Addition of Contingency Management to Stop Smoking Services in Opiate Users A Pilot and Feasibility Study

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Addition of Contingency Management to Stop Smoking Services in Opiate Users:

A Pilot and Feasibility Study

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In loving memory of my grandfather, Arthur Millington (1933-2015).

Without your impromptu (and often unsolicited) science lessons throughout my childhood, I may never have walked this path. I regret that you are not here to see me complete this journey, but you have accompanied me in my thoughts every step of the way. Thank you.

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Abstract

Prevalence of tobacco smoking amongst those in treatment for opiate dependence is almost five times greater than that of the general population. Despite this, very few of those undergoing treatment for opiate addiction receive help to stop smoking. Contingency management (CM) is a behavioural intervention, based on the principles of operant conditioning, where desired behaviours are positively reinforced with some form of reward. CM may represent a potentially useful addition to standard stop smoking treatments for those in opiate addiction treatment, but has never been tested in this context in the UK. This thesis describes the development and piloting of an intervention, investigating the addition of a contingency management intervention for tobacco smoking, to standard stop smoking services treatment, in individuals undergoing treatment for opiate addiction.

A meta-analysis was first conducted, investigating the use of CM as an intervention for the use of non-prescribed drug use during opiate addiction treatment. CM was found to be to be more effective than control in engendering abstinence from a wide range of drugs. Moderator analysis showed CM to be more effective than control in preventing use of cocaine, cocaine and opiates, tobacco, and poly-substance use, but not of opiates.

Whilst carrying out the meta-analysis, it was discovered that no tool currently existed for assessing the quality of CM studies. This was addressed by the design and testing of a new tool, the CMQAT (Contingency Management Quality Assessment Tool). The tool underwent three stages of reliability and validity testing. Inter-rater reliability increased from slight at stage one, to fair at stage two, and was better than that of an established quality assessment tool (EPHPP) that achieved only slight agreement. Predictive validity could not be established at any stage.

The results of the meta-analysis and CMQAT development were used to design a feasibility and pilot study, testing the addition of a CM intervention, to standard stop smoking services treatment. Forty opiate addiction patients were recruited into the study, and 37 were randomised to either an experimental (CM for smoking abstinence) or control (CM for attendance at the clinic) condition. The rate of recruitment was greater than that of other similar studies, yet only ten participants completed the intervention, two from the experimental condition and eight from the control, with none of the participants attending follow-up. The most widely reported reason for dropping out of the study was that the smoking clinic was not run at convenient times.

Overall, I believe this thesis constitutes a significant contribution to the CM literature. The findings of the meta-analysis offer further support for the efficacy of CM as an intervention for non-prescribed drug use during opiate addiction treatment. The CMQAT forms the foundation for future work to improve both the accuracy of quality assessments of CM trials, and the reporting of methods and data in published reports of CM trials. The feasibility/pilot study represented the first time in the UK that CM had been used as an intervention for tobacco smoking during opiate addiction treatment. The primary observation from this study was that with the CM protocol used, retention in treatment was poor, with only 25% of participants completing the five-week intervention. Taken together, the findings have a number of implications for research, practice and policy. Perhaps the most important of these though, is that implementing CM in a clinical setting alongside standard stop smoking services treatment, introduces a number of new challenges not encountered in a laboratory setting. Further feasibility and pilot work is required before a full scale randomised controlled trial can be carried out.

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Abbreviations

CM	Contingency Management
CMQAT	Contingency Management Quality Assessment Tool
CO	Carbon Monoxide
EPHPP	Effective Public Health Practice Project
HRA	Health Research Authority
IRAS	Integrated Research Application System
LDA	Longest Duration of Abstinence
NCSCT	National Centre for Smoking Cessation and Training
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NRT	Nicotine Replacement Therapy
PNS	Percentage of Negative Samples
ppm	Parts Per Million
RCT	Randomised Controlled Trial

Chapter 1:

Introduction

1.1 Tobacco Smoking

1.1.1 Tobacco and Health

Prevalence of tobacco smoking varies dramatically between countries, with rates in 2015 ranging from as little as 6.6% of a country's population (Nigeria) to 97.5% of the population (Kiribati) [1]. Globally, approximately 820 million men and 176 million women are smokers [2]. Prevalence of smoking has been steadily decreasing globally, with age-standardised prevalence of daily tobacco smoking in men declining from 41.2% to 31.1%, an average annual rate of decline of 0.9% and for women declining from 10.6% to 6.2% between 1980 and 2012 [3]. Recently, smoking prevalence in the UK dropped below 17% nationally for the first time ever [4]. Despite this, however, the increasing global population means that the number of daily smokers has actually increased, from 721 million in 1980, to 967 million in 2012 [3].

Tobacco smoking is the leading cause of premature death in the western world [5], currently killing 6 million people per year across the globe and predicted to kill 8 million people annually by 2030 [6]. Smokers have between a two and fourfold greater risk of premature death than those who do not smoke [7,8] and in England alone smoking killed 74 thousand people in 2014 [9]. The main cause of smoking-related premature death occurs through cancer [10]; smoking tobacco causes over a quarter of all cancer deaths in the UK [11], with 270,000 new cases of cancer per year in Europe directly attributable to it [12]. Tobacco smoke contains 5000 chemicals, of which 98 are harmful to humans when inhaled and 60 are carcinogenic [13]. Twenty of the chemicals in cigarettes have been found to cause lung cancer tumours in lab studies, with polycyclic aromatic hydrocarbons of particular concern [14], and causal links have now been made between tobacco smoking and at least 14 different types of cancer [15]. Smoking also increases mortality through a number of other negative health outcomes, and in the UK smoking is responsible for 23% of all hospital admissions for respiratory disease and over 10% of admissions for circulatory diseases [9]. These deleterious health effects translate to profound economic costs, costing the NHS £2 billion a year to treat, and costing the UK economy £13.9 billion per year in total [16].

1.1.2 Tobacco Dependence Mechanisms

It is now widely accepted that the primary substance responsible for the addictive nature of tobacco smoking (but not its negative health effects [17,18]) is nicotine [19,20]. However, this was not always the case, and it was not until the surgeon general's report in the late 1980s [21] that nicotine was placed on a parity with other drugs of abuse [19]. Nicotine's

primary target in the brain is nicotinic acetylcholine receptors (nAChRs) [22]. These are found throughout both the central and peripheral nervous systems. Two main cholinergic projection subsystems exist, one of which projects to the dopaminergic neurons of the substantia nigra and ventral tegmental area (VTA) [23]. Nicotine has been shown to produce dopamine release in this region of the brain that is qualitatively similar to that of other drugs of abuse [24]. Dopamine release in these brain regions has been identified as playing a critical role in drug addiction [23,25]. This is therefore the proposed mechanism by which tobacco smoking becomes addictive, with the rapid rate of nicotine absorption in the brain and high amounts of nicotine attained in the brain from smoking thought to be crucial factors that promote and sustain nicotine addiction [26].

1.1.3 Tobacco Smoking and Opiate Addiction

Despite smoking prevalence in the UK falling below 17% nationally for the first time [4], smoking prevalence amongst those in treatment for opiate addiction remains far higher, between 84-98% [27–31]. Worryingly, despite a large proportion of this group expressing interest in smoking cessation [27,28], very few are ever offered smoking cessation treatment during treatment. In the South London and Maudsley NHS trust for example, only 15% of those in treatment for drug abuse were offered smoking cessation help during treatment in 2014 [32].

Currently, the mechanisms underlying this high co-morbidity of tobacco smoking and opiate use are not well understood, with several potential explanations identified. One potential explanation is that of the common pathway of addiction, where addiction to multiple substances is thought to be mediated through the dopamine reward pathway [23–25]. Another possible explanation is that some aspects of tobacco dependence may be mediated through the effects of endogenous opiates [33]. For example, smoking is associated with lower availability of opioid receptors in the thalamus and basal ganglia, an effect related to craving and severity of addiction [34]. There is still debate about the effects of this on tobacco smoking, however, as opiate antagonists have thus far not proven to be effective in smoking cessation [35]. This said, the opiate receptor agonist methadone has been shown to increase tobacco smoking [36], and nicotine dependence to increase discomfort from opiate withdrawal during detoxification [37].

Another potential joint pathway for this co-morbidity is that of cue-reactivity, the term given to a broad range of physiological arousals and psychological desires that occur when drug users are presented with drug related cues [38]. It is thought that these responses to cues are learnt associations, and have been shown to occur in both tobacco smokers and

opiate users [39]. Research has shown how neutral stimuli (coloured cards) can quickly become conditioned as cues for smoking [40], and how this can elicit a greater urge to smoke [41]. Related to this is the phenomenon of state dependent memory, where the internal state of an individual impacts memory storage and retrieval [42]. This has been successfully shown to occur for tobacco smoking in humans [43] and opiates in mice [44,45]. Taken together with the high co-morbidity of tobacco smoking and opiate use, it seems logical to suggest that tobacco and opiates may act in some individuals as cues for each other, and that the use of one may induce a desire for the other. This is as yet to be substantiated with research but offers another potential explanation for the high co-morbidity of tobacco smoking and opiate use.

1.1.4 Smoking Cessation

Smoking cessation precipitates several different adverse withdrawal symptoms [46,47]. These can include irritability, anxiety, difficulty concentrating, increased appetite, restlessness, depressed mood, insomnia [48], mood swings and cigarette cravings. Anticipation of withdrawal symptoms has been identified as a barrier to the initiation of a quit attempt [40], and severity of withdrawal symptoms is associated with relapse to smoking during cessation [49]. Resultantly, quit rates from tobacco smoking are relatively low, with NHS services achieving quit rates of 53% at 4 weeks, falling to only 15% at one year [50]. Despite this, those receiving behavioural support combined with pharmacological support for their smoking addiction are still four times more likely to quit than those not receiving help [51].

When smoking cessation treatment first began in the late 1960s, the approach to treatment was somewhat sporadic. One of the earliest large scale trials into smoking cessation, “The Smoking Control Research Project”, trialled a combination of counselling and tranquilising drugs to aid cessation [50,52,53]. Cessation rates were good, with an average success rate of 20% at one year follow up [53]. However, the different counsellors employed wildly different treatment strategies, ranging from an “aggressive crusading approach” to “rational persuasion” [54], somewhat obscuring the findings. In the early 1980s, however, the model for current smoking cessation interventions began to take form, now known as the “Maudsley Model” [50]. This approach to smoking cessation was one of the first to concentrate on nicotine withdrawal, with a primary focus on therapy being able to tackle the initial difficult period of acute nicotine withdrawal [55]. This early treatment implemented five evening visits organised over 4 weeks, with clients expected to quit immediately after the first meeting [55]. Nicotine gum was also provided as part of the

treatment, with appropriate training as to how to use it, along with measurements of breath carbon monoxide (CO) levels to chart progress [55].

Over the intervening years, this approach has been adapted and changed in line with new evidence, to what is now used across the NHS and in many other countries, the "Standard Treatment Program" of the NCSCT (National Centre for Smoking Cessation Training) [56]. These programs are now run by local authorities rather than the NHS, but still focus on dealing with initial nicotine withdrawal, and still require clients to set a quit date within the first week. However, the standard treatment now runs over 6 weeks, with one session per week. As well as providing behavioural support, the treatment also encourages the use of evidence-based pharmacotherapies, namely nicotine replacement therapy (NRT). It is also emphasised how best to use these, and clients are encouraged to try a variety of different types in order to determine which best suits their individual needs [57]. Each of the six treatment sessions has a clearly-defined purpose and focus. The manualised nature of the program has allowed its widespread use in various health care settings throughout the UK, and its easy adaption to specialist client groups such as those in addiction treatment and mental health care settings. The pharmacotherapy options now available to smokers are far broader than they were in the initial days of the Maudsley model and are not limited to NRT. NRT options now include patches, strips, nasal spray, gum, lozenges, inhalator, microtabs and mouth spray, whilst non NRT pharmacotherapy options include varenicline and bupropion [56]. A large body of evidence now exists showing that both NRT and non-nicotine-based pharmacotherapies are effective and efficacious in encouraging cessation [58–60], with the partial nicotine receptor agonist varenicline showing the greatest efficacy and effectiveness [61,62]. Other treatments, for example, contingency management (see below) have also been utilised in smoking cessation, with results suggesting that incentives increase cessation rates over 40% compared to control (60).

1.1.5. Smoking Cessation in Opiate Use

Smoking cessation during treatment for opiate addiction remains a relatively under-researched area compared to smoking cessation in the general public. This is somewhat surprising given the high rates of smoking prevalence amongst this group [27–30]. Even more so when it is considered that smoking tobacco during opiate detoxification results in significantly greater opiate craving and significantly lower rates of detoxification completion [37], and is associated with higher levels of illicit drug use [63]. To compound this issue, not only does smoking tobacco

have a negative effect on drug treatment, but illicit drug use can negatively impact on smoking cessation attempts, reducing efficacy of normal NHS smoking cessation treatment by nearly half [64].

Moreover, until very recently, smoking cessation has been viewed by drug treatment staff as of significantly lower importance than treating clients' main drug of abuse, with less than of a third of staff across seven community and residential addictions services in one UK trust thinking it should be treated early in a client's primary addiction treatment [32]. In an assessment of 408 methadone clinics in the USA, only 18% offered individual or group smoking cessation counselling, and only 12% prescribed NRT [65]. Contrary to this, however, a number of studies have now shown that stopping smoking has no negative impact on drug addiction treatment outcomes, with some studies suggesting a positive effect [66].

Several different treatments for smoking cessation have been trialled in the US in those in treatment for opiate addiction, with varying degrees of success. In one study, varenicline significantly increased quit rates and smoking reduction compared to placebo, however, this effect ceased once treatment was removed [67]. Similar results in cessation and smoking reduction have been observed with combined bupropion and nicotine replacement therapy [68]. Electronic cigarettes have also been shown to significantly reduce the number of cigarettes smoked per day in opiate addiction treatment [69]. A more widely researched intervention for smoking cessation during treatment for opiate addiction treatment is contingency management (see below). Four studies have shown significant increases in smoking abstinence and reduction in cigarette smoking in those in opiate addiction treatment [70–73] using contingency management. However, these small studies were again all carried out in the USA, tested a total of only 132 participants in contingency management conditions using a mixture or reward schedules, and had experimental phases lasting between two and 12 weeks. At current, no studies have been conducted in the UK investigating the use of contingency management as an intervention for tobacco smoking during treatment for opiate addiction.

1.2 Contingency Management

1.2.1 Underlying Theory

Contingency management (CM) is founded on the principles of operant conditioning, developed by B.F. Skinner during the first half of the 20th century, from the earlier work of Konorski, and later Thorndike [74]. According to operant conditioning theory, changes in behaviour are

brought about by either positive or negative reinforcement, with positive reinforcers encouraging behaviours with desirable outcomes, and negative reinforcers discouraging behaviours that have aversive outcomes [74]. These basic behavioural principles (positive and negative reinforcement) have been used to explain a variety of human behaviours, including addiction. In terms of addiction, it is posited that the positive effects of drugs operate as positive reinforcers for further consumption with the desire to avoid the negative effects experienced during withdrawal acting as negative reinforcement [75]. The proposed neurological underpinnings of positive reinforcement identify the mesocorticolimbic dopamine system as being the primary brain circuit responsible for the rewarding nature of drugs [76]. It is argued that the positive reinforcing effects of drugs are driven by the increased dopamine release observed after their administration [77,78], as well as the extinction of the reinforcing effects of drugs after selective destruction of the system [20,79,80]. The negative reinforcing effects of drugs are thought to be mediated by the same dopamine system, and be linked to a reduction in reward function [76]. Namely, a decrease in dopamine and serotonin neurotransmission after prolonged exposure to drugs of abuse [81] causing the anhedonic effects associated with acute drug withdrawal [76]. CM utilises these same reward mechanisms to encourage healthier behaviours, in this case the reduction or cessation of drug use [82]. Importantly, CM focuses on the use of positive reinforcement rather than negative. Not only is this more pleasant for both clients and staff [82], but curtails the high attrition rates seen with negative reinforcement [83], and is generally more effective in substance misuse than negative reinforcement [84].

1.2.2 Development of CM Over Time and Use in Addiction Treatment

CM was first developed by F.S. Keller in the early 1960s as a means of teaching psychology to university students [85]. It was quickly adopted as a means of altering a number of behaviours, from obesity [86] to household energy use [87]. One of the first investigations of CM in the addictions field was carried out on tobacco smokers in the late 1960s. Participants handed over their own money at the beginning of the experiment and were paid it back in increments for every time they recorded being abstinent at each check-up [88]. Of the 25 participants, 21 remained abstinent for the course of the experiment, and at 12-month follow up, 38% were still abstinent.

Contemporary CM interventions operate on a similar premise; however, in line with the modern focus on positive reinforcement over negative participants receive rewards without staking anything of their own. Cash is also no longer used and participants now normally receive

monetary vouchers that can be used against the purchase of particular goods (sometimes referred to as voucher-based reinforcement therapy) (Higgins & Silverman in [89]). Other rewards for desired behaviour can include clinical privileges, or on-site prize distribution [90]. Although this is the general format for CM interventions, there are a number of different variations that have been developed and tested. A body of evidence now exists showing CM to be effective in treating a wide range of substance use (illicit drugs, alcohol and tobacco) disorders, often performing better than other behavioural interventions [91–95]. CM has been observed to be particularly efficacious in engendering abstinence from opiates [93].

CM for the treatment of addiction usually takes the form of voucher-based reinforcement therapy, where patients are rewarded with vouchers for displaying the desired behaviour (for example returning negative drug samples, or clinic attendance). Commonly, the value of the vouchers received escalates with each successive display of the desired behaviour up to a set maximum (escalating schedule). If patients do not exhibit the desired behaviour (i.e. relapse), then the reward value will reset to the minimum level and begin to increase at the same rate as before. More recently, a new CM protocol has been developed aimed at reducing the overall costs of implementing CM interventions, known as the fishbowl method [96]. This operates on the same basic principle as conventional CM but rather than participants receiving vouchers, they instead receive the chance to draw tickets. These tickets give them the chance to earn high, medium or low value gifts, or win nothing at all (25% of tickets in the original study) [96]. This form of CM was highly effective in encouraging abstinence amongst alcohol dependent patients [96].

The most recent development in the way that CM interventions are conducted, is percentile shaping [97–99]. Percentile shaping (or simply shaping) aims to increase patient contact with rewards, thereby increasing the likeliness of them achieving the desired treatment outcome. This is achieved by making rewards contingent, not on absolute abstinence, but on providing biochemically verified levels of a drug in progressively lower percentiles. An investigation of this in tobacco smoking cessation tested the effects of providing contingent rewards based on producing breath CO samples in the either the 10th, 30th, 50th or 70th percentile group. The percentile group in this case is linked to a participant's last 10 breath samples. In the 70th percentile group, for example, receiving the reward is contingent on producing a breath sample with CO levels lower than the 7th lowest sample of the last nine samples delivered. In the 10th percentile group, on the other hand, a breath sample needs to be lower than the lowest of the previous 9. All percentage schedules resulted in reduced

breath CO levels, but those in the 70th percentile group delivered the lowest CO samples. Similarly, the number of participants delivering breath samples indicating complete abstinence was far lower in the 10th percentile group than any of the others [98].

It has been noted, however, that shaping schedules can result in participants receiving rewards of far greater magnitude for their first abstinent sample than those in non-shaping trials. This means that it may not be the increased contact with rewards that makes shaping successful, but instead simply the magnitude of reward. When this was tested, it was observed that standardising the rate at which rewards escalate in a shaping schedule (i.e. increasing only for samples showing abstinence, not for being lower than the previous), then non-shaping CM performs far better than shaping. Participants not only achieved cessation earlier, but also maintained it longer than those in a shaping condition [100].

1.2.3 CM for Smoking Cessation

CM for the treatment of tobacco smoking is relatively under-researched when compared to its use as an intervention for illicit drug use. However, a small number of studies finding CM to be an effective intervention for tobacco smoking have been conducted in a range of treatment settings. For example, CM has been used successfully to treat smoking in pregnancy [101], adolescence [102,103], schizophrenia [104], and post-traumatic stress disorder [105]. Although all of these studies observed significantly greater cessation rates or reductions in breath CO in CM conditions compared to control, only one [101] of these studies was carried out in the context of standard stop smoking treatment. This study offered pregnant smokers up to £400 in vouchers, over a 12-week period, for CO verified smoking cessation. At the primary outcome assessment, significantly more participants receiving rewards than not receiving rewards had stopped smoking (22.5% vs 8.6%). Moreover, a Cochrane review of 21 studies using incentives to encourage smoking cessation found that the odds ratio for quitting with incentives compared to without was 1.42 [106]. This suggests that overall, CM can act as a successful intervention for smoking cessation, across a number of different treatment populations.

1.2.4 Efficacy of CM on Discontinuation of Rewards

Although CM is often highly effective during treatment, the primary issue encountered with CM interventions is the high remission rates observed at follow-up once contingent rewards are stopped. For example, in the Cochrane review mentioned above, only three of the 21 studies showed any advantage of CM over control after 6-month follow-up. For example, when CM was compared to cognitive behavioural therapy (CBT) in

secondary-school smokers [107], CM engendered significantly greater 7-day abstinence (36% of participants) than CBT (0%). At one month follow up though, only 7% of CM participants were still abstinent, compared to 4% in the CBT. The same has been observed in substance abuse settings, with a meta-analysis showing a decrease in effect size from d = 0.52 to d = 0.37 in the three months following treatment completion [93].

Different CM schedules do appear, however, to have differential effects on the longevity of treatment effects. Escalating with reset CM, for example, has been found to show significantly lower tobacco smoking relapse in follow-up than fixed-schedule CM [108]. Similarly, in tests of escalating schedules with and without reset, as well as fixed reward schedules, escalating with reset schedules performed significantly better at engendering an initial period of abstinence that remained unbroken for the rest of the study [109]. Little research has been carried out directly addressing the high remission rates observed in CM, however, Kellogg and colleagues have identified seven key factors affecting the efficacy of CM interventions (target behaviour, choice of target population, choice of reinforcer, incentive magnitude, frequency of incentive distribution, timing of incentive, and duration of intervention) [82].

1.2.5 CM for Smoking During Treatment for Opiate Addiction

The use of CM as an intervention for smoking cessation during opiate addiction treatment is markedly under researched. To our knowledge, there are currently only four studies published that have researched CM in this context [70–73], all of which were carried out in the US, two by the same research group [70,73]. All took place in drug treatment centres (but not standard smoking cessation treatment, see below), with one taking place in a centre specifically for the treatment of drug use in pregnant women [71]. The total value of rewards available ranged between $362.50 to $857.50, and two [70,72] of the four studies offered pharmacotherapy alongside the CM intervention, namely bupropion [70] and NRT [72]. All studies employed an escalating with reset CM schedules, with one of the studies also using a percentile shaping schedule [71]. However, there is a significant divide between studies in the length of intervention used and the number of times per week that participants were required to biochemically verify abstinence from tobacco smoking and receive rewards. The two studies run by the same research groups [70,73] lasted only 14 days, but recorded smoking and administered rewards on every day. The two remaining studies, conversely, were conducted over a much longer period of time (12 weeks), but biochemically measured smoking and administered rewards only three times a week. Notably, despite these studies representing the only instances of CM being used for treating

tobacco smoking during opiate addiction treatment, only two of the studies [71,73] are classified as a pilot or feasibility studies, with the other two [70,72] reported as full trials. These two pilot studies only reported efficacy data, however, not pilot or feasibility findings.

Overall, all studies reported significantly greater smoking abstinence in CM conditions than in control conditions at the end of treatment. However, the outcomes used to measure this differ from those used to measure clinical efficacy in the UK. The Russell Standard [110] suggests that the minimum standard required of an effective treatment is for 40% of participants to be abstinent four weeks after the quit date. The two, two-week long interventions measured abstinence rates of only 30% [73] and 10% [70] at the 30-day follow-ups. Of the two reaming studies, one [71] reported a cessation rate of 31% after 12 weeks of the intervention, whilst the final study reported cessation rates of 25-30% at week four [72]. This mirrors the findings regarding the long-term effects of CM outlined above. It is worth noting that the Russell standard is used for smoking cessation in the general population, and the lower rates of cessation in those undergoing opiate addiction treatment may still represent a clinically significant reduction.

There are also a number of other limitations in the findings of these studies. Firstly, none of the studies was carried out in what could be considered a 'normal' treatment environment. None of the CM interventions ran as an adjunct to normal stop smoking treatment, or even attempted to emulate the one appointment per week normally seen in smoking cessation treatment, instead assessing participants multiple times per week. Secondly, all of these studies were carried out in the US, making it hard to generalise their findings outside of a US opiate addiction treatment setting. Therefore, although CM appeared to show promise as an intervention for tobacco during opiate addiction treatment, it remained unclear not only how these results transferred to normal medical practice, but whether CM could even be implemented in this context at all.

1.3 Conclusion and Aims

1.3.1 Conclusion

In conclusion, tobacco smoking during treatment for drug addiction, specifically in opiate addiction, poses a major barrier to treatment success. Moreover, very little has been done thus far to encourage this group to stop smoking, despite the steady downward trend in smoking prevalence observed in the general public. The result of this is not only undue financial stress on the already over-stretched resources of the NHS, but the

needless premature death of a huge number of already disadvantaged people. Not only is there now a great deal of evidence supporting this premise, but research has begun to highlight potentially effective means by which this can be stopped. CM has been used widely in the drug addictions field for a number of years, and has developed a strong supporting evidence base [91–95]. Moreover, it has been used not only to treat opiate addiction itself, but also the use of various other drugs during opiate addiction treatment. The use of CM for treating tobacco smoking during opiate addiction still remains under researched, however, and has never been tested in the UK. The purpose of this thesis is to address this issue, and aims to do so using the MRC guidelines for developing and evaluating complex interventions [111].

1.3.2 Intervention Development

Due to the specific nature of the target population and behaviour, a CM intervention of this type falls under that of a "complex" intervention. The intervention will therefore be designed under the Medical Research Council (MRC) guidelines for the development of complex interventions [111]. These guidelines constitute the important steps and processes to be followed when developing a complex intervention. Initially, the guidelines described the design process as progressing linearly through clearly defined phases in an iterative process. This constituted four phases; Phase I: Modelling, Phase II: "Exploratory Trial", Phase III: Definitive "Randomised Controlled Trial", and Phase IV: Long Term Implementation. These were preceded by a pre-clinical theory stage and follow a continuum of increasing evidence (see Figure 1) [112].

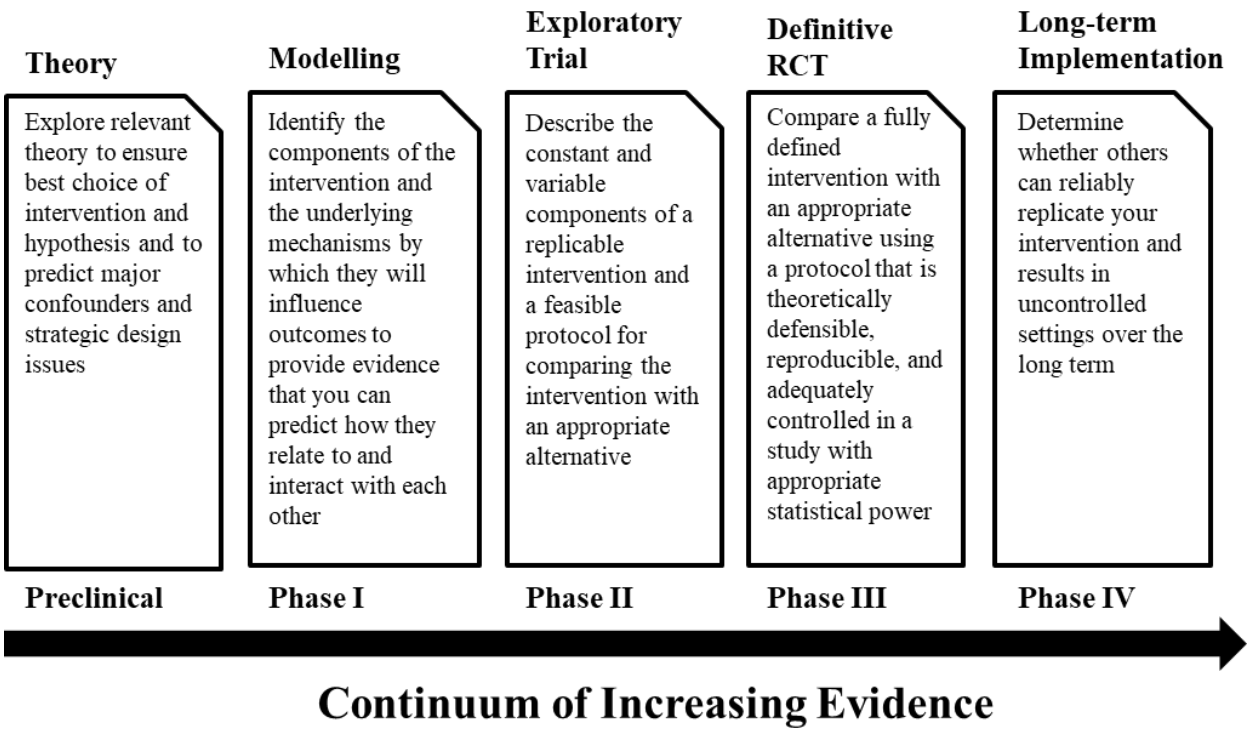

Figure 1 Stages of intervention development as adapted from the 2008 MRC guidelines for the development of complex interventions

The most recent version of these guidelines, however, note that the development of interventions may not necessarily progress in a linear or even cyclical manner [111]. The updated guidelines instead recommend that the development of complex interventions should be performed systematically, incorporating the best quality evidence and theory available, and tested using a phased approach. It is these updated guidelines that will be implemented in this thesis (see Figure 11, chapter 4).

1.3.3 Aims

There are three primary aims for this thesis:

1. To update the literature on the efficacy of CM for treating drug use in the context of opiate addiction, by performing a systematic review and meta-analysis. At the time of commencing my PhD, the most recent review assessing this was published in 2000. The reason for the broad focus of this is due to the lack of research focussing on CM for tobacco smoking during opiate addiction treatment.
2. To use the information gathered during this process to identify key effective components of CM interventions in this field in order to formulate a CM intervention for tobacco smoking during opiate addiction treatment.

3. To test the feasibility of implementing this intervention in a UK outpatient drug treatment clinic, making recommendations for the potential testing of such an intervention in a full scale randomised control trial.

Chapter 2:

Contingency Management for the Treatment of Drug Use in Opiate Addiction Treatment: A Systematic Review and Meta-Analysis

2.1 Rationale

The MRC guidelines for the development and evaluation of complex interventions [113] suggest that most interventions will initially go through a development phase. The purpose of the development stage is to identify the evidence base, to identify and develop theory, and in some cases, to model processes and outcomes. For this initial development stage, it is therefore commonplace to undertake some sort of formal review of the literature. Such a review was undertaken for this thesis to inform the design of the intervention and is detailed below. As mentioned in the previous chapter, a review on incentives for smoking cessation has already been carried out by the Cochrane Collaboration [106]. However, this review was not focussed on the treatment of tobacco smoking during opiate addiction treatment, necessitating the conduct of a review addressing this question directly. The protocol for this review is published on the PROSPERO website (registrations number 42016015621, available from: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016015621). See appendix 1 for a copy of the published article.

2.2 Background and Aims

Amongst those in treatment for opiate addiction, use of non-prescribed drugs is very common. Hair samples from 99 recently deceased opiate addiction treatment patients identified a range of 21 different drugs being used during treatment, including cocaine, amphetamine, morphine and diazepam [114]. Other studies have observed that over a third of patients entering opiate addiction treatment were also DSM-IV dependent on a drug other than heroin (not including nicotine) [115], and poly drug use has been reported to be as high as 68% [116]. These high levels of drug use are not limited to illicit substances. Tobacco smoking is highly prevalent in drug treatment in general [32], with prevalence rates of over 90% observed in individuals undergoing methadone treatment for opiate addiction [28,117]. Methadone itself has been linked to increased tobacco cigarette consumption, smoke intake and self-reported satisfaction of cigarette smoking [118] and to increased alcohol consumption compared with heroin use [119].

Use of non-prescribed drugs during methadone treatment for opiate addiction has been associated with a range of adverse effects such as poor treatment retention and outcomes [120]. Use of a single drug during opiate addiction treatment is associated with a threefold greater risk of dropping out of treatment, with use of multiple drugs quadrupling the risk [121]. For example, cocaine use during methadone treatment has been linked to persistence of heroin use [122]. Similarly, as mentioned earlier, tobacco

smoking during opiate detoxification results in significantly greater opiate craving and significantly lower rates of detoxification completion [37] and is associated with higher levels of illicit drug use [63].

High prevalence rates and the links to adverse treatment outcomes indicate a need for effective interventions for non-prescribed drug use during opiate addiction treatment. One of the most widely used behavioural interventions is contingency management (CM). CM uses rewards (for example vouchers, clinical privileges or desirable items to be won as prizes) to positively reinforce abstinence from or reduce use of drugs during treatment for opiate addiction. CM differs from other common psychological interventions in that the focus of treatment is not on introspective analysis of discrepancies between goals and behaviour (as in motivational interviewing) or modification of flawed cognitive processing (as in CBT), but instead on directly influencing the reinforcement mechanisms involved in addiction [123]. Despite a number of recent reviews assessing the efficacy of CM for substance use in general [91,92,95,124], very little is known about the use of CM for treating use of non-prescribed drugs in the context of opiate addiction treatment, where treatment outcomes may differ.

Whilst some of these reviews included studies assessing the use of CM in this context, none directly addressed the efficacy of CM for substance use during opiate addiction treatment. The most recent review of this specific use of CM is a meta-analysis published over 16 years ago [125]. CM was observed to perform better overall than control, and the effects of CM for drug use during opiate addiction treatment were observed to be moderated by five factors (type of reinforcer, time to reinforcement delivery, targeted CM drug(s), number of urine specimens collected per week and type of subject assignment). However, this review did not search the literature systematically, increasing the risk of bias in the selection of study data. Similarly, it did not assess the effects of different drugs targeted with CM, instead only assessing the moderating effects of targeting single or poly drug use. The aim of the present review was to assess the efficacy of CM for treating the use of different non-prescribed drugs during treatment for opiate addiction, by systematically searching the literature and assessing the effects of potentially moderating variables.

2.3 Methods

2.3.1 Search Strategy

The review was carried out in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [126]. Studies were identified using a keyword search of the online databases Embase, PsychInfo, PsychArticles using the Ovid SP interface and Medline using PubMed, with the following search terms: "Contingency Management" or "Reward" or "Payment" or "Incentive" or Prize" and "Substance" or "Misuse" or "Drug" or "Narcotic*" or "Tobacco" or "Smok*" or "Stimulan*" or "Cocaine" or "Alcohol" and "Opiate" or "Opioid" or "Heroin" or "Methadone". The search was limited to studies published between each database's inception and March 2015, published in the English language and including only humans. See appendix 2 for full search strategy.

2.3.2 Inclusion and Exclusion Criteria

Studies were eligible for inclusion if they: i) Tested one or more CM intervention(s) aimed at substance use reduction or abstinence in patients receiving treatment for opiate addiction; ii) used a controlled trial design– either a no/delayed treatment control group or an alternative therapy control group, or controlled by repeated participation in two or more treatment arms; iii) randomised participants to conditions; iv) provided reinforcement or punishment contingent on biological verification of substance use/abstinence; v) used consistent measures of substance use at baseline and follow-up; vi) published in a peer reviewed journal. Studies were excluded if: i) Participation was non-voluntary – e.g. court orders, prison inmates etc.; ii) means and standard deviations for treatment effects were not available from the published data or the authors.

2.3.3 Study Selection

Studies were reviewed for inclusion by three independent reviewers, with all studies being reviewed for inclusion twice. One reviewer (myself) processed all titles and abstracts as first reviewer, and two other reviewers (RC and LB) jointly processed half each as second reviewers. An agreement rate of 96% was reached between reviewers; disagreements were discussed and resolved by a separate reviewer.

2.3.4 Quality Assessment

We were unable to identify a quality assessment tool specifically for CM studies. Therefore, the EPHPP's (Effective Public Health Practice Project) 'Quality Assessment Tool for Quantitative Studies' [127] (referred to hereon as the EPHPP tool), was used to assess the internal and external validity of all studies, as well as any biases and confounds. This assesses

the quality of studies as strong, moderate or weak on six domains (selection bias, study design, confounds, blinding, data collection and withdrawals/dropouts) providing an overall score for the quality of the evidence in the study. A study is rated as providing strong evidence only when all domains are rated as moderate or strong, and a moderate rating when strong or moderate ratings are achieved for all bar one of the domains. Inter-rater reliability for the EPHPP tool has been shown to be 'fair' across the six domains and 'excellent' overall, often performing better than the Cochrane Collaboration Risk of Bias Tool [128] which is why it was selected for use here. All quality assessments were performed by a single assessor (myself).

2.3.5 Data Extraction and Synthesis

All data extraction was completed by a single reviewer (myself) using an extraction table designed specifically for the current review and agreed by all reviewers (see supplementary materials). Where studies did not contain means and standard deviations for treatment effects, authors were contacted up to two times to obtain the data. Requests for data were sent to authors of 35 studies, with data for six studies being received [129–134]. Where means and standard deviations were not obtained, alternative data including F tests, t tests and chi square were used to calculate an effect size where feasible [70,72,135,136].

2.3.6 Outcome Measures

Standardised mean differences (Cohen's d [137]) were calculated for each individual study using either 1) longest duration of abstinence (LDA) data or 2) percentage of biochemically verified negative samples (PNS). LDA refers to the longest continuous period of abstinence from a drug, often measured in days or weeks. PNS is a measure of the number of drug-negative samples submitted as a percentage of the total number of samples submitted over the course of a trial [138]. As follow-up data were available for only four [70,133,139,140] of the 10 studies that included a follow-up period, all data used in analyses are those recorded during treatment.

