any CM vs. no CM ($p = ns$)
Chutuape et al. (2001), USA	53 opioid-dependent patients (DSM-IV diagnostic criteria) Mean age: 38 years Male: 60 %	Maintenance treatment (1) MMT CM take home monthly ($n = 18$) (2) MMT CM take home weekly ($n = 16$) (3) MMT + take home random no CM ($n = 19$)	CM based on negative urine results for opioids and cocaine. Take home weekly: one urine sample per week randomly selected and tested for the presence of opioids and cocaine. A drug-negative sample resulted in awarding of three take-home doses per week. Take home monthly: urine samples used for take home determination were randomly selected, on average, once per month rather than once per week. Take home random: patients received take homes based on the results of individual weekly drawings rather than drug-free urine results. The probability of earning take homes at each drawing was 50 %	Treatment retention Opioid use and cocaine (urine analysis) – as (i) proportion of negative urine samples, (ii) consecutive abstinence (mean longest duration in weeks) and (iii) consecutive abstinence (% with at least 8 weeks of abstinence)	7 months	Retention: (1) MMT CM take home monthly: 83.3 % (2) MMT CM take home weekly: 62.5 % (3) MMT + take home random no CM: 94.7 % ($p < 0.05$ in favour of no CM) Opioid and cocaine use (urine analysis): (i) Proportion of negative urine samples: results showed in figure ($p < 0.04$ in favour of any CM) (ii) Consecutive abstinence (mean longest duration in weeks) (1) MMT CM take home monthly: 8.4 (2) MMT CM take home weekly: 10.5 (3) MMT + take home random no CM: 5.4 ($p = ns$) (iii) Consecutive abstinence (% with at least 8 week of abstinence) (1) MMT CM take home monthly: 38.9 % (2) MMT CM take home weekly: 56.6 % (3) MMT + take home random no CM: 10.5 % ($p < 0.002$)

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
DeFulio et al. (2012), USA	38 opioid-dependent patients (DSM-IV diagnostic criteria) Mean age: 43.5 years Male: 58 %	Naltrexone maintenance treatment (1) Naltrexone + CM (n = 19) (2) Naltrexone (n = 19)	CM on naltrexone ingestion. Naltrexone patients received drugs and were allowed to attend the therapeutic workplace. CM patients were allowed to attend the therapeutic workplace only if they ingest naltrexone. They could participate again if they resumed taking naltrexone	Treatment retention Opioid and/or cocaine use (urine analysis) – as proportion of negative urine samples for opioids and cocaine (missing urine samples considered positive)	6 months	Retention: (1) Naltrexone + CM: 74 % (2) Naltrexone: 26 % (p = 0.004) Opioid use (urine analysis) as proportion of negative urine samples for opioids: (1) Naltrexone + CM: 71.6 (2) Naltrexone: 65.3 % (p = ns) Cocaine use (urine analysis) as proportion of negative urine samples for cocaine: (1) Naltrexone + CM: 57.9 % (2) Naltrexone: 53.7 % (p = ns)
Dunn et al. (2013, 2014), USA	68 opioid-dependent patients (DSM-IV diagnostic criteria) Mean age: 44.9 years Male: 61.5 %	Naltrexone maintenance treatment (1) Naltrexone + CM (n = 35) (2) Naltrexone (n = 32)	CM on naltrexone ingestion. Naltrexone patients received drugs and were allowed to attend the therapeutic workplace. CM patients were allowed to attend the therapeutic workplace only if they ingest naltrexone. They could participate again if they resumed taking naltrexone	Treatment retention Opioid and/or cocaine use (urine analysis) – as proportion of negative urine samples for opioids and cocaine (missing urine samples considered positive)	6 months (end of the study) 12 months' follow-up	Retention: (1) Naltrexone + CM: 54 % (2) Naltrexone: 16 % (p < 0.01) Opioid use (urine analysis) as proportion of negative urine samples for opioids: (1) Naltrexone + CM: 71 (2) Naltrexone: 60 % (p = ns) Cocaine use (urine analysis) as proportion of negative urine samples for cocaine: (1) Naltrexone + CM: 56 % (2) Naltrexone: 53 % (p = ns) 12 months' follow-up Opioid use (urine analysis) as proportion of negative urine samples for opioids: (1) Naltrexone + CM: 44 % (2) Naltrexone: 42 % (p = ns) Cocaine use (urine analysis) as proportion of negative urine samples for cocaine: (1) Naltrexone + CM: 56 % (2) Naltrexone: 59 % (p = ns)
Everly et al. (2011), USA	35 opioid-dependent patients (DSM-IV diagnostic criteria) Mean age: 42.5 years Male: 51.5 %	Naltrexone maintenance treatment (1) Naltrexone + CM (n = 18) (2) Naltrexone (n = 17)	CM on naltrexone ingestion. Naltrexone patients received drugs and were allowed to attend the therapeutic workplace. CM patients were allowed to attend the therapeutic workplace only if they ingest naltrexone. They could participate again if they resumed taking naltrexone	Treatment retention Opioid and/or cocaine use (urine analysis) – as proportion of negative urine samples for opioids and cocaine (missing urine samples considered positive)	6 months	Retention: (1) Naltrexone + CM: 77 % (2) Naltrexone: 77 % (p = ns) Opioid use (urine analysis) as proportion of negative urine samples for opioids: (1) Naltrexone + CM: 73.6 (2) Naltrexone: 61.8 % (p = ns) Cocaine use (urine analysis) as proportion of negative urine samples for cocaine: (1) Naltrexone + CM: 55.6 % (2) Naltrexone: 54.4 % (p = ns)