2.3.7 Moderators

A number of possible moderators were assessed, based on those shown in previous reviews to impact on the efficacy of CM [93,125]. These included the drug targeted for intervention, the decade in which the study was carried out, the quality of the study, duration of the intervention, the type of reinforcer used, and the form of opiate treatment participants were undergoing. Some moderators previously suggested to affect the efficacy of CM [93,125] could not be investigated due to a lack of suitable data in the included studies or because all studies used the same approach. For

example, the number of times abstinence was verified per week could not be investigated as 16 studies recorded this three times a week compared to only five recording it twice a week and one study recording it every day. Similarly, type of incentive (positive, negative, mixed) was not tested as all except two studies in both analyses used a mixed incentive. Time to reinforcement could not be tested as all included studies delivered immediate reinforcements.

2.3.8 Data Analysis

Meta-analyses were carried out using RevMan v5.3 [141] software. Data were entered into a generic inverse variance analysis in RevMan that analysed the efficacy of CM compared with control across all drug use during treatment for opiate addiction, using both LDA and PNS. All meta-analyses were carried out as random effects analyses due to the wide variety of CM interventions included [142]. To allow comparison of CM to control, some multi-arm trials were collapsed into a two arm design by averaging the effects across the treatment conditions [143]. This was only done, however, when each arm used CM in isolation (other than normal pharmacological treatment for opiate addiction); if a study arm included CM in combination with another behavioural or pharmacological treatment not part of standard treatment, then this arm was not included in the meta-analysis. This was done in order to match the design of the included studies with only single experimental and control arms. Control arms were not collapsed unless each was a standard treatment control. For example, one study [144] had four conditions (CM with either methadone or buprenorphine and performance feedback with either methadone or buprenorphine), so the two CM conditions were collapsed together, as were the two performance feedback conditions. Another study [145] also had four conditions (CM, methadone increase, CM + methadone increase and a usual care control), but no conditions were collapsed and only the CM and usual care control conditions were used in the analysis. The I^2 statistic was used to assess the percentage of variability in treatment effect estimates attributable to between-study heterogeneity.

Moderator analysis was performed using Comprehensive Meta-analysis software V.3 [146]. Results were computed using random effects statistics and indicate the extent to which each moderator accounts for variability in effect sizes with respect to drug use outcomes. A significant value of Q-between indicates significant differences among effect sizes between the categories of the moderator variable. This method also calculates the mean pooled effect size for each category within the moderator variable being tested and whether this is significant. For the drug targeted for intervention, studies fell into five categories: opiates,

cocaine, opiates and cocaine combined, tobacco, and polysubstance use. For study decade, studies were grouped as being published from 1990-1999, 2000-2009 and 2010 onwards (study publication dates ranged from 1993 to 2015). Study quality followed the strong, moderate and weak ratings of the 'Quality Assessment Tool for Quantitative Studies' [127]. Intervention durations were grouped as <12 weeks, 12 weeks, and >12 weeks. Reinforcer type was categorised as monetary vouchers and 'other'. Opiate treatment similarly contained two categories, methadone treatment and 'other'.

Publication bias was assessed using the 'failsafe N' technique [147], calculated using Comprehensive Meta-analysis software V.3 [146]. This calculates the number of studies averaging a Z-value of zero that would be required to make the overall pooled effect size non-significant [147].

2.4 Results

2.4.1 Included Studies

A total of 3144 studies were identified in the search, yielding a total of 22 studies meeting inclusion criteria that could be included in the meta-analysis (see PRISMA flow diagram, Figure 2). The included studies randomised a total of 2333 patients to 39 CM conditions and 33 non-CM control conditions. This included three studies with two CM conditions each collapsed into a single CM condition, four studies with three CM conditions each collapsed into a single CM condition, and two studies with two CM and two control conditions each collapsed into single CM and control conditions.

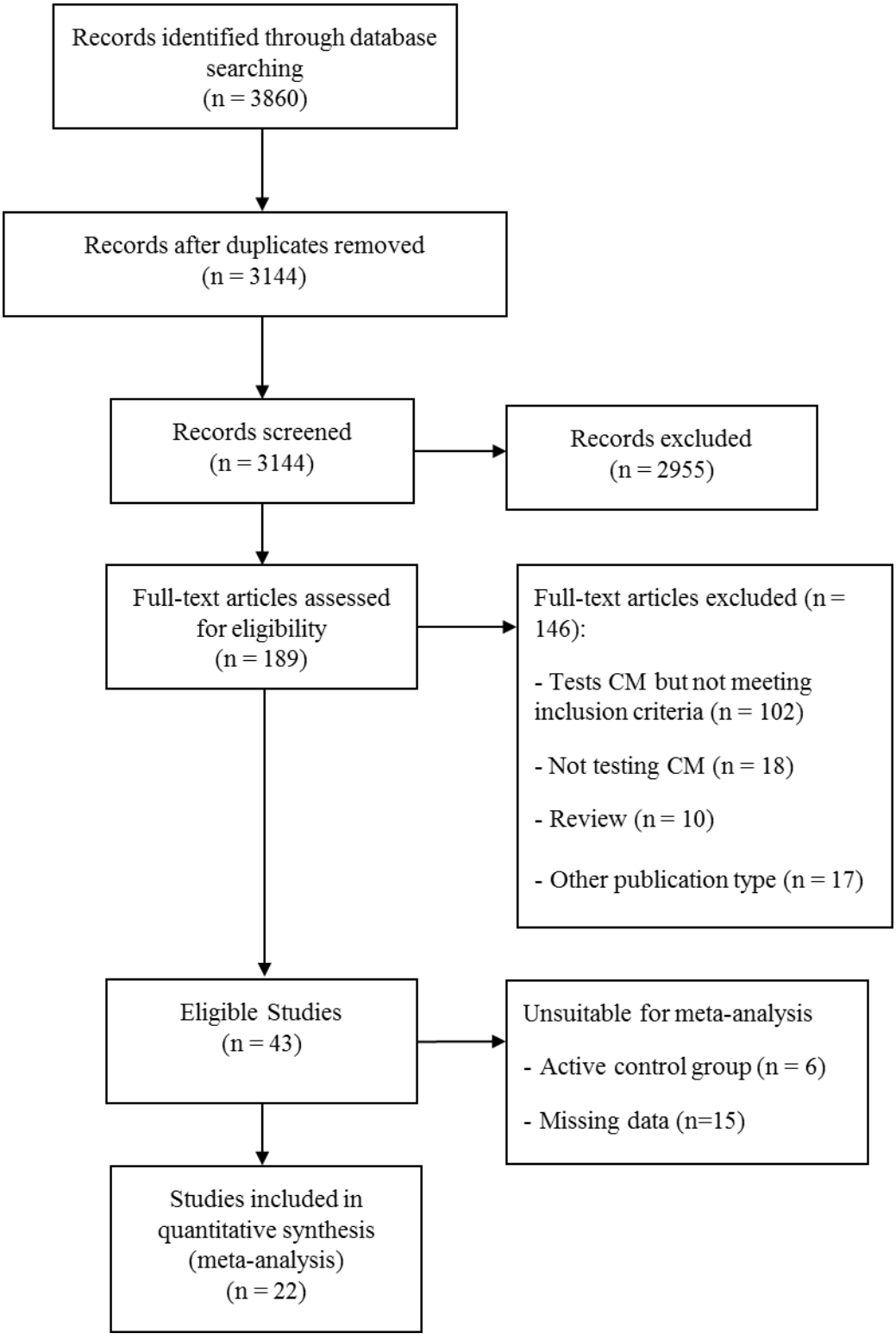

Figure 2 PRISMA flow diagram

2.4.2 Study Description and Quality Assessment

Eight of the 22 studies tested the effects of CM for cocaine use, two for opiate use, one for tobacco smoking, six for the combined use of opiates and cocaine, and five for polysubstance use. Twenty-one studies included some form of opiate substitution therapy (18 methadone, one

buprenorphine, one a mixed buprenorphine and naloxone tablet, and one suboxone), with only a single study not utilising any form of opiate substitution therapy. The duration of CM interventions used ranged between 11 days and 31 weeks, with the number of participants in each study ranging between 12 and 388. Seventeen studies reported retention rates, resulting in an average retention rate of 76.4% (range 51.2% - 97.7%). All studies were carried out in the US, with 13 being carried out in the same state (Maryland). See Table 4 at the end of this chapter for a full description of included studies and interventions. Methodological quality assessment using the EPHPP rated two studies as overall providing strong evidence, 10 studies moderate evidence and 10 studies weak evidence (Table 1).

Table 1 EPHPP ratings for all included studies organised by drug target of CM intervention

Study	Selection Bias	Study Design	Confounds	Blinding	Data Collection	Withdrawals/ Dropouts	Overall
Cocaine							
Epstein et al. 2003	2	1	1	2	1	2	Strong
Katz et al. 2002	2	1	3	2	1	1	Moderate
Kidorf et al. 1993	3	1	1	2	1	1	Moderate
Petry et al. 2007	3	1	1	3	1	2	Weak
Silverman et al. 1996	3	1	1	2	1	1	Moderate
Silverman et al. 1998	2	1	1	2	1	3	Moderate
Umbricht et al. 2014	3	1	1	1	1	2	Moderate
Vandrey et al. 2007	3	1	3	2	1	3	Weak
Opiates							
Ling et al. 2013	2	1	3	2	1	2	Moderate
Preston et al. 2000	3	1	3	1	1	1	Weak
Opiates and Cocaine							
Chutuape et al. 2000	3	1	1	2	1	3	Weak
Epstein et al. 2009	3	1	1	2	1	2	Moderate
Groß et al. 2006	3	1	1	2	1	2	Moderate
Katz et al. 2002	2	1	1	2	1	3	Moderate
Petry et al. 2002	2	1	1	2	1	1	Strong
Schottenfeld et al. 2005	3	1	1	1	1	3	Weak
Tobacco							
Dunn et al. 2010	2	1	1	3	1	2	Moderate
Poly-substance							
Chutuape et al. 1999	3	1	3	2	1	3	Weak
Downey et al. 2000	3	3	3	2	1	3	Weak
Kidorf et al. 1996	3	1	3	2	1	3	Weak
Peirce et al. 2006	3	1	1	3	1	2	Weak
Petry et al. 2015	3	1	1	2	1	3	Weak

1 = Strong, 2 = Moderate, 3 = Weak

2.4.3 Meta-Analysis

The meta-analysis for LDA (longest duration of abstinence) from all substances combined contained 18 studies randomising 2059 patients to 31 CM conditions and 25 non-CM control conditions. The random effects meta-analysis produced a pooled effect size of *d*=0.57 (95% CI: 0.42 - 0.72), with CM performing significantly better than control (Figure 3). A moderate [143] level of the variability of effects between studies was due to between-study heterogeneity (I^2 = 51%).

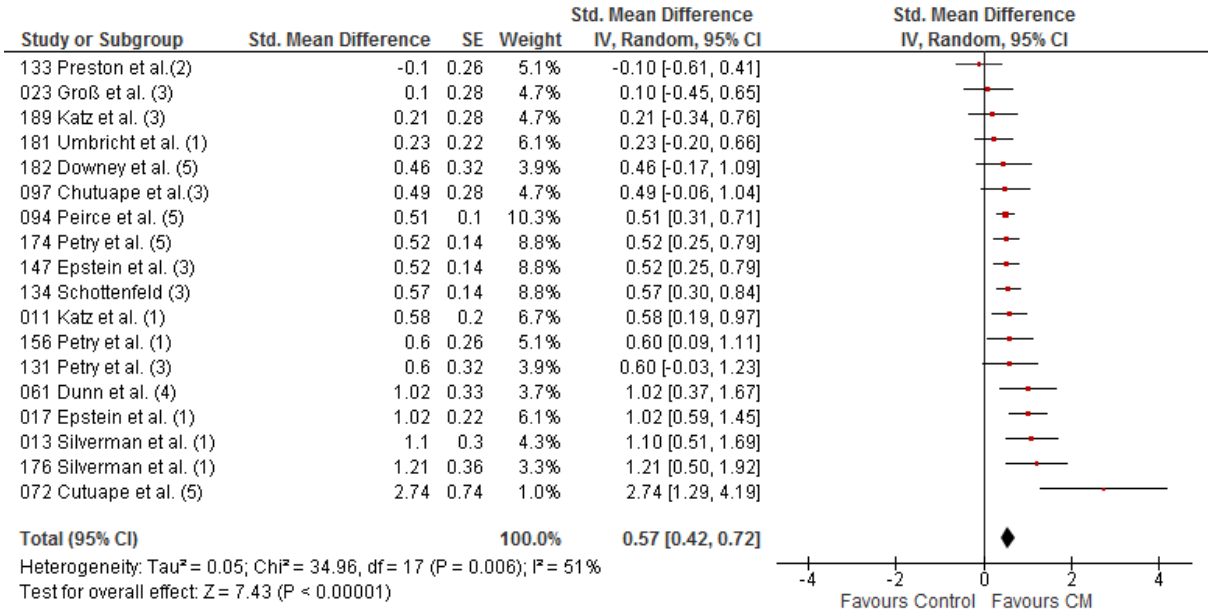

Figure 3 Forest plot for LDA during treatment of all substances combined. (1) = Cocaine, (2) = opiates, (3) = opiates and cocaine, (4) = Tobacco, (5) = Poly-substance

For PNS (percentage of negative samples), 12 studies randomising 1387 patients to 24 CM conditions and 21 non-CM control conditions were included and the pooled effect size was *d*=0.41 (95% CI: 0.28 - 0.54), again with CM performing significantly better than control (Figure 4). Variability of effects was not due to between-study heterogeneity (I^2 = 0%).

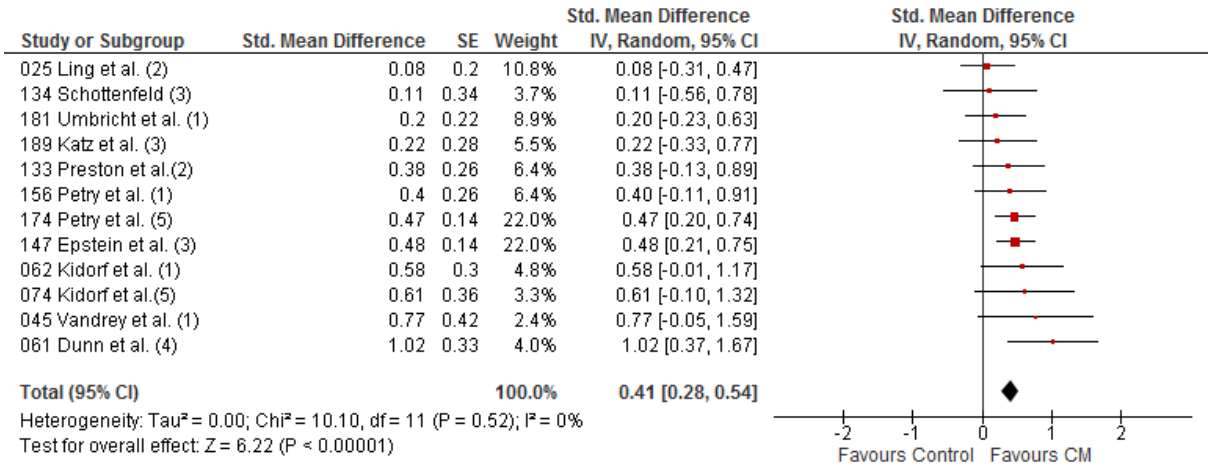

Figure 4 Forest plot for PNS during treatment of all substances combined. (1) = Cocaine, (2) = opiates, (3) = opiates and cocaine, (4) = Tobacco, (5) = Poly-substance

2.4.4 Moderator Analysis

The only moderator found to have a significant effect on the efficacy of CM was intervention drug target, but only for LDA (Tables 2 and 3). Within each of the categories of the six moderators, CM performed significantly better than control in all but three instances. Within drug targeted for intervention, CM performed no better than control for treating non-prescribed opiate use for both LDA and PNS. Within intervention duration, CM failed to encourage significantly better LDA than control in studies with intervention duration of less than 12 weeks. Within opiate treatment type, CM did not result in significantly greater PNS than control for studies where participants were in the 'other' category.

Table 2 Random effects moderator analysis results for LDA

Moderator	k[1]	Effect Size (d)[2]	95% CI	Z Value	P value	Q between (df)[3]	P of Q between
Drug targeted for intervention	18					10.75 (4)	0.03
Cocaine	6	0.75	0.45-1.04	4.91	<0.001		
Opiates	1	-0.10	-0.61-0.41	-0.40	0.70		
Opiates and cocaine	6	0.48	0.32-0.64	5.85	<0.001		
Tobacco	1	1.02	0.37-1.67	3.10	<0.01		
Poly substance	4	0.62	0.27-0.98	3.45	<0.01		
Study decade						1.31 (2)	0.52
1990-1999	4	1.08	0.14-2.02	2.23	0.02		
2000-2009	10	0.53	0.41-0.65	8.67	<0.001		
2010 onwards	4	0.53	0.32-0.74	4.92	<0.001		
Study Quality						2.66 (2)	0.23
Strong	2	0.87	0.48-1.27	4.37	<0.001		
Moderate	8	0.57	0.32-.82	4.47	<0.01		
Weak	8	0.51	0.30-0.72	4.75	<0.001		
Intervention Duration						1.30 (2)	0.52
< 12 Weeks	2	0.26	-0.41-0.93	0.77	0.44		
12 Weeks	12	0.63	0.44-0.82	6.42	<.001		
> 12 Weeks	4	0.53	0.27-0.79	4.04	<.001		
Reinforcer type						0.022	0.88
Monetary Vouchers	16	0.57	0.41-0.74	6.86	<.001		
Other'	2	0.54	0.13-0.95	2.55	0.01		
Opiate treatment						0.65	0.42
Methadone	13	0.61	0.42-0.80	6.45	<0.001		
Other	5	0.47	0.20-0.74	3.46	<0.01		

[1]Number of studies, [2]Weighted random effects, [3] A significant value of Q-between indicates significant differences among effect sizes between the categories of the moderator variable

Table 3 Random effects moderator analysis results for PNS

Moderator	k[1]	Effect Size (d)[2]	95% CI	Z Value	P value	Q between (df)[3]	P of Q between
Drug targeted for intervention						6.43 (4)	0.17
Cocaine	4	0.4	0.13-0.67	2.89	<0.01		
Opiates	3	0.18	-0.11-0.46	1.23	0.22		
Opiates and cocaine	2	0.43	0.18-0.67	3.42	<0.01		
Tobacco	2	1.02	0.37-1.67	3.09	<0.01		
Poly substance	1	0.49	0.23-0.74	3.74	<0.001		
Study decade						1.10 (2)	0.58
1990-1999	2	0.51	0.25-0.77	3.83	<0.001		
2000-2009	3	0.30	0.01-0.59	2.01	0.05		
2010 onwards	7	0.40	0.20-0.60	3.93	<0.001		
Study Quality						0.36 (2)	0.84
Strong	1	0.48	0.21-0.75	3.43	<.01		
Moderate	5	0.36	0.06-0.66	2.32	0.02		
Weak	6	0.44	0.30-0.58	0	<0.001		
Intervention Duration						0.32 (2)	0.85
< 12 Weeks	5	0.47	0.28-0.67	4.73	<.001		
12 Weeks	2	0.42	0.18-0.67	3.35	0.04		
> 12 Weeks	5	0.37	0.02-0.71	2.06	<0.01		
Reinforcer type						0.41 (1)	0.52
Monetary Vouchers	9	0.39	0.23-0.54	4.82	<0.001		
Other'	3	0.51	0.17-0.85	2.94	<0.01		
Opiate treatment						0.35 (1)	0.55
Methadone	8	0.45	0.30-0.60	6.00	<0.001		
Other	4	0.32	-0.08-0.72	1.58	0.12		

[1]Number of studies, [2]Weighted random effects, [3] A significant value of Q-between indicates significant differences among effect sizes between the categories of the moderator variable

2.4.5 Publication Bias

There is widespread acceptance of the fact that studies reporting positive results are far more likely to be published than studies reporting null findings, resulting in an over representation of positive results within the literature [148–150]. The 'failsafe N' [147] calculates the number of studies reporting null results that would be required to overturn the statistically significant difference between CM and control observed above. For LDA, 560 papers reporting null results would be required, and 101 for PNS.

2.5 Discussion

Overall, the random effects analyses showed CM performed significantly better than control in encouraging abstinence from a range of different drugs in patients undergoing treatment for opiate addiction. This was the case when measuring both LDA and PNS, producing medium and small [137] pooled effect sizes respectively. Moderator analysis performed on drug targeted for intervention, decade in which the study was carried out, quality of the study, duration of the intervention, type of reinforcer used, and form of opiate treatment, showed drug target for LDA data to be the only characteristic significantly moderating the efficacy of CM, driven primarily by the ineffectiveness of CM in treating opiate use. Despite only a single significant moderator effect, within each of the six moderator categories CM was found to perform significantly better than control in all but three cases. CM performed no better than control in encouraging abstinence from non-prescribed opiates during treatment for opiate addiction, measuring both LDA and PNS. CM also performed no better than control for LDA in studies with interventions less than 12 weeks long, and PNS in studies where usual opiate treatment was anything but methadone treatment. CM for other non-prescribed drug use in treatment for opiate addiction had no negative impact on usual treatment retention compared to three-month follow-up retention rates observed in usual opiate treatment [151–153].

This review has a number of limitations. One aim of the moderator analysis was to analyse the effects of CM by target drug type. To improve on the work of Griffith et al., (2000), five categories of drugs were used rather than two. However, one of them, polysubstance use, combined studies with four differing definitions of this, making results hard to integrate. CM still performed better in this category though, suggesting a robustness of effects across a variety of different drug combinations. Another limitation is that the review does not contain any grey literature. This means that any CM studies that have been conducted yet never published are not included in the analysis.

The current review does have a number of strengths however. It is the first review in over 16 years to address directly the efficacy of CM for encouraging abstinence from non-prescribed drug use during treatment for opiate addiction. This is important as CM has gained considerable support in this time, having been recommended since 2007 as a treatment for drug misuse by the National Institute for Health and Care Excellence [154]. The findings of the current review support those of the previous reviews carried out in the field; finding an overall positive small to medium [137] effect size for CM in treating drug use in opiate addiction treatment

[125]. This is in contrast to the usual small effect size of psychological interventions in the field [94]. Findings of the present review are also similar to those of previous reviews assessing the use of CM for drug use overall, regardless of treatment setting, which found similar small to medium effect sizes for drug use in general [91–93,95,124]. The robustness of the effects of CM across different client groups suggests potential utility in treating a diverse range of individuals and needs within the addictions field.

We found no evidence of CM working better than control in encouraging abstinence from non-prescribed opiates during treatment, which is in contrast to Prendergast et al., (2006) who identified CM as one of the most effective treatments for opiate use. The current review included only two studies of this type, compared to four (different) studies included in the previous review because of differing review aims. Moreover, three of the four opiate studies in the previous review systematically reduced methadone doses to zero over the course of the intervention, thereby increasing the likelihood of relapse to opiates and perhaps handing those receiving CM a competitive advantage over those not. Studies in the current review, however, maintained medication doses throughout the duration of the intervention, possibly eliminating this advantage and leading to the observed non-significant finding. With more data, however, results for opiates may more closely follow the trends observed with other drugs.

The moderator analysis performed in the current review has also produced contradictory results to previous reviews. Previous reviews [93,125] found four of the six moderators analysed here to have a significant effect on the efficacy of CM (drug targeted for intervention, the decade in which the study was carried out, the quality of the study evidence, the length of the intervention period). The current study only found a significant effect for drug targeted for intervention. A possible explanation for this is differences in analysis, with the previous reviews adopting a fixed effects analysis, and the current the more conservative and more widely recommended [143] random effects analysis. Support for this comes from more recent reviews that have adopted this same random effects analysis. Lussier et al., (2006) for example analysed the effects of three (drug targeted for intervention, the decade in which the study was carried out, the quality of the study evidence) moderators also analysed in the current and previous reviews, finding none of them to have a significant effect.

More general limitations within the field have also been identified, for example a lack of data available for meta-analysis. In the current

review, a total of 21 studies that met all other inclusion criteria could not be included in the quantitative data synthesis. This lack of available data is even more pronounced for follow-up, with only 10 of the 22 included studies utilising some sort of follow-up element in their study design, with data available for only four. These four studies [70,133,139,140] had follow-up periods ranging between 30 days and nine months, with none of the studies observing a significant difference between CM and control conditions at follow-up. CM is often criticised for poor follow-up results, but given the paucity of data reported in the included studies, we were not able to explore this here. Another concern is the quality of the studies included, with only two studies being rated by the EPHPP as providing strong evidence, and 20 papers providing weak evidence. Notably, every study in the current review was performed in the US, with at least 13 performed in the same state and 17 having at least one co-author from the same institution. This significantly limits the generalisability of the currently available evidence on CM for non-prescribed drug use in opiate addiction treatment.

This lack of evidence particularly highlights the need for more research on the effectiveness of CM as an intervention for tobacco dependence during opiate addiction treatment. The systematic search returned only four studies testing interventions for tobacco smoking in this treatment context, only one of which [70] could be included in the meta-analysis due to missing data in the other three. This small study (n=40) tested a 14-day escalating with reset CM intervention, against a yoked control group (voucher earnings were yoked to those of a participant in the experimental condition). CM participants achieved over double the number of PNS than controls (55% vs 17%), and a LDA nearly triple that of controls (7.7 vs 2.4 days). These promising findings further reinforce the need for more studies investigating the effectiveness of CM as an intervention for tobacco smoking during treatment for opiate addiction. It is similarly important that future research studies are carried out in a wider range of countries, include follow-ups to investigate relapse after the removal of rewards, and focus on improving the overall quality of the data that are published.

In conclusion, CM appears to be an efficacious treatment of the use of cocaine, non-prescribed opiates and cocaine, tobacco, and polysubstance use during opiate addiction treatment, but not for use of non-prescribed opiates. Evidence of longer-term efficacy in this treatment context remains lacking, as is research into the effects of CM on tobacco, providing the rationale for the intervention for the intervention developed as part of this thesis.

Table 4 Description of included studies

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow-up
Tobacco									
Dunn et al. 2010 Experimental and Clinical Psychopharmacology Vermont, USA	Two conditions: CM and non-contingent voucher Meth. 107.6 ± 8.8 mg/day or Bup. 14.9 ± 1.3 mg/day	Rand - 40 Post - 25	Biochemical verification taken every day with vouchers for abstinence delivered daily. Numerous bonuses available for abstinence at certain points	Escalating with reset 90 days Max $362.50	None reported	Percentage of biochemical samples meeting abstinence criteria	Abstinence defined as breath CO ≤ 6 ppm during days 1 to 5 and a urine cotinine ≤ 80 ng/ml on Days 6 to 14 PNS and LDA	Exp. Ppt submitted significantly more negative samples than ctrl. Ppt (t (30.1) = 3.24, p < .01)	No significant difference between the two conditions at any follow up
Katz et al. 2002 Experimental and Clinical Psychopharmacology Baltimore, Maryland, USA	Repeated measures - single, continuous, interrupted or no voucher Meth. 100 mg/day	Rand - 40 Post - Not reported	Urines collected Mon, Wed and Fri. Vouchers awarded dependent on condition (one large voucher, continuous or interrupted vouchers, or no voucher)	Multiple Each phase lasted 11 days Max reward dependent on condition	Weekly individual and group counselling	Number of consecutive days cocaine abstinence	50% reduction in Benzo. or Benzo <300ng/ml LDA	Mean abstinence duration was 2 days for no voucher, 3.2 days for single-voucher, and 4.9 and 4.8 days for continuous and interrupted voucher conditions, respectively, F(3, 117)=7.3, p=<.001.	N/A

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow-up
Kidorf et al. 1993 Experimental and Clinical Psychopharmacology Baltimore, Maryland, USA	CM or Yoked Control group. Ppt were accepted into the 2 years meth. treatment once the exp had done so Meth. 50mg/day	Rand - 44 Post - 43	Urines collected Mon, Wed and Fri. The single reward was awarded after two consecutive weeks of cocaine abstinence which had to occur within the 7-week probationary period	Fixed schedule 7 weeks Single reward of 2 years meth. treatment	Group and individual counselling at least once per week	Two consecutive weeks of cocaine abstinence	Definition not reported PNS	50% of CM and 14 % of control achieved 2 weeks of continuous cocaine abstinence. No significant difference was found between conditions for the number of negative urines returned	No significant difference between the two conditions was found for the proportion of cocaine negative urines submitted
Petry et al. 2007 Journal of Consulting and Clinical Psychology Connecticut, USA	Prize based (fishbowl) or voucher based CM, or standard care control Meth. Mean dose between 78.4 and 83 mg/day dependent on condition	Rand - 76 Post - 59	Urines collected twice per week with an average of 4 days between submissions. Negative samples resulted in draws from the prize earn, or vouchers.	Fishbowl or voucher escalating with reset. 12 weeks Max up to $300 and $585 respectively	Weekly individual and/or group counselling	Cocaine abstinence	Not reported LDA and PNS	Fishbowl CM ppt achieved significantly greater LDA than control ppt. Voucher CM ppt did not.	No significant difference between percentage of participants submitting negative samples in any condition at 9 months

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow-up
Silverman et al. 1998 Journal of Consulting and Clinical Psychology Baltimore, Maryland, USA	Three conditions, Escalating CM, Escalating CM with start bonus, and yoked control Meth. Mean dose 62mg/day	Rand -59 Post - Average retention 10.3 to 11.3 weeks dependent on condition	Urines collected Mon, Wed and Fri. Vouchers dispensed after urines tested	Escalating with reset, with bonuses in one condition. 12 weeks Max reward $1950 without bonuses	Offered weekly individual counselling	Not reported	Benzo. <300ng/ml LDA	Both CM conditions achieved significantly longer durations of abstinence	Difference between CM groups and control remained significant at 8 weeks
Silverman et al. 1996 Archives of General Psychiatry Baltimore, Maryland, USA	Two conditions, escalating with reset CM and yoked control Meth. 50mg/day	Rand - 37 Post - 89% of exp ppt and 83% of ctrl ppt retained for full 12 weeks	Urines taken Mon, Wed and Fri. Vouchers given for abstinence	Escalating with reset and bonus. 12 weeks Max $1155	Weekly individual counselling (45 minutes per week)	Not reported	Benzo. <300ng/ml LDA	Exp patients achieved significantly longer durations of sustained cocaine abstinence than ctrl ppt (F(1.35) =13.5; p=<.001)	No significant difference found between groups 4 weeks post intervention
Umbricht et al. 2014 Drug and Alcohol Dependence Baltimore, Maryland, USA	2x2 Design. CM or Yoked control and Topiramate or placebo. Meth. 100 mg/day	Rand - 171 Post - 113	Urines collected Mon, Wed and Fri. Vouchers awarded for abstinence	Escalating with reset. 31 weeks Max $1155	Weekly individual and group counselling	Cocaine abstinence between weeks 9 and 20	Benzo. <300ng/ml PNS and LDA	No significant difference found between any of the conditions	N/A

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow-up
Vandrey et al. 2007 Experimental and Clinical Psychopharmacology	2x4 design - 2 types of reward type (voucher or cheque) and 4 types of reward magnitude ($0, $25, $50 or $100) Meth., dose not reported	Rand - 12 Post - Not reported	Urines collected Mon, Wed and Fri. Rewards were provided for evidence of abstinence Mon to Wed, on the Thur	Fixed, with a single voucher or cheque available in each condition. 16 weeks (two 8-week periods) Largest voucher value $100	Group and individual counselling	Not reported	Benzo. <300ng/ml PNS	No main effect of incentive type. Planned comparisons found that high value cheques resulted in significantly greater abstinence than high value vouchers	N/A
Opiates									
Ling et al. 2013 Addiction Los Angeles, USA	4 conditions, 4 CM, CBT, CM+CBT and no behavioural treatment Control Suboxone, variable dose	Rand - 202 Post - 134	Urines collected twice weekly, with escalating numbers of draws for vouchers dependent on drug free urines	Fishbowl with escalating draws. 16 weeks Max initially $2196, later reduced to $14600	Counselling	Proportion of opiate negative urines	Exact criteria not reported PNS	Mean number of consecutive opioid-negative UA results did not differ significantly by group.	Same results 52-week follow-up as post treatment

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow-up
Preston et al. 2000 Archives of General Psychiatry Baltimore, Maryland, USA	4 Conditions: CM, Increased meth. with non-contingent vouchers, CM + meth. increase, usual treatment control with non-contingent vouchers Meth. dose not reported	Rand - 120 Post - 112	Urines collected Mon, Wed and Fri. Vouchers administered for evidence of abstinence	Escalating with reset. 8 weeks Max $554	Weekly individual counselling	Opiate negative urine samples	<300ng/ml opiates PNS and LDA	LDA significantly increased with contingent vouchers (F(1,116)= 10.02, p = .002)	N/A
Cocaine and Opiates									
Chutuape et al. 2000 Drug and Alcohol Dependence Baltimore, Maryland, USA	3 conditions: CM with weekly or monthly urine testing, and a control where take home meth. was awarded randomly Meth. 60mg/day	Rand - 53 Post - 43	Urines collected Mon, Wed and Fri. One urine randomly selected either weekly or monthly dependent on condition to decide whether vouchers awarded	Escalating with reset. 28 weeks Max reward was take home doses for all weeks	Weekly individual and group counselling sessions	Not reported	Not reported	The mean LDA was 10.5 (SD 8.9), 8.4 (SD 8.5), and 5.4 (SD 7) weeks for the Weekly, Monthly, and Random Drawings groups, respectively (F(2,52) 1.9, PB0.16).	N/A

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow-up
Epstein et al. 2009 Drug Alcohol Dependence Baltimore, Maryland, USA	3x2 dose by contingency design - meth. dose of either 70 mg or 100mg and yoked control, CM for cocaine or split CM for cocaine and opiates	Rand - 252 Post - 23% of ppt dropped out before the end of the intervention	Urines collected Mon, Wed and Fri. Vouchers were awarded for abstinence from cocaine and opiates either together or separately dependent on condition	Escalating with reset. 12 weeks Max not reported	Weekly individual counselling	Percentage of urine specimens negative for heroin, cocaine, and both simultaneously	<300 ng/ml for both opiates and cocaine PNS and LDA	Main effect of contingency on cocaine-negative urines, ($F(2,244) = 7.36$, $p = .0008$) and on urines simultaneously negative for opiates and cocaine, ($F(2,244) = 3.61$, $p = .0285$) but not in opiate-negative urines, ($F(2,244) = 2.51$, $p = .0830$)	N/A

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow-up
Groß et al. 2006 Experimental and Clinical Psychopharmacology Vermont, USA	Three conditions: CM vouchers, Reduction in medication, and standard treatment control Bup, maintained on either 4 mg/70 kg or 8 mg/70 kg for the duration of the study	Rand - 60 Post - 45	Urines collected Mon, Wed and Fri. Dependent on condition, ppt either earned points, or did not have their bup dose decreased on evidence of abstinence	Escalating with reset and bonus. 12 weeks Max $269	Behavioural drug counselling	Mean duration of continuous abstinence, total number of weeks abstinent (non-continuous), and number of missing visits.	<300ng/ml of cocaine or opiates LDA	Contingent medication ppt achieved significantly greater durations of continuous abstinence (M=5.9 weeks, SD=4.6) than ppt in the voucher group (M=2.9 weeks, SD=3.3; Fisher's LSD, p=.05).	N/A
Katz et al. 2002 Experimental and Clinical Psychopharmacology Baltimore, Maryland, USA	Two conditions, CM or Standard care Meth. 100mg/day	Rand - 52 Post - Mean 35.9 days (of 180) in treatment	Urines collected three times per week and vouchers administered for negative samples	Escalating with reset and bonus 12 weeks Max $1,087.50	Weekly individual cognitive behavioural counselling	Not reported	<300ng/ml for both opiates and cocaine LDA and PNS	No statistically significant condition effects found	N/A

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow-up
Petry et al. 2002 Journal of Consulting and Clinical Psychology Connecticut, USA	CM or standard treatment Meth. Average 69 or 70 mg/day in standard treatment and CM	Rand - 42 Post - 39	Urines collected Mon, Wed and Fri. Ppt received on draw for abstinence from either cocaine or opiates, and four for abstinence from both. Continuous weekly abstinence earned bonus draws	Fishbowl, escalating draws. 12 weeks Max number of draws dependent on abstinence from different drugs	Monthly individual counselling	Weeks of continuous abstinence from both opioids and cocaine	Not reported LDA	There were significant group difference in the percentage of urine samples negative for both drugs (F(1, 40)=4.01, p=.05	The percentage of urine samples negative for both opioids and cocaine was higher in exp than ctrl ppt (U=112.0, p=.05.) at 6 month follow up
Schottenfeld et al. 2005 The American Journal of Psychiatry USA	2x2 design: meth. or buprenorphine and CM or performance feedback Maximum daily meth. dose of 85 mg or bup. dose of 16 mg	Rand - 162 Post - Cumulative proportion: meth. + CM - 0.6, meth. + performance feedback - 0.75, Bup + CM - 0.45, Bup + Performance feedback - 0.5	Urines collected Mon, Wed and Fri and vouchers administered for evidence of abstinence	Escalating with reset. 24 weeks Max $1033.50	Individual counselling twice weekly for the first 12 weeks and weekly for the last 12	Maximum number consecutive weeks of abstinence and proportion of drug-free urine tests	<300 ng/ml for both opiates and cocaine LDA	Meth. ppt achieved significantly longer periods of abstinence than bup. There were no significant effects of CM (F=0.09, df=1, 158, p=0.76) and no significant interaction between medication and CM (F=0.10, df=1, 158, p=0.75)	N/A

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow-up
Poly substance use									
Chutuape et al. 1999 Drug and Alcohol Dependence Baltimore, Maryland, USA	Two conditions: CM and usual care control Meth. 71 mg/day or 77 mg/day in CM and standard care conditions	Rand - 14 Post - 12	Urines collected Mon, Wed and Fri. Vouchers or take homes administered for evidence of abstinence dependent on ppt choice	Fixed. 12 weeks Max $900 or three take homes per week dependent on ppt choice	Twice-weekly counselling sessions (one individual and one group session)	Number of drug free urines	<200ng/ml for meth., opiates, cocaine and benzodiazepines LDA	Mean LDA for exp ppt was 8.4 and 1 week for ctrl ppt (t(8)=5.9, p=<0.001.)	5 ppt relapsed after the CM intervention. ended, generally within the first week
Downey et al. 2000 Experimental and Clinical Psychopharmacology USA	Two conditions: CM and Yoked control Mixed Bup. Naloxone tablets. Dose not reported	Rand - 41 Post - 21	Urines taken Mon, Wed and Fri. Vouchers administered for evidence of abstinence	Escalating with reset and bonus. 12 weeks Max not reported	Weekly cognitive behavioural substance abuse therapy	Not reported	<300ng/ml for all drugs other than phencyclidine which was <25ng/ml LDA	No sig. difference between the two groups on % drug free urines, LDA or total abstinence for heroin, cocaine or poly drug use during the voucher phase	N/A

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow-up
Kidorf et al. 1996 Behavior Therapy Baltimore, Maryland, USA	Two conditions: CM and usual care control Meth. 60mg/day	Rand - 16 Post - 14	Urines collected twice per week and take homes administered for evidence of abstinence. Samples positive for drugs resulted in meth. being administered in a split dose	Fixed with negative consequences for drug positive samples. 2-month cross-over Max 2 take homes per week	Weekly individual counselling	Percentage of drug free urines	Breath alcohol < 0.5, other drug cut-offs not reported PNS	A condition main effect was found, ($F(2, 30) = 4.43$, $p=< .05$.) Patients submitted more drug-free urines when exposed to exp (M = 29%; SE = 9.0) than ctrl (M = 9%; SE = 3.0)	N/A
Peirce et al. 2006 Archives of General Psychiatry USA	Two conditions: CM and usual care control Meth. doses ranging between 67.9mg/day to 108 mg/day dependent on recruitment centre	Rand - 388 Post - 67.1% of exp ppt and 64.8% ctrl ppt retained	Urines collected twice per week and prize draws allowed for evidence of abstinence	Fishbowl, escalating with reset. 12 weeks Max 204 draws, resulting in a maximum of approx. $400 in prizes, plus one guaranteed $20 prize.	Individual and group consoling. Frequency ranged from 3 times per week to once per month	Not reported	Not reported LDA	Exp ppt were significantly more likely to submit stimulant- and alcohol-negative samples than were ctrl ppt (OR, 1.98; 95% CI, 1.42-2.77; missing samples coded as missing)	No group differences in percentage of submitted samples negative for stimulants and alcohol (χ^2=0.08, P=.78)

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow-up
Petry et al. 2015 Journal of Consulting and Clinical Psychology USA	Four conditions: $300 prize CM, $900 prize CM, $900 voucher CM and usual care control Meth. doses ranging between 77 mg/day and 85.4 mg/day	Rand - 240 Post - Not reported	Urines taken at least twice a week with at least 2 days between tests. Abstinence resulted in either fishbowl draws or vouchers	Escalating with reset for either fishbowl draws or vouchers dependent on condition. 12 weeks Max either $300 or 900$	Weekly group counselling	LDA and proportion of samples submitted negative for cocaine and alcohol	Not reported PNS and LDA	The longest duration of abstinence and proportion of samples testing negative were significantly greater in each of the three CM conditions relative to usual care ($F(3,236) = 3.39$, $p = .02$ and $F(3,236) = 3.94$, $p = .009$ respectively)	At the 12-month follow-up, 113 of 225 (50.2%) patients submitted negative samples

Abbreviations - **Rand**- Randomised to conditions, **Post**- Post intervention, **Exp** - Experimental condition(s), **Ctrl** - Control condition, **CM** - Contingency Management, **TLFB** - Time Line, Follow Back, **LDA** - Longest Duration of Abstinence, **PNS** - Percentage of Negative Samples, **Meth.** - Methadone, **Bup.** - Buprenorphine, **Pbo.** - Placebo, **ppt** – Participants, **Benzo** – Benzoylecgonine, **OST** – Opiate substitution therapy.

Chapter 3:

Contingency Management Quality Assessment Tool

3.1 Introduction and Aims

3.1.1 Introduction

During the process of conducting the meta-analysis, it became clear that there was no quality assessment tool set up specifically for use with CM papers. Due to the complex nature of CM interventions, there are a number of specific elements of the interventions that can impact their efficacy as previously discussed [82]. It can therefore be argued that the currently available means of assessing study quality assess only the generic methodological qualities of CM studies. This is because the most widely used quality assessment tools (for example the Cochrane Collaboration's tool for assessing risk of bias [143]) are designed to assess the quality of any randomised controlled trial regardless of the nature of the intervention used. What this effectively means, is that any current quality assessment made of a CM study disregards the quality of the CM intervention itself. Moreover, it can result in unfair appraisals of study quality, due to the incompatibility of some common trial practices with CM interventions, for example, allocation concealment. Due to the importance of accurately assessing study quality in systematic reviews and meta-analyses, the decision was made to attempt to create, for the first time, a quality assessment tool that could be used specifically for CM studies. This chapter details the design and preliminary reliability and validity testing of such a tool. Development took place in two stages: stage one included the initial development of the tool and reliability and validity testing; stage two included refining the tool in light of the stage one findings and the re-testing of reliability and validity.

3.1.1 Existing Quality Assessment Tools

The first step in development of the new quality assessment tool was identifying an extant quality assessment tool that could act as a template. A recent meta-analysis of quality assessment tools identified a total of 21 different tools [155]. Quality assessment tools for RCTs were most prevalent, with six different tools being identified. Quality assessment tools were also found for assessing studies of various other methodologies. These included: two tools for assessing non-randomised intervention studies; three for case-control, cohort, cross-sectional and case series studies; three for diagnostic accuracy studies; three for animal studies; three for systematic reviews and meta-analyses, and one for assessing clinical practice guidelines.

Due to the majority of CM studies being tested using an RCT design [91,93–95,125,156], RCT quality assessment tools were most pertinent to

the design of the new tool for assessing quality in CM studies. The six studies identified in the meta-analysis included: the Cochrane Collaboration's tool for assessing risk of bias [143]; the PEDro scale (Physiotherapy Evidence Database scale) [157]; the JADAD scale [158]; the Delphi list [159]; CASP (Critical Appraisal Skills Programme) checklist RCTs [160]; and the NICE (National Institute For Health and Clinical Excellence) Methodology Checklist for RCTs [161]. I additionally identified a further two tools used to assess the quality of RCTs: the EPHPP Quality Assessment tool for Quantitative Studies, identified whilst carrying out my meta-analysis, [127] and the National Institute of Health's Quality Assessment of Controlled Intervention Studies [162].

In 2008 the JADAD scale was the most widely used as well as the most reliable and valid [163], however, the Cochrane Collaboration's tool has also become equally widely used and accepted [155]. More recently, however, the EPHPP Quality Assessment tool for Quantitative Studies [127] has grown in prominence, not only being recommended by the Cochrane Collaboration [143] but also being shown experimentally to outperform the Cochrane Collaboration's tool for assessing risk of bias as previously discussed[128].

Despite the relatively large number of different quality assessment tools available, the majority of tools, including the three most widely used, all follow a very similar format. Each of the tools includes a series of different criteria used to assess studies on a two or three-point scale. The EPHPP tool, for example, assesses studies on six criteria (selection bias, study design, confounds, blinding, data collection and withdrawals and dropouts) each of which is rated as either strong, moderate or weak. The Cochrane Collaboration's tool assesses papers along seven criteria (random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting and other sources of bias) rating them as either low, high, or unknown risk of bias [164]. The modified JADAD uses a series of nine yes or no questions (Is this an RCT study?; Reported as randomised?; Randomisation is appropriate?; Double blinding is reported?; Double blinding is appropriate?; Withdrawals are reported by number and reasons her arm?; Method used to assess adverse events is described?; Method of statistical analysis is described?; Inclusion and/or exclusion of the requirements is described?) to rate the quality of papers. However, as important as these generic methodological aspects are for the overall quality of a study, their generic nature necessarily means that intervention specific aspects are overlooked. Consequently, when these tools are applied to complex behavioural interventions such as CM, an

objective rating of quality cannot be achieved. Another important element of study quality is the implementation of an intervention, namely, the degree to which the implementation of an intervention follows recommended practice. This issue of implementation in the appraisal of study quality is something that all current quality assessment tools fail to address [155], again compromising the ability of these tools to assess study quality objectively when used in practice.

A number of different process evaluation frameworks aimed at addressing this dual issue of including both intervention specific aspects and treatment implementation in quality appraisal have been suggested [165–167]. One area where this is beginning to be addressed is in behavioural interventions for smoking cessation, where a taxonomy of the behaviour change techniques used has been developed [168,169]. The application of this for the improvement of treatment was assessed in a recent study. Thirty different group support manuals used by English stop smoking services were assessed using the taxonomy. An average of seven behaviour change techniques were identified in each manual, with two positively associated with short term quit rates [170]. This not only highlights the importance and utility of assessing the active elements of behavioural interventions, but also draws into question why more detail on behaviour change techniques are not included in quality assessment tools. The issue of poor reporting of implementation in behavioural interventions is still widespread, with only 5-30% of experimental studies reporting their interventions in detail [166]. Resultantly, treatment implementation also remains largely unreported despite its documented importance for the quality of both the design and implementation of interventions [171]. With complex behavioural interventions such as CM, the efficacy of the intervention is so closely linked to its design and implementation that any quality rating that neglects these issues is severely limited. Any new quality assessment tool for a complex intervention should therefore attempt to include this in its design.

3.1.2 Aims of Developing the CMQAT (Contingency Management Quality Assessment Tool)

The rationale for designing the current quality assessment tool was to create a tool that allowed a fairer appraisal of quality than allowed by current quality assessment tools, that includes not only methodological quality but also assesses how factors shown to impact efficacy are implemented. The aims of this study therefore were to:

1. Develop a quality assessment tool specifically for use with CM studies.

2. Test the reliability and validity of the newly developed tool, and compare this against an established quality assessment tool.

3.2 Stage One: Development and Testing of the Quality Assessment Tool

3.2.3 Developing Assessment Criteria

In order to achieve these aims, it was imperative to identify key intervention elements that have been shown to impinge on the overall quality of CM interventions; the rationale behind this being that these could then be used as criteria against which to rate the quality of CM studies. In 2007 the NIDA (National Institute on Drug Abuse) and SAMHSA (Substance Abuse and Mental Health Services Administration) engaged the leading researchers in the CM field to create a document outlining the foundations and principles of CM, including the key elements impacting efficacy of CM [82]. The seven core elements of CM interventions were identified in the introductory chapter (chapter 1) and are discussed in detail below:

1. Target behaviour: All CM interventions, regardless of the target behaviour, should incentivise behaviour using a "reinforcement" rather than "reward" schedule [90]. A "reward" schedule entails the completion of a large, often long-term goal (for example 4 weeks abstinence), whereas a "reinforcement" schedule breaks behaviours down into smaller steps that are each rewarded. This is important as it is the inability to achieve these longer-term goals that CM is designed to remedy. The desired target behaviour and exactly what is expected from those receiving the intervention should be clearly and formally laid out at the beginning of treatment [82], and the target behaviour should be readily measurable and objectively verifiable [172].

The target behaviour that rewards are made contingent upon is very important, especially in terms of differentiating between the goal of the intervention and target behaviour. In interventions for substance use disorders, for example, the ultimate goal and hence the most obvious target behaviour, is long-term abstinence. However, a number of different behaviours can be targeted either individually or in combination, for example, treatment adherence [173,174]. Similarly, percentile shaping, where the goal of the intervention is abstinence but the target behaviour is gradual reduction of use, may work better than making rewards contingent on abstinence from the outset [97,98,100,175].

2. Choice of target population: As resources are often limited, it is important to identify a target population most in need of treatment, even though it would be ideal to treat an entire population. Using the fishbowl method of CM (where tickets representing different value rewards are picked from a container) can often be useful in this context as it reduces the overall cost of delivering the intervention, allowing a wider population to be treated than a standard CM intervention of the same cost. Also, different formulations of reward schedule may work better for different populations. Percentile shaping for example has been found to be particularly successful in the treatment of "hard to treat" smokers [97,98]. Target populations can also differ by treatment centre location. For example, when testing CM to encourage methadone clinic attendance in China, prize-based CM was significantly better at retaining patients in methadone maintenance therapy than usual treatment. However, the difference in the two conditions was only significant in the treatment centre based in a rural part of China and not for the centre in the urban area [176].

3. Choice of reinforcer: The most widely used CM reinforcer in addictions research is monetary vouchers, however, they are not necessarily the most effective. When asked, individuals in treatment for opiate addiction report they would rather receive take-home methadone doses than cash incentives [177,178]. This is borne out in meta-analysis findings, where take-home doses of methadone have been observed to be most effective in treating substance use disorder (SUD) amongst those in treatment for opiate addiction [125]. This means that a key factor in choosing the right reinforcer may well involve polling the treatment population or participants to ascertain the most popular incentives. However, this must also be balanced with what the treatment centres, where these interventions are carried out, feel is most suitable for their clients. For example, a common concern amongst clinicians and to some degree researchers is that providing cash vouchers may result in relapsed drug use. This fear is not supported by research, however, where cash has been shown to be of no greater risk than monetary vouchers [129,179]. Some research has shown cash rewards to be more effective than both goods based and voucher based rewards in drug treatment [129,180]. Other research, though, has shown there to be no difference in efficacy between using cash or voucher incentives [129,179]

4. Incentive Magnitude: According to theories of operant conditioning (the behavioural principle on which CM is built) the larger the magnitude of the reward the more appealing it is and the more effective it will be at encouraging the desired behaviour [181]. Incentive magnitude has also

been observed in a meta-analysis to moderate the efficacy of CM, with large incentives performing significantly better than smaller ones in encouraging abstinence [91].

5. Frequency of incentive distribution: This is closely related to the behaviour being encouraged, and the ease with which it can be verified. In substance use disorders, CM interventions normally follow an "FR1" (fixed ratio 1) pattern, meaning that every time the desired behaviour is observed, the incentive is given. The necessity for this schedule of incentive distribution in CM for substance use disorders can make the treatment prohibitively expensive, especially when it is taken into account that higher magnitudes of reward will result in greater efficacy of the intervention. The "fishbowl" method of CM was created in order to combat this issue, where rather than being given rewards outright, participants are instead allowed to draw tickets from a container for each display of the desired behaviour. The proportion of "winning" tickets and the monetary values of these are assigned dependent on the study being conducted. This allows an FR1 schedule to be maintained, even with large magnitude rewards, with the actual attainment of tangible goods controlled at whatever fixed ratio rate is deemed necessary, simply by altering the proportion of "winning tickets".

6. Timing of the incentive: The time delay between the verification of a desired behaviour taking place, and receiving the reward for doing so, can be instrumental in the efficacy of a CM intervention. This is especially the case in individuals with SUDs, who show increased bias toward immediate reinforcement than delayed reinforcement [182]. A meta-analysis has shown that timing of incentive operates as a moderator to the efficacy of CM, with immediate rewards performing significantly better than delayed rewards in encouraging abstinence [91]. It is recommended that rewards should be received within 48 hours of displaying the behaviour to be most effective [82]. This is especially important in the treatment of SUDs due to the exaggerated delay discounting observed in those with addictions [182]. This is a result of the temporal order of reinforcement in addiction. The positive reinforcing effects of a drug's use happen very quickly after its use, whereas any negative effects usually happen a lot later, meaning that the negative effects of drugs do not act as negative reinforcers [89].

7. Duration of the intervention: As noted above, one of the primary shortfalls of CM is that once rewards for behaviour are removed, participants will often return to using drugs. It would therefore seem to be imperative that interventions are run for long enough to allow patients to change their behaviour for a sustained period of time so that the risk of relapse is low. There is very little research that addresses duration of

intervention as a moderator of treatment efficacy. One meta-analysis suggested that there may be no effect on treatment outcomes [125] at all, however, significant methodological heterogeneity between the included studies was likely to explain this observation. Conversely, the results of my own meta-analysis show that, at least for the LDA outcome, CM performed no better than control in interventions under 12 weeks long. Until experimental research is carried out directly investigating this, there is no "ideal" length of CM intervention, and cues should instead be taken from the standard treatment techniques used for each individual drug.

3.2.4 Creating Rating Criteria and Calculating Study Quality

The EPHPP quality assessment tool was chosen as the template from which to create the new tool as it is recommended for use with RCTs by the Cochrane Collaboration [143], and has also been shown to have excellent inter-rater reliability [128]. Resultantly, I translated the seven core principles of CM outlined above to fit this template, creating the new quality assessment scale, to which I gave the acronym CMQAT (Contingency Management Quality Assessment Tool).

As discussed in the previous chapter, the EPHPP tool rates studies as either strong (one), moderate (two) or weak (three) across six criteria (selection bias, study design, confounders, blinding, data collection method, and withdrawals and dropouts). The overall quality rating given to a study is then based on the number of weak ratings that the study receives over these six criteria. Studies receiving no weak ratings are rated as providing strong evidence overall, studies receiving one weak rating as providing moderate evidence and all other studies as providing weak evidence. For the CMQAT, we wanted to implement a similar system of scoring, however felt that it was more logical to assign higher scores for higher quality (i.e. reversing the scoring system of the EPHPP). Therefore, the assessments for each criterion in the new quality assessment tool would be three for strong, two for moderate and one for weak. The initial descriptions of strong, medium and weak ratings on each of the seven criteria are outlined below in section 3.5, alongside the changes made to criteria in light of stage one testing, and the resulting new criteria used during stage two testing.

Four different methods for calculating the overall quality of the studies were assessed during reliability and validity testing because of concerns that the strict method of rating studies implemented by the EPHPP tool had the potential of being overly stringent, resulting in studies being rated as providing poorer quality evidence than they actually do.

Scoring method 1 “Strict”: This was a replication of the scoring used in the EPHPP tool but with scores reversed (i.e. 3 for strong and 1 for weak).

Scoring method 2 “Lenient”: The second was a less stringent version of the EPHPP method, allowing studies with a single weak rating and at least three strong ratings to be classified as providing strong evidence, and studies receiving two weak ratings to be classified as providing moderate strength evidence. This again used the reverse scoring system to the EPHPP method (3 for strong and 1 for weak)

Scoring method 3 “Sum”: Global rating based on the sum of quality rating scores across the six rating criteria

Scoring method 4 “Average”: Global rating based on the average of quality rating scores across the six rating criteria.

3.3 Stage One: Reliability and Validity Testing Methods

3.3.1 Study Selection

In order for validation testing to be performed, a selection of CM studies that could be tested using the CMQAT was required. Having previously performed a systematic search for CM studies whilst carrying out the meta-analysis, it was decided that the 22 studies returned by this search would be used for testing the new tool. All of the included studies assessed the efficacy of CM in encouraging abstinence from non-prescribed drug use during opiate addiction treatment. Full details of the systematic search and included studies can be found in Chapter 2, and also in appendix 2.

3.3.2 Reliability and Validity Measures

Current evidence suggests that very few of the tools commonly used to assess the quality of studies have actually gone through validation testing [163]. This posed some problems for the development of the current tool as there is very little precedent in the literature as to how to go about validity and reliability testing in this specific context. It was therefore decided that two common measures of validity and reliability would be measured, namely inter-rater reliability and predictive validity.

3.3.3 Inter-Rater Reliability Testing

Inter-rater reliability is a quantitative measure of the degree of agreement between different coders on the same scale [183]. I and two other researchers (Assessors 1, 2 and 3) rated each of the studies, and then I

calculated the level of agreement between the three. This was calculated as Fleiss's Kappa, a statistical measure that allows for comparisons of rater agreement between two or more raters [184]. This produces a score between zero and one, with scores of 0.01-0.2 representing slight agreement, 0.21-0.40 fair agreement, 0.41-0.60 moderate agreement, 0.61-0.80 substantial agreement and 0.81-1.00 almost perfect agreement [184].

3.3.4 Predictive Validity Testing

Predictive validity tests the degree to which the scores of one scale are predictive of those of another [185]. In the current case, this was tested by calculating the correlation between the overall quality scores of studies using the CMQAT by each of the three assessors and the effect size of each study. The effect sizes of 22 studies across two different treatment outcomes were used to conduct this testing: twelve studies with effect sizes calculated based on percentage of negative samples, and 18 with effect sizes based on longest duration of abstinence. In performing the predictive validity testing, the quality scores of the relevant studies for each treatment outcome and the effect sizes of studies for each of these treatment outcomes were correlated. This predictive validity testing was also performed using the EPHPP quality assessment tool, in order to investigate whether this established quality assessment tool was predictive of the strength of study outcome. Correlations between effect size and EPHPP score were calculated using the ratings assigned to studies by Assessor 3 (myself) only. Ratings assigned using the EPHPP tool were performed following the instructions supplied with the tool. Due to the small sample size of studies being rated, and the large number of similar scores resulting from the strong, moderate or weak rating scale, correlations were calculated as Kendall's tau with pairwise deletion.

3.4 Stage One: Results

3.4.1 Missing Data

Whilst carrying out the quality assessments, it was discovered that a number of the published articles were missing data pertaining to the "frequency of incentive distribution" and "timing of the incentive" criteria. In total, 19 of the 22 studies were missing information required to complete the quality assessment. For the studies with missing data, each was provisionally marked as weak for the criteria for which data were missing. The authors of these studies were then contacted to clarify these details. Twelve of the authors contacted replied, all of which clarified the missing details on the papers.

3.4.2 CMQAT Quality Ratings and Inter-Rater Reliability

Criterion and global quality ratings for all papers, along with percentage agreement between the three assessors, are shown in Figures 5 and 6 below. The number of studies rated overall as providing strong, moderate or weak evidence by each of the three reviewers is shown in Table 5.

Criterion Ratings

Study	Target behaviour			Target population			Reinforcer			Incentive magnitude			Frequency of distribution			Timing of incentive			Duration of intervention		
	A1	A2	A3	A1	A2	A3	A1	A2	A3	A1	A2	A3	A1	A2	A3	A1	A2	A3	A1	A2	A3
Katz 2002	2	3	3	2	3	3	2	3	2	3	3	3	2	3	2	1	1	1	1	2	2
Silverman 1998	3	3	3	3	3	3	2	3	2	3	3	3	3	3	2	1	3	1	2	2	2
Epstein 2003	3	3	3	3	1	2	2	3	2	2	2	2	3	3	1	1	3	2	2	2	2
Groß et al. 2006	3	3	3	2	2	3	2	3	2	1	1	1	3	3	1	3	3	3	1	3	1
Ling 2013	3	3	3	2	2	3	2	1	2	2	2	2	2	3	2	1	3	2	1	3	1
Vandrey 2007	3	3	3	2	3	2	2	3	3	1	1	1	2	3	2	2	1	2	2	2	1
Dunn 2010	3	3	3	2	2	3	2	3	2	3	3	3	3	3	3	3	1	1	2	2	1
Kidorf et al. 1993	2	3	1	1	2	3	1	1	1	1	1	1	3	1	1	1	1	3	1	1	1
Chutuape et al. 1999	3	3	3	3	3	1	3	3	3	2	2	2	3	3	1	2	3	1	1	3	3
Kidorf et al. 1996	3	3	3	2	3	1	2	1	3	3	3	3	2	3	1	1	3	1	1	2	1
Peirce et al. 2006	3	3	3	2	3	3	2	3	2	1	1	1	2	3	2	3	3	2	1	3	2
Chutuape et al. 2000	3	3	3	2	3	3	2	3	3	3	3	3	3	1	1	1	1	1	1	3	1
Petry et al. 2002	3	3	3	2	3	3	2	3	2	2	2	2	3	3	2	2	3	3	1	3	2
Preston 2000	3	3	3	2	3	2	2	3	2	2	2	2	3	3	2	2	1	2	1	3	1
Schottenfeld et al. 2005	3	3	3	3	3	2	2	3	2	2	2	2	3	3	1	3	3	3	1	3	1
Epstein et al. 2009	3	3	3	3	2	3	2	3	2	2	2	2	3	3	2	3	3	2	1	3	2
Petry 2007	3	3	3	3	3	3	2	3	2	2	2	2	2	3	2	2	3	1	1	3	2
Petry et al. 2015	3	3	3	2	3	3	2	3	2	1	1	1	2	3	2	2	3	3	2	3	2
Silverman 1996	3	3	3	1	3	3	2	3	2	2	2	2	2	2	2	2	3	1	1	3	2
Umbricht 2014	3	3	3	3	3	2	2	3	2	2	2	2	2	3	2	1	3	1	1	3	1
Downey et al. 2000	3	3	3	3	2	1	2	3	2	2	2	2	3	3	2	1	1	1	1	3	1
Katz et al. 2002	3	3	3	2	2	2	2	3	2	2	2	2	3	3	2	3	3	3	1	3	1

Percentage Agreement[1]	Target behaviour			Target population			Reinforcer			Incentive magnitude[2]			Frequency of distribution			Timing of incentive			Duration of intervention		
	A1	A2	91%	A1	A2	41%	A1	A2	9%	A1	A2	N/A	A1	A2	55%	A1	A2	41%	A1	A2	23%
	A3	A1	91%	A3	A1	27%	A3	A1	86%	A3	A1	N/A	A3	A1	41%	A3	A1	50%	A3	A1	59%
	A3	A2	95%	A3	A2	41%	A3	A2	18%	A3	A2	N/A	A3	A2	18%	A3	A2	41%	A3	A2	23%

Figure 5 Stage one criterion ratings for CMQAT. A1= Assessor 1, A2= Assessor 2, A3= Assessor 3, [1] Percentage agreement calculated as the number of the same rating given to studies for each criterion, expressed as a percentage. [2] Percentage agreement was not calculated for Incentive Magnitude as this is based on the ranking of studies and therefore is the same for all raters.

	Strict			Lenient			Sum Score			Average Score		
	A1	A2	A3	A1	A2	A3	A1	A2	A3	A1	A2	A3
Katz 2002	1	2	2	2	3	3	13	18	16	1.86	2.57	2.29
Silverman 1998	2	3	2	3	3	3	17	20	16	2.43	2.86	2.29
Epstein 2003	2	2	2	3	3	2	16	17	18	2.29	2.43	2.00
Groß et al. 2006	1	2	1	2	3	1	15	18	14	2.14	2.57	2.00
Ling 2013	1	2	2	2	3	2	14	18	19	2.00	2.57	2.11
Vandrey 2007	2	1	1	2	1	2	14	16	14	2.00	2.29	2.00
Dunn 2010	3	2	1	3	3	3	17	16	16	2.43	2.29	2.29
Kidorf et al. 1993	1	1	1	1	1	1	11	11	11	1.57	1.57	1.57
Chutuape et al. 1999	1	2	1	1	3	1	16	19	14	2.29	2.71	2.00
Kidorf et al. 1996	1	2	1	2	3	1	13	17	13	1.86	2.43	1.86
Peirce et al. 2006	2	3	2	2	3	2	15	20	19	2.14	2.86	2.11
Chutuape et al. 2000	1	1	1	2	2	1	15	17	15	2.14	2.43	2.14
Petry et al. 2002	2	3	3	2	3	3	15	20	17	2.14	2.86	2.43
Preston 2000	2	2	2	2	3	2	15	18	14	2.14	2.57	2.00
Schottenfeld et al. 2005	2	3	1	3	3	2	17	20	14	2.43	2.86	2.00
Epstein et al. 2009	2	3	3	3	3	3	17	19	16	2.43	2.71	2.29
Petry 2007	1	2	2	2	3	2	14	19	19	2.00	2.71	2.11
Petry et al. 2015	3	3	2	3	3	3	15	20	16	2.14	2.86	2.29
Silverman 1996	1	3	2	2	3	2	14	20	19	2.00	2.86	2.11
Umbricht 2014	1	2	1	1	3	2	13	19	13	1.86	2.71	1.86
Downey et al. 2000	1	2	1	2	3	1	15	17	14	2.14	2.43	1.56
Katz et al. 2002	2	3	2	3	3	2	16	19	15	2.29	2.71	2.14

Percentage Agreement[1]	Strict			Lenient			Sum Score[2]			Average Score[2]		
	A1	A2	23%	A1	A2	75%	A1	A2	*r*= 0.508 *p*= 0.016	A1	A2	*r*= 0.510 *p*= 0.015
	A3	A1	55%	A3	A1	55%	A3	A1	*r*= 0.255 *p*= 0.252	A3	A1	*r*= 0.481 *p*= 0.024
	A3	A2	45%	A3	A2	32%	A3	A2	*r*= 0.523 *p*= 0.012	A3	A2	*r*= 0.588 *p*= 0.004

Figure 6 Stage one overall ratings for the CMQAT. A1= Assessor 1, A2= Assessor 2, A3= Assessor 3, [1] Percentage agreement calculated as the number of the same rating given to studies for each criterion, expressed as a percentage. [2] Pearson's correlation and associated *p* value.

Table 5 Number of studies rated by each assessor as providing strong, moderate and weak evidence on CMQAT

	Overall Quality Ratings (N, %)		
Assessor and rating method	Strong	Moderate	Weak
Assessor 1, Strict	2 (9.09%)	9 (40.91%)	11 (50.00%)
Assessor 2, Strict	8 (36.36%)	11 (50.00%)	8 (36.36%)
Assessor 3, Strict	2 (9.09%)	10 (45.45%)	10 (45.45%)
Assessor 1, Lenient	7 (31.82%)	12 (54.55%)	3 (13.64%)
Assessor 2, Lenient	19 (86.36%)	1 (4.45%)	2 (9.09%)
Assessor 3, Lenient	6 (27.27%)	10 (45.45%)	6 (27.27%)

Inter-rater reliability testing yielded an overall kappa value of k= .095 (*p*= .293) for the strict scoring system and k= .065 (*p*= .479) for the lenient scoring system, both signifying only slight agreement. Significant positive correlations were observed between assessors one and two, and assessors two and three for the sum scoring method, and between all assessors for the average scoring method.

3.4.3 CMQAT and EPHPP Predictive Validity

Correlations between the four different overall scoring methods for the CMQAT (strict, lenient, sum score and average score) and the effect sizes of the studies rated are shown in Table 6. No significant correlations were observed between any of the CMQAT scoring methods for the three assessors, and effect sizes of the studies rated.

Table 6 Correlations between CMQAT quality scores and study effect sizes for each of the three assessors

	Marking Criteria			
Effect Size Type	**Strict**	**Lenient**	**Sum Score**	**Average Score**
Assessor 1				
Longest Duration of Abstinence (N= 18)	τ = 0.380 (*p*= 0.855)	τ = 0.075 (*p*= 0.714)	τ = 0.174 (*p*= 0.368)	τ = 0.174 (*p*= 0.368)
Percentage of Negative Samples (N= 12)	τ = 0.250 (*p*= 0.315)	τ = 0.000 (*p*= 1.000)	τ = -0.065 (*p*= 0.779)	τ = -0.065 (*p*= 0.779)
Assessor 2				
Longest Duration of Abstinence (N= 18)	τ = 0.137 (*p*= 0.510)	τ = 0.131 (*p*= 0.539)	τ = 0.191 (*p*= 0.325)	τ = 0.191 (*p*= 0.325)
Percentage of Negative Samples (N= 12)	τ = -0.297 (*p*= 0.226)	τ = -0.385 (*p*= 0.133)	τ = -0.408 (*p*= 0.078)	τ = -0.408 (*p*= 0.078)
Assessor 3				
Longest Duration of Abstinence (N= 18)	τ = 0.113 (*p*= 0.582)	τ = 0.206 (*p*= 0.306)	τ = 0.249 (*p*= 0.198)	τ = 0.249 (*p*= 0.198)
Percentage of Negative Samples (N= 12)	τ = -0.250 (*p*= 0.315)	τ = 0.000 (*p*= 1.000)	τ = 0.050 (*p*= 0.831)	τ = 0.050 (*p*= 0.831)

Correlations between the EPHPP quality scores and the effect sizes of the studies rated are shown below in Table 7. No significant correlations were observed between EPHPP scores of the three assessors, and effect sizes of the studies rated.

Table 7 Correlations between EPHPP quality scores and study effect sizes

Effect Size Type	EPHPP Score
Longest Duration of Abstinence (N=18)	$\tau = 0.212$ ($p = 0.268$)
Percentage of Negative Samples (N= 12)	$\tau = 0.032$ ($p = 0.888$)

3.5 Assessment Criteria Revisions

3.5.1 Alteration Process

Between stage one and two testing, the three reviewers discussed their experiences of using the rating criteria for the CMQAT. Particular attention was given to those criteria on which agreement during stage one was especially low. This process led to a number of changes being made to the stage one criteria before stage two testing. The stage one criteria, along with the changes made and the resulting new criteria are outlined below in section 3.5.2. As well as these changes to criteria, a number of other changes were made including the addition of a set of instructions for the application of the tool. The formatted versions of the stage two rating criteria and instructions are shown in appendix 3.

3.5.2 Changes Made to Criteria

General instructions (introduced after stage one):

- Each of the quality rating criteria is marked on a three-point scale that rates the paper as strong (3), medium (2) or weak (1) for that criterion.
- Where the information required for a rating to be made is missing in the published paper, the study should be rated as weak for that criterion. Authors should then be contacted to clarify this information and the assessment altered accordingly.
- All contingency management schedules should fall under that of "**reinforcement**" rather than "**reward**" [90]. The "reward" model entails the completion of a large, often long-term goal (for example two weeks of abstinence), whereas the "reinforcement" model breaks behaviours down into smaller steps (for example 2 days of abstinence) that are each rewarded. Any study implementing a "reward" schedule of reinforcement should not be rated, and should be excluded from any analyses.

1. **Target behaviour:**

Stage one rating criteria and instructions:

The type of target behaviour that is incentivised should fall under that of "reinforcement" rather than "reward" [90]. Any schedule falling under the "reward" definition should be given a weak rating. The "reward" model entails the completion of a large, often long-term goal, whereas the "reinforcement" model breaks behaviours down into smaller steps that are each rewarded.

Strong – Both observable and measurable with biochemical verification or treatment staff / experimenter verification

Moderate – Both observable and measurable with participant self-report data only

Weak – Neither observable nor measurable, ill-defined target behaviour or not related to condition being treated

Changes made:

- Any schedule falling under the "reward" definition should be excluded rather than given a weak rating
- Use of self-report data for contingent rewards now to result in a weak rating.
- Behaviour must be both measurable AND observable in order for a strong rating to be awarded.
- If behaviour measurable but not observable then a moderate rating should be given.
- Added stipulation that the CM schedule needs to be maintained throughout duration of the study.

Stage two instructions:

- **"Measurable"** refers to a behaviour that can be measured using an objective recording method, for example, urine, blood or breath levels of a drug [186].
- **"Observable"** refers to the behaviour being directly observable and validated by a member of the treatment team. For example observed or pH or heat tested urine samples [186].
- The same contingency management schedule should be maintained for the duration of the intervention, unless there is an a priori

investigative motive for not doing so. Any study that alters the contingency management schedule without this being part of the initial study design should be marked as weak for this criterion.

Stage two rating criteria:

Strong (3) – Both observable AND measurable, with biochemical verification or treatment staff / experimenter verification

Moderate (2) – Measurable but not observable

Weak (1) – Neither observable nor measurable, ill-defined target behaviour or not related to condition being treated OR self-report

2. **Target population:**

Stage one rating criteria and instructions:

Strong – Highly specific and very well-defined target population / condition, with few potentially confounding between-participant differences, and with good justification for the use of CM.

Moderate – Less specific and less well-defined target population / condition OR some potentially confounding between-participant differences, with some justification for the use of CM.

Weak – Non-specific and ill-defined target population / condition with a great deal of potentially confounding between-participant differences; little or no justification for the use of CM OR differences between participants not reported.

Changes made:

- Instructions added to make it clearer where the data for this criterion come from – i.e. from the testing of between-participant variables.
- Removed the need for a justification of the use of CM as this was too subjective.

Stage two instructions:

- **"Between-participant differences"** – Demographic variables/ participant characteristics statistically tested for differences between groups (e.g. experimental vs control)

Stage two rating criteria:

Strong (3) – Specific and well-defined target population / condition AND no significant between-participant differences

Moderate (2) – Specific and well-defined target population / condition AND any significant between participant differences have been controlled for in analysis.

Weak (1) – Non-specific and ill-defined target population / condition AND/OR significant between-participant differences, that have NOT been controlled for in analysis OR between-participant differences not reported (contact authors to request data)

3. **Choice of reinforcer:**

Stage one rating criteria and instructions:

Strong – The choice of reinforcer has been influenced by the participants taking part in the study or has been shown empirically to be of maximum utility in the particular treatment population.

Moderate – The choice of reinforcer has been shown in previous research to be of some efficacy, but may not be of optimum efficacy.

Weak – The choice of reinforcer is not based on consultation with participants and has either no or limited empirical support.

Changes made:

- Altered to make it clearer that participant input into the choice of rewards needs to be made prior to the initiation of the study.

Stage two instructions:

- The choice of reinforcers used should only be considered to have been influenced by participants if this was done prior to the initiation of the study. For example, the exchange of earned vouchers for goods of participants' choice would not fall under this definition, unless participants had input as to whether they wanted rewards to take this form or not.

Stage two rating criteria:

Strong (3) – The choice of reinforcer has been influenced by the participants taking part in the study AND shown empirically to be of utility in the particular treatment population.

Moderate (2) – The choice of reinforcer has been shown in previous research to be of some efficacy, but participants have not been consulted.

Weak (1) – The choice of reinforcer is neither based on consultation with participants nor has empirical support.

4. Incentive magnitude

Stage one rating criteria and instructions:

Monetary vouchers should be adjusted for inflation and the average weekly value calculated based on receiving all rewards. Clinical privileges should be ranked based on their intrinsic value to patients.

Strong – Studies with reward values in the top quartile of ranked studies.

Moderate – Studies with reward values in the middle two quartiles of ranked studies.

Weak – Studies with reward values in the bottom quartile of ranked studies.

Changes made:

- Made clearer as to how this should be calculated and also added more information to the instructions to allow the ranking of non-monetary vouchers.

Stage two instructions:

- For monetary vouchers/cash rewards, the total available reward value for each study should be adjusted for inflation from the year the study was conducted to the current year. This value should then be divided by the number of weeks that the study ran for, and the studies ranked based on these average weekly reward values.
- Studies using other reward types, for example, clinical privileges should be ranked as moderate, unless there is evidence in the literature that these are of greater intrinsic value than monetary vouchers/cash rewards ranked in the middle quartile.
- If quality assessments are being conducted on only a small number of studies, or outside of the context of a systematic review/meta-analysis, the reward values of similar studies in the relevant field should instead be used a reference point for rating incentive magnitude. Incentives of a greater magnitude than those commonly

used in the field should be rated as strong, those on a par with those commonly used in the field as moderate, and those of lower magnitude than those commonly used in the field as weak.