Author (Year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Higgins et al. (1986), USA	39 opioid-dependent patients (DSM-IV diagnostic criteria) Mean age: 32 years Male: 100 %	Detoxification treatment (1) Detoxification + no CM dose increase ($n = 13$) (2) Detoxification + CM dose increase ($n = 13$) (3) 10-week detoxification with methadone ($n = 13$)	CM based on negative urine results for opioids. CM dose increase group received dose increases of 5, 10, 15, 20 mg on days 22–77. Dose increase no CM group received the same dose increase	Treatment retention Opioid use (urine analysis) – as proportion of positive urine samples for opioids	2.5 months	Retention: Days in treatment (1) Detoxification + no CM dose increase: 75 (2) Detoxification + CM dose increase: 78 (3) 10-week detoxification with methadone: 64 ($p = ns$) Opioid use (urine analysis) as proportion of positive urine samples for opioids: (1) Detoxification + no CM dose increase: 17 % (2) Detoxification + CM dose increase: 13 % (3) 10-week detoxification with methadone: 35 % ($p = ns$)
Hser et al. (2011), China	320 opioid-dependent patients (DSM-IV diagnostic criteria) Mean age: 38 years Male: 76.2 %	Maintenance treatment (1) MMT + CM ($n = 160$) (2) MMT ($n = 159$)	CM based on negative urine results for opioids and methadone A computerised method was used to determine each draw amount. Half of the draws had incentive rewards (1 Yuan: USD 0.15), 30 % had small incentives (5 Yuan: USD 0.74), 15 % had medium incentives (10 Yuan: USD 1.47) and 15 % had high incentives (20 Yuan: USD 2.94)	Treatment retention Opioid use (urine analysis) – as (i) proportion of negative urine samples for opioids and (ii) longest duration of sustained abstinence (weeks)	3 months	Retention: (1) MMT + CM: 80.6 % (2) MMT: 66.7 % ($p < 0.05$) Opioid use (urine analysis): (i) Proportion of negative urine samples for opioids (1) MMT + CM: 45.5 % (2) MMT: 39.8 % ($p = ns$) (ii) Longest duration of sustained abstinence (weeks) (1) MMT + CM: 5.1 (2) MMT: 4.1 ($p < 0.05$)
Jiang et al. (2012), China	160 opioid-dependent patients (DSM-IV diagnostic criteria) Mean age: 38.9 years Male: 78.1 %	Maintenance treatment (1) MMT + CM ($n = 80$) (2) MMT ($n = 80$)	CM based on negative urine results for opioids and methadone The size of the reward or the prize could increase based on the number of times the client sequentially received MMT or had continuous negative urine samples. The total award provided was 527 Yuan (USD 83.60)	Treatment retention Opioid use (urine analysis) – as (i) proportion of negative urine samples for opioids and (ii) longest duration of sustained abstinence (weeks)	6 months	Retention: (1) MMT + CM: 78.8 % (2) MMT: 77.5 % ($p = ns$) Opioid use (urine analysis): (i) Proportion of negative urine samples for opioids (1) MMT + CM: 9.2 % (2) MMT: 9.6 % ($p = ns$) (ii) Longest duration of sustained abstinence (weeks) (1) MMT + CM: 15.4 (2) MMT: 13 ($p = ns$)
McCaul et al. (1984), USA	20 opioid-dependent patients (DSM-IV diagnostic criteria) Mean age: 29 years Male: 100 %	Detoxification treatment (1) Detoxification + CM ($n = 10$) (2) 9-week detoxification with methadone ($n = 10$)	CM based on negative urine results for opioids. Patients received take-home methadone privilege and USD 10 for each opioid-free urine sample	Treatment retention Opioid use (urine analysis) – as (i) proportion of negative urine samples for opioids and (ii) number of patients with longest duration of sustained abstinence (up to 10 weeks)	2 months	Retention : (1) Detoxification + CM: 70 % (2) Detoxification: 20 % ($p < 0.05$) Opioid use (urine analysis): (i) Proportion of negative urine samples for opioids (1) Detoxification + CM: 60 % (2) Detoxification: 80 % ($p < 0.05$) (ii) Number of patients with longest duration of sustained abstinence (up to 10 weeks) (1) Detoxification + CM: 50 % (2) Detoxification: 0 % ($p < 0.05$)