Stage two rating criteria:

Strong (3) – Studies with reward values in the top quartile of all studies being rated

Moderate (2) – Studies with reward values in the middle two quartiles of all studies being rated

Weak (1) – Studies with reward values in the bottom quartile of all studies being rated

5. Frequency of incentive distribution

Stage one rating criteria and instructions:

Strong – Explicit evidence of this being set to establish total compliance with agreed behavioural goals (e.g. drug abstinence)

Moderate – Evidence of some consideration of this being set to establish total compliance with agreed behavioural goals (e.g. drug abstinence)

Weak – No evidence of this being set to establish total compliance with agreed behavioural goals (e.g. drug abstinence)

Changes made:

- This was altered so that the moderate rating now applies to any study that uses a frequency of incentive distribution capable of capturing total compliance with behavioural goals, but does not explicitly report this as the motivation for implementing the frequency of incentive distribution used.

Stage two instructions:

- If data are missing for frequency of incentive distribution, score the study as moderate if the frequency would capture total compliance with agreed behavioural goals (for example testing for cocaine every two days [187]). Consistent with the general instructions, authors should still be contacted for explicit verification of this and the quality assessment adjusted accordingly.

Stage two rating criteria:

Strong (3) – Explicit evidence of this being set to establish total compliance with agreed behavioural goals (e.g. drug abstinence)

Moderate (2) – Evidence of this having the ability to establish total compliance with agreed behavioural goals (e.g. drug abstinence) OR no evidence of the frequency to establish total compliance provided but the frequency would catch all drug use

Weak (1) – No evidence of this being set to establish total compliance with agreed behavioural goals (e.g. drug abstinence)

6. Timing of the incentive

Stage one rating criteria and instructions:

Based on the meta-analysis of (Griffith et al., 2000):

Strong – Immediate reward on display of desired behaviour

Moderate – Reward administered within 24 hours of display of desired behaviour

Weak – Reward administered after 24 hours of display of desired behaviour OR timing of incentive administration unclear

Changes made:

- Clarified so that a strong rating constitutes rewards administered the same calendar day as evidence of desired behaviour, moderate the next calendar day and weak any time after this.

Stage two instructions:

- It should be noted that for "fishbowl" type interventions (where for each verified display of the desired behaviour, participants earn the right to draw tickets from a bowl that can represent money or prizes), it is the earning of draws from the "fishbowl" that constitutes the reward, not the later exchange of these earned rewards for physical goods.

Stage two rating criteria:

Based on the meta-analysis of (Griffith et al., 2000)

Strong (3) – Reward administered on the same calendar day as display of desired behaviour

Moderate (2) – Reward administered one calendar day after the display of desired behaviour

Weak (1) – Reward administered more than one calendar day after display of desired behaviour OR timing of incentive administration not reported (contact authors to request data)

7. Duration of the intervention

Stage one rating criteria and instructions:

Strong – Explicit justification of the intervention duration based on previous research or the length of other treatments being administered to patients (e.g. methadone treatment, drug detox etc.)

Moderate – No explicit justification of the intervention duration but it is evident that it follows either a precedent in the literature or other treatments being administered to patients (e.g. methadone treatment, drug detox etc.)

Weak – No explicit justification of the intervention duration and no evidence of following either a precedent in the literature or other treatments being administered to patients (e.g. methadone treatment, drug detox etc.)

Changes made:

- Clarified criteria so that strong rating is only available to studies that explicitly justify length of intervention.

Stage two instructions:

- Aligning with other treatment: This refers to the length of the contingency management treatment following the length of another treatment being administered to participants. For example, treatment for illicit drug use often takes place over 12 weeks [188] or for smoking cessation (in the UK) over six weeks [56]. Therefore, a contingency management that followed the duration of another treatment given to participants, but did not explicitly state this as the motivation for the treatment duration used, would be rated as providing moderate strength evidence. Authors should still be contacted for explicit verification of intervention duration and the quality assessment adjusted accordingly.

Stage two rating criteria:

Strong (3) – Explicit justification of the intervention duration being based on empirical support of efficacy

Moderate (2) – No explicit justification of the intervention duration but it follows clinical precedent or aligns with other treatments being administered to patients (e.g. methadone treatment, drug detox etc.)

Weak (1) – No explicit justification of the intervention duration and no evidence of following either a precedent in the literature or other treatments being administered to patients (e.g. methadone treatment, drug detox etc.)

3.6 Stage Two: Validation Testing Methods

3.6.1 General Methods

After the changes outlined above had been made to the rating criteria, inter-rater reliability testing was re-conducted. One of the stage one assessors (A1) was no longer available, so an alternative reviewer (A4) performed the stage two ratings alongside myself and the other reviewer who rated studies during stage one. Inter-rater reliability was calculated in the same way as during stage one, and the same method of calculating the four overall quality scores for the CMQAT was also implemented.

3.6.2 Study Selection

The 20 studies used for stage two assessments were identified in the same systematic search as those in stage one. However, these studies were not included in the meta-analysis due to it not being possible to calculate effect sizes for any of these studies.

3.6.3 Predictive Validity

As effect sizes could not be calculated for the studies being assessed during stage two, it was not possible to perform predictive validity testing during this stage of testing.

3.6.4 EPHPP Quality Assessments

As predictive validity testing was not possible during stage two, the inter-rater reliability of the EPHPP was additionally tested. All three assessors therefore rated stage two studies using the EPHPP tool as well as the CMQAT. The aim of this was to assess whether the CMQAT could achieve similar levels of inter-rater reliability as an established quality assessment tool, i.e. the EPHPP. Ratings assigned using the EPHPP tool were carried out in accordance with the instructions supplied with the tool.

3.7 Stage Two: Results

3.7.1 CMQAT Quality Ratings and Inter-Rater Reliability

Criterion and global quality ratings for all papers, along with percentage agreement between the three assessors, are shown in Figures 7 and 8 below. The number of studies rated overall as providing strong, moderate or weak evidence by each of the three assessors is shown in Table 8.

Criterion Ratings

Study	Target behaviour			Target population			Reinforcer			Incentive magnitude			Frequency of distribution			Timing of incentive			Duration of intervention		
	A1	A4	A3	A1	A4	A3	A1	A4	A3	A1	A4	A3	A1	A4	A3	A1	A4	A3	A1	A4	A3
Katz et al. 2004	2	2	2	2	2	2	2	2	2	2	2	2	3	1	3	2	1	3	2	2	2
Sigmon 2004	3	3	3	1	3	1	2	2	2	1	1	1	2	2	3	1	1	1	3	1	1
Rawson 2002	2	3	2	3	3	3	2	2	2	2	2	2	3	2	2	3	3	2	2	2	3
Correia 2005	3	3	3	2	3	3	2	2	2	2	2	2	3	2	3	1	1	1	3	1	1
Hall 1979	3	3	3	1	1	1	2	1	2	2	2	2	2	2	2	1	1	1	2	2	2
McCaul 1984	3	3	3	1	1	3	2	1	2	1	1	1	1	1	1	3	1	1	3	2	2
Tuten 2012	2	3	3	3	3	3	2	2	2	2	2	2	2	2	1	1	1	1	1	1	2
Iguchi 1996	3	3	3	3	3	3	2	2	2	3	3	3	2	1	3	3	1	3	3	1	1
Stitzer 1992	3	3	3	3	1	1	2	2	2	3	3	3	3	1	2	1	1	3	2	1	1
Kosten 2003	2	3	3	3	3	3	2	2	2	2	2	2	3	2	2	1	3	1	2	2	2
Carpenedo 2010	3	3	3	3	1	1	2	3	2	2	2	2	2	3	2	1	3	1	3	2	3
Winstanley 2011	3	3	3	2	2	3	2	2	2	2	2	2	2	2	2	1	1	1	3	2	2
Iguchi 1997	3	3	3	3	3	3	2	1	2	1	1	1	2	2	2	1	3	1	2	2	2
Preston 2001	2	3	3	2	2	2	2	2	2	2	2	2	2	2	2	2	3	1	1	2	2
Correira 2003	2	2	2	3	1	1	2	2	2	1	1	1	2	1	2	1	1	1	3	1	3
Shoptaw 2002	3	3	2	3	3	2	2	2	2	1	1	1	1	1	2	1	3	1	2	2	2
Cutuape 1999	3	3	3	3	1	3	2	2	2	3	3	3	2	2	2	1	3	3	2	1	2
Dunn 2008	3	3	3	3	3	3	2	2	2	3	3	3	3	3	3	3	3	3	3	1	1
Silverman 1999	3	3	3	3	3	1	2	2	2	3	3	3	2	2	2	3	3	3	2	1	1
Robles 2002	3	3	3	1	3	3	2	2	2	2	2	2	2	3	2	1	3	1	3	2	1

Percentage Agreement[1]	**Target behaviour**			**Target population**			**Reinforcer**			**[2]Incentive magnitude**			**Frequency of distribution**			**Timing of incentive**			**Duration of intervention**		
	A1	A4	80%	A1	A4	65%	A1	A4	80%	A1	A4	N/A	A1	A4	55%	A1	A4	50%	A1	A4	35%
	A3	A1	80%	A3	A1	55%	A3	A1	100%	A3	A1	N/A	A3	A1	60%	A3	A1	70%	A3	A1	40%
	A3	A4	90%	A3	A4	70%	A3	A4	80%	A3	A4	N/A	A3	A4	45%	A3	A4	50%	A3	A4	70%

Figure 7 Stage two criterion ratings for CMQAT. A1= Assessor 1, A2= Assessor 2, A3= Assessor 3, [1] Percentage agreement calculated as the number of the same rating given to studies for each criterion, expressed as a percentage. [2] Percentage agreement was not calculated for Incentive Magnitude as this is based on the ranking of studies and therefore is the same for all raters.

Overall Ratings

	Strict			Lenient			Sum Score			Average Score		
Study	**A1**	**A4**	**A3**	**A1**	**A4**	**A3**	**A1**	**A4**	**A3**	**A1**	**A4**	**A3**
Katz et al. 2004	3	1	3	3	2	3	15	12	16	2.14	1.71	2.29
Sigmon 2004	1	1	1	1	1	1	13	13	12	1.86	1.86	1.71
Rawson 2002	3	3	3	2	3	3	17	17	16	2.43	2.43	2.29
Correia 2005	2	1	1	3	2	2	16	14	15	2.29	2.00	2.14
Hall 1979	1	1	1	2	1	2	13	12	13	1.86	1.71	1.86
McCaul 1984	1	1	1	1	1	1	14	10	13	2.00	1.43	1.86
Tuten 2012	1	1	1	2	2	2	13	14	14	1.86	2.00	2.00
Iguchi 1996	3	1	2	3	1	3	19	14	18	2.71	2.00	2.57
Stitzer 1992	2	1	1	3	1	2	17	12	15	2.43	1.71	2.14
Kosten 2003	2	3	2	2	3	2	15	17	15	2.14	2.43	2.14
Carpenedo 2010	2	2	1	3	3	2	16	17	14	2.29	2.43	2.00
Winstanley 2011	2	2	2	2	2	2	15	14	15	2.14	2.00	2.14
Iguchi 1997	1	1	1	2	2	2	14	15	14	2.00	2.14	2.00
Preston 2001	2	3	2	2	3	2	13	16	14	1.86	2.29	2.00
Correira 2003	1	1	1	2	3	1	14	9	12	2.00	1.29	1.71
Shoptaw 2002	1	1	1	1	2	2	13	15	12	1.86	2.14	1.71
Cutuape 1999	2	1	2	3	2	3	16	15	17	2.29	2.14	2.43
Dunn 2008	3	2	2	3	3	3	20	18	18	2.86	2.57	2.57
Silverman 1999	3	2	1	3	3	2	18	17	15	2.57	2.43	2.14
Robles 2002	1	3	1	2	3	2	14	18	14	2.00	2.57	2.00

Percentage Agreement

Strict		
A1	A4	50%
A3	A1	70%
A3	A4	60%

Lenient		
A1	A4	40%
A3	A1	65%
A3	A4	45%

Sum Score [2]		
A1	A4	r= 0.359, p= 0.120
A3	A1	r= 0.827, p=<0.001
A3	A4	r= 0.408, p= 0.074

Average Score [2]		
A1	A4	r= 0.360, p= 0.119
A3	A1	r= 0.823, p=<0.001
A3	A4	r= 0.405, p= 0.076

Figure 8 Stage two overall ratings for the CMQAT. A1= Assessor 1, A2= Assessor 2, A3= Assessor 3, [1] Percentage agreement calculated as the number of the same rating given to studies for each criterion, expressed as a percentage. [2] Pearson's correlation and associated *p* value.

Table 8 Number of studies rated by each assessor as providing strong, moderate and weak evidence on CMQAT stage two

	Overall Quality Ratings (N, %)		
Assessor and rating method	Strong	Moderate	Weak
Assessor 1, Strict	5 (25.00%)	7 (35.00%)	8 (40.00%)
Assessor 2, Strict	4 (20.00%)	4 (20.00%)	12 (60.00%)
Assessor 3, Strict	2 (10.00%)	6 (30.00%)	12 (60.00%)
Assessor 1, Lenient	8 (40.00%)	9 (45.00%)	3 (15.00%)
Assessor 2, Lenient	8 (40.00%)	7 (35.00%)	5 (25.00%)
Assessor 3, Lenient	5 (25.00%)	12 (60.00%)	3 (15.00%)

In stage two testing, there was a general improvement in percentage agreement between assessors across all rating criteria, and also overall for the strict, but not the lenient scoring method. However, agreement for criterion one decreased between stage one and two. Inter-rater reliability testing yielded an overall kappa value of k= .335 (p=>.001) for the strict rating system and k= .201 (p= .034) for the lenient scoring system, both signifying "fair" agreement. A significant positive correlation was observed between A1 and A3 (the two assessors testing at stages one and two) for both the sum and average scoring methods. No significant correlations were observed between A4 and either of the other two assessors.

3.7.2 EPHPP Quality Assessment Tool Quality Ratings and Inter-Rater Reliability

Criterion and global quality ratings for all papers assessed with the EPHPP quality assessment tool, along with percentage agreement between the three assessors, are shown in Figure 9 below. The number of studies rated overall as providing strong, moderate or weak evidence by each of the three assessors is shown in Table 9.

EPHPP Ratings

	Selection Bias			Study Design			Confounds			Blinding			Data Collection			Withdrawals/ Dropouts			Overall		
Study	**A1**	**A4**	**A3**	**A1**	**A4**	**A3**	**A1**	**A4**	**A3**	**A1**	**A4**	**A3**	**A1**	**A4**	**A3**	**A1**	**A4**	**A3**	**A1**	**A4**	**A3**
Katz et al. 2004	2	3	3	1	1	1	1	1	1	2	3	2	1	1	1	1	1	3	1	3	3
Sigmon 2004	3	3	2	1	1	1	3	1	3	2	3	2	1	1	1	2	1	1	3	3	2
Rawson 2002	3	3	3	1	1	1	1	1	1	2	3	2	2	1	1	3	3	3	3	3	3
Correia 2005	3	3	2	3	2	1	3	NA	3	2	3	2	1	1	1	3	3	3	3	3	3
Hall 1979	1	1	3	1	1	1	3	3	3	2	3	2	1	1	1	3	3	3	3	3	3
McCaul 1984	3	3	3	1	1	1	1	1	1	2	2	2	1	1	2	2	3	3	2	3	3
Tuten 2012	2	1	3	1	1	1	1	1	1	2	3	2	2	1	1	3	3	3	2	3	3
Iguchi 1996	2	2	3	1	1	1	1	1	1	2	3	2	1	1	1	2	2	2	1	2	2
Stitzer 1992	2	3	3	1	3	1	1	1	3	2	3	2	1	1	1	1	2	2	1	3	3
Kosten 2003	2	2	3	1	1	1	1	1	1	1	3	1	1	1	1	3	3	3	2	3	3
Carpenedo 2010	2	2	2	1	1	1	1	3	1	2	3	2	1	1	1	3	3	3	2	3	2
Winstanley 2011	2	2	3	1	1	1	1	1	1	2	3	2	1	1	1	3	2	2	2	2	2
Iguchi 1997	2	1	2	1	1	1	1	1	1	2	3	3	1	2	1	2	2	2	1	2	2
Preston 2001	2	3	3	1	1	1	2	1	1	2	3	2	1	1	1	1	1	1	1	3	2
Correira 2003	2	3	3	3	2	1	3	NA	1	2	3	3	1	1	1	2	3	3	3	3	3
Shoptaw 2002	2	2	3	1	1	1	1	1	1	2	3	2	2	2	1	2	3	1	1	3	2
Cutuape 1999	2	3	3	1	1	1	1	1	3	2	3	2	1	1	1	1	3	3	1	3	3
Dunn 2008	2	3	3	1	1	1	1	1	1	2	3	2	2	1	1	2	3	2	1	3	2
Silverman 1999	2	2	3	3	2	1	1	NA	3	2	3	2	1	1	1	2	2	3	2	2	3
Robles 2002	3	3	3	1	1	1	1	1	1	2	3	2	1	1	1	3	3	1	3	3	2

Percentage Agreement [1]

Selection Bias		
A1	A4	60%
A3	A1	25%
A3	A4	50%

Study Design		
A1	A4	80%
A3	A1	85%
A3	A4	80%

Confounds		
A1	A4	70%
A3	A1	75%
A3	A4	65%

Blinding		
A1	A4	5%
A3	A1	90%
A3	A4	15%

Data Collection		
A1	A4	80%
A3	A1	75%
A3	A4	85%

Withdrawals/ Dropouts		
A1	A4	60%
A3	A1	50%
A3	A4	75%

Overall		
A1	A4	40%
A3	A1	30%
A3	A4	40%

Figure 9 EPHPP criterion and overall ratings of all three assessors for stage two studies, with overall quality ratings calculated as according to the EPHPP instructions (the same system as the strict rating method of the CMQAT). A1= Assessor 1, A2= Assessor 2, A3= Assessor 3. [1] Percentage agreement calculated as the number of the same rating given to studies for each criterion, expressed as a percentage.

Table 9 Number of studies rated by each assessor using the EPHPP quality assessment tool as providing strong, moderate and weak evidence

Assessor and rating method	**Overall Quality Ratings (N, %)**		
	Strong	Moderate	Weak
Assessor 1	8 (40.00%)	6 (30.00%)	6 (30.00%)
Assessor 2	0	4 (20.00%)	16 (80.00%)
Assessor 3	0	9 (45.00%)	11 (55.00%)

Inter-rater reliability testing of the EPHPP quality assessment tool yielded an overall kappa value of k= .051 (*p*= .607), signifying only slight agreement.

3.8 Stage Three Methods

For stage three testing, the assessor from stage two (A4) that did not assess the studies from stage one, used the updated rating criteria to assess the stage one studies. This was conducted in order to ascertain whether the updated rating criteria had increased the predictive validity of the tool. As in stage one, correlations were calculated between the quality ratings of the studies and the effect sizes for both longest duration of abstinence and percentage of negative samples.

3.9 Stage Three Results

3.9.1 CMQAT Quality Ratings

Criterion and overall quality ratings and shown below in Figure 10. The number of studies rated overall as providing strong, moderate or weak evidence by the assessor is shown in Table 10.

Study	Target behaviour	Target population	Reinforcer	Incentive magnitude	Frequency of incentive distribution	Timing of the incentive	Duration of the intervention	Strict	Lenient	Sum	Average
Katz 2002	3	3	2	3	2	1	3	2	3	17	2.43
Silverman 1998	3	2	2	3	2	1	2	2	2	15	2.14
Epstein 2003	2	2	2	2	2	1	2	2	2	13	1.86
Groß et al. 2006	3	3	1	1	2	1	2	1	1	13	1.86
Ling 2013	2	2	2	2	1	3	3	2	2	15	2.14
Vandrey 2007	3	1	2	1	2	2	2	1	2	13	1.86
Dunn 2010	2	3	2	3	3	1	1	1	2	15	2.14
Kidorf et al. 1993	2	3	1	1	1	3	1	1	1	12	1.71
Chutuape et al. 1999	3	1	2	2	2	3	2	2	2	15	2.14
Kidorf et al. 1996	3	1	2	3	1	3	1	1	1	14	2.00
Peirce et al. 2006	3	3	2	1	1	3	3	1	2	16	2.29
Chutuape et al. 2000	3	3	2	3	3	2	2	3	3	18	2.57
Petry et al. 2002	3	3	2	2	2	3	2	3	3	17	2.43
Preston 2000	3	3	2	2	3	1	1	1	2	15	2.14
Schottenfeld et al. 2005	3	3	2	2	2	1	2	2	2	15	2.14
Epstein et al. 2009	3	3	2	2	2	3	3	3	3	18	2.57
Petry 2007	2	3	2	2	1	3	3	2	3	16	2.29
Petry et al. 2015	3	3	2	1	2	1	2	1	2	14	2.00
Silverman 1996	3	2	2	2	2	1	2	2	2	14	2.00
Umbricht 2014	3	3	2	2	2	1	2	2	2	15	2.14
Downey et al. 2000	2	3	2	2	2	2	3	3	3	16	2.29
Katz et al. 2002	2	1	2	2	2	1	2	1	2	12	1.71

Figure 10 Stage three criterion and overall quality ratings

Table 10 Number of studies rated by the assessor using the CMQAT as providing strong, moderate and weak evidence in stage three

Rating Method	Overall Quality Ratings (N, %)		
	Strong	Moderate	Weak
Assessor 4, Strict	4 (18%)	9 (41%)	9 (41%)
Assessor 4, Lenient	6 (27%)	13 (59%)	3 (14%)

3.9.2 Predictive Validity

Correlations between the four different overall scoring methods for the CMQAT (strict, lenient, sum score and average score) and the effect sizes of the studies rated are shown in Table 11. No significant correlations were observed between any of the CMQAT scoring methods and effect sizes of the studies rated.

Table 11 Correlations between CMQAT quality scores and study effect sizes for each of the three assessors

	Marking Criteria			
Effect Size Type	**Strict**	**Lenient**	**Sum Score**	**Average Score**
Longest Duration of Abstinence (N= 18)	$\tau = 0.154$ ($p = 0.455$)	$\tau = 0.040$ ($p = 0.848$)	$\tau = 0.160$ ($p = 0.932$)	$\tau = 0.161$ ($p = 0.932$)
Percentage of Negative Samples (N= 12)	$\tau = -0.453$ ($p = 0.069$)	$\tau = -0.164$ ($p = 0.507$)	$\tau = -0.066$ ($p = 0.774$)	$\tau = -0.067$ ($p = 0.774$)

3.10 Discussion

The seven core principles of CM, as laid out by the leading researchers in the field [82], were translated into quality rating criteria using the EPHPP quality assessment tool as template. Preliminary reliability and validity assessments of the resulting quality assessment tool, the CMQAT, were then assessed involving four assessors in three stages. During stage one testing, inter-rater reliability between the three assessors was only "slight" [184]. In predictive validity testing, all correlations between CMQAT scores and the effect sizes for the rated studies were non-significant. Correlations between the EPHPP quality scores and effect sizes of rated studies were also non-significant. Rating criteria were improved in light of stage one results, and in stage two testing, the inter-rater reliability between the three assessors increased to "fair" [184]. The inter-rater reliability for the same assessors, assessing the same studies, using the EPHPP quality assessment tool, was only "slight" [45]. Predictive validity testing was not possible during stage two as effect sizes could not be calculated for the studies used during this stage of testing. Stage three testing re-rated stage

one studies with the updated criteria, allowing assessment of predictive validity. No significant correlations were observed between the CMQAT quality ratings and study effect sizes.

There are a number of limitations to this research. The main limitation is the restricted amount of reliability and validity testing that the CMQAT has undergone. Although both inter-rater reliability and predictive validity testing have been performed twice, a number of other types of reliability and validity testing should also be undergone in order to examine the potential of using the tool for assessing the quality of studies. Similarly, the tool has only been tested by a very limited number of assessors, with a small number of studies taken from a narrow spectrum of the CM literature (pertaining to SUD CM interventions). Related to this, there is the potential that as I both created the initial outline for the CMQAT and acted as an assessor during stages one and two, a certain amount of bias may exist in the ratings assigned in both these stages. Another limiting factor of the current work is that although predictive validity testing has been conducted twice, no significant correlations were observed either time, with no discernible improvement in predictive validity. This draws into question the methods being used to test predictive validity. It was the assumption here, that studies rated as being of higher quality should produce larger effect sizes. However, a study assessing the relationship between study quality and effect size, using a random selection of RCTs investigating interventions used for circulatory and digestive diseases, mental health, and pregnancy and childbirth, observed that lower quality studies overestimated the effectiveness of an intervention, artificially inflating effect sizes [189]. This may explain why more of the correlations observed in stage three are negative than those from stage one, with those that are not negative in stage three still being closer to zero than those in stage one. This has quite serious implications for future testing of the validity of the CMQAT. Whether this over-estimation of effect size by lower quality studies also occurs in CM studies, and the implications of this for ascertaining the predictive validity of the CMQAT, merits further investigation. The potential implications of this are discussed in more detail in the discussion chapter (chapter six).

Despite these limitations, there are strengths to the current work. This is the first time that a quality assessment tool has been created and tested for use specifically with CM studies, and therefore represents a significant contribution to the contingency management field. At the current time, any quality assessment of CM studies does not reflect an objective appraisal of study quality. The CMQAT therefore, even in its early stage of development, begins to address this issue, offering a more

objective assessment of the quality of CM studies than is currently available. Despite the limited scope of the results presented here, and the limitations outlined above, the current work provides a foundation for the further development of the tool.

There are a number of directions for future research and the further development of the tool, with a number of important issues that require addressing before the use of the tool can progress. Firstly, it should be considered what forms of further reliability and validity testing should be performed on the tool. It would seem that measuring the test-retest reliability of the tool, for example, may represent a potentially useful means of further ascertaining the reliability of the CMQAT. Similarly, testing split-half reliability [190] may be a useful means for ascertaining the internal consistency of the tool. Testing with methods developed under item response theory [191] may help uncover whether any latent quality constructs exist within the tool. Other types of validity testing however, for example convergent validity, may be of only limited utility given the relative uniqueness of the CMQAT and the difficulties involved in finding another tool against which to compare the CMQAT in this context. It may also be necessary to better define what should be expected from the validity and reliability testing already implemented. For example, the inter-rater reliability achieved in the second stage of testing is low, representing only "fair" agreement. Despite this, inter-rater reliability was greater than "slight" agreement achieved with the EPHPP quality assessment tool, raising the question of exactly what level of agreement is enough to recommend the tool for use in research. Furthermore, as mentioned in the previous chapter, a prior study [128] showed the EPHPP to have "excellent" inter-rater reliability, which contrasts starkly with our observation of only slight agreement. It may be that there is some sort of practice effect [192] taking place, or alternatively it may be that the EPHPP is more difficult to apply to CM studies as opposed to more conventional RCTs. Whatever the underlying cause of this discrepancy in inter-rater reliability may be, it merits further investigation. Another focus of future research should be to determine which of the different scoring methods trialled here is best. The percentage agreement between assessors increased for the strict rating system from stage one to two, but decreased for the lenient. This improvement in agreement may implicate the strict method as potentially the more useful of the two. It may be, however, that the sum or average scoring systems are of greater utility for weighting analyses during meta-analysis, as implementing these continuous scale scoring methods offers a finer grain appraisal of quality than grouping studies under the three categories of strong moderate or weak. Interestingly, significant positive correlations between ratings were found

amongst more of the assessors in stage one than in stage two, but the correlations observed in stage two were stronger and more significant. As the improvement in the strength of correlation between stage one and two was in the two assessors that took part in both stages, this may suggest that some sort of practice effect is taking place. More research, and consultation with a wide range or researchers is required before the most appropriate scoring method can be agreed.

Perhaps the most important element in the further development of the tool however, is its application by a broader range of assessors in a wider range of research fields. Validity and reliability testing of the CMQAT by experts implementing CM interventions for a wide range of behaviours, not just addictions, is imperative for ensuring that the CMQAT is suitable for use with all varieties of CM study. Given that the principles of CM that the CMQAT criteria are based on were constructed from the perspective of addictions interventions, it may be useful to perform some sort of Delphi experiment with researchers in other fields, similar to that used in the development of the Cochrane Collaborations risk of bias tool [193]. This would allow the development of the rating criteria to reflect more accurately the breadth of behaviours that CM interventions can be used to treat. Further to this, there is the potential that the formulation of the CMQAT paves the way for the development of reporting guidelines for CM studies, similar to the CONSORT statement [194] designed to improve the reporting of randomised controlled trials. This may even feed into the design of future CM studies, improving the quality of evidence concerning its efficacy, and improving outcomes for service users. An associated issue is that of treatment implementation. As mentioned earlier, implementation plays a pivotal role in the quality of any intervention, but is often poorly reported and at current, not included in the assessment of study quality. The CMQAT contains some elements related to the implementation of CM, but does not currently include a direct appraisal of this in its assessment. The initial intent of the CMQAT was to assess study quality based on the seven identified core components of CM, and only once this has been successfully completed can assessment of implementation be further built into the tool.

Overall, the work reported here signifies the first steps towards the objective reporting of quality in CM studies. This has implications not only for the synthesis of systematic reviews and meta-analysis of CM studies, but also for the design and conduct of trials. There is a great deal of further testing and refinement required before the tool can be implemented in practice, namely in testing the CMQAT across a broader range of CM literature, but a foundation now exists on which to build this future work.

Chapter 4:

Addition of Contingency Management to Stop Smoking Services in Opiate Users: A Pilot and Feasibility Study

Methods

4.1 Background

From the results of the meta-analysis, it was clear that there was a significant gap in the literature concerning the use of contingency management (CM) as an intervention for tobacco smoking during opiate addiction treatment. As previously mentioned, only four studies [70–73] testing CM for tobacco dependence during opiate addiction treatment were identified in the systematic search, only one [70] of which could be meta-analysed. CM has also never been tested in this context in the UK before, forming the basis for the decision to develop an intervention to test this. Due to the specific nature of the target population and behaviour, an intervention of this type falls under that of a "complex" intervention, and was therefore designed under the Medical Research Council (MRC) guidelines for the development of complex interventions [111] (see Figure 11).

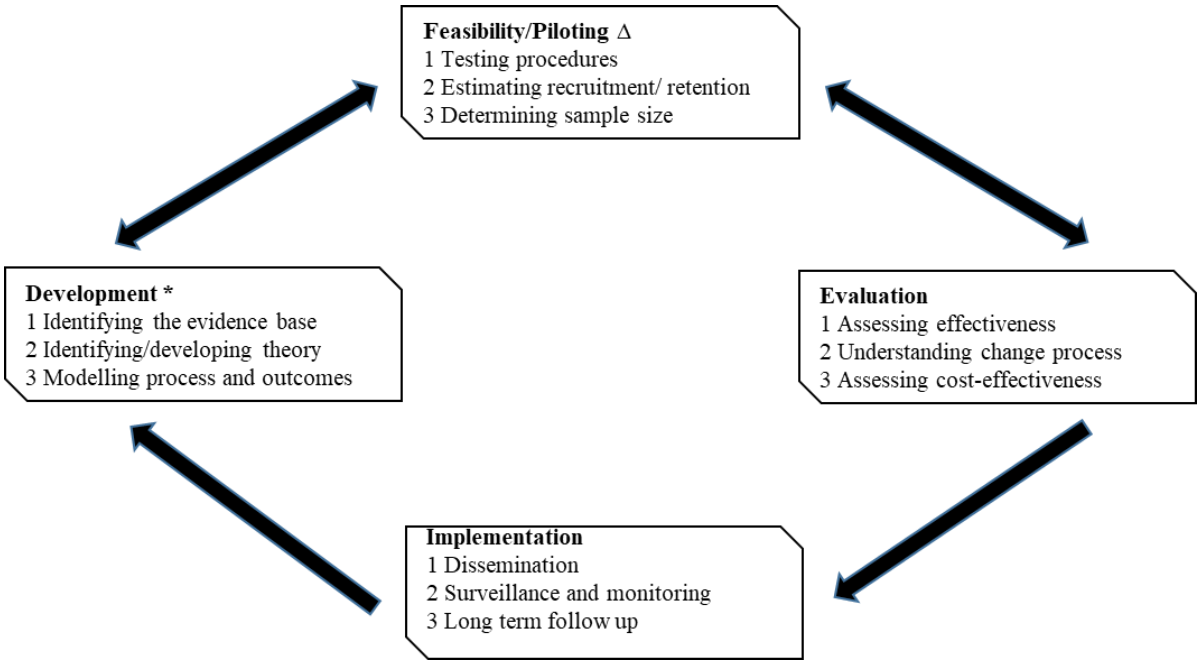

Figure 11 Key elements of the development and evaluation process, as adapted from the 2016 MRC guidelines. *The element represented by the work carried out in the Meta-analysis and CMQAT (Chapters 2 and 3). ΔThe element represented by the pilot/feasibility study (chapters 4 and 5)

These guidelines constitute the key elements required in the development of a complex intervention, starting at the development stage with research progressing systematically from this point [111]. The systematic review and meta-analysis, and the development of the quality assessment tool (CMQAT), constituted the first two elements of the development element of intervention design. These two projects highlighted the necessary evidence and theory regarding the use of CM in this treatment population that was required to develop the current

intervention. We then further decided that, given a small number of studies had already explored the use of CM for tobacco smoking during opiate addiction treatment [70–73], and that CM is so widely used across many types of drug addiction treatment, that modelling processes would be unnecessary. The next key element in the development of the current intervention therefore, is that of feasibility and piloting. The purpose of this is to test the procedures involved with the intervention in order to ascertain their acceptability, whilst allowing the estimation of likely recruitment and retention rates [111]. It also allows for the preliminary testing of any potential intervention effects as secondary outcomes, as was done here.

As mentioned previously, not only is there a large body of evidence outlining the use of CM in drug addiction, but there are a few studies published investigating its use for tobacco smoking in opiate addiction treatment [70–73]. Additionally, the study centre (an outpatient drug addiction treatment centre) where I had chosen to conduct the current intervention had previously implemented CM interventions in its opiate addiction treatment clients, including a large, cluster randomised trial investigating the efficacy of CM for hepatitis B vaccination completion [195]. The decision was therefore made that a pilot/feasibility study would be the most appropriate design. The methods for this pilot study are outlined below and have also been published in the journal BMJ Open (appendix 4).

4.2 Methods and Design

4.2.1 Objectives

Primary objective: To investigate whether a CM intervention can be successfully added to standard stop smoking services treatment, in patients undergoing outpatient treatment for opiate addiction, in order to identify any elements that need changing before carrying out a full scale randomised controlled trial (RCT).

Secondary objectives: To gather preliminary findings regarding the effects of the CM intervention on smoking behaviours in this group, and any possible effects the intervention may have on opiate addiction treatment outcomes.

4.2.2 Study Site

A pivotal element of the pilot study was that CM was integrated into standard stop smoking services treatment in the UK. This required the identification of an addiction treatment centre that also ran a stop smoking clinic. A number of potential study sites were considered, however, only

one of these had an extant stop smoking clinic and was therefore chosen as the study site. This centre was also locally accessible, and had a close working relationship with my department, making it an ideal location for the study.

Between August 2014 and July 2015, smoking cessation treatment was run by the team at the treatment centre. Prior to this, it had been run by a specialised local authority stop smoking team. In the period between July 2015 and the initiation of the current study, there was no stop smoking service run at the treatment site, necessitating the re-training of staff at the treatment staff before the study could commence. During the period of time that the service was being run by the treatment centre, a total of 34 drug addiction clients were admitted into the service. These clients attended an average of 2.65 (SD=2.42) sessions, with seven of these achieving CO validated abstinence at week 4 (19).

4.2.3 Participants, Recruitment, Inclusion Criteria and Randomisation

As this was a pilot study, the primary outcome was not the efficacy of the study intervention. Consequently, the sample size was not calculated to ascertain efficacy. Instead, the method outlined by Viechtbauer et al [196] for calculating the sample size based on the probability of any issues that may arise was been used. A sample size of 40 using the above rationale is powerful enough to provide over 90% certainty of detecting any issues that occur with a probability of over 5%. The study therefore aimed to recruit 40 patients, all undergoing current treatment for opiate addiction.

Participants were recruited from the study site either through self-referrals in response to advertisements shown in the treatment centre, directly recruited by myself in the treatment centre, or through referrals from treatment centre staff.

Participants were eligible for inclusion if they wanted to quit smoking (complete abstinence), were between 18 and 65 years old, undergoing pharmacological treatment for opiate addiction, smoked a minimum of ten cigarettes per day (in order to capture anything from ‘light smoking’ and over [197,198]), and provided informed consent. Participants were ineligible for inclusion in the study if they exhibited insufficient English skills to understand study protocols, were currently undergoing treatment for other drugs of abuse or were taking part in other research. Pregnant women were not excluded.

Participants interested in taking part in the study were given an information sheet and then asked to return to the treatment centre no

sooner than 24 hours later to sign their consent to take part in the study. If participants had already been given an information sheet by a member of staff, and had had at least 24 hours to consider whether they wanted to take part in the study, they were consented immediately. Once consent was obtained, participants were then immediately randomised into either experimental (CM for abstinence) or control (CM for attendance) conditions. Randomisations were performed by myself using the service provided by the company 'sealed envelope ltd.' [199], utilising random permuted blocks within strata. Randomisation was stratified based on participants' current smoking frequency (between 10 and 20 per day, and more than 20 per day [32]).

4.2.4 Study Design

A two-arm, randomised controlled design was utilised for the pilot study. A CM intervention was provided as an adjunct to the standard stop smoking services treatment provided at the treatment centre, with CM rewards available during weeks 2 to 5 of the stop smoking treatment. In light of our meta-analysis findings that little is known regarding the longer-term effects of CM, a six-month follow-up was included in the design of the pilot study. The study was conducted in compliance with the principles of the Declaration of Helsinki [200], the principles of Good Clinical Practice, and all applicable regulatory requirements. The rationale for the chosen design is described in the following sections and the main elements of the study are outlined in the flow chart (Figure 12).

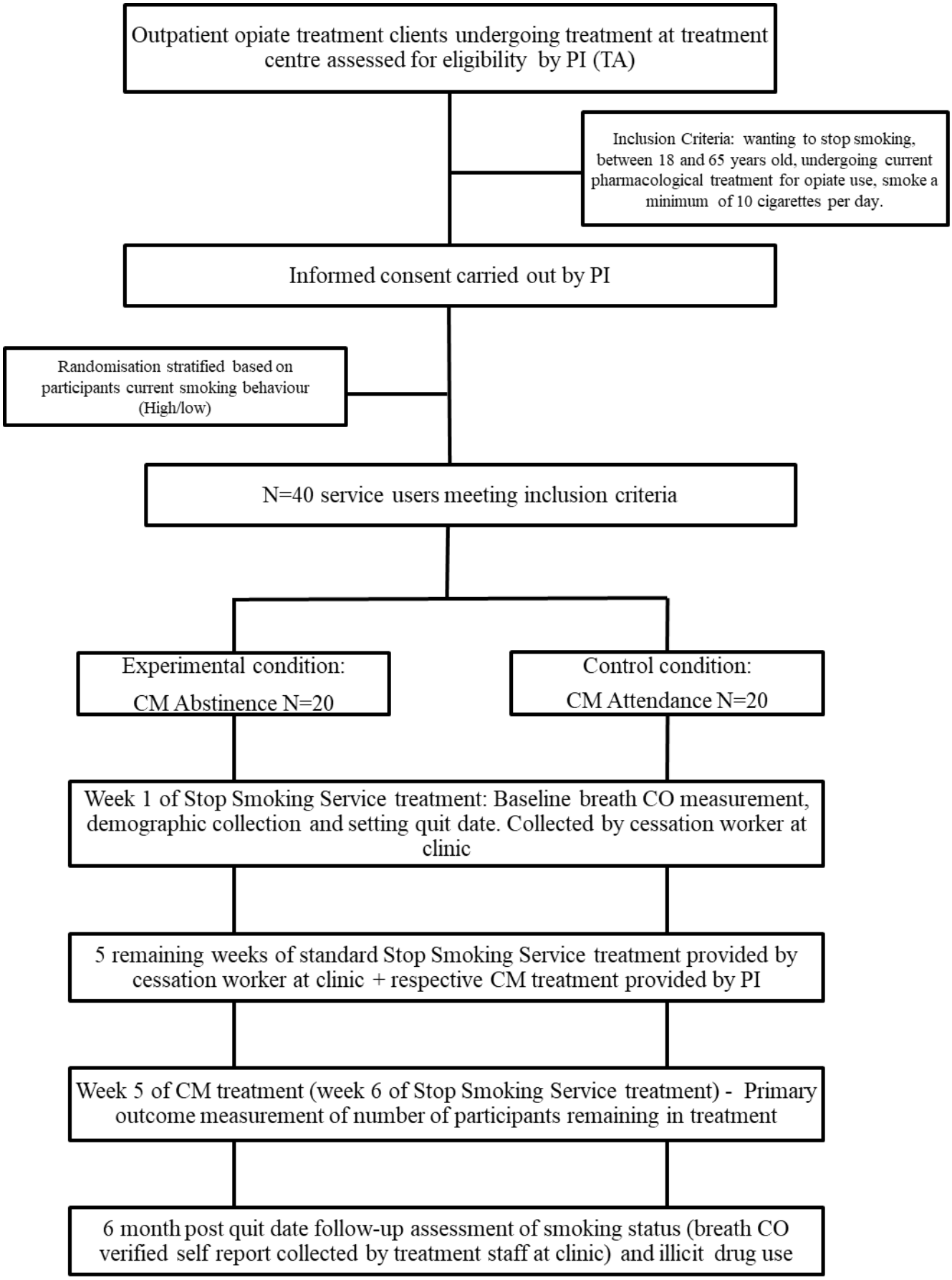

Figure 12 Flow diagram of the main elements of the study

4.2.5 Standard Treatment

The standard smoking cessation treatment provided at the treatment centre follows the treatment program set out by the National Centre for Smoking Cessation and Training (NCSCT) [56] and The National Institute for Health and Care Excellence (NICE) guidelines for smoking cessation [201]. This treatment combines manualised behavioural support to stop smoking with nicotine replacement therapy (NRT) and takes place over six weeks with one session per week. In the first meeting, the service user's readiness and ability to quit is assessed, information for the remainder of the treatment program is given and a quit date for the next week is set. For the remaining five weeks, clients attend the clinic to receive behavioural support and have their abstinence biochemically verified. In the study clinic, NRT is available free of charge to all individuals engaged with smoking cessation treatment, in the form of nicotine patches, gum, inhalators, mouth or oral spray, and oral strips. At the time of the study, the clinic also additionally offered e-cigarettes (on a trial basis), which had a nicotine content of 18mg/ml. These e-cigarettes were disposable and securely sealed, initially designed for use in high-security environments such as prisons [202]. The smoking cessation treatment provided at the treatment centre does not include treatment with bupropion or varenicline.

During the six weeks of treatment, service users are given a week's supply of NRT or e-cigarettes at a time. At the end of the six weeks, service users are given a two-week supply of NRT or e-cigarettes before exiting the treatment. The type of NRT received is decided by clients with guidance from the cessation worker and can constitute a single form of NRT or a combination of different types. Clients' breath carbon monoxide (CO) levels are measured using a Bedfont piCO+ Smokerlyzer breath CO monitor. Measurements are taken at the initial visit and at each subsequent visit over the next five weeks, to biochemically verify self-reported abstinence from smoking (CO<10ppm [110]). NRT and e-cigarette use is recorded throughout treatment.

4.2.6 Contingency Management Intervention

Target Behaviour

The target behaviour chosen for the current intervention was smoking abstinence, which was chosen over other similar target behaviours for a variety of reasons. The primary reason for this being chosen over, for example, a gradual reduction in smoking, is that the intervention is designed to run as an adjunct to the NCSCT tobacco cessation treatment used at the treatment centre [203]. One of the key requirements of this

treatment is that service users set a quit date for the week following their initial visit, to which they are then expected to adhere. Meta-analysis of behavioural and pharmacological smoking cessation treatments has shown there to be no difference in cessation rates when smoking is reduced gradually compared to quitting abruptly [204]. It was initially thought that CM encouraging a gradual reduction in smoking (known as percentile shaping) was more effective than CM encouraging abstinence [97,98,175]. It was later shown however, that this increased efficacy over CM schedules rewarding abstinence was driven simply by higher reward values for initial abstinence; when this was controlled for, no difference between the schedules was observed [100]. The decision not to implement gradual reduction was also a pragmatic one, as this would have been far harder to implement than abstinence due to the stop smoking clinic running only once per week.

Use of an Active Control Group

Central to the concept of all controlled trials, is that the experimental and control conditions differ only in the treatment that they receive, allowing conclusions to be drawn from any differences observed in results obtained [205]. Normally, this would involve assigning participants to one of two conditions: an experimental group receiving a treatment or a control group receiving either no treatment, or treatment as usual. The design of CM treatments, however, complicates the use of this simple experimental design. Due to the nature of CM, in order to receive rewards participants must not only display the desired behaviour(s) being encouraged, but also display a variety of other associated behaviours, for example attending the treatment centre, attending on a specific day at a specific time, submitting to biochemical testing of abstinence etc. This effectively means that participants in the experimental condition of a CM study are effectively being reinforced for performing a number of separate actions. Therefore, without an appropriate control, it is impossible to disentangle the effects of these two separate reinforced actions on observed changes in behaviour.

One method of circumventing this issue, employed in six of the 21 studies included in the meta-analysis presented earlier (and three of the four previous studies using CM as an intervention for tobacco smoking during opiate addiction treatment [70,71,73]), is the use of a yoked control condition. This is an active control condition where participants in the control condition also receive rewards. Each participant in the control condition is yoked to a participant in the experimental condition, receiving the same rewards as them but unaware of this yoking. This method was considered for the current study but given the limited resources available

and the complex nature of its implementation, an alternative method was required. A simpler and more easily implemented version of this method was therefore used, namely, rewarding participants for attendance at the treatment centre independent of their smoking status. This allowed any effects of the intervention on tobacco smoking to be isolated from those of attendance at the study centre. It would have been preferable to have included a third, no treatment condition, but again, limited resources meant that this was not possible.

Contingency Management Schedule

The CM intervention followed an escalating with reset schedule, where reward values increase in a set increment value for each successive verified display of the desired behaviour. When the desired behaviour is not observed, no reward is given, and the reward value for the next verified display of the desired behaviour is reset to that of the initial reward. Reward values then begin to rise again in the same way as before. This CM schedule was chosen as not only is this one of the most common schedules used in the CM literature [206], but was used in all four of the previously conducted CM studies for smoking in opiate addiction treatment [70–73]. However, unlike these previous studies, the length of the CM intervention to be used in the current study was based on the length of the NCSCT smoking cessation treatment [56]. The CM intervention, therefore, ran for five weeks in total, starting in week two of the standard stop smoking services treatment and ending in week six (Table 12). Participants in the experimental condition were rewarded for smoking abstinence, defined as producing a breath CO reading of <10ppm [110]. Participants in the control condition were rewarded for attending the smoking cessation clinic. After each smoking cessation treatment session, the cessation worker completed a slip of paper that recorded each participant's individual participant number, and their breath CO reading for that session. This was then given to me, as I sat in an adjacent room and administered rewards where appropriate. Due to the nature of the CM intervention, it was not possible to blind participants to treatment allocation. Cessation workers were not made aware of treatment allocation, but could not be considered to be blinded to treatment allocation as it is possible that clients may have discussed this with them. Similarly, as I was responsible for both participant randomisation and incentive distribution I was similarly un-blinded. At the end of the CM intervention, participants were asked to complete a client satisfaction and well-being survey, previously used to assess client satisfaction of stop smoking services treatment [207].

Reward Values

Setting an appropriate reward value was particularly complex due to an intervention of this type having never been conducted previously in the UK. The initial calculation of reward value was modelled on the reward values of four studies previously conducted in the US, all investigating CM for tobacco cessation in opiate addiction treatment [70–73] . The maximum possible amount that could be earned over the course of the intervention in each study was adjusted for inflation from the year that the study was conducted to the year 2016, and an average reward value per day calculated. The average daily reward value calculated from these studies was £12.45 (SD £7.13). However, if this reward value had been implemented in the current study this would have resulted in an overall maximum incentive magnitude of £522.90, potentially costing £20,916 if delivered successfully to all 40 participants. This was not only far beyond the available funding for the current PhD study, but would not have been feasible if it was later implemented as a RCT, or integrated nationally into normal treatment.

However, a recent UK study investigating the efficacy of CM in encouraging completion of a hepatitis B vaccination programme, found that a reward magnitude of only £30 administered over a four-week period (£0,£5, £10, £15), significantly increased completion of the vaccination programme compared to control [195]. Although this study was conducted over a four-week period, participants only attended three treatment sessions compared to the six sessions over a six-week period in the current intervention. The decision was therefore made to approximately double the average daily reward values of this study (£1.07), increasing them slightly to fit with the escalating with reset CM schedule being used. This resulted in a maximum possible reward value of £115, averaging £2.73 per day over the six-week study.

Reward values were the same in both conditions, beginning at £5 and doubling each time the incentivised behaviour was recorded, up to a maximum of £40. All rewards were delivered as “Love2Shop” vouchers (see below). Over the course of the whole intervention, participants could earn a maximum of £115 (Table 12).

Table 12 Reward schedule for a participant that remains abstinent and/or attends all smoking cessation treatment meetings (dependent on condition) for the duration of the intervention. Maximum total reward: £115

Smoking Cessation Treatment Week Number	1	2	3	4	5	6
CM Week Number		1	2	3	4	5
Reward Value	£0.00	£5.00	£10.00	£20.00	£40.00	£40.00

Vouchers Rather Than Other Reward Types

Current evidence suggests that the most effective reward type for participants in opiate addiction treatment are increases in opiate substitution medication, or the ability to take this home rather than supervised consumption at the treatment centre [125,208]. This was not possible to implement in the treatment centre chosen for the current trial however, forcing the use of an alternative reward type (for a more detailed discussion of reward types, see Chapter 3, section 3.2.3). The most commonly used reward in CM studies is money, primarily due to it being an almost universally conditioned reinforcer [179], and therefore rewards in the current intervention took the form of monetary vouchers ("Love2Shop" vouchers).

4.2.7 Measures

Outcome measures

The primary outcome was assessed by recording the number of participants completing the five weeks of the intervention in each condition. Success was defined as 60% or more of participants completing treatment, in-line with retention rates observed in similar studies [70,73].

The secondary objectives of the study were to gather preliminary findings regarding the effects of the CM intervention on smoking behaviour in this group, and any possible effects the intervention may have on opiate addiction treatment outcomes. The smoking abstinence outcome was recorded as point prevalence abstinence, and biochemically verified with abstinence defined as a breath CO reading of under 10ppm at each session [110]. Data concerning the opiate addiction treatment outcome were assessed by accessing participant medical records to ascertain participants' opiate addiction treatment, including drug types (methadone, buprenorphine etc.) and dosage as well as illicit drug use throughout the period of the trial.

Follow-Up Measures

At the six-month follow up (see below for follow-up procedures), the following measures were recorded:

Point prevalence smoking abstinence: Self-reported smoking abstinence for 7 days before follow-up and exhaled air CO <10pm [110].

Continuous abstinence: Self-reported smoking abstinence since end of treatment and exhaled air CO<10ppm. Participants smoking five or fewer cigarettes during the six-month follow-up will be considered self-reported quitters using the continuous outcome measure [110].

Illicit drug use and treatment, collected at the end of the study from participants' medical records.

All those lost to follow-up will be treated as though smoking [110].

Other Measures

At the first stop smoking treatment session, a number of demographic and smoking behaviour variables were recorded. Demographic variables included gender, ethnic group, employment status, how they heard about the service and whether pregnant and breastfeeding. Smoking behaviour variables included the type of tobacco that participants smoked, how many cigarettes per day they smoked, how soon after waking they had their first cigarette, how many years they had been smoking, what ages they started smoking and whether they lived with a smoker. Other variables collected included quitting confidence, importance, confidence and readiness (all measured on a ten-point scale), whether they had tried to quit smoking before and if so how many times, the number of weeks since their last quit attempt, their longest duration of abstinence from smoking, whether they had ever tried NRT and if so the number of types and the length of time used for, whether they had ever tried bupropion, and if they had ever used any other cessation aid. The collection form showing the information collected can be found in appendix 5. As many contact details as possible were recorded for each participant in order to increase the probability of participants being able to be followed up. This included the details of relevant friends and family members.

4.2.8 Follow-Up Procedures

Six months after their set quit date, I contacted participants up to three times, in order to ascertain their self-reported smoking status. In order to test the optimal follow-up method, participants were pseudo-randomised

by recruitment order to be contacted by text and phone call, or email and phone call. All participants were asked to return to the clinic in order to have their breath CO levels tested to verify abstinence. Once this was done, participants would have completed their participation in the study. Participants then received a £10 voucher for completing the follow up procedure.

4.2.9 Planned Analysis

As the primary objective of the intervention was retention rather than efficacy, this was reported using descriptive statistics, namely means and standard deviations for the number of participants retained at the end of treatment in each condition. Any differences between conditions were reported using t-tests for continuous and chi square for categorical data, or their non-parametric equivalents. Baseline demographics, smoking behaviour and opiate treatment and drug use behaviour were compared between conditions using t-tests for continuous and chi square for categorical data, or their non-parametric equivalents.

For the secondary objectives, differences between the groups in point prevalence smoking abstinence were investigated using t-tests for continuous and chi square for categorical data, or their non-parametric equivalents. Data for opiate use and opiate treatment outcomes were also compared between conditions using t-tests and chi square tests, or their non-parametric equivalents, dependent on data. Any questionnaire data were reported using descriptive statistics. All statistics were performed as two tailed tests using an alpha value of 0.05.

4.3 Ethics

There were a number of delays experienced during the application for ethical approval. The application for sponsorship of the study by the university's R&D service was made on the 17/03/2016, and this was granted on the 22/04/2016. After this was granted, the IRAS (Integrated Research Application System) form was completed, and submitted on the 10/05/2016. The application was submitted during the time where HRA approval systems were being changed, causing some further delays. The study received final ethical approval from the London – City and East ethics committee on the 16th of June 2016 (reference 16/LO/0990).

4.3.1 Risks to Participants

There is no known risk associated with the CM behavioural intervention. Smoking cessation can precipitate a number of uncomfortable withdrawal symptoms. These will be attenuated by the stop smoking services treatment provided at the treatment centre, an evidence-based treatment

that includes nicotine replacement therapy, e-cigarettes and behavioural support. Any information recorded from participants will be anonymised using a participant ID number, the master sheet for which will be stored in a locked cabinet at the treatment centre. This ensures that no identifiable information will ever leave the treatment centre.

4.3.3 Informed Consent

The participant information sheet and consent form can be found in appendix 6. Participants will receive both the study intervention and standard stop smoking services treatment at no cost.

Chapter 5:
Addition of Contingency Management to Stop Smoking Services in Opiate Users: A Pilot and Feasibility Study

Results

5.1 Recruitment and Participants

5.1.1 Recruitment

A total of 40 participants were recruited. Recruitment took place over an 18-week period, beginning in October 2016 and ending in February 2017. The recruitment rate over this 18-week period is shown in Figure 13 below. There was a plateau in recruitment between weeks eight and 11 due to the Christmas holiday period. The Christmas break also resulted in a break in the experimental procedures for some participants. The break fell between study sessions three (19/12/2016) and four (09/01/2017), for three participants (one in the experimental condition and two in the control), resulting in a three week break in treatment. Recruitment began so close to the Christmas period due to delays in obtaining approval for the trial from the Health Research Authority (HRA). An overhaul of their application process resulted in a significant backlog of applications, delaying the start date of the study. After ethical approval was granted, it then transpired that clinical pressures within the treatment centre had led to the smoking cessation clinic being temporarily closed. This necessitated the re-training of staff and re-launch of the smoking cessation clinic, causing further significant delays to the initiation of the pilot study.

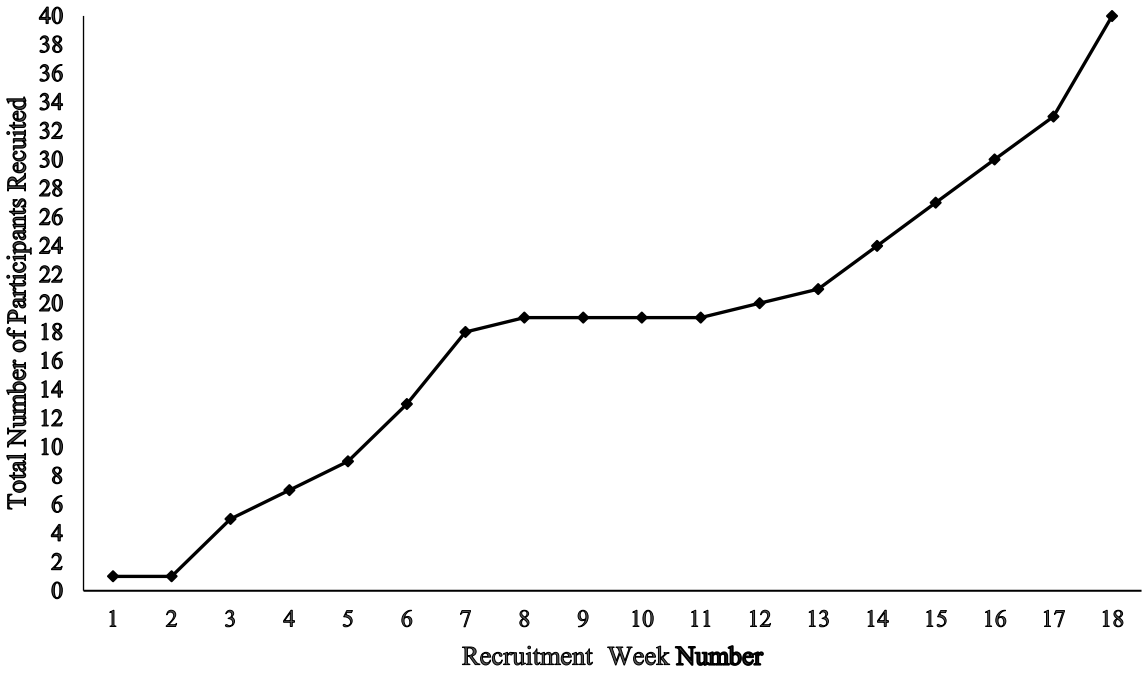

Figure 13 Recruitment Rate over the 18-week recruitment period

5.1.2 Participant Flow Through Study

Figure 14 below shows participant flow through the study. Due to implementation of multiple methods of recruitment, the number of participants approached and assessed for eligibility is unknown. For example, key workers were asked to consider their caseloads for participants, but it was not possible to record the number of participants they approached.

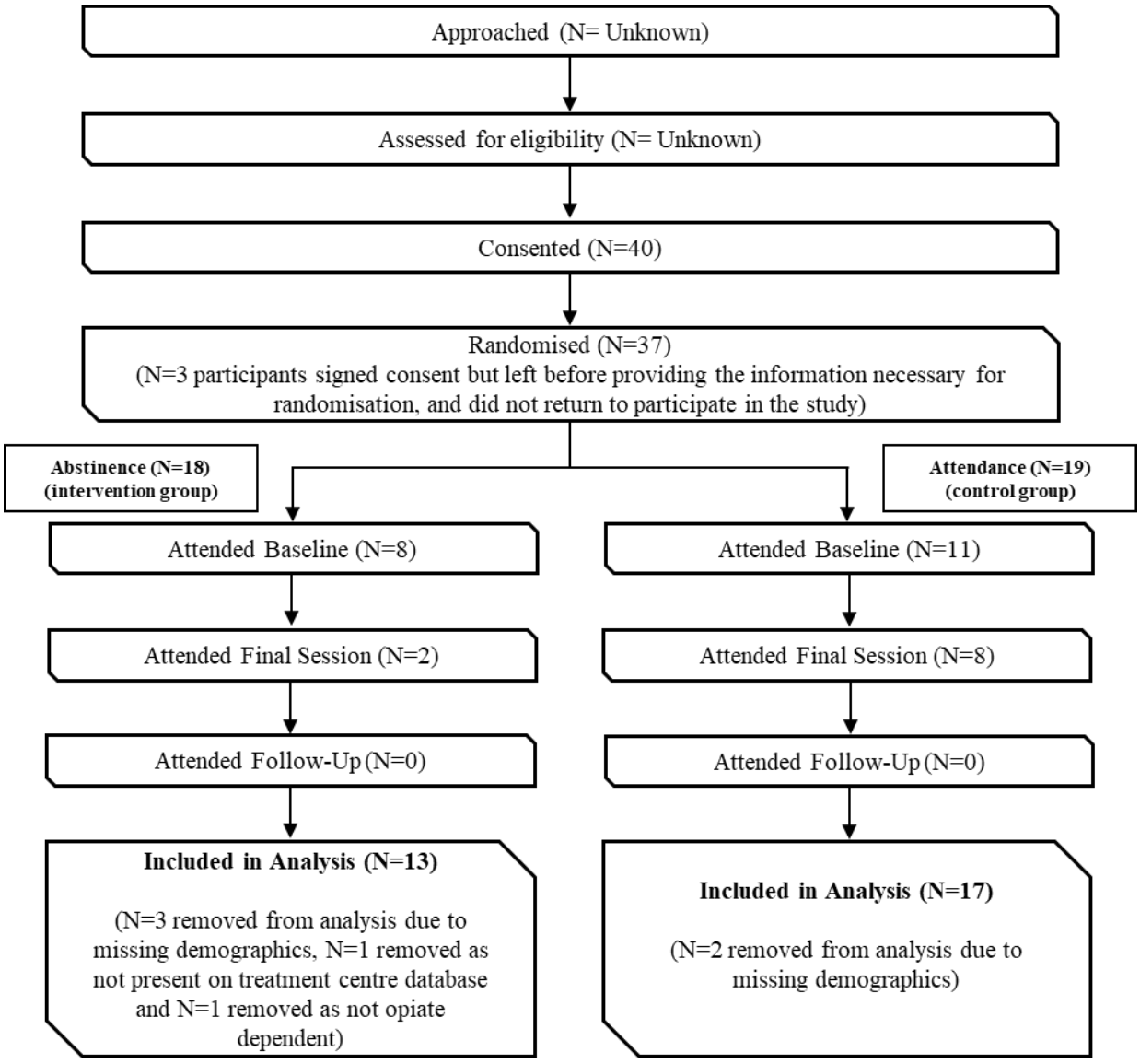

Figure 14 Participant flow through study

At the outset of the study, participants were asked how many cigarettes they smoked per day, randomised to conditions, and informed of their allocation to condition at the time of signing consent. However, the first participant consented into the study immediately dropped out after being assigned to the experimental condition (CM for abstinence), so participants were subsequently informed of their allocation after their

baseline session. Conversely, the recording of demographic information was switched from the baseline session to when consent was signed. This was done when it was noted that a number of participants were signing consent but not turning up for their baseline session. Collection of demographics was not possible for some participants though as they simply left the treatment centre after signing consent and did not return for their baseline session.

Of the 40 participants initially recruited, 10 were removed from the analysis. Three participants were removed from the analysis after not being randomised after not providing the information necessary for randomisation and not returning to participate, and five for not returning to provide demographic variables after signing consent. Two further participants were removed from the analysis after study completion, one for not being found on the treatment centre's database and another when it transpired that they were not in treatment for opiate dependence, but for cocaine abuse. All analyses, unless otherwise stated, include the remaining 30 participants, 13 in the experimental condition (CM for abstinence) and 17 in the control (CM for attendance).

5.1.3 Recruitment Method

As described in chapter 4, a number of different methods of recruitment were utilised: self-referral in response to advertisements shown in the treatment centre, direct recruitment by the PI in the treatment centre, or through referrals from treatment centre staff. (Table 13).

Table 13 Method of recruitment by treatment condition

	Intervention (CM for abstinence), n (%)	**Control (CM for attendance), n (%)**	**Comparison**
How did you hear about the service?			
Key worker	4 (31%)	5 (29%)	χ^2= 1.292
Study advert/word of mouth	3 (23%)	7 (41%)	(p=0.524)
Direct recruitment by experimenter	6 (46%)	5 (29%)	

χ^2= Chi-square test

5.1.4 Participant Demographics

Overall, participants were predominantly male (n=19, 63%) and white (n=19, 63%). All participants were eligible for free prescriptions and the majority (n=29, 97%) had been unemployed for 12 months or more. Participants did not differ significantly across conditions on the demographic variables where tests could be carried out (Table 14).

Table 14 Demographic variables by condition

	Intervention (CM for abstinence), N (%)	**Control (CM for attendance), N (%)**	**Comparison**
Age			
20-30	2 (15%)	1 (6%)	
30-40	5 (39%)	3 (18%)	
40-50	3 (23%)	10 (59%)	**N/A[1]**
50-60	2 (15%)	3 (18%)	
60+	1 (8%)	0	
Gender			
Female	5 (39%)	6 (35%)	χ^2= 0.320
Male	8 (61%)	11 (65%)	(*p*= 0.858)
Eligible for free prescriptions?			
Yes	13 (100%)	17 (100%)	**N/A[2]**
Ethnic Group			
Black	7 (54%)	4 (24%)	χ^2= 0.910
White	5 (39%)	12 (71%)	(*p*=0.635)
Other	1 (8%)	1 (5%)	
Employment Status			
Unemployed	13 (100%)	16 (94%)	**N/A[1]**
Employed	0	1 (6%)	

χ^2= Chi-square test, [1]Difference not tested due to empty cells, [2]Difference not tested as no difference

5.1.6 Smoking Behaviour

Overall, participants smoked an average of 19.67 cigarettes per day (Median= 20, SD=7.87), began smoking at an average age of 15.33 (Median= 15.00, SD=3.82) years old, and had smoked for an average of 26.80 (Median= 27.00, SD=9.37) years. Most participants (N=25, 83%) smoked hand-rolled cigarettes and consumed their first cigarette of the day less half an hour after waking up (N=24, 80%). The majority of participants (N=21, 70%) had tried to quit smoking at least once before, having tried to quit an average of 3.23 (Median= 1.00, SD=4.92) times prior to the study, with an average of 153.23 (Median= 104.00, SD=163.77) weeks since their last quit attempt and average longest duration of abstinence of 41.84 (Median=12.00, SD=65.00) days. Just over half (N=17, 57%) of participants had tried nicotine replacement therapy (NRT), using it for an average of 13.01 (Median=2.25, SD=22.36) weeks and tried an average of 2.64 (Median=2.00, SD=1.27) types. The majority (N=19, 63%) of participants had not previously used an e-cigarette, and just under half of the participants (N= 14, 47%) lived with another smoker. Average scores for quitting importance, readiness and confidence (out of ten) were 9.10 (Median=10.00, SD=1.86), 7.83 (Median=8.00, SD=2.06) and 6.70 (Median= 7.00, SD=1.91) respectively. Participants randomised to the control (attendance) condition reported significantly greater quitting confidence

than those in the experimental (abstinence) conditions. Participants did not differ significantly across conditions on any other smoking behaviour measure (Table 15).

Table 15 Smoking behaviour variables by condition

	Intervention (CM for abstinence) mean (SD)/ Median (range)/ N (%)	**Control (CM for attendance) mean (SD)/ Median (range)/ N (%)**	**Comparison**
Cigarettes smoked per day	20.00 (5.77)	19.41 (9.33)	t=-0.199 (*p*=0.843)
Type of Tobacco used			
Hand-rolled	13 (100%)	12 (71%)	
Manufactured	0	5 (29%)	
Age began smoking	15.00 (9.00)	15.00 (21.00)	U=94.000 (*Z*=-0.694, *p*=0.487)
Number of years smoking	25.31 (11.92)	27.94 (7.93)	t=0.757 (*p*=0.455)
Live with another smoker			
Yes	4 (31%)	10 (58.80%)	χ^2= 2.330 (*p*=0.127)
No	9 (69%)	7 (41.20%)	
Time to first cigarette			
<30 minutes	11 (85%)	13 (77%)	χ^2= 0.305 (*p*=0.580)
>30 minutes	2 (15%)	4 (23%)	
Previously tried to quit smoking			
Yes	10 (77%)	11 (65%)	t=0.524 (*p*=0.469)
No	3 (23%)	6 (35%)	
Number of previous quit attempts	1.00 (20.00)	1.00 (10.00)	U=92.000 (*Z*=-0.795, *p*=0.457)
Weeks since last quit attempt	104.00 (492.00)	156.00 (620.00)	U=51.500 (*Z*=-0.594, *p*=0.553)
Longest period of smoking abstinence (days)	16.00 (77.80)	7.25 (259.80)	U=75.000 (*Z*=-0.110, *p*=0.912)
Previously tried NRT			
Yes	8 (62%)	9 (53%)	χ^2= 0.222 (*p*=0.638)
No	5 (39%)	8 (47%)	
Weeks NRT used for	8.00 (77.70)	2.00 (31.50)	U=27.500 (*Z*=-0.425, *p*=0.671)
Number of NRT types tried	3.00 (4.00)	2.00 (4.00)	U=24.500 (*Z*=-1.143, *p*=0.277)
Ever used an e-cigarette			
Yes	4 (31%)	7 (41%)	χ2= 0.344 (*p*=0.558)
No	9 (69%)	10 (59%)	
Quitting importance	10.00 (9.00)	10.00 (2.00)	U=93.500 (*Z*=-0.810, *p*=0.483)
Quitting readiness	7.46 (2.07)	8.12 (2.09)	t=0.857 (*p*= 0.399)
Quitting confidence	5.00 (5.00)	8.00 (6.00)	U=54.000 (*Z*=-2.424, *p*=0.015)

t= t-test, χ^2= Chi-square test, U= Mann-Whitney test

5.2 Primary Outcome: Intervention Adherence

5.2.1 Treatment Completion

Overall, 10 participants completed the five-week intervention, attending all five study sessions, resulting in a retention rate of 33% (25% retention of the original 40 recruited). The number of participants in each condition attending at each session is shown below in Table 16.

Table 16 Number of participants in each condition attending each treatment session

	Overall	Abstinence (intervention)	Attendance (control)
Attendance N (%)			
Baseline	19	8 (62%)	11 (65%)
Session 1	14	5 (38%)	9 (53%)
Session 2	12	3 (32%)	9 (53%)
Session 3	12	4 (31%)	8 (47%)
Session 4	11	3 (31%)	8 (47%)
Session 5	10	2 (15%)	8 (47%)

A total of 19 (63%) participants attended their baseline session, with a mean of 2.33 (SD=2.78) of the five study sessions attended. Whilst a greater proportion of control participants completed treatment, there was no significant difference between conditions for any of the primary outcome measures (Table 17).

Table 17 Primary outcome data by condition

	Abstinence (intervention) N (%)/ Median (range)	Attendance (control) N (%)/ Median (range)	Comparison
Attended baseline			
Yes	8 (62%)	11 (65%)	χ^2= 0.320
No	5 (38%)	6 (35%)	(*p*=0.858)
Completed treatment			
Yes	2 (15%)	8 (47%)	χ^2= 3.326
No	11 (85%)	9 (53%)	(*p*=0.068)
Number of study sessions attended	1 (6)	2 (6)	U= 85.500 (*Z*= -1.154, *p*=0.248)

χ^2= Chi-square test, U= Mann-Whitney test

5.3 Secondary Outcomes: Smoking Behaviour and Opiate Treatment

5.3.1 Issues encountered measuring smoking

Given the very high levels of attrition observed, testing the effects of the intervention on smoking was difficult. Moreover, part way through the study, a major flaw was discovered in the use of breath CO validation in administering the rewards. At the outset of the study, self-reported smoking data were not recorded by the experimenter, as CO validation was being used to assign rewards to participants in the experimental condition. However, once self-reported smoking data collection was introduced, it became evident that a large number of the participants that self-reported smoking were providing breath CO samples signifying abstinence (i.e. lower than 10ppm). This meant that participants in the experimental condition were smoking yet receiving rewards for being abstinent. Resultantly, the decision was made to begin recording the number of cigarettes that participants were smoking per week and also the number of days per week that they were smoking cigarettes (this is a measure commonly used in the illicit drugs field, but not the smoking field). Data collection for this began in December 2016, meaning data were recorded for only 11 of the 30 participants included in the main analysis. These data should not be considered as representing the efficacy of the intervention for treating tobacco smoking and, therefore, only a brief overview of these results is presented. A number of interesting observations were made, however. These are considered in detail in the discussion below.

5.3.2 Smoking behaviour

Self-reported point prevalence abstinence (CO verified) at each treatment session was calculated for all 30 participants, with failure to attend a study session treated as smoking (in either condition). Overall, point prevalence abstinence was low across all five sessions, with a high of only 7% at session one. Breath CO recordings were also analysed, with missing data at each session removed from calculation of averages. Overall, mean breath CO was 19.6ppm at baseline and 9.3 ppm at session 5, though this reduction was non-significant.

As mentioned above, the number of cigarettes that participants smoked per week and the number of days per week smoking were recorded for 11 of the 30 participants in the final analysis. The number of cigarettes smoked in the last seven days across both conditions reduced from an overall average of 137.73 (SD=62.82, median=140.00, range=220.00) at

baseline to 14.10 (SD=30.59, median=4.00, range=100.00). A Wilcoxon signed-rank test showed this reduction to be significant (Z=-2.023, p=0.043), though given the small sample size this should be interpreted with caution. The number of days smoking in the last seven days reduced from an overall average of 7 (SD=0, median=7.00, range=0, n=11) at baseline to 4.33 (SD=3.28, median=7.00, range=7.00, n=9) at session 5. A Wilcoxon signed-rank test showed this change to be non-significant (Z=-1.000, p=0.317).

5.3.3 Opiate Treatment

When designing the study, it was intended that details of participants' opiate treatment data at both baseline and the final session could be recorded from participant medical records. The treatment centre agreed that this was something that we could do, and the appropriate access credentials were obtained prior to completion of the study. However, when the retrieval of these data was undertaken, it was discovered that the recording of these data was not adequate enough to allow this to be done. For all participants, there was only a single entry for their opiate treatment and in the majority of cases this was over 12 months old. For this reason, it was not possible to investigate any potential effects of the intervention on opiate treatment.

5.4 End of Treatment Questionnaire

Of the 10 participants who completed treatment, nine completed the end of treatment questionnaire; eight from the attendance condition and one from the abstinence condition. As discussed in the methods chapter (chapter 4), all of these participants received vouchers during the intervention and although not part of the intervention tested here, all participants had received e-cigarettes. The responses of participants to these questions are shown below in Tables 18, 19 and 20.

Overall, participants reactions were positive, with the majority of participants reporting that they would recommend the service to others (N=8), would return to the service if they resumed smoking (N=7), and that the information dispensed regarding medications available was useful (N=9). Two thirds of respondents (N=6) reported that they would have attempted to quit smoking even if vouchers were not available. The majority of respondents (N=7) were either satisfied or very satisfied with the support that they received to stop smoking and how supportive the staff were. Vouchers, e-cigarettes and weekly breath CO measurements were all rated as either helpful or very helpful by the majority of respondents. Notably, e-cigarettes were rated as helpful or very helpful by more participants than vouchers (N=6 vs N=8). Most of the respondents

(N=5) received only a single form of NRT (alongside e-cigarettes), with nicotine gum rated as being the most useful.