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Neufeld et al. (2008), USA	100 opioid-dependent patients with antisocial personality disorder (DSM-III diagnostic criteria) Mean age: 39 years Male: 77%	Maintenance treatment (1) MMT + counselling + CM (n = 51) (2) MMT + counselling (n = 49)	CM based on counselling session attendance and negative urine analysis for illicit drugs (no further specification). Patients who attend counselling sessions and give negative urine samples can increase dose, select medication time and have take-home methadone dosage	Opioid and cocaine use (urine analysis) – as proportion of negative urine samples for opioids and cocaine	6 months	Opioid use (urine analysis) as proportion of negative urine samples for opioids: (1) MMT + counselling + CM: 80.5 % (2) MMT + counselling: 73.7 % (p = ns) Cocaine use (urine analysis) as proportion of negative urine samples for cocaine: (1) MMT + counselling + CM: 77.3 % (2) MMT + counselling: 66.7 % (p = ns)
Nunes et al. (2006), USA	69 opioid-dependent patients (DSM-IV diagnostic criteria) Mean age: 35.3 years Male: 79%	Naltrexone maintenance treatment (1) Naltrexone + CM (n = 36) (2) Naltrexone (n = 33)	CM based on naltrexone ingestion and negative urine analysis. Voucher points, worth USD 2.00 each and exchangeable for goods and services consistent with the treatment plan, were awarded at one point for each day of urine-confirmed abstinence and one point for each day of monitored naltrexone compliance. There is the potential for USD 28 per week and USD 672 total for complete abstinence and naltrexone adherence throughout the 6-month trial	Treatment retention Opioid and cocaine use (urine analysis) – as subjects with >80 % of negative urine samples for opioids and proportion of cocaine-positive urine samples (proportion of positive urine samples and percentage of opioid-free urine samples are during treatment, prior to dropout)	6 months	Retention: (1) Naltrexone + CM: 22.2 % (2) Naltrexone: 9.1 % (p < 0.05) Opioid use (urine analysis) as subjects with >80 % of negative urine samples for opioids: (1) Naltrexone + CM: 47.2 % (2) Naltrexone: 63.6 % (p = ns) Cocaine use (urine analysis) as proportion of cocaine-positive urine samples: (1) Naltrexone + CM: 21 % (2) Naltrexone: 26 % (p = ns)