Table 18 Participant (N=9) responses to the end of treatment questionnaire questions, N (%)

	Response, N (%)		
Question	Yes	No	Unsure
Would you recommend this service to other smokers who want to stop smoking?	8 (89%)	1 (11%)	0
In the event that you started smoking again would you go back to the service for help with stopping smoking?	7 (78%)	1 (11%)	1 (11%)
If you returned to the service for help with stopping smoking in the future do you think that you would be welcomed back?	7 (78%)	0	2 (22%)
When you contacted the service were you given an appointment date or told how long you would have to wait?	7 (78%)	2 (22%)	0
Was the length of time you had to wait for your first appointment acceptable to you?	8 (89%)	1 (11%)	0
Are the appointment times you were given convenient for you?	9 (100%)	0	0
Is the place where you go for your appointments convenient for you to get to?	9 (100%)	0	0
Was the information that you were given about the choice of medication helpful?	9 (100%)	0	0
Was it easy to get hold of your medicine once you had chosen which medication you were going to use for your stop smoking attempt?	9 (100%)	0	0
Would you have tried to quit smoking if there were no vouchers being offered?	6 (67%)	3 (33%)	0

Table 19 Participant (N=9) responses to the end of treatment questionnaire questions, N (%)

	Response, N (%)					
Question	Very Unsatisfied / Unhelpful	Unsatisfied / Unhelpful	Unsure	Satisfied / Helpful	Very Satisfied / Helpful	Not applicable
Overall, how satisfied are you with the support you have received to stop smoking?	1 (11%)	0	1 (11%)	2 (22%)	5 (56%)	0
How satisfied are you with how supportive staff have been?	1 (11%)	0	1 (11%)	2 (22%)	5 (56%)	0
How helpful has the information and advice that staff have given to you during your appointment been?	1 (11%)	0	0	3 (33%)	5 (56%)	0
How helpful has the written information that staff have given to you been?	0	0	0	5 (56%)	3 (33%)	1 (11%)
Do you find having your carbon monoxide (CO) reading done at every visit helpful?	1 (11%)	0	0	2 (22%)	6 (67%)	0
How helpful were the vouchers in stopping smoking?	1 (11%)	0	2 (22%)	1 (11%)	5 (56%)	0
How helpful were e-cigarettes for stopping smoking?	1 (11%)	0	0	3 (33%)	5 (56%)	0

Table 20 Participant (N=9) responses to the end of treatment questionnaire questions, N (%)

Question	Nicotine Patches	Nicotine Gum	Nicotine Lozenges	Inhalator	Mouth Spray	Nasal Spray	Oral Strips
Which of the following types of nicotine replacement therapy did you receive?							
Single NRT (N=5)	2 (22%)	1 (11%)	1 (11%)	1 (11%)	0	0	0
Dual NRT (N=3)	1 (11%)	2 (22%)	0	2 (22%)	1 (11%)	0	0
Multiple NRT (N=1)	1 (11%)	1 (11%)	1 (11%)	1 (11%)	0	0	0
Which of the following types of nicotine replacement therapy did you find most useful?	2 (22%)	4 (44%)	1 (11%)	2 (22%)	0	0	0

Participants were additionally asked "If you were to do the study again, what would be more likely to make you take part if you got: Vouchers, Free e-cigarettes, both, or other". Three participants (33%) said they would be more likely to take part if given free e-cigarettes, and five (56%) said they would be more likely to take part if given both free e-cigarettes and vouchers. One participant did not answer this question.

5.5 Non-Completer Questionnaire

As such a high attrition rate was observed in the study, it seemed prudent to attempt to understand the reasons behind this. For this reason, a short questionnaire was created, and participants who had consented to take part in the study but not completed treatment were contacted by telephone to answer the four questions. Six (21%) of the 29 participants who did not complete the treatment were willing to answer the questionnaire. The response of participants to each of the questions is shown below in Table 21.

Table 21 Participant responses to the non-completer questionnaire, N (%)

Question 1	What made you decide to take part in the study in the first place? (Tick all that apply)
Answer 1	**Wanted to stop smoking**: 6 (100%) **Wanted to get the vouchers**: 3 (50%) **Wanted e-cigarettes**: 0 **Other**: 0
"Other" responses and comments	"I did like the e-cigs but didn't know about them originally" "Mainly to give up smoking but also the vouchers, I thought I would get the money in one go though, but I guess I could have saved up. Don't get cravings for cigarettes anymore and I use the spray that gets rid of the cravings if I do."
Question 2	Why did you decide to stop taking part in the study? (Tick all that apply)
Answer 2	**Didn't really want to stop smoking**: 0 **Life factors:** 2 (33%) **Decided I could stop smoking alone**: 0 **Voucher values weren't high enough**: 0 **None of the treatments were suitable for me**: 0 **Not enough sessions**: 0 **Session times didn't work with my schedule**: 0 **Other**: 4 (67%)
"Other" responses and comments	"I pulled out as knew couldn't stop straight away as was in the stop smoking condition" "I went back home and have only just returned" "I couldn't smoke cannabis without using tobacco" "I went on holiday to Barbados" "I moved down to Kent so had to stop coming. They don't offer e-cigarettes here so I have started smoking again"
Question 3	What would have made you stay in the study? (Tick all that apply)
Answer 3	**Higher value vouchers:** 0 **More regular sessions (more than once per week)**: 3 (50.00%) **More sessions on different days**: 3 (50.00%) **Guaranteed access to e-cigarettes**: 0 **Other**: 3 (50.00%)
"Other" responses and comments	"Maybe higher vouchers but it was the smoking not the vouchers that made me want to take part the most" "Wasn't working at the time but now I work 8-5 so don't have time" "Being able to smoke with the weed and not smoking cigarettes" "Nothing, I would have taken part if it wasn't for the fact that I was going to go on holiday" "If I hadn't moved away I would have stayed in the study"
Question 4	If you think that more vouchers would have made you stay, how much would you need paying over the six weeks to make you stay? (Tick the one that applies most)
Answer 4	**£150**: 0, **£170**: 0, **£190**: 0, **£200**: 0 (No participants answered this question)

5.5 Follow-Up

Only a single participant could be contacted for six-month follow-up. They reported not having smoked since the end of treatment, but CO verification of this could not be obtained.

5.6 Discussion

5.6.1 Summary of Results

Overall, 40 participants were recruited into the study, taking a total of 18 weeks. Of the 40 participants recruited, ten completed the five-week intervention. This retention rate of 25% is far lower than the 60% retention rate required to deem the study successful (based on retention rates in other similar studies [70,73]). More attendance condition participants completed treatment than abstinence condition participants, but this difference was not statistically significant. It was impossible to ascertain any effects of the intervention on opiate addiction treatment or drug use due to the paucity of data recorded on the treatment centre's electronic database. Of the 10 participants that completed the intervention, nine completed the end of study questionnaire. Eight of these respondents reported that they would recommend the intervention to other people, six found vouchers either helpful or very helpful in giving up smoking but would have attempted to give up smoking had vouchers not been available. Six of the 29 participants that did not complete the intervention agreed to answer the non-completer questionnaire. All respondents reported wanting to take part in the study to give up smoking and would have stayed in the study had more sessions been available on more days. Taken together, these findings may suggest that the frequency and provision of smoking cessation are the key barriers in engendering smoking cessation in those undergoing treatment for opiate addiction. The provision of e-cigarettes also seemed to be attractive. A number of smoking behaviour variables were collected but given the high attrition rate and consequent small sample size, the data produced are of only limited utility and results should be interpreted with caution. Neither point prevalence nor breath CO changed significantly over the course of the intervention. The number of cigarettes smoked in the last seven days did reduce significantly.

Overall, the CM intervention did not appear to be effective. Retention rates were far lower than anticipated, with too few participants remaining in treatment across the two conditions to allow any meaningful comparison of secondary outcomes across conditions.

5.6.2 Pilot and Feasibility Results

Although the results of the primary and secondary objectives of the study are hampered by high attrition rates, a number of very important pilot and feasibility observations were made as the study progressed. These will be discussed in the order in which each became apparent during the running of the study.

Standardising Treatment

The first important pilot/feasibility finding became apparent before the study had even begun recruiting. When initially securing the study site, we were informed that the treatment centre had a functioning smoking cessation service. When the study was ready to be implemented, however, it transpired that this was no longer the case and that re-training of staff in using the NCSCT stop smoking programme [56] was required. This raises an important concern for interventions that run as an adjunct to standard care. Additionally, ensuring that all participants receive the same fidelity of standard care treatment is vital if the results obtained are to accurately reflect the effects of the intervention being implemented. It would seem important, then, to at least record the fidelity of all behavioural interventions delivered to participants, both standard care and the adjunct intervention. This itself raises another question over standardising normal care procedures and the effects that this may have on treatment. It may be, for example, that attempting to standardise normal treatment practices across participants and/or treatment centres artificially elevates the fidelity of the standard care intervention above what it would normally be. This may in turn lead to the intervention appearing to be of different efficacy than it would be if implemented in an environment outside of the study.

Recruitment

A number of other important pilot/feasibility findings came early on in the implementation of the study. For example, the three-week interruption of recruitment over Christmas period. A break in recruitment like this is not in itself particularly detrimental. What is more concerning, is that there were a number of participants already recruited into the study by this point. The efficacy of CM is based on there being constant and uninterrupted reinforcement for the desired behaviours [82]. As a result, disruptions to the reward schedule can severely curtail the efficacy of the intervention. Had there been time, the start date of the current study would have been delayed to accommodate this, but, with the study having already been severely delayed, this was not possible. Any future studies should therefore ensure that all participants have an uninterrupted period in which they can participate in the study, with initiation of their participation delayed if necessary. An additional observation linked to recruitment was our inability to record the number of participants that were approached or assessed for eligibility. This was because multiple methods of recruitment were employed, including the use of key workers at the study site. Given their busy schedules and high client load, it was not reasonable to expect the keyworkers to record these data. It would be

beneficial, however, if in the future this information could be recorded somehow, as it gives an impression of the level of interest in the intervention among potential participants. Related to this, given the number of keyworkers at the treatment centre and their contact with potential participants, it is somewhat surprising to see that slightly more participants were recruited directly by the investigator than by keyworkers. Although we held a pre-study meeting with keyworkers to introduce the study and allow them to ask questions, additional meetings and training would be advisable as a means of potentially boosting recruitment by keyworkers. It has, however, been reported that treatment staff in addictions treatment may not see quitting smoking as important, or even as advisable, during treatment for illicit drug use [32]. It may, therefore, be a difficult task engaging key workers with interventions such as the one in the current study, that aim to encourage smoking cessation in those undergoing treatment for opiate addiction.

Treatment Allocation and Data Recording

Another important finding is the changes that were made when participants were told of their randomisation and when demographic information was recorded. As mentioned above, the first participant recruited had hoped to be randomised to the attendance condition but dropped out when allocated to the abstinence condition. For this reason, we began informing participants of their allocation to at the end of the baseline session. There was another change early on in the study of when collection of demographic data took place. Initially, this was planned to be collected at the baseline session, however, when very few participants returned for their baseline session, this was instead recorded at the signing of consent. It is possible that these two issues could have been avoided had there been a single data collection and treatment assignment session that occurred at baseline. One of the problems inherent in the study that may have exacerbated the issues encountered with informing participants of treatment allocation and data recording, is that the smoking clinic ran for only two hours on Monday afternoon. Therefore, if a participant signed consent on a Monday afternoon after the smoking cessation clinic had finished, it was an entire week before their baseline session and two weeks before they would have a chance of receiving their initial reward of only £5. Therefore, as well as having a single baseline session where demographics are collected and treatment allocations made, having two or three of these sessions each week and rewarding participants for attending these session, may be beneficial additions to the design of future trials.

Biochemical Verification of Smoking Abstinence

Another learning point from the study was the use of breath CO as the measure on which rewards in the experimental group were made contingent. As noted above, part way through the study it became clear that participants were providing breath CO samples indicative of not smoking (<10ppm), despite self-reporting smoking. As the rewards for abstinence group participants were based on this measure and not self-report, participants could continue smoking whilst receiving rewards for quitting. This undermines the intervention's intended means of effectiveness. Future studies should implement the use of both self-report and biochemical measures to assess abstinence, as recommend in the Russell Standard [110].

Quality of Participant Drug Treatment Records

A final pilot/feasibility finding was observed at the end of the study, when an attempt was made to access the electronic treatment records of the participants. The aim of this was to investigate any potential effects of the intervention on opiate addiction treatment outcomes and illicit drug use. When these data were accessed, though, it was found that the recording of the data rendered any of these aims impossible. Not only were a number of the records on the system over 12 months out of date, but one participants did not even have an entry on the system. This participant were therefore removed from the analysis, further limiting sample size. It would be beneficial, both to research and treatment, if efforts were made to increase the quality of the recording of this information. Until then, it may be better to instead obtain this information directly from the treatment staff at the beginning and end of the intervention. Alternatively, it may instead be preferable to check at consent whether a participant is present on the system and the quality of the information recorded about them.

5.6.3 Limitations

The current study has a number of limitations. One of the main limitations of the study is the poor retention rates achieved, with only 10 participants completing treatment. Similar studies have observed retention rates of 60% or more [70,73], over double that observed in the current study. It is unclear why retention in the current study was so low. Although this is a pilot and feasibility study, designed and conducted to detect issues such as poor retention, this still poses a problem. The issue with so few participants being retained is that this severely limits any inferences that can be made regarding the secondary outcomes. An associated limitation is the inability to follow-up any participants long-term to verify smoking

abstinence, compromising the ability to determine any potential long-term effects of the intervention.

Another limiting factor of the current study, is that it coincided with the redesign of the stop smoking service in the treatment centre and the simultaneous introduction of e-cigarettes as a novel form of NRT. E-cigarettes have been shown in a number of studies [209–212] to aid smoking cessation. As all participants completing treatment were given e-cigarettes during treatment, it is, therefore, very difficult to separate the effects of the intervention from those of e-cigarettes. This also severely limits the generalisability of the pilot study findings, as the study was effectively carried out in a stop smoking service unlike any other in the UK, as to our knowledge e-cigarettes are not currently offered as part of standard smoking cessation treatment in substance misuse centres in the UK. The introduction of e-cigarettes to the stop smoking treatment provided at the clinic was a snap decision made by the management at the treatment centre, which could not have been anticipated at the outset.

A final limitation of the study is having only two conditions. As mentioned in the previous chapter, the nature of CM interventions means that participants are effectively rewarded for two things; in the case of this study, attending the treatment centre and abstinence from tobacco smoking. Because of this, it is important to have a control condition that allows the effects of rewarding for attendance and abstinence to be differentiated. This was the rationale behind the two conditions used in the current study. However, what the current trial did not include, was a condition where participants received standard care, without any rewards. This was because limited resources allowed for only two conditions. Without such a standard care condition, it is impossible to draw conclusions about the feasibility or efficacy of CM as compared to usual treatment. Future studies should, therefore, not only include a condition that differentiates between rewarding attendance and abstinence, but also a condition that allows comparison between rewarding attendance or abstinence with treatment as usual.

5.6.4 Strengths

Despite a number of limitations, the current study has some strengths. For example, despite the limited number of participants attending baseline, the randomisation method used created a balanced sample. Participants did not differ significantly across conditions on any of the demographic or opiate treatment and drug use variables and for all but one (quitting confidence) of the smoking behaviour variables. The primary strength of this pilot study, though, is that it is the first study of CM for smoking cessation during opiate addiction treatment conducted in the UK and the

first of its kind outside of the US. It therefore represents the first step towards the potential use of CM for smoking cessation in UK drug addictions services. Related to this, a further strength is that, to my knowledge, this is the first study of its type anywhere in the world to integrate CM techniques with stop smoking services in routine clinical practice. As a result, this pilot study suggests a shift in the focus of research is needed, from the efficacy of CM in treating smoking cessation during opiate addiction treatment, to its integration with standard care.

5.6.5 Implications and Recommendations for Future Research

Although the findings of this pilot study are somewhat limited by low retention rates, they still present a number of important implications for future research. The poor retention rates observed in this study, particularly amongst participants randomised to the abstinence condition, suggest that implementing a CM intervention for smoking cessation during treatment for opiate addiction may be more difficult than initially envisaged. However, recruitment did not seem to be an issue. The recruitment rate observed during this pilot study is better than that of Tuten et al. [71], who investigated the efficacy of contingent rewards for reducing cigarette smoking amongst pregnant women receiving treatment with methadone for opiate addiction. Moreover, the number of participants recruited into the stop smoking service over the four-month study recruitment period, is greater than the number recruited in the 12 months that the stop smoking services were run by the treatment centre before initiation of the pilot study. This suggests that CM may have the potential to engage a larger portion of individuals in this environment and population for smoking cessation treatment. This also illustrates that there is a demand for smoking cessation treatment among these individuals. It is important to note, however, that it is unclear to what extent the e-cigarettes being offered as part of smoking cessation treatment played a role in this rate of recruitment. Notably, of the nine respondents to the end of treatment questionnaire, a third reported they would be more likely to take part again if given free e-cigarettes and over half of respondents reported that they would be more likely to take part if given both free e-cigarettes and vouchers. None of the respondents reported that they would be more likely to take part if just given vouchers. These findings only represent a small portion of the participants that did not complete treatment, but, suggest that e-cigarettes may have played some role in the observed recruitment rates.

It is also unclear exactly why this recruitment rate did not translate into higher rates of study completion. Given that in CM interventions allocation concealment is not possible, it may simply be that participants

agreed to take part in the study hoping that they would be randomised to the attendance condition, deciding not to take part once randomised to the abstinence condition. However, as later in the study, participants were not randomised to conditions until their baseline assessment, this does not account for the large number of participants that consented to take part in the study yet did not attend their baseline session. An alternative explanation for this may simply be that the lives of the participants recruited were not suited to the regular and repeated attendance required by a CM intervention. Another potential explanation may be that the stop smoking service runs for only two hours, one day a week, making it too restrictive to fit in with the lives of most participants. Some support for this is seen in the non-completer questionnaire, where all respondents reported that either more regular treatment sessions (more than once per week), or more sessions on different days, would have made them stay in treatment. Yet another potential explanation may be that the reward values implemented in this pilot study were simply not high enough to encourage study completion in the majority of participants. The four studies previously conducted using CM to encourage smoking cessation during opiate addiction treatment [70–73], all offered participants substantially larger monetary rewards than the current pilot study. As previously discussed (Chapter 4, section 4.2.6), the reason for the use of lower value rewards in this pilot study was in part due to the fact that these higher value rewards could never be implemented in usual practice, as they are simply too expensive. If this is the case, the implication would be that although CM may represent an effective intervention for tobacco smoking in this population, the economic burden of treatment precludes it from ever being implemented in practice. Without further research, however, any explanation as to the low rates of study completion is simply speculation, and this should therefore be a focus of future research.

The main implications for future research, however, come from observations from the pilot/feasibility study. One implication is that the method of biochemical verification upon which rewards are made contingent, requires careful consideration for future studies. In CM studies, it is imperative that abstinence is biochemically verified at all times, with no opportunity for non-abstinence being rewarded as abstinence. If participants can earn rewards for abstinence whilst being non-abstinent, it becomes impossible to ascertain for certain whether any observed effect of the intervention is actually valid. The Russell Standard [110], which outlines the standards for the measurement of efficacy in smoking cessation studies, recommends that abstinence be measured using biochemically verified self-report. Biochemical validation usually takes the form of breath CO, as used in the current study. That is, if a

participant self-reports abstinence from smoking, they are required to provide a negative breath sample (this was not implemented in the current study as efficacy was not of primary concern). Although this methodology is in many ways compatible with CM interventions (using breath CO verified self-reported smoking status to administer rewards), this would only be possible if it was certain that the method of biochemical verification could detect any cases of non-abstinence. Making provision of rewards contingent on biochemical verification of self-reported abstinence using breath CO levels may, therefore, not be viable when participants are seen only once per week. This leaves two options for accurate biochemical verification: either participants are required to attend the clinic multiple times per week, or another biochemical measure of smoking abstinence is used, for example, urine cotinine levels. Cotinine is a metabolite of the nicotine in cigarettes and can remain in the body for several days after smoking [213]. It therefore offers for more accurate verification of smoking status than breath CO, that is only effective over a 12-24 hour period [213]. However, when using NRT products, as is standard practice in UK smoking cessation treatment, cotinine levels cannot be used to verify smoking status as NRT treatments also metabolise to cotinine [214]. Resultantly, metabolites of tobacco smoking that do arise with NRT use, such as anabasine or anatabine should instead be used to verify smoking abstinence [214]. The issue with using these measures, however, is that at the current time there are no commercially available tests that allow immediate testing and results. This precludes their use with CM interventions, as one of the core principles underlying the efficacy of CM is the immediacy of rewards on the display of the desired behaviour [82]. This leaves only the first option, testing multiple times a week, as the only currently viable option. The feasibility of this should be another key focus of future research in the field.

Testing participants more than once a week, although more expensive and time consuming, may also provide an answer to a number of the other pilot/feasibility results observed. Offering multiple testing sessions per week would also reduce the potential for long periods of time between signing consent and baseline sessions, as seen in this study. This would also increase the feasibility of the idea of having participants attend a single session where they sign consent, demographics are collected and the baseline session completed. Whether or not these sessions should be rewarded would require further investigation and may negatively impact the economic viability of the interventions.

Given that this is the first time such an intervention has been carried out in the UK, and the results reported here, perhaps the primary focus of

future research should be in the design of a study protocol more amenable to the needs of potential participants. For example, qualitative interviews with both potential participants and also treatment staff would offer vital insight into methods or elements of experimental design that either may or may not work. Limited resources meant that this was not possible in the current study, but doing so may have avoided some of the issues, such as low treatment completion and low attendance at baseline, that were observed.

5.6.6 Conclusion

Overall, the desired retention rates and results of previous CM intervention studies investigating tobacco smoking in opiate addiction [70–73] could not be replicated here. Whether this was due to the higher reward values used in these other studies, the availability of e-cigarettes in our study, or due to their interventions not being integrated with standard stop smoking treatment, is unclear. What is clear, is that despite the re-launch of the treatment centre's stop smoking service, the offer of free e-cigarettes and the potential to earn a total of £115 in vouchers, very few participants could be maintained in smoking cessation treatment or encouraged to attend their baseline appointment. This suggests that in the current climate in addiction treatment centres, the methods used in this pilot and feasibility study are not enough to have the desired impact on smoking in substance misusers. However, although the desired retention rates could not be achieved, this pilot study brings to light a number of important issues for the application of CM as an adjunct to normal smoking cessation treatment in opiate addiction treatment. These issues included difficulties in standardising treatment, methods of recruitment, notifying participants of treatment allocation, timing of recording demographic data, biochemical verification of abstinence, and quality of the recoding of drug treatment data. Future research should focus on the value of rewards required to achieve acceptable retention rates in this client group, the utility of more accurate biochemical verification of smoking status, the effects of combining standard care with multiple testing sessions per week, and on the other issues outlined above such as implementing multiple trial sessions per week. Finally, this is the first time that an intervention of this kind had been conducted in the UK. As such, it lays the foundation for further investigation into the use of CM for smoking cessation in opiate addiction treatment. It is important that similar interventions are conducted in an effort to combat the high prevalence of smoking in this already disadvantaged group.

Chapter 6:

Discussion

6.1 Summary of Findings

Smoking rates amongst opiate dependent individuals range from 80-98% [27–31], nearly five times higher than that of the general population [4]. Moreover, smoking tobacco during methadone treatment for opiate addiction increases discomfort from opiate withdrawal, posing a major barrier to treatment success [37]. Research has shown that a large majority (79%) of individuals receiving substance misuse treatment in the UK want to quit smoking, but that very few (15%) are offered support to do so [32]. Additionally, stopping smoking during treatment for drug addiction can actually improve treatment outcomes [215], indicating an urgent need for the development of effective smoking cessation treatments for those undergoing treatment for opiate addiction. Contingency management (CM) is a widely used behavioural intervention in addictions treatment, and uses positive reinforcement to encourage desired behaviours [82]. A meta-analysis of CM treatments for substance dependence concluded that CM is one of the most effective substance abuse treatments, with those undergoing treatment for opiate addiction responding best [93]. Furthermore, in the US, CM has been used with some success as an intervention for tobacco smoking during treatment for opiate addiction [70–73]. Despite a growing body of evidence, no study has yet combined CM with standard UK stop smoking services treatment, in individuals receiving treatment for opiate addiction. Therefore, the aim of this thesis was to use the behavioural intervention CM to address the high prevalence of tobacco smoking in those undergoing treatment for opiate addiction. In order to achieve this aim, the thesis followed the MRC guidelines for the development of complex interventions [111].

6.1.1 Meta-Analysis

The initial stage of the MRC guidelines for the development of complex interventions, entails a comprehensive search for existing theory and evidence. CM is a widely researched intervention in the addictions field, with a number of recent systematic reviews and meta-analyses [91–95] supporting its efficacy for this purpose. Despite this, the last review that specifically addressed the use of CM for treating the use of non-prescribed drugs during opiate addiction treatment, was performed in 1999 [125]. Moreover, this review was not performed systematically, raising concerns over potential bias in the selection of included studies. For this reason, it was decided that the best course of action was to perform an updated meta-analysis. It was initially thought that this new meta-analysis should be performed solely on the use of CM for tobacco smoking during opiate addiction. However, it was later decided that this should be broadened to include use of all non-prescribed drugs during opiate addiction treatment.

The reasons for doing this were twofold: firstly, during initial searches, there were very few studies investigating CM for tobacco smoking during opiate addiction treatment; secondly, as a motivating factor for conducting the review was to inform the design of a pilot study, including a broader range of literature had the potential to enable a more optimal design of the pilot study.

The systematic search returned a total of 43 studies meeting inclusion criteria, however, only 22 studies were included in the quantitative synthesis, primarily due to missing data. Overall, the meta-analysis found CM to be more effective than control in engendering abstinence from a wide range of drugs during opiate addiction. This was the case for both of the outcome measures assessed, longest duration of abstinence and percentage of negative samples. Target substance was the only significant moderator of CM efficacy. Moderator analysis showed CM to be more effective than control in preventing use of cocaine, cocaine and opiates, tobacco, and poly-substance use, but not of opiates. The largest effect size for CM was observed in the study investigating the efficacy of CM for tobacco smoking.

6.1.2 Design and Development of the CMQAT

Whilst carrying out the quality assessment of studies included in the meta-analysis, I discovered that there was no existing tool specifically for the assessment of quality in CM studies. This not only posed quite serious issues for the way that the quality of CM studies was currently being assessed, but also represented an opportunity to investigate in more detail, the elements of CM that impact its efficacy as an intervention. As a result, the decision was made to create a new quality assessment tool, the CMQAT (Contingency Management Quality Assessment Tool), that would address this issue. The first step in the development of this tool was to construct the rating criteria that would be used to assess quality. For this, I used the seven core principles of CM, as defined by leading researchers in the field [82]. These were then translated into rating criteria, using the EPHPP (Effective Public Health Practice Project) quality assessment tool as a template, with a three-point scoring scale both for each criterion and overall quality ratings. The tool was then subject to three stages of validity and reliability testing. Inter-rater reliability was tested using Fleiss's Kappa, a statistical measure that allows for comparisons of rater agreement between two or more raters [184]. Predictive validity was tested by correlating the CMQAT ratings with the effect sizes of the studies being rated, the rationale being that higher quality studies should produce larger effect sizes.

In stage one testing, inter-rater reliability was only slight, and predictive validity testing found no significant correlations between the CMQAT or EPHPP score and study effect size. Between testing stages one and two, a number of changes were made to the rating criteria based on the comments of the stage-one assessors. Stage two testing observed an improvement in inter-rater reliability to "fair". Inter-rater reliability of the EPHPP was also tested during this stage, to allow a comparison of an established quality assessment tool with the CMQAT. EPHPP inter-rater reliability was only slight. In stage three, the updated rating criteria were tested for predictive validity, however, no significant correlations were observed between CMQAT score and study effect size. There is a potential explanation for our inability to ascertain predictive validity at both stages one and three. Namely, that our assumption that higher quality studies will produce larger effect sizes may have been incorrect. One study has shown, that in some circumstances, lower quality studies can actually overestimate the effectiveness of an intervention, artificially inflating effect sizes [189]. Although there is more work to be done before the CMQAT can be used in a research context, the work performed here provides a strong base on which this future work can build.

6.1.3 Pilot Study

The findings from both the meta-analysis and CMQAT were then used to inform the development of a pilot/feasibility study. Given that CM had never been tested as an intervention for tobacco smoking during opiate addiction treatment in the UK before, but had been tested successfully in this context in the US, it was decided that a pilot/feasibility study, rather than a larger scale trial, was the most appropriate choice of study design. This study was statistically powered, using the method of Viechtbauer et al. [196], to detect with over 90% certainty, any issues that might occur with a probability of over 5%. An integral part of the pilot/feasibility study was that CM was integrated into routine stop smoking services treatment in the UK, requiring the identification of an addiction treatment centre that also ran a stop smoking clinic. A number of potential study sites were considered, however, only one of these had an extant stop smoking clinic and was, therefore, chosen as the study site. After ethical approval for the study had been granted, it then transpired that due to other clinical pressures, the smoking cessation clinic was temporarily closed, necessitating the retraining of staff at the treatment centre and the relaunch of the smoking cessation clinic for this study. This caused significant delays in the implementation of the pilot. In the pilot/feasibility study, participants were randomised to one of two conditions, CM for smoking abstinence (experimental condition) and CM for attendance at the smoking clinic (control condition). Participants in the

experimental condition received vouchers for providing breath CO recordings of <10ppm, and those in the control condition for attending the smoking cessation clinic.

Of the 40 participants recruited into the study, only 10 completed the five-week intervention. This 25% retention rate was much lower than the 60% target. Moreover, no participants attended the six-month follow-up, with only one participant being contacted successfully. The most widely reported reason for study withdrawal was that the smoking clinic was not run at convenient times. Although the study was not statistically powered to detect intervention efficacy, CM also appeared to have little impact on tobacco smoking behaviours, with no significant differences apparent between conditions for point prevalence smoking or breath CO recordings. There was a significant decrease in the number of cigarettes smoked between baseline and week five for those remaining in the study. However, the poor retention rates and consequent small sample size mean that this should be interpreted with caution.

6.2 Implications for Research

One of the main implications for research, is the direction in which future research concerning the use of CM for smoking cessation during opiate addiction treatment should take. Although the focus of the final study of this thesis was concerned solely with the pilot and feasibility testing of the treatment of tobacco smoking in those undergoing treatment for opiate addiction, this narrow focus may not be the most appropriate. As was seen in the demographics of participants in the pilot study, all participants were receiving treatment for more than one drug of abuse, with many receiving treatment for three. This has also been observed in much larger samples of drug users. In one study carried out in the US, of nearly 70,000 admissions to drug addiction treatment between 1998 and 2004, just under half were for polydrug abuse [216]. Smoking prevalence is far higher than in the general population, not only in opiate addiction treatment, but across treatment for all drug addictions [32]. Additionally, CM interventions have been implemented in the treatment of addiction to a range of different drugs [91–95]. From a research perspective, it is desirable to focus on smoking cessation in a treatment population using only a single illicit substance (for example those in treatment for opiate addiction), as this better fits with the experimental method and circumvents the difficulties that arise from differing dosages, means of administration etc. that vary across different substances [217]. However, this focus on the use on participants using only a single substance does not represent the true make-up of drug use observed in treatment centres, with a growing body of evidence suggesting that patients presenting with

abuse of only a single substance are becoming progressively more scarce [218–223]. Given this, it may be better to broaden the focus of future research on CM for smoking in drug treatment, to individuals in treatment for addiction to any substances rather than focussing on smoking solely in those in treatment for opiate addiction.

Another important implication of the work carried out pertains to the efficacy of CM interventions at follow-up, after rewards have been withdrawn. The meta-analysis that I conducted, analysing the efficacy of CM as an intervention for non-prescribed drug use during opiate addiction treatment, updated and enhanced the findings of a similar, but unsystematic, meta-analysis performed in 1999 [125]. In comparing the findings of these two meta-analyses, what was particularly interesting, was that neither our meta-analysis, nor that of Griffith et al. [125], was able to investigate the effects of CM in this context at follow-up. In the original review, of the 30 studies included only two implemented a follow-up, and of the 22 included in our meta-analysis, 10 studies included a follow-up, but data were only available for two of these. One of the main criticisms of CM is that its effects often deteriorate rapidly after rewards are removed, with one meta-analysis showing that after six months, positive effects of treatment were no longer apparent [95]. It would therefore appear that the longer-term effects of CM, particularly with regard to what happens when rewards are no longer available, needs to be a clear focus of future research.

This also highlights another broad issue affecting CM research, namely the poor reporting of data in published articles. In the systematic search for the meta-analysis, a total of 43 studies meeting inclusion criteria were identified. However, only 22 of these studies could be included in the quantitative synthesis. The primary reason for this was a lack of usable data within the published articles that would allow the meta-analysis to be performed. Moreover, without seeking data from the authors of the studies identified in the search, the number of studies included in the quantitative synthesis would have been even smaller. In total, data requests were sent to the authors of 35 studies, with data for six studies being received. Resultantly, 15 studies were excluded from the analysis due to missing data. Losing over a third of studies due to poor reporting of data seriously compromises the findings of a meta-analysis, as the inclusion of data from such a large number of studies has the potential to dramatically change the overall results. A similar issue was encountered during the development of the CMQAT. During stage one, it was found that a majority of the published articles were missing the requisite information to allow for assessment of quality, particularly with regard to the

"frequency of incentive distribution" and "timing of the incentive" criteria. In total, the authors of 19 of the 22 studies used during stage one testing were contacted to obtain additional information regarding the implementation of their studies. This lack of detail regarding the way in which studies were conducted, severely limited the ability to rate the quality of studies, and compromised the assessment of the CMQAT. It therefore seems clear that the poor reporting of CM studies is an issue that requires addressing before meta-analysis can offer a truly accurate representation of the efficacy of CM interventions. The introduction of the CMQAT may act as a first step towards improving the way in which CM studies are reported. If studies were to report the data required for assessment with the CMQAT, a great deal of the difficulties with poor reporting of data may have been avoided. It may be that the CMQAT itself could be translated into a set of instructions for the reporting of CM trials. The CONSORT (Consolidated Standards of Reporting Trials) statement is a series of guidelines designed to improve the reporting of randomised trials [194], first introduced in 1996. However, as with the development of the CMQAT, there are currently no existing guidelines designed specifically to improve the reporting of CM studies. Development of guidelines like those of the CONSORT statement specifically for CM studies, would ensure that important methodological elements of CM interventions are all reported with sufficient detail. These could include design elements such as how soon after the display of a desired behaviour rewards are administered, the rationale behind the length of the intervention, or whether participants were consulted on the types of rewards used in the intervention. Given the increasingly widespread use of CM interventions both within addictions research and in other fields, the development of a set of guidelines for CM studies, similar to the CONSORT statement, should be a priority of future research.

Perhaps a more important implication, is the extent to which CM can be implemented in routine practice as an effective treatment for tobacco smoking during treatment for opiate addiction. The systematic search performed for my meta-analysis identified four studies [70–73] reporting CM to be an effective intervention for tobacco smoking in this client group. CM has also been observed to be effective for smoking cessation in a number of other treatment contexts, including pregnancy [101], adolescence [102], schizophrenia [104], and post-traumatic stress disorder [105]. There is, therefore, little question that CM can be effective for smoking cessation in a variety of contexts. However, whether this can be translated to routine treatment is a question that remains unaddressed, as only one of these studies implemented its intervention in standard UK stop smoking services [101]. A potential barrier to this is highlighted in the

research undertaken here, relating to the cost of treatment. When formulating the protocol for the pilot study, one of the major considerations was the value of rewards that would be made available to participants. Initially, this was designed using the values of rewards in the four existing studies researching CM for tobacco smoking in opiate addiction treatment [70–73] in line with the assessment for the CMQAT. However, once the total cost was calculated, it transpired that this would have exceeded £20,000 for the 40 participants to be included in the pilot study. Not only was this far beyond the resources available for the pilot study, it also represented an amount that could not realistically be funded during the normal course of treatment. Resultantly, the reward values for the study were reduced, instead being based on those of a study using financial incentives to encourage completion of Hepatitis B vaccinations by opiate addiction treatment patients [195]. The results of our pilot study though are very different to those of the studies identified during the meta-analysis or in the Hepatitis B study. Rather than the significant reduction in tobacco smoking or increased adherence to vaccination protocols in the CM groups observed in other studies, only two participants in the CM for smoking cessation even finished treatment. With the design of the study, and the results obtained, it is not possible to assess what role, if any, reward values played in this discrepancy. What is clear, however, is that reward value should be a focus of any future work in this area. If the reward value required for CM to be effective for encouraging smoking cessation amongst those in treatment for opiate addiction is higher than that viable for implementation in the real world, then there would be little use in continuing its research in this capacity.

This is not to say, however, that CM cannot play an important role within addictions research. If, with future research, it transpires that CM interventions that reward participants for abstinence are not economically viable, there may still be a place for CM in this treatment context. As can be seen from the results of the study investigating the use of CM for adherence to Hepatitis B vaccinations [195], even relatively low reward values (in this case £30) seem to be effective at engaging those in treatment for opiate addiction with treatment. A similar effect is also suggested by the results of our pilot study, where participants in the control condition (CM for attendance) appeared to reduce the number of cigarettes that they were smoking. This result should be interpreted with caution due to the small N and high attrition, but may point towards the ability of CM to engage and maintain those undergoing treatment for opiate addiction, in smoking cessation treatment. Further support for this comes from a study investigating the efficacy of CM for adherence to naltrexone treatment. Naltrexone is a pharmacological treatment for opiate addiction, and blocks

the reinforcing effects of opioids by acting as a long-acting competitive opioid agonist (i.e. it blocks opioid receptors in the brain, diminishing the ability of opiates to bind with receptors) [224]. CM incentives not only resulted in ingestion of a significantly greater number of naltrexone doses, but in a retention rate more than double that of the control condition. It may therefore be more prudent to shift the focus of future research of the efficacy of CM for smoking during opiate addiction treatment from abstinence, to engaging clients with, and maintaining them in, smoking cessation treatment.

Based on the evidence presented here, though, it is not possible to assert that CM does not represent a potentially effective treatment for smoking cessation during opiate addiction treatment. In order for this to be determined, further studies like the one reported here are necessary and the findings of our pilot/feasibility study hold a number of important implications for this research. Primary amongst which, is that access to the treatment should be made as convenient as possible for potential participants. In our pilot/feasibility study, participants could only attend on a Monday afternoon across a two-hour period. This restrictive access to treatment may not only have dissuaded potential participants from taking part, but also contributed to the poor retention rates observed. As previously mentioned, the most commonly cited reason for participants dropping out was that the smoking clinic was not run at convenient times. An additional benefit of this increased access, would be in allowing for the use of Russell Standard [110] guidelines for testing the efficacy of the intervention as discussed in the discussion section of the previous chapter. However, the increased contact required for attending multiple sessions may in turn be too much of a commitment, again dissuading participants from taking part in the study. Related to this is another important implication of the pilot/feasibility findings for the demographic make-up of the participants. Ninety seven percent of our sample were unemployed, with it being unclear whether this was driven by the sample of individuals undergoing treatment at the clinic, or by some other factor. It may be, for example, that those who were unemployed were the only people who could attend a smoking clinic held between 2pm and 4pm on a Monday. It would seem logical then, in a future study, to ensure that recruitment is stratified based on the demographic make-up of the clinical population.

Overall, the findings of this thesis hold a number of important implications for future research into the use of CM interventions for tobacco smoking, in those undergoing treatment for opiate addiction. Despite tobacco smoking having posed a major issue in UK drug treatment

for a number of years and CM having been successfully implemented in a number of drug treatment settings, this is the first time that CM has been investigated as a potential intervention for tobacco smoking during opiate addiction treatment in the UK. The primary implication of the research conducted in this thesis is that despite the efficacy of CM within an experimental context, its ability to be successfully implemented in a clinical setting alongside standard care, is both unclear and potentially far more complex than initially envisaged. Future research should focus on the role that CM may be able to play within standard care, the optimal use of CM within this context (whether that be encouraging abstinence, treatment adherence, or other relevant behavioural targets), and on improving our current understanding of the longer-term effects of CM interventions. Notably, in accordance with MRC guidelines [111] as highlighted in the introduction and methods chapters (Chapters 1 and 4 and figure 11), the ultimate aim of pilot and feasibility work is to feed into the development of a full-scale RCT. Future research efforts should, therefore, reflect this goal. In order to progress to a full scale RCT of CM's efficacy in this treatment context, a great deal more pilot and feasibility work remains to be done. The main issue that requires addressing is the high rate of attrition and poor follow-up rate. How best to test this remains unclear, with a number of potential options including increasing the number of sessions per week, increasing reward values, changing the CM procedures and many more. Perhaps, then, the first work that should be carried out, and that was not carried out in the current study, is some form of user involvement research. For example, a piece of qualitative research assessing the motivations of those in treatment for opiate addiction to quit smoking, the acceptability of different treatments, and the necessary requirements of treatment to maintain their participation in an intervention, would allow for the design of a far more effective and better attended intervention.

6.3 Implications for Clinical Practice

Although this thesis reports the conduct and findings of a pilot/feasibility study, there are still important implications for clinical practice arising from the findings observed. For example, the number of participants recruited by keyworkers at the clinic is lower than the numbers recruited by the experimenter. Given their greater number and contact with potential participants, this is somewhat surprising. However, it has been shown that addictions treatment staff often view smoking cessation as far less important than treating primary drug use [32,225–227], so perhaps this should not be unexpected. This feeling amongst treatment staff is mirrored in the poor provision of smoking cessation treatment for those

in treatment for opiate addiction. As few as 18% of clinics in the US offer individual or group smoking cessation counselling, with only 12% prescribing NRT [65]. This is in stark contrast to the demand for smoking cessation treatment amongst both those in treatment for opiate addiction [228] and the broader drug treatment population [32]. This was also evident in the current study, with the average rating of the importance of stopping smoking amongst participants reported as ten out of ten. Moreover, of the participants that completed the end of treatment questionnaire, the majority reported that their main motivation for taking part in the study was to quit smoking and that they would have tried to quit even if no rewards were available. Resultantly, one of the main implications of this study for clinical practice, is the need for an increased awareness amongst treatment centre staff of the demand amongst their clients for smoking cessation services. Linked to this, a concerted effort must be made both within opiate addiction treatment and wider drug treatment settings to increase provision of smoking cessation treatment. Without this, the demand for these services amongst those in treatment will continue to go unanswered.

Related to this is the issue of the shift in focus of addiction treatment in the UK from abstinence, to harm reduction. Traditionally, drug addiction was conceptualised as being akin to a disease, the logical implication of this being that it could, in some way, be cured [229]. The result of this was that abstinence became the primary focus of addiction treatment [229]. More recently, however, the literature has developed to support a different conceptualisation of addiction, as a chronic relapsing condition [230,231]. Consequently, it is now recognised that for some individuals, long-term abstinence may never be achievable [232]. Therefore, harm reduction strategies have become more widely accepted in treatment. For example, the National Institute for Health and Care Excellence (NICE) now have guidelines specifically for harm reduction in tobacco cessation, which support the use of NRT for as long as they both reduce the desire to smoke and prevent relapse to smoking [233]. E-cigarettes, which are becoming increasingly popular [234], may represent a further evolution of this harm reduction approach. Although not a licensed NRT product, e-cigarettes have already been shown to aid smoking cessation both in the general population [209–212] and in those undergoing treatment for opiate addiction [69]. They were also well received in the current study, with e-cigarettes rated as helpful or very helpful in giving up smoking by more participants than vouchers. Given that the majority of those undergoing treatment for opiate addiction receive methadone maintenance treatment [235], a harm reduction treatment itself, it is reasonable to suggest that a harm reduction approach to smoking may garner more approval among

staff in addictions centres than an abstinence approach. Moreover, as those in treatment for opiate addiction are already accustomed to harm reduction techniques in their opiate treatment, it stands to reason that this may be a potentially useful technique in their smoking cessation treatment. Importantly, the implementation of this approach without improvement in the provision of smoking cessation treatment in general would be of little use. Therefore, a combined focus on both the improvement and formulation of treatment is imperative.

Another implication for clinical practice stems from our inability to use electronic participant records to ascertain potential effects of the intervention on illicit drug use and treatment. This was simply the result of poor recording of these data, with very few records providing up to date information. Without accurate recording of medical information, it is impossible to understand the potential effects of any intervention on a participant's current medical treatment. Electronic patient records also have a number of benefits for general medical practice, including improving quality of care and patient safety [236–241]. It is, therefore, also beneficial to general medical practice to have this information maintained properly. The poor recording of addiction treatment observed here may be symptomatic of falling budgets within drug treatment [242], but nevertheless requires urgent attention and rectification if treatment standards are to be maintained.

6.4 Implications for Policy

The findings of this thesis also highlight one important implication for policy. Namely, the need for smoking cessation to have a more prominent role in the care of those undergoing treatment of opiate addiction. Smoking prevalence in those in opiate addiction treatment is nearly five times that of the general population [27–31], yet the provision of smoking cessation treatment for this group is minimal. As mentioned above, studies in the US have found that less than 20% of methadone clinics offered individual or group smoking cessation counselling or 12% prescribed NRT [65]. This low priority of tobacco smoking in opiate addiction treatment is borne out in the wider literature. In our meta-analysis, of the 22 included studies, only one investigated CM for smoking cessation, whereas eight studies investigated CM for cocaine use and a further six for combined opiate and cocaine use. This is despite the fact the smoking prevalence in opiate addiction treatment has been recorded to be as high as 98% [30], yet prevalence of smoking among cocaine users is under 50% [223]. This low priority of smoking cessation in opiate addiction treatment cannot be attributed to disinterest in those undergoing treatment. Of the participants recruited into our pilot study, 70% had previously tried to quit smoking,

with an average of over three previous quit attempts. This is mirrored in a larger-scale study, where a majority of opiate addiction patients have expressed interest in smoking cessation [243]. There is, therefore, a great deal to be done in terms of policy-making, to elevate the importance of smoking cessation within the context of opiate addiction treatment. A large body of evidence now exists showing the positive impact of smoking cessation during treatment for opiate addiction and the demand for this service from those in treatment, but that provision of this is lacking.

6.5 Conclusion

Overall, I believe this thesis constitutes a significant contribution to the CM literature and the findings have a number of important implications for research, clinical practice, and policy. Firstly, the findings of the meta-analysis offer further support for the efficacy of CM as an intervention for non-prescribed drug use during opiate addiction treatment. As a result of this meta-analysis, it was discovered that no quality assessment tool for CM studies existed. Resultantly, the CMQAT was developed and tested in three stages. This can now form the foundation for future development of the tool and better reporting of CM trials in the literature. The findings of the meta-analysis and the research carried out in constructing the CMQAT were then used to develop a CM intervention for tobacco smoking in individuals undergoing treatment for opiate addiction, which was tested in a pilot study. This was the first time that CM had been tested in this context in the UK. The pilot study led to a number of important observations regarding the ability of CM to be implemented in this context. Namely, that with the CM protocol used, retention in treatment was poor, with only ten of 40 recruited participants completing the five-week intervention.

Taken together, these findings have a number of implications. Perhaps the most important of these though, is that despite the now well-documented efficacy of CM for encouraging abstinence from a wide range of both illicit and licit drugs during opiate addiction treatment, when this is transferred out of an experimental environment and into standard care, implementation seems to be severely compromised. More research is required to ascertain whether CM does or does not represent an effective means of encouraging abstinence from smoking during opiate addiction treatment, but it may well be that better integration with routine opiate treatment provision will enhance engagement with smoking cessation. Similarly, targeting behaviours other than abstinence, such as attendance at cessation treatment, may represent a more fruitful avenue for future CM research. Methodologically, I have introduced a new tool, the CMQAT to support improved reporting and implementation of CM trials. There is the

potential for this to be further developed alongside a statement similar to CONSORT, to improve the reporting of CM research.

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Appendices

Appendix 1: Published Meta-Analysis Paper

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Review

Contingency Management interventions for non-prescribed drug use during treatment for opiate addiction: A systematic review and meta-analysis

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ABSTRACT

Background and aims: Use of non-prescribed drugs during treatment for opiate addiction reduces treatment success, creating a need for effective interventions. This review aimed to assess the efficacy of contingency management, a behavioural treatment that uses rewards to encourage desired behaviours, for treating non-prescribed drug use during opiate addiction treatment.

Methods: A systematic search of the databases Embase, PsychInfo, PsychArticles and Medline from inception to March 2015 was performed. Random effects meta-analysis tested the use of contingency management to treat the use of drugs during opiate addiction treatment, using either longest duration of abstinence (LDA) or percentage of negative samples (PNS). Random effects moderator analyses were performed for six potential moderators: drug targeted for intervention, decade in which the study was carried out, study quality, intervention duration, type of reinforcer, and form of opiate treatment.

Results: The search returned 3860 papers; 22 studies met inclusion criteria and were meta-analysed. Follow-up data was only available for three studies, so all analyses used end of treatment data. Contingency management performed significantly better than control in reducing drug use measured using LDA (d = 0.57, 95% CI: 0.42–0.72) or PNS (d = 0.41) (95% CI: 0.28–0.54). This was true for all drugs other than opiates. The only significant moderator was drug targeted (LDA: Q = 10.75, p = 0.03).

Conclusion: Contingency management appears to be efficacious for treating most drug use during treatment for opiate addiction. Further research is required to ascertain the full effects of moderating variables, and longer term effects.

1. Introduction

Amongst those in treatment for opiate addiction, use of non-prescribed drugs is very common. Hair samples from 99 recently deceased opiate addiction patients identified a range of 21 different drugs being used during treatment, including cocaine, amphetamine, morphine and diazepam (Nielsen et al., 2015). Other studies have observed that over a third of patients entering opiate addiction treatment were also DSM-IV dependent on a drug other than heroin (not including nicotine) (Puigdollers et al., 2009), and poly drug use has been reported to be as high as 68% (Taylor, 2015). These high levels of drug use are not limited to illicit substances. Tobacco smoking is highly prevalent in drug treatment in general (Cookson et al., 2014), with prevalence rates of over 90% observed in individuals undergoing methadone treatment for opiate addiction (Best et al., 2009; Clemmey et al., 1997). Methadone itself has been linked to increased tobacco cigarette consumption, smoke intake and self-reported satisfaction of cigarette smoking (Chait and Griffiths, 1984), and to increased alcohol consumption compared with heroin use (Backmund et al., 2003).

Use of non-prescribed drugs during methadone treatment for opiate addiction has been associated with a range of adverse effects such as poor treatment retention and outcomes (Magura et al., 1998). Use of a single drug during opiate addiction treatment is associated with a threefold greater risk of dropping out of treatment, and use of multiple drugs quadruples the risk of dropping out (White et al., 2014). For example, cocaine use during methadone treatment has been linked to persistence of heroin use (Hartel et al., 2011). Similarly, tobacco smoking during opiate detoxification results in significantly greater opiate craving and significantly lower rates of detoxification completion (Mannelli et al., 2013) and is associated with higher levels of illicit drug use (Frosch et al., 2000).

High prevalence rates and the links to adverse treatment outcomes indicate a need for effective interventions for non-prescribed drug use during opiate addiction treatment. One of the most widely used

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behavioural interventions is contingency management (CM). CM is based on the theory of operant conditioning (Skinner, 1938), which states that the administering of a reward for a particular behaviour increases the likelihood of that behaviour being repeated. In the current context, CM uses rewards (vouchers, clinical privileges or desirable items to be won as prizes for example) to positively reinforce abstinence from or reduced use of drugs during treatment for opiate addiction. CM differs from other common psychological interventions in that the focus of treatment is not on introspective analysis of discrepancies between goals and behaviour (as in motivational interviewing) or modification of flawed cognitive processing (as in CBT), but instead on directly influencing the reinforcement mechanisms involved in addiction (Jhanjee, 2014). Previous reviews have shown CM to be moderately effective in treating substance use (illicit drugs, alcohol and tobacco) disorders in general (Benishek et al., 2014; Davis et al., 2016; Dutra et al., 2008; Lussier et al., 2006; Prendergast et al., 2006), particularly so for opiate addiction (Prendergast et al., 2006). Despite a number of recent reviews assessing the efficacy of CM for substance use in general, very little is known about the use of CM for treating use of non-prescribed drugs in the context of opiate addiction treatment, where treatment outcomes may differ.

Whilst some of these reviews included studies assessing the use of CM in this context (Benishek et al., 2014; Castells et al., 2009; Davis et al., 2016; Lussier et al., 2006), none directly addressed the efficacy of CM for substance use during opiate addiction treatment. The most recent review of this specific use of CM is a meta-analysis published over 16 years ago (Griffith et al., 2000). CM was observed to perform better overall than control, and the effects of CM for drug use during opiate addiction treatment were observed to be moderated by five factors (type of reinforcer, time to reinforcement delivery, targeted CM drug(s), number of urine specimens collected per week and type of subject assignment). However, this review did not search the literature systematically, increasing the risk of bias in the selection of study data. Similarly, it did not assess the effects of different drugs targeted with CM, instead only assessing the moderating effects of targeting single or poly drug use. The aim of the present review was to assess the efficacy of CM for treating the use of different non-prescribed drugs during treatment for opiate addiction, by systematically searching the literature and assessing the effects of potentially moderating variables.

2. Method

A protocol for the current review is available online (see appendix of Supplementary file).

2.1. Search strategy

The review was carried out in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Moher, 2009). Studies were identified using a keyword search of the online databases Embase; PsychInfo; PsychArticles using the Ovid SP interface and a MeSH search of Medline using the PubMed interface; with the following search terms: "Contingency Management" **or** "Reward" **or** "Payment" **or** "Incentive" **or** Prize" **and** "Substance" **or** "Misuse" **or** "Drug" **or** "Narcotic*" **or** "Tobacco" **or** "Smok*" **or** "Stimulan*" **or** "Cocaine" **or** "Alcohol" **and** "Opiate" **or** "Opioid" **or** "Heroin" **or** "Methadone". The search was limited to studies published between each database's inception and March 2015; published in the English language and including only humans. See appendix[1] for full search strategy.

2.2. Inclusion and exclusion criteria

Studies were eligible for inclusion if they: *i)* Tested one or more CM intervention(s) aimed at substance use reduction or abstinence in patients receiving treatment for opiate addiction. CM included any intervention that consistently administered rewards to positively reinforce substance use reduction or abstinence in patients receiving treatment for opiate addiction; *ii)* used a controlled trial design–either a no/delayed treatment control group or an alternative therapy control group, or controlled by repeated participation in two or more treatment arms; *iii)* randomised participants to conditions; *iv)* provided reinforcement or punishment contingent on biological verification of substance use/abstinence; *v)* used consistent measures of substance use at baseline and follow-up; *vi)* Published in a peer reviewed journal. Studies were excluded if: *i)* Participation was non-voluntary – e.g., court orders, prison inmates etc.; *ii)* means and standard deviations for treatment effects were not available from the published data or the authors.

2.3. Study selection

Studies were reviewed for inclusion by three independent reviewers, with all studies being reviewed for inclusion twice. TA processed all titles and abstracts as first reviewer, RC and LB jointly processed half each as second reviewers. An agreement rate of 96% was reached between reviewers; disagreements were discussed and resolved by a separate reviewer, AM.

2.4. Quality assessment

The 'Quality Assessment Tool for Quantitative Studies' (Effective Public Health Practice Project, 2003) was used to assess the internal and external validity of all studies, as well as any biases and confounds. This assesses the quality of studies as strong, moderate or weak on six domains (selection bias, study design, confounds, blinding, data collection and withdrawals/dropouts), providing an overall score for the quality of the evidence in the study. A study is rated as providing strong evidence only when all domains are rated as moderate or strong, and a moderate rating when strong or moderate ratings are achieved for all bar one of the domains. Inter-rater reliability has been shown to be 'fair' across the six domains and 'excellent' overall, often performing better than the Cochrane Collaboration Risk of Bias Tool (Armijo-Olivo et al., 2012).

2.5. Data extraction and synthesis

All data extraction was completed by a single reviewer (TA) using an extraction table designed specifically for the current review and agreed by all reviewers (see supplementary materials). Where studies did not contain means and standard deviations for treatment effects, authors were contacted up to two times to obtain the data. Requests for data were sent to authors of 35 studies, with data for six studies being received (Carpenedo et al., 2010; Downey et al., 2000; Epstein et al., 2009; Kirby et al., 2013; Petry et al., 2007; Vandrey et al., 2007). Where means and standard deviations were not obtained, alternative data including F tests, *t*-tests and chi square were used to calculate an effect size where feasible (Dunn et al., 2010; Shoptaw et al., 2002; Silverman et al., 1998, 1996).

2.6. Outcome measures

Standardised mean differences (Cohen's *d* (Cohen, 1988)) were calculated for each individual study using either: 1) longest duration of abstinence (LDA) data or 2) percentage of biochemically verified negative samples (PNS). As follow-up data were available for only three of the 10 studies that included a follow-up period, all data used in analyses are those recorded during treatment.

2.7. Moderators

A number of possible moderators were assessed, based on those

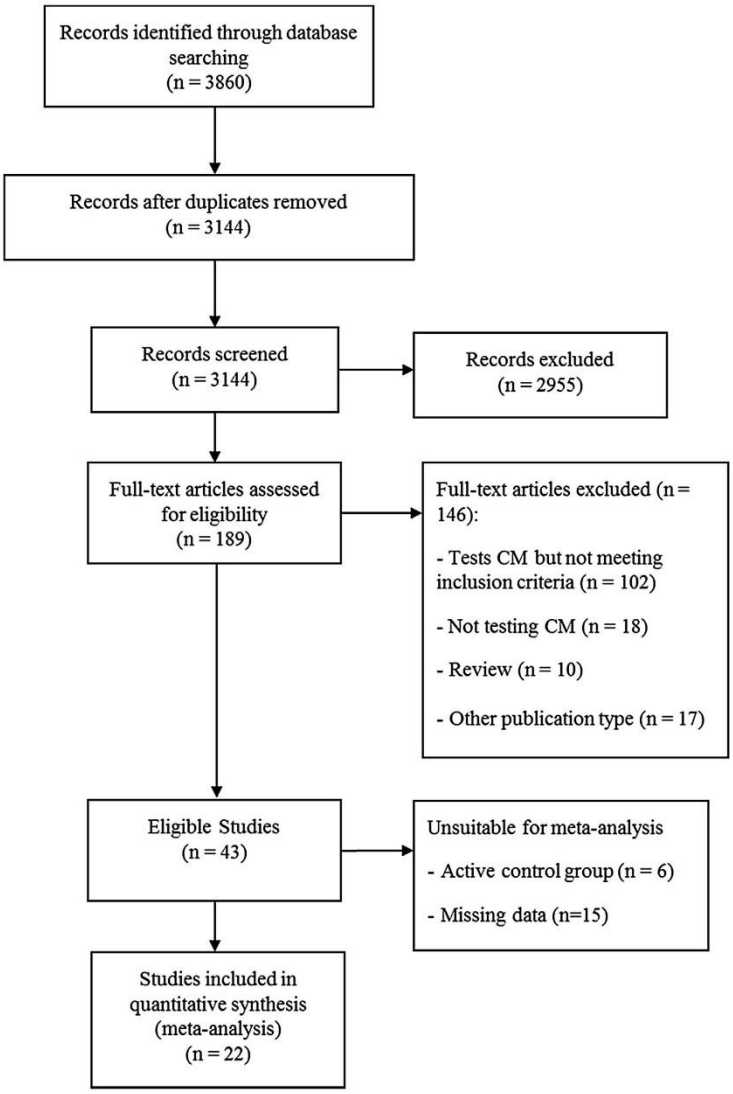

Fig. 1. PRISMA flow diagram.

shown in previous reviews to impact on the efficacy of CM (Griffith et al., 2000; Prendergast et al., 2006). These included the drug targeted for intervention, the decade in which the study was carried out, the quality of the study, duration of the intervention, the type of reinforcer used, and the form of opiate treatment participants were undergoing. Some moderators previously suggested to affect the efficacy of CM (Griffith et al., 2000; Prendergast et al., 2006) could not be investigated due to a lack of suitable data in the included studies or because all studies used the same approach. For example, the number of times abstinence was verified per week could not be investigated as 16 studies recorded this three times a week compared to only five recording it twice a week and one study recording it every day. Similarly, type of incentive (positive, negative, mixed) was not tested as all bar two studies in both analyses used a mixed incentive. Time to reinforcement could not be tested as all included studies delivered immediate reinforcements.

2.8. Data analysis

Meta-analyses were carried out using RevMan v5.3 (Cochrane Collaboration, 2014) software. Data were entered into a generic inverse variance analysis in RevMan that analysed the efficacy of CM compared with control across all drug use during treatment for opiate addiction, using both LDA and PNS. All meta-analyses were carried out as random effects analyses due to the wide variety of CM interventions included (Riley et al., 2011). To allow comparison of CM to control, some multi-

Table 1
Description of each included study and intervention, organised by drug target of CM intervention.

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow up
Cocaine									
Epstein et al. (2003)	2 × 2 factorial design. CM or no CM, and CBT or Social support	Rand – 193	Urines collected every Mon, Wed and Fri, and vouchers administered dependent on condition	Escalating with reset and bonus for three consecutive negative samples	Individual counselling sessions focussing on cessation of all drugs	Number of drug negative urines	Benzo < 300 ng/ml	Throughout intervention, BZE levels were lower in the CM-only and combination groups than in the other two groups. F (1, 185) = 15.94, p < 0.001	No significant difference between any of the groups at 12 month follow up
Psychology of Addictive Behavior Baltimore, Maryland, USA	Meth., between 50 and 80 mg/day	Post – 147		12 Weeks					
Katz et al. (2002a,b)		Rand – 40		Max $1155 Multiple Each phase lasted 11 days			50% reduction in Benzo. or Benzo < 300 ng/ml		
Experimental and Clinical Psychopharma-	Repeated measures – single, continuous, interrupted or no voucher meth. 100 mg/day	Post – Not reported	Urines collected Mon, Wed and Fri. Vouchers awarded dependent on condition (one large	Max reward dependent on condition	Weekly individual and group counselling	Number of consecutive days cocaine abstinence	LDA	Mean abstinence duration was 2 days for no voucher, 3.2 days for single-voucher, and 4.9 and	N/A

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Table 1 *(continued)*

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow up
cology Baltimore, Maryland, USA			voucher, continuous or interrupted vouchers, or no voucher)					4.8 days for continuous and interrupted voucher conditions, respectively, $F(3, 117) = 7.3$, $p = < 0.001$.	
Kidorf et al. (1993)		Rand − 44		Fixed schedule			Definition not reported		
Experimental and Clinical, Psychopharmacology Baltimore, Maryland, USA	CM or Yoked Control group. Ppt were accepted into the 2 years meth. treatment once the exp had done so Meth. 50 mg/day	Post − 43	Urines collected Mon, Wed and Fri. The single reward was awarded after two consecutive weeks of cocaine abstinence which had to occur within the 7 week probationary period	7 Weeks Single reward of 2 years meth. treatment	Group and individual counselling at least once per week	Two consecutive weeks of cocaine abstinence	PNS	50% of CM and 14% of control achieved 2 weeks of continuous cocaine abstinence. No significant difference was found between conditions for the number of negative urines returned	No significant difference between the two conditions was found for the proportion of cocaine negative urines submitted
Petry et al. (2007)		Rand − 76		Fishbowl or voucher escalating with reset.			Not reported		
Journal of Consulting and	Prize based (fishbowl) or voucher based CM, or standard care control Meth. Mean	Post − 59	Urines collected twice per week with an average of 4 days between	12 weeks Max up to $300 and $585 respectively	Weekly individual and/or group counselling	Cocaine abstinence	LDA and PNS	Fishbowl CM ppt achieved significantly greater LDA than	No significant difference between

(continued on next page)

Table 1 *(continued)*

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow up
Clinical Psychology, Connecticut, USA	dose between 78.4 and 83 mg/day dependent on condition		submissions. Negative samples resulted in draws from the prize earn, or vouchers.					control ppt. Voucher CM ppt did not.	percentage of participants submitting negative samples in any condition at 9 months
Silverman et al. (1998)		Rand −59		Escalating with reset, with bonuses in one condition. 12 weeks			Benzo. < 300 ng/ml		
Journal of Consulting and Clinical Psychology Baltimore, Maryland, USA	Three conditions, Escalating CM, Escalating CM with start bonus, and yoked control Meth. Mean dose 62 mg/day	Post − Average retention 10.3–11.3 weeks dependent on condition	Urines collected Mon, Wed and Fri. Vouchers dispensed after urines tested	Max reward $1950 without bonuses	Offered weekly individual counselling	Not reported	LDA	Both CM conditions achieved significantly longer durations of abstinence	Difference between CM groups and control remained significant at 8 weeks
Silverman et al. (1996)	Two conditions, escalating with reset CM and yoked control	Rand − 37	Urines taken Mon, Wed and Fri.	Escalating with reset and bonus.			Benzo. < 300 ng/ml		
Archives	Meth.	Post −	Vouchers	12 weeks Max $1155	Weekly	Not	LDA	Exp	No

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Table 1 (*continued*)

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow up
of General Psychiatry, Baltimore, Maryland, USA	50 mg/day	89% of exp ppt and 83% of ctrl ppt retained for full 12 weeks	given for abstinence		individual counselling (45 min per week)	reported		patients achieved significantly longer durations of sustained cocaine abstinence than ctrl ppt ($F = (1.35) = 13.5$; $p = < 0.001$)	significant difference found between groups 4 weeks post intervention
Umbricht et al. (2014)	2 × 2 Design. CM or Yoked control and Topiramate or placebo.	Rand – 171		Escalating with reset.			Benzo. < 300 ng/ml		
Drug and Alcohol Dependence, Baltimore, Maryland, USA	Meth. 100 mg/day	Post – 113	Urines collected Mon, Wed and Fri. Vouchers awarded for abstinence	31 weeks Max $1155	Weekly individual and group counselling	Cocaine abstinence between weeks 9 and 20	PNS and LDA	No significant difference found between any of the conditions	N/A
Vandrey et al. (2007)		Rand – 12		Fixed, with a single voucher or cheque available in each condition.			Benzo. < 300 ng/ml		
Experimental and	2 × 4 design – 2 types of reward	Post – Not reported	Urines collected Mon, Wed and Fri.	16 weeks (two 8 week periods)	Group and individual counselling	Not reported	PNS	No main effect of incentive type.	N/A

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Table 1 (*continued*)

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow up
Clinical Psychopharmacology	type (voucher or cheque) and 4 types of reward magnitude ($0, $25, $50 or $100) Meth., dose not reported		Rewards were provided for evidence of abstinence Mon to Wed, on the Thur	Largest voucher value $100				Planned comparisons found that high value cheques resulted in significantly greater abstinence than high value vouchers	
Opiates									
Ling et al. (2013)	4 conditions, 4 CM, CBT, CM + CBT and no behavioural treatment Control	Rand – 202		Fishbowl with escalating draws.			Exact criteria not reported		
Addiction, Los Angeles, USA	Suboxone, variable dose	Post – 134	Urines collected twice weekly, with escalating numbers of draws for vouchers dependent on drug free urines	16 weeks Max initially $2196, later reduced to $14600	Counselling	Proportion of opiate negative urines	PNS	Mean number of consecutive opioid-negative UA results did not differ significantly by group.	Same results 52 week follow up as post treatment
Preston et al. (2000)		Rand – 120		Escalating with reset.			< 300 ng/ml opiates		
Archives of General Psyc-	4 Conditions: CM, Increased meth. with non	Post – 112	Urines collected Mon, Wed and Fri. Vouchers	8 weeks Max $554	Weekly individual counselling	Opiate negative urine samples	PNS and LDA	LDA significantly increased with contingent	N/A

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Table 1 (*continued*)

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow up
hiatry, Baltimore, Maryland, USA	contingent vouchers, CM + meth. increase, usual treatment control with non contingent vouchers Meth. dose not reported		administered for evidence of abstinence					vouchers (F (1116) = 10.02, p = 0.002)	
Cocaine and Opiates									
Chituape et al. (2000)		Rand − 53		Escalating with reset.					
Drug and Alcohol Dependence, Baltimore, Maryland, USA	3 conditions: CM with weekly or monthly urine testing, and a control where take home meth. was awarded randomly Meth. 60 mg/day	Post − 43	Urines collected Mon, Wed and Fri. One urine randomly selected either weekly or monthly dependent on condition to decide whether vouchers awarded	28 weeks Max reward was take home doses for all weeks	Weekly individual and group counselling sessions	Not reported	Not reported	The mean LDA was 10.5 (SD 8.9), 8.4 (SD 8.5), and 5.4 (SD 7) weeks for the Weekly, Monthly, and Random Drawings groups, respectively (F(2.52) 1.9, PB0.16).	N/A
Epstein et al. (2009)		Rand − 252		Escalating with reset.			< 300 ng/ml for both opiates and cocaine		
Drug	3 × 2 dose by	Post − 23% of ppt	Urines collected	12 weeks Max not	Weekly individual	Percentages of urine	PNS and LDA	Main effect of	N/A

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Table 1 *(continued)*

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow up
Alcohol Dependence, Baltimore, Maryland, USA	contingency design – meth. dose of either 70 mg or 100 mg and yoked control, CM for cocaine or split CM for cocaine and opiates	dropped out before the end of the intervention	Mon, Wed and Fri. Vouchers were awarded for abstinence from cocaine and opiates either together or separately dependent on condition	reported	counselling	specimens negative for heroin, cocaine, and both simultaneously		contingency on cocaine-negative urines, (F (2244) = 7.36, p = 0.0008) and on urines simultaneously negative for opiates and cocaine, (F (2244) = 3.61, p = 0.0285) but not in opiate-negative urines, (F (2244) = 2.51, p = 0.0830)	
Groß et al. (2006) Experimental and Clinical Psychopharm-	Three conditions: CM vouchers, Reduction in medication, and standard treatment control Bup, maintained on either 4 mg/70 kg or 8 mg/70 kg for the duration of the study	Rand – 60 Post – 45	Urines collected Mon, Wed and Fri. Dependent on condition, ppt either earned	Escalating with reset and bonus. 12 weeks Max $269	Behavioural drug counselling	Mean duration of continuous abstinence, total number of weeks abstinent (non-	< 300 ng/ml of cocaine or opiates LDA	Contingent medication ppt achieved significantly greater durations of	N/A

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Table 1 (*continued*)

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow up
macology, Vermont, USA			points, or did not have their bup dose decreased on evidence of abstinence			continuous), and number of missing visits.		continuous abstinence (M = 5.9 weeks, SD = 4.6) than ppt in the voucher group (M = 2.9 weeks, SD = 3.3; Fisher's LSD, p = 0.05).	
Katz et al. (2002a,b)	Two conditions, CM or Standard care	Rand – 52					< 300 ng/ml for both opiates and cocaine		
Experimental and Clinical Psychopharmacology, Baltimore, Maryland, USA	Meth. 100 mg/day	Post – Mean 35.9 days (of 180) in treatment	Urines collected three times per week and vouchers administered for negative samples	Escalating with reset and bonus 12 weeks Max $1,087.50	Weekly individual cognitive behavioural counselling	Not reported	LDA and PNS	No statistically significant condition effects found	N/A
Petry et al. (2002)	CM or standared treatment	Rand – 42		Fishbowl, escalating draws.			Not reported		
Journal of Consulting	Meth. Average 69 or 70 mg/day in standard	Post – 39	Urines collected Mon, Wed and Fri. Ppt received on	12 weeks Max number of draws dependent	Monthly individual counselling	Weeks of continuous abstinence from both opioids and	LDA	There were significant group difference in the	The percentage of urine samples

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Table 1 (*continued*)

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow up
and Clinical Psychology, Connecticut, USA	treatment and CM		draw for abstinence from either cocaine or opiates, and four for abstinence from both. Continuous weekly abstinence earned bonus draws	on abstinence from different drugs		cocaine		percentage of urine samples negative for both drugs ($F(1, 40) = 4.01$, $p = 0.05$	negative for both opioids and cocaine was higher in exp than ctrl ppt ($U = 11\text{-}2.0$, $p = 0.05$.) at 6 month follow up
Schottenfeld et al. (2005)		Rand – 162		Escalating with reset.			< 300 ng/ml for both opiates and cocaine		
The American Journal of Psychiatry, USA	2 × 2 design: meth. or buprenorphine and CM or performance feedback Maximum daily meth. dose of 85 mg or bup. dose of 16 mg	Post – Cumulative proportion: meth. + CM – 0.6, meth. + performance feedback – 0.75, Bup + CM – 0.45, Bup + Performance feedback – 0.5	Urines collected Mon, Wed and Fri and vouchers administered for evidence of abstinence	24 week Max $1033.50	Individual counselling twice weekly for the first 12 weeks and weekly for the last 12	Maximum number consecutive weeks of abstinence and proportion of drug-free urine tests	LDA	meth. ppt achieved significantly longer periods of abstinence than bup. There were no significant effects of CM ($F = 0.09$, $df = 1, 158$, $p = 0.76$) and no significant interaction between medication and CM ($F = 0.10$, $df = 1, 158$,	N/A

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Table 1 (*continued*)

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow up
								p = 0.75)	
Tobacco									
Dunn et al. (2010)		Rand − 40		Escalating with reset 90 days					
Experimental and Clinical Psychopharmacology Vermont, USA	Two conditions: CM and non contingent voucher Meth. 107.6 ± 8.8 mg/day or Bup. 14.9 ± 1.-3 mg/day	Post − 25	Biochemical verification taken everyday with vouchers for abstinence delivered daily. Numerous bonus's available for abstinence at certain points	Max $362.50	None reported	Percentage of biochemical samples meeting abstinence criteria	Abstinence defined as breath CO ≤ 6 ppm during days 1–5 and a urine cotinine ≤ 80 ng/ml on Days 6–14 PNS and LDA	Exp. Ppt submitted significantly more negative samples than ctrl. Ppt (t (30.1) = 3.24, p < 0.01)	No significant difference between the two conditions at any follow up
Poly substance use									
Chutuape et al. (1999)	Two conditions: CM and usual care control	Rand − 14					< 200 ng/ml for meth., opiates, cocaine and benzodiazepines		
Drug and Alcohol Dependence, Baltimore,	Meth. 71 mg/day or 77 mg/day in CM and standard care conditions	Post − 12	Urines collected Mon, Wed and Fri. Vouchers or take homes administered for	Fixed. 12 weeks Max $900 or three take homes per week dependent on ppt choice	Twice-weekly counselling sessions (one individual and one group session)	Number of drug free urines	LDA	mean LDA for exp ppt was 8.4 and 1 week for ctrl ppt (t (8) = 5.9, p = < 0.001.)	5 ppt relapsed after the CM intervention. ended, generally within

(*continued on next page*)

Table 1 (*continued*)

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow up
more, Maryland, USA			evidence of abstinence dependent on ppt choice						the first week
Downey et al. (2000)	Two conditions: CM and Yoked control	Rand − 41	Urines taken Mon, Wed and Fri.	Escalating with reset and bonus.			< 300 ng/ml for all drugs other than phencyclidine which was < 25 ng/ml		
Experimental and Clinical Psychopharmacology, USA	Mixed Bup. Naloxone tablets. Dose not reported	Post − 21	Vouchers administered for evidence of abstinence	12 weeks Max not reported	Weekly cognitive behavioural substance abuse therapy	Not reported	LDA	No sig difference between the two groups on% drug free urines, LDA or total abstinence for heroin, cocaine or poly drug use during the voucher phase	N/A
Kidorf et al. (1996)		Rand − 16		Fixed with negative consequences for drug positive samples.					
Behavior Therapy, Baltimore, Maryland, USA	Two conditions: CM and usual care control Meth. 60 mg/day	Post − 14	Urines collected Twice per week and take homes administered for evidence of abstinence. Samples	2 month cross over Max 2 take homes per week	Weekly individual counselling	Percentage of drug free urines	Breath alcohol < 0.5, other drug cut-offs not reported PNS	A condition main effect was found, ($F(2, 30) = 4.43$, $p = < 0.05$.) Patients submitted more drug-	N/A

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Table 1 (*continued*)

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow up
			positive for drugs resulted in meth. being administered in a split dose					free urines when exposed to exp (M = 29%; SE = 9.0) than ctrl (M = 9%; SE = 3.0)	
Peirce et al. (2006) Archives of General Psychiatry USA	Two conditions: CM and usual care control Meth. Doeses ranging between 67.9 mg/day to 108 mg/day dependent on recruitment centre	Rand – 388 Post – 67.1% of exp ppt and 64.8% ctrl ppt retained	Urines collected twice per week and prize draws allowed for evidence of abstinence	Fishbowl, escalating with reset. 12 weeks Max 204 draws, resulting in a maximum of approx. $400 in prizes, plus one guaranteed $20 prize.	Individual and group consoling. Frequency ranged from 3 times per week to once per month	Not reported	Not reported LDA	Exp ppt were significantly more likely to submit stimulant- and alcohol-negative samples than were ctrl ppt (OR, 1.98; 95% CI, 1.42-2.77; missing samples coded as missing)	No group differences in percentage of submitted samples negative for stimulants and alcohol (χ^2 = 0.-08, P = 0.78).
Petry et al. (2015) Journal of Con-	Four conditions: $300 prize CM, $900	Rand – 240 Post – Not reported	Urines taken at least twice a week	Escalating with reset for either fishbowl draws or vouchers dependent on condition. 12 weeks Max either $300 or 900$	Weekly group counselling	LDA and proportion of samples submitted	Not reported PNS and LDA	The longest duration of abstinence and	At the 12-month follow-

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Table 1 *(continued)*

Study, publication date, publishing journal and location carried out	Design and usual opiate substitution therapy treatment	Participants randomised pre and post intervention	Intervention procedure	CM Schedule, length of intervention and max reward	Additional treatments	Primary Outcome	Abstinence Criteria	Substance use post intervention	Substance use at longest follow up
sulting and Clinical Psychology, USA	prize CM, $900 voucher CM and usual care control Meth. Doses ranging between 77 mg/day and 85.4 mg/day		with at least 2 days between tests. Abstinence resulted in either fishbowl draws or vouchers			negative for cocaine and alcohol		proportion of samples testing negative were significantly greater in each of the three CM conditions relative to usual care (F(3236) = 3.39, p = 0.02 and F (3236) = 3.94, p = 0.009 respectively)	up, 113 of 225 (50.2%) patients submitted negative samples

Abbreviations – **Rand**- Randomised to conditions, **Post**- Post intervention, **Exp** – Experimental condition(s), **Ctrl** – Control condition, **CM** – Contingency Management, **TLFB** – Time Line Follow Back, **LDA** – longest duration of abstinence, **PNS** – percentage of negative samples, **Meth.** – methadone, **Bup.** – buprenorphine, **Pbo.** – placebo, **ppt** – participants, **Benzo** – benzoylecgonine, **OST** – Opiate substitution therapy.

Table 2
EPHPP ratings for all included studies organised by drug target of CM intervention.

Study	Selection Bias	Study Design	Confounds	Blinding	Data Collection	Withdrawals/ Dropouts	Overall
Cocaine							
Epstein et al. (2003)	2	1	1	2	1	2	Strong
Katz et al. (2002a,b)	2	1	3	2	1	1	Moderate
Kidorf et al. (1993)	3	1	1	2	1	1	Moderate
Petry et al. (2007)	3	1	1	3	1	2	Weak
Silverman et al. (1996)	3	1	1	2	1	1	Moderate
Silverman et al. (1998)	2	1	1	2	1	3	Moderate
Umbricht et al. (2014)	3	1	1	1	1	2	Moderate
Vandrey et al. (2007)	3	1	3	2	1	3	Weak
Opiates							
Ling et al. (2013)	2	1	3	2	1	2	Moderate
Preston et al. (2000)	3	1	3	1	1	1	Weak
Opiates and Cocaine							
Chutuape et al. (2000)	3	1	1	2	1	3	Weak
Epstein et al. (2009)	3	1	1	2	1	2	Moderate
Groß et al. (2006)	3	1	1	2	1	2	Moderate
Katz et al. (2002a,b)	2	1	1	2	1	3	Moderate
Petry et al. (2002)	2	1	1	2	1	1	Strong
Schottenfeld et al. (2005)	3	1	1	1	1	3	Weak
Tobacco							
Dunn et al. (2010)	2	1	1	3	1	2	Moderate
Poly-substance							
Chutuape et al. (1999)	3	1	3	2	1	3	Weak
Downey et al. (2000)	3	3	3	2	1	3	Weak
Kidorf et al. (1996)	3	1	3	2	1	3	Weak
Peirce et al. (2006)	3	1	1	3	1	2	Weak
Petry et al. (2015)	3	1	1	2	1	3	Weak

1 = Strong, 2 = Moderate, 3 = Weak

arm trials were collapsed into a two-arm design by averaging the effects across the treatment conditions (Cochrane Colaboration, 2011). This was only done however when each arm used CM in isolation (other than normal pharmacological treatment for opiate addiction); if a study arm included CM in combination with another behavioural or pharmacological treatment not part of standard treatment, then this arm was not included in the meta-analysis. This was done in order to match the design of the included studies with only single experimental and control arms. Control arms were not collapsed unless each was a standard treatment control. For example, one study (Schottenfeld et al., 2005) had four conditions (CM with either methadone or buprenorphine and performance feedback with either methadone or buprenorphine), so the two CM conditions were collapsed together, as were the two performance feedback conditions. Another study (Preston et al., 2000) also had four conditions (CM, methadone increase, CM + methadone increase and a usual care control), but no conditions were collapsed and only the CM and usual care control conditions were used in the analysis. The I^2 statistic was used to assess the percentage of variability in treatment effect estimates attributable to between-study heterogeneity.

Moderator analysis was performed using Comprehensive Meta-analysis software V.3 (Borenstein et al., 2014). Results were computed using random effects statistics and indicate the extent to which each moderator accounts for variability in effect sizes with respect to drug use outcomes. A significant value of Q-between indicates significant differences among effect sizes between the categories of the moderator variable. This method also calculates the mean pooled effect size for each category within the moderator variable being tested and whether this is significant. For the drug targeted for intervention, studies fell into five categories: opiates, cocaine, opiates and cocaine combined, tobacco, and polysubstance use. For study decade, studies were grouped as being published from 1990 to 1999, 2000 to 2009 and 2010 onwards (study publication dates ranged from 1993 to 2015). Study quality followed the strong, moderate and weak ratings of the 'Quality Assessment Tool for Quantitative Studies' (Effective Public Health Practice Project, 2003). Intervention durations were grouped as < 12 weeks, 12 weeks, and > 12 weeks. Reinforcer type was categorised as monetary vouchers and 'other'. Opiate treatment similarly contained two categories, methadone treatment and 'other'.

Publication bias was assessed using the 'failsafe N' technique (Rosenthal, 1979), calculated using Comprehensive Meta-analysis software V.3 (Borenstein et al., 2014). This calculates the number of studies averaging a Z-value of zero that would be required to make the overall pooled effect size non-significant (Rosenthal, 1979).

3. Results

3.1. Included studies

A total of 3144 studies were identified in the search, yielding a total of 22 studies meeting inclusion criteria and included in the meta-analysis (Chutuape et al., 2001, 1999; Downey et al., 2000; Dunn et al., 2010; Epstein et al., 2009, 2003; Gross et al., 2006; Katz et al., 2002a; Katz et al., 2002b; Kidorf and Stitzer, 1993, 1996; Ling et al., 2013; Peirce et al., 2006; Petry et al., 2014, 2007; Petry and Martin, 2002; Preston et al., 2000; Schottenfeld et al., 2005; Silverman et al., 1998, 1996; Umbricht et al., 2014; Vandrey et al., 2007) (see PRISMA flow diagram, Fig. 1). The included studies randomised a total of 2333 patients to 39 CM conditions and 33 non-CM control conditions. This included three studies with two CM conditions each collapsed into a single CM condition, four studies with three CM conditions each collapsed into a single CM condition, and two studies with two CM, and two control, conditions each collapsed into single CM and control conditions.

3.2. Study description and quality assessment

Eight of the 22 studies tested the effects of CM for cocaine use, two for opiate use, one for tobacco smoking, six for combined use of opiates and cocaine and five for polysubstance use. Twenty-one studies

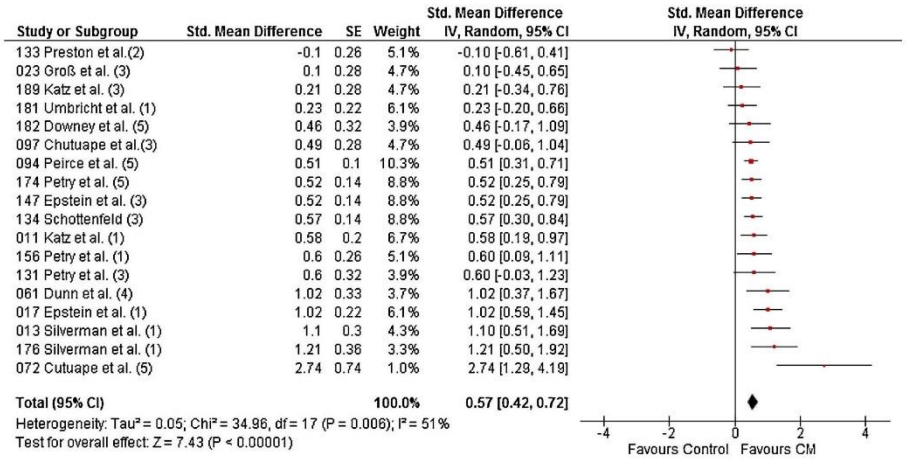

Fig. 2. Forest plot for LDA during treatment of all substances combined. (1) = Cocaine, (2) = opiates, (3) = opiates and cocaine, (4) = Tobacco, (5) = Poly-substance.

included some form of opiate substitution therapy (18 methadone, one buprenorphine, one a mixed buprenorphine and naloxone tablet, and one suboxone), with only a single study not utilising any form of opiate substitution therapy. The duration of CM interventions used ranged between 11 days and 31 weeks, with the number of participants in each study ranging between 12 and 388. Seventeen studies reported retention rates, resulting in an average retention rate of 76.4% (range 51.2%–97.7%). All studies were carried out in the US, with 13 being carried out in the same state (Maryland) (See Table 1 for full description of studies and interventions). Methodological quality assessment rated two studies as overall providing strong evidence, 10 studies moderate evidence and 10 studies weak evidence (Table 2).

3.3. Meta-Analysis

The meta-analysis for LDA (longest duration of abstinence) from all substances combined contained 18 studies randomising 2059 patients to 31 CM conditions and 25 non-CM control conditions. The random effects meta-analysis produced a pooled effect size of $d = 0.57$ (95% CI: 0.42–0.72), with CM performing significantly better than control (Fig. 2). A moderate (Cochrane Colaboration, 2011) level of the variability of effects between studies was due to between-study heterogeneity ($I^2 = 51\%$).

For PNS (percentage of negative samples), 12 studies randomising 1387 patients to 24 CM conditions and 21 non-CM control conditions were included and the pooled effect size was $d = 0.41$ (95% CI: 0.28–0.54), again with CM performing significantly better than control (Fig. 3). Variability of effects was not due to between-study heterogeneity ($I^2 = 0\%$).

3.4. Moderator analysis

The only moderator found to have a significant effect on the efficacy of CM was intervention drug target, but only for LDA (Tables 3 and 4). Within each of the categories of the six moderators, CM performed significantly better than control in all but three instances. Within drug targeted for intervention, CM performed no better than control for treating non-prescribed opiate use for both LDA and PNS. Within intervention duration, CM failed to encourage significantly better LDA than control in studies with intervention duration of less than 12 weeks. Within opiate treatment type, CM did not result in significantly greater PNS than control for studies where participants were in the 'other' category.

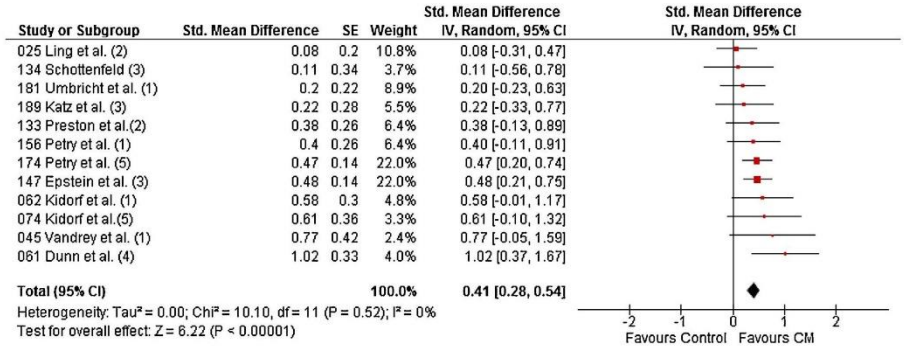

Fig. 3. Forest plot for PNS during treatment of all substances combined. (1) = Cocaine, (2) = opiates, (3) = opiates and cocaine, (4) = Tobacco, (5) = Poly-substance.

Table 3
Random effects moderator analysis results for LDA.

Moderator	k[1]	Effect Size (d)[2]	95% CI	Z Value	P value	Q between (df)[3]	P of Q between
Drug targeted for intervention	18					10.75 (4)	0.03
Cocaine	6	0.75	0.45–1.04	4.91	< 0.001		
Opiates	1	−0.10	−0.61–0.41	−0.40	0.70		
Opiates and cocaine	6	0.48	0.32–0.64	5.85	< 0.001		
Tobacco	1	1.02	0.37–1.67	3.10	< 0.01		
Poly substance	4	0.62	0.27–0.98	3.45	< 0.01		
Study decade						1.31 (2)	0.52
1990–1999	4	1.08	0.14–2.02	2.23	0.02		
2000–2009	10	0.53	0.41–0.65	8.67	< 0.001		
2010 onwards	4	0.53	0.32–0.74	4.92	< 0.001		
Study Quality						2.66 (2)	0.23
Stong	2	0.87	0.48–1.27	4.37	< 0.001		
Moderate	8	0.57	0.32–.82	4.47	< 0.01		
Weak	8	0.51	0.30–0.72	4.75	< 0.001		
Intervention Duration						1.30 (2)	0.52
< 12 Weeks	2	0.26	−0.41–0.93	0.77	0.44		
12 Weeks	12	0.63	0.44–0.82	6.42	< 0.001		
> 12 Weeks	4	0.53	0.27–0.79	4.04	< 0.001		
Reinforcer type						0.022	0.88
Monetary Vouchers	16	0.57	0.41–0.74	6.86	< 0.001		
Other[i]	2	0.54	0.13–0.95	2.55	0.01		
Opiate treatment						0.65	0.42
Methadone	13	0.61	0.42–0.80	6.45	< 0.001		
Other	5	0.47	0.20–0.74	3.46	< 0.01		

[1]Number of studies, [2]Weighted random effects, [3]A significant value of Q-between indicates significant differences among effect sizes between the categories of the moderator variable

3.5. Publication bias

There is widespread acceptance of the fact that studies reporting positive results are far more likely to be published than studies reporting null findings, resulting in an over representation of positive results within the literature (Rosenthal, 1991; Rosenthal and Rubin, 1988; Schmid, 2016). The 'failsafe N' (Rosenthal, 1979) calculates the number of studies reporting null results that would be required to overturn the statistically significant difference between CM and control observed above. For LDA, 560 papers reporting null results would be required, and 101 for PNS.

Table 4
Random effects moderator analysis results for PNS.

Moderator	k[1]	Effect Size (d)[2]	95% CI	Z Value	P value	Q betweeen (df)[3]	P of Q between
Drug targeted for intervention						6.43 (4)	0.17
Cocaine	4	0.4	0.13–0.67	2.89	< 0.01		
Opiates	3	0.18	−0.11–0.46	1.23	0.22		
Opiates and cocaine	2	0.43	0.18–0.67	3.42	< 0.01		
Tobacco	2	1.02	0.37–1.67	3.09	< 0.01		
Poly substance	1	0.49	0.23–0.74	3.74	< 0.001		
Study decade						1.10 (2)	0.58
1990–1999	2	0.51	0.25–0.77	3.83	< 0.001		
2000–2009	3	0.30	0.01–0.59	2.01	0.05		
2010 onwards	7	0.40	0.20–0.60	3.93	< 0.001		
Study Quality						0.36 (2)	0.84
Stong	1	0.48	0.21–0.75	3.43	< 0.01		
Moderate	5	0.36	0.06–0.66	2.32	0.02		
Weak	6	0.44	0.30–0.58	0	< 0.001		
Itntervention Duration						0.32 (2)	0.85
< 12 Weeks	5	0.47	0.28–0.67	4.73	< 0.001		
12 Weeks	2	0.42	0.18–0.67	3.35	0.04		
> 12 Weeks	5	0.37	0.02–0.71	2.06	< 0.01		
Reinforcer type						0.41 (1)	0.52
Monetary Vouchers	9	0.39	0.23–0.54	4.82	< 0.001		
Other[i]	3	0.51	0.17–0.85	2.94	< 0.01		
Opiate treatment						0.35 (1)	0.55
Methadone	8	0.45	0.30–0.60	6.00	< 0.001		
Other	4	0.32	−0.08–0.72	1.58	0.12		

[1]Number of studies, [2]Weighted random effects, [3]A significant value of Q-between indicates significant differences among effect sizes between the categories of the moderator variable.

4. Discussion

Overall, the random effects analyses showed CM performed significantly better than control in encouraging abstinence from a range of different drugs in patients undergoing treatment for opiate addiction. This was the case when measuring both LDA and PNS, producing medium and small (Cohen, 1988) pooled effect sizes respectively. Moderator analysis performed on drug targeted for intervention, decade in which the study was carried out, quality of the study, duration of the intervention, type of reinforcer used, and form of opiate treatment, showed drug target for LDA data to be the only characteristic significantly moderating the efficacy of CM, driven primarily by the ineffectiveness of CM in treating opiate use. Despite only a single significant moderator effect, within each of the six moderator categories CM was found to perform significantly better than control in all but three cases. CM performed no better than control in encouraging abstinence from non-prescribed opiates during treatment for opiate addiction, measuring both LDA and PNS. CM also performed no better than control for LDA in studies with interventions less than 12 weeks long, and PNS in studies where usual opiate treatment was anything but methadone treatment. CM for other non-prescribed drug use in treatment for opiate addiction had no negative impact on usual treatment retention compared to three-month follow-up retention rates observed in usual opiate treatment (Burns et al., 2015; Hansen et al., 1990; Soyka et al., 2008).

This review has a number of limitations. One aim of the moderator analysis was to analyse the effects of CM by target drug type. To improve on the work of Griffith et al. (2000), five categories of drugs were used rather than two. However, one of them, polysubstance use, combined studies with four differing definitions of this, making results hard to integrate. CM still performed better in this category though, suggesting a robustness of effects across a variety of different drug combinations. Another limitation is that the review does not contain any grey literature. This means that any CM studies that have been conducted yet never published are not included in the analysis.

The current review does have a number of strengths however. It is the first review in over 16 years to address directly the efficacy of CM for encouraging abstinence from non-prescribed drug use during treatment for opiate addiction. This is important as CM has gained considerable support in this time, having been recommended since 2007 as a treatment for drug misuse by the National Institute for Health and Care Excellence (Pilling et al., 2007). The findings of the current review support those of the previous reviews carried out in the field; finding an overall positive small to medium (Cohen, 1988) effect size for CM in treating drug use in opiate addiction treatment (Griffith et al., 2000). This is in contrast to the usual small effect size of psychological interventions in the field (Dutra et al., 2008). Findings of the present review are also similar to those of a previous reviews assessing the use of CM for drug use overall, regardless of treatment setting which found similar small to medium effect sizes for drug use in general (Benishek et al., 2014; Castells et al., 2009; Davis et al., 2016; Lussier et al., 2006; Prendergast et al., 2006). The robustness of the effects of CM across different client groups suggests potential utility in treating a diverse range of individuals and needs within the addictions field.

We found no evidence of CM working better than control in encouraging abstinence from non-prescribed opiates during treatment, which is in contrast to Prendergast et al. (2006) who identified CM as one of the most effective treatments for opiate use. The current review included only two studies of this type, compared to four (different) studies included in the previous review because of differing review aims. Moreover, three of the four opiate studies in the previous review systematically reduced methadone doses to zero over the course of the intervention, thereby increasing the likelihood of relapse to opiates and perhaps handing those receiving CM a competitive advantage over those not. Studies in the current review however maintained medication doses throughout the duration of the intervention, possibly eliminating this advantage and leading to the observed non-significant finding. With more data however, results for opiates may more closely follow the trends observed with other drugs.

The moderator analysis performed in the current review has also produced contradictory results to previous reviews. Previous reviews (Griffith et al., 2000; Prendergast et al., 2006) found four of the six moderators analysed here to have a significant effect on the efficacy of CM (drug targeted for intervention, the decade in which the study was carried out, the quality of the study evidence, the length of the intervention period). The current study only found a significant effect for drug targeted for intervention however. A possible explanation for this is differences in analysis, with the previous reviews adopting a fixed effects analysis, and the current the more conservative and more widely recommended (Cochrane Colaboration, 2011) random effects analysis. Support for this comes from more recent reviews that have adopted this same random effects analysis. Lussier et al. (2006) for example analysed the effects of three (drug targeted for intervention, the decade in which the study was carried out, the quality of the study evidence) moderators also analysed in the current and previous reviews, finding none of them to have a significant effect.

More general limitations within the field have also been identified, for example a lack of data available for meta-analysis. In the current review, a total of 21 studies that met all other inclusion criteria could not be included in the quantitative data synthesis. This lack of available data is even more pronounced for follow-up, with only 10 of the 22 included studies utilising some sort of follow-up element in their study design, with data available for only three. CM is often criticised for poor follow-up results, but given the paucity of data we were not able to explore this here. Another concern is the quality of the studies included, with only two studies being rated as providing strong evidence, and 20 papers providing weak evidence. Notably, every study in the current review was performed in the US, with at least 13 performed in the same state and 17 having at least one co-author from the same institution. This significantly limits the generalisability of the currently available evidence on CM for non-prescribed drug use in opiate addiction treatment.

This lack of evidence does however present avenues for future research, particularly the use of CM for tobacco smoking in opiate addiction treatment. This is especially relevant considering that tobacco smoking is the most prevalent form of drug use in opiate addiction treatment (Best et al., 2009; Clemmey et al., 1997), and it has been shown that individuals in treatment for opiate addiction treatment have a mortality rate four times that of non-smokers (Hser et al., 1994). It is similarly important that future research studies are carried out in a wider range of countries, include follow-ups to investigate relapse after the removal of rewards, and focus on improving the overall quality of the data that are published.

In conclusion, CM appears to be an efficacious treatment of the use of cocaine, non-prescribed opiates and cocaine, tobacco, and polysubstance use during opiate addiction treatment, but not for use of non-prescribed opiates. Evidence about longer-term efficacy in this treatment context remains lacking, as is research into the effects of CM on tobacco, the most prevalent secondary addiction in this population.

Contributors

LB and RC acted as second reviewers during study selection. AM, LB and JS had editorial input during manuscript preparation. All authors approved of the final manuscript before submission.

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Conflict of interest

None declared.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.drugalcdep.2017.05.028.

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Appendix 2: Meta-Analysis Search Strategy

Search carried out in Embase, PsychInfo and PsychArticles, from inception to March 2015:

Search #	Search term	Number of records
1	"contingency management".mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	4180
2	reward.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	81032
3	payment.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	32841
4	incentive.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	25567
5	prize.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	9309
6	substance.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	294314
7	misuse.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	30461
8	drug.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	6941070
9	narcotic*.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	49362
10	tobacco.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	152660
11	smok*.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	443219
12	stimulan*.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	48239
13	cocaine.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	79734
14	alcohol.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	572022
15	opiate.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	123411
16	opioid.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	88148
17	heroin.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	28038
18	methadone.mp. [mp=ti, ab, hw, tn, ot, dm, mf, dv, kw, tx, ct, tc, id, tm]	36461
19	1 or 2 or 3 or 4 or 5	143581
20	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14	7790725
21	15 or 16 or 17 or 18	194478
22	19 and 20 and 21	4873
23	limit 22 to english language [Limit not valid in Journals@Ovid; records were retained]	4747
24	limit 23 to human [Limit not valid in Journals@Ovid; records were retained]	2870
25	limit 24 to humans [Limit not valid in Journals@Ovid,PsycINFO; records were retained]	2870
26	remove duplicates from 25	2447

Search carried out in PubMed, from inception to March 2015:

(Contingency Management) OR (Reward) OR (Payment) OR (Incentive) OR (Prize) AND (Substance) OR (Misuse) OR (Drug) OR (Narcotic*) OR (Tobacco) OR (Smok*) OR (simulan*) OR (Cocaine) OR (Alcohol) AND (opiate) OR (opioid) OR (heroin) OR (methadone) AND Humans[Mesh] AND English[lang]

Results: 3807

New Results: 1414 (number of results not also returned by searching Embase, PsychInfo and PsychArticles).

Appendix 3: CMQAT Stage Two Rating Criteria

CMQAT: Instructions for use

General Instructions:

- Each of the quality rating criteria are marked on a three-point scale that rates the paper as strong (3), medium (2) or weak (1) for that criterion.
- Where the information required for a rating to be made is missing, the study should be rated for that criterion based on the information available in the published paper. Authors should then be contacted to clarify this information and the assessment altered accordingly.
- All contingency management schedules should fall under that of "**reinforcement**" rather than "**reward**" [90]. The "reward" model entails the completion of a large, often long-term goal (for example two weeks of abstinence), whereas the "reinforcement" model breaks behaviours down into smaller steps (for example 2 days of abstinence) that are each rewarded. Any study implementing a "reward" schedule of reinforcement should not be rated, and should be excluded from any analyses.

1. Target behaviour and contingency schedule

- **"Measurable"** refers to a behaviour that can be measured using an objective recording method, for example urine, blood or breath levels of a drug [186].
- **"Observable"** refers to the behaviour being directly observable and validated by a member of the treatment team. For example observed or pH or heat tested urine samples [186].
- The same contingency management schedule should be maintained for the duration of the intervention, unless there is an a priori investigative motive for not doing so. Any study that alters the contingency management schedule without this being part of the initial study design should be marked as weak for this criterion.

2. Target population:

"Between participant differences" – Demographic variables/participant characteristics statistically tested for differences between groups (e.g. experimental vs control).

3. Choice of reinforcer:

- The choice of reinforcers used should only be considered to have been influenced by participants if this was done prior to the initiation of the study. For example, the exchange of earned vouchers for goods of

participants' choice would not fall under this definition, as participants had no input as to whether the wanted rewards to take this form or not.

4. Incentive Magnitude:

- For monetary vouchers/cash rewards, the total available reward value for each study should be adjusted for inflation from the year the study was conducted to the current year. This value should then be divided by the number of weeks that the study ran for, and the studies ranked based on these average weekly reward values.
- Studies using other reward types, for example clinical privileges, should be ranked as moderate, unless there is evidence in the literature that these are of greater intrinsic value than monetary vouchers/cash rewards ranked in the middle quartile.
- If quality assessments are being conducted on only a small number of studies, or outside of the context of a systematic review/meta-analysis, the reward values of similar studies in the relevant field should instead be used a reference point for rating incentive magnitude. Incentives of a greater magnitude than those commonly used in the field should be rates as strong, those on a par with those commonly used in the field as moderate, and those of lower magnitude than those commonly used in the field as weak.

5. Frequency of incentive distribution

- If data are missing for frequency of incentive distribution, score the study as moderate if the frequency would capture all drug use (for example testing for cocaine every two days [187]). Authors should still be contacted for explicit verification of this and the quality assessment adjusted accordingly.

6. Timing of the incentive

- It should be noted that for "fishbowl" type interventions (where for each verified display of the desired behaviour, participants earn the right to draw tickets from a bowl that can represent money or prizes), it is the earning of draws from the "fishbowl" that constitutes the reward, not the later exchange of these earned rewards for physical goods.

7. Duration of the intervention

- For example, treatment for illicit drug use often takes place over 12 weeks as it is widely accepted that this is the minimum duration of treatment required to derive benefit [188]. A study that did not explicitly state this but followed this treatment duration would be rated as

moderate. Authors should still be contacted for explicit verification of intervention duration and the quality assessment adjusted accordingly.

CMQAT: Rating Criteria

1. Target behaviour and contingency schedule

Strong (3) – Both observable AND measurable, with biochemical verification or treatment staff / experimenter verification

Moderate (2) – Measurable but not observable

Weak (1) – Neither observable nor measurable, ill-defined target behaviour or not related to condition being treated OR self-report

2. Target population:

Strong (3) – Specific and well-defined target population / condition AND no significant between participant differences

Moderate (2) – Specific and well-defined target population / condition AND any significant between participant differences have been controlled for in analysis.

Weak (1) – Non-specific and ill-defined target population / condition AND/OR significant between participant differences, that have NOT been controlled for in analysis OR between participant differences not reported (contact authors to request data).

3. Choice of reinforcer:

Strong (3) – The choice of reinforcer has been influenced by the participants taking part in the study AND shown empirically to be of utility in the particular treatment population.

Moderate (2) – The choice of reinforcer has been shown in previous research to be of some efficacy, but participants have not been consulted.

Weak (1) – The choice of reinforcer is neither based on consultation with participants nor has empirical support.

4. Incentive Magnitude:

Strong (3) – Studies with reward values in the top quartile of all studies being rated.

Moderate (2) – Studies with reward values in the middle two quartiles of all studies being rated.

Weak (1) – Studies with reward values in the bottom quartile of all studies being rated.

5. Frequency of incentive distribution:

Strong (3) – Explicit evidence of this being set to establish total compliance with agreed behavioural goals (e.g. drug abstinence)

Moderate (2) – Evidence of this having the ability to establish total compliance with agreed behavioural goals (e.g. drug abstinence) OR no evidence of the frequency to establish total compliance provided but the frequency would catch all drug use

Weak (1) – No evidence of this being set to establish total compliance with agreed behavioural goals (e.g. drug abstinence)

6. Timing of the incentive

Based on the meta-analysis of (Griffith et al. (2000)

Strong (3) – Reward administered on the same calendar day as display of desired behaviour

Moderate (2) – Reward administered the one calendar day after the display of desired behaviour

Weak (1) – Reward administered more than one calendar day after display of desired behaviour OR timing of incentive administration not reported (contact authors to request data).

7. Duration of the intervention

Strong (3) – Explicit justification of the intervention duration being based on empirical support of efficacy

Moderate (2) – No explicit justification of the intervention duration but it follows clinical precedent or aligns with other treatments being administered to patients (e.g. methadone treatment, drug detox etc.)

Weak (1) – No explicit justification of the intervention duration and no evidence of following either a precedent in the literature or other

treatments being administered to patients (e.g. methadone treatment, drug detox etc.)

Appendix 4: Published Pilot Study Protocol

BMJ Open

Contingency management for tobacco smoking during opioid addiction treatment: a randomised pilot study

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ABSTRACT

Introduction Smoking rates among individuals in treatment for opioid addiction are close to five times that of the general public. Moreover, drug-addicted smokers have a premature mortality rate four times greater than drug-addicted non-smokers. The aim of this pilot study was to investigate whether contingency management (CM) can be successfully added to evidence-based stop smoking treatment in individuals undergoing treatment for opioid addiction and assess preliminary evidence for its impact.

Participants Forty tobacco smokers currently undergoing treatment for opioid addiction.

Intervention Escalating with reset CM as an adjunct to standard smoking cessation treatment. Financial incentives will be administered over a 5-week period for either biochemically verified abstinence from smoking or attendance at the clinic. Participants will be randomised to conditions stratified on current levels of smoking (high or low).

Objectives and analyses To assess whether a CM intervention can be successfully added to standard stop smoking services treatment, in patients undergoing outpatient treatment for opioid addiction. This will be measured as the number of people completing the 5 weeks of the intervention.

Ethics and dissemination Ethics approval for the study was granted on the 16 June 2016 by the London—city and east (reference 16/LO/0990) ethics committee. The pilot study was retrospectively registered on clincaltrials.gov in January 2017 (ID: NCT03015597). A SPIRIT checklist and figure are available for this protocol. It is planned that the results of this study will be published in an academic journal.

Strengths and limitations of this study

- ► Extends an extensively tested evidence-based intervention to a novel treatment population.
- ► Implements a randomised controlled experimental design.
- ► Due to constraints of the intervention, blinding of both participants and treatment centre staff is not possible.

BACKGROUND

Tobacco smoking is the leading cause of premature death in the Western world,[1] currently killing six million people per year across the globe, predicted to rise to eight million people annually by 2030.[2] In England alone, smoking killed 74 000 people in 2014.[3] Consequently, tobacco smoking places a large economic burden on both the National Health Service and the larger UK economy. It has been estimated that tobacco smoking costs the NHS approximately two billion pounds per year, with a total cost to the UK economy of approximately 13 billion pounds annually.[4]

In 2016, smoking prevalence in the general UK population fell below 17% for the first time.[5] However, despite this encouraging downwards trend, smoking prevalence among those in treatment for drug addiction remains high, with a prevalence of 88% recorded in the UK in 2013[6] and little change observed in the 20 years from 1988 to 2008.[7] Drug-addicted smokers also have a fourfold greater premature mortality rate than non-smokers.[8] This situation is further exacerbated by evidence showing that the efficacy of the standard stop smoking treatment currently used is nearly halved when an individual has used illicit drugs in the past 30 days.[9] There is, therefore, a great need for the development of novel interventions for tobacco smoking for those in drug addiction treatment that can bolster the efficacy of current interventions. One of the highest rates of smoking prevalence in substance abuse treatment is observed in opioid addictions treatment, ranging between 84% and 98%.[7 10–13] Moreover, those in treatment for opioid addiction report high rates of interest in stop smoking treatment,[10 11] making them an ideal population for the development of interventions for tobacco smoking in substance abuse treatment.

Contingency management (CM) is a behavioural intervention based on the principles of operant conditioning, whereby

changes in behaviour are brought about by positively rewarding desired behaviours. CM has been shown to be an effective intervention for drug use during opioid addiction[14] and has been recommended for use in opioid addictions in the UK for some time.[15] Some studies show promising results for CM in smoking cessation during treatment for opioid addiction[16–20]; however, this remains under-researched. Moreover, none of the currently published studies investigating this were carried out in the UK, or alongside standard stop smoking treatment.

The aim of the proposed pilot study was to assess whether a CM intervention can be successfully added to standard stop smoking services treatment in patients undergoing outpatient treatment for opioid addiction.

ETHICS

Risks to participants

There is no known risk associated with the CM behavioural intervention. Smoking cessation can precipitate a number of uncomfortable withdrawal symptoms. These will be attenuated by the stop smoking services treatment provided at the treatment centre, an evidence-based treatment that includes nicotine replacement therapy (NRT), e-cigarettes and behavioural support. Any information recorded from participants will be anonymised using a participant ID number, the master sheet for which will be stored in a locked cabinet at the treatment centre. This ensures that no identifiable information will ever leave the treatment centre.

Vouchers rather than cash

The treatment centre where the pilot study is being carried out did not want participants to be paid in cash so as not be able to buy cigarettes, alcohol or drugs. The 'Love2Shop' vouchers used as an alternative can be spent in a number of high street stores. Although cash vouchers have been shown to be more effective than vouchers in some case,[21] other research has shown cash and monetary vouchers to be of equal efficacy.[22 23] The use of monetary vouchers, therefore, should not negatively impinge on the efficacy of the current intervention. Participants will receive both the study intervention and standard stop smoking services treatment at no cost.

METHODS/DESIGN

This protocol was designed in accordance with the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) statement. See online supplementary material for SPIRIT checklist and online supplementary figure.

Objectives

Primary objective: To investigate whether a CM intervention can be successfully added to standard stop smoking services treatment, in patients undergoing outpatient treatment for opioid addiction, in order to identify any elements that need changing before carrying out a full-scale randomised controlled trial (RCT).

Secondary objective: To gather preliminary findings regarding the effects of the CM intervention on smoking in this group, and any possible effects the intervention may have on opioid addiction treatment outcomes.

Participants, recruitment, inclusion criteria and randomisation

As this is a pilot study, the primary outcome is not the efficacy of the study intervention. Consequently, the sample size has not been calculated to ascertain efficacy. Instead, the method outlined by Viechtbauer *et al*[24] for calculating the sample size based on the probability of any issues that may arise has been used. A sample size of 40 using the above rationale is powerful enough to provide over 90% certainty of detecting any issues that occur with a probability of over 5%.

The study therefore aims to recruit 40 patients, all undergoing current treatment for opioid addiction and who smoke ten or more cigarettes a day. Participants will be recruited from the study site, an outpatient drug addiction treatment centre, either through self-referrals in response to advertisements shown in the treatment centre or referrals from treatment centre staff. Participants are eligible for inclusion if they want to quit smoking (complete abstinence), are aged between 18 and 65 years, undergoing pharmacological treatment for opioid addiction, smoke a minimum of 10 cigarettes per day and provide informed consent. Use of smoking cessation medication is not a criterion for exclusion. Participants will be ineligible for inclusion in the study if they exhibit insufficient English skills to understand study protocols, are currently undergoing treatment for other drugs of abuse or if taking part in other research. Pregnant women will not be excluded.

Participants will be randomised into either experimental (CM for abstinence) or control (CM for attendance) conditions when recruited into the trial. Randomisation will be performed by the principal investigator (PI), using the service provided by the company 'sealed envelope',[25] and will be performed using random permuted blocks within strata. Randomisation will be stratified based on participants' current smoking frequency (between 10 and 20 per day, and more than 20 per day[6]). All participants will be given at least 24 hours after being given an information sheet to decide whether to take part, and will provide written consent, collected by the PI (TSA).

Study design

A two-arm randomised controlled pilot study with 6-month follow-up. The intervention will be provided as an adjunct to the standard smoking cessation treatment provided at the treatment centre, with CM rewards available during 2–5 weeks of the smoking cessation treatment. The study will be conducted in compliance with the principles of the Declaration of Helsinki,[26] the principles of Good Clinical Practice and all applicable regulatory requirements.

Opioid treatment

As part of the standard opioid treatment programme, the clinic offers both behavioural and pharmacological treatments. Pharmacological treatments include methadone, buprenorphine and in some cases a combination of buprenorphine and naloxone; each of these progresses from a daily supervised dose, to a daily unsupervised pickup to a weekly unsupervised pickup. All medication prescriptions are reviewed every 6 months. Clients are also allocated a key worker with whom they meet in person every 2 weeks to discuss their treatment, and who can refer them to a number of different behavioural support programmes. These include psychological therapies or group therapy for their drug use, or a number of other services for issues related to their drug use such as needle exchanges, bloodborne virus testing and domestic violence support. In the past, the clinic has implemented CM interventions as part of other research projects; however, CM has never been implemented as part of the standard opioid treatment programme.

Standard treatment

Prior to the initiation of this study, the smoking clinic had not operated for several months; smoking cessation training was therefore readministered to clinic staff and the smoking cessation treatment relaunched prior to the start of the trial. The treatment runs at the same time each week, on a Monday