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Preston et al. (1999), USA	57 opioid-dependent patients (DSM-III diagnostic criteria) Mean age: 33.4 years Male: 63.6 %	Naltrexone maintenance treatment (1) Naltrexone + CM (n = 19) (2) Naltrexone + voucher non-CM (n = 19) (3) Naltrexone (n = 19)	CM based on naltrexone ingestion. The value of the vouchers began at USD 2.50 and increased in value by USD 1.50 for each consecutive dose ingested. In addition, for every three consecutive naltrexone doses ingested, subjects earned an additional voucher worth USD 10.00. A subject who ingested all naltrexone doses for 12 consecutive weeks could earn a total of USD 1 155. Patients in the non-CM control group received vouchers independent of whether or not they ingested naltrexone. Vouchers in this group were matched to those given in the CM group	Treatment retention Opioid and cocaine use (urine analysis) – as proportion of opioid-positive urine samples and proportion of cocaine-positive urine samples (missing samples ignored)	3 months	Retention: (1) Naltrexone + CM: 50 % (2) Naltrexone + voucher non-CM: 25 % (3) Naltrexone: 5 % ($p = 0.002$) Opioid use (urine analysis) as proportion of opioid-positive urine samples: (1) Naltrexone + CM: 14 % (2) Naltrexone + voucher non-CM: 27 % (3) Naltrexone: 24 % ($p = ns$) Cocaine use (urine analysis) as proportion of cocaine-positive urine samples: (1) Naltrexone + CM: 30 % (2) Naltrexone + voucher non-CM: 32 % (3) Naltrexone: 39 % ($p = ns$)
Preston et al. (2000), USA	57 opioid-dependent patients (DSM-III diagnostic criteria) Mean age: 37.4 years Male: 61.2 %	Maintenance treatment (1) MMT + CM (n = 29) (2) MMT (n = 28)	CM based on negative urine results for opioids. The value of the vouchers began at USD 2.50 and increased in value by USD 1.50 for each consecutive dose ingested. In addition, for every three consecutive naltrexone doses ingested, subjects earned an additional voucher worth USD 10.00. A subject who met voucher criteria for 8 consecutive weeks could earn a total of USD 554. Patients in the non-CM control group received vouchers independent of whether or not they met the criteria. Vouchers in this group were matched to those given in the CM group	Treatment retention Opioid and cocaine use (urine analysis) – as (i) proportion of opioid-negative urine samples and proportion of cocaine-negative urine samples and (ii) number of consecutive opioid-negative urine samples	2 months	Retention: (1) MMT + CM: 93.1 % (2) MMT: 96.4 % ($p = ns$) Opioid use (urine analysis): (i) Proportion of opioid-negative urine samples (1) MMT + CM: 47.4 % (2) MMT: 33.8 % ($p < 0.05$) (ii) Sustained abstinence (number of consecutive opioid-negative urine samples): results not reported ($p < 0.05$ in favour of CM) Cocaine use (urine analysis) as proportion of cocaine-negative urine samples: (1) MMT + CM: 93.1 % (2) MMT: 96.4 % ($p = ns$)

Author (year), country	Participants	Experimental and control intervention	Contingency management intervention	Outcome measures	Length of follow-up	Results
Stitzer et al. (1992), USA	53 opioid-dependent patients (DSM-III diagnostic criteria) Mean age: 34 years Male: 72 %	Maintenance treatment (1) MMT + CM take home ($n = 26$) (2) MMT + take home no CM ($n = 27$)	CM based on negative urine results for opioids, cocaine and benzodiazepines. CM take home: subjects earned the first take-home dose after six consecutive negative urine samples (3 weeks). Additional take homes were gained for every 3 weeks of continuous abstinence. No CM take home: subjects earned 0, 1, 2 or 3 take-home doses per week at random	Treatment retention Opioid and cocaine use (urine analysis) – as proportion of opioid-positive urine samples and proportion of cocaine-negative urine samples	7 months	Retention: (1) MMT + CM take home: 74 % (2) MMT + take home no CM: 61.5 % ($p = ns$) Opioid use (urine analysis) as proportion of opioid-positive urine samples: results not shown ($p = ns$) Cocaine use (urine analysis) as proportion of cocaine-negative urine samples: results not shown ($p = ns$)

MMT, methadone maintenance treatment; ns, not significant; ST, standard treatment.

Annex 2

Excluded studies and studies awaiting assessment

Excluded studies

Cannabis-dependent patients

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Patients dependent on both cocaine and opioids

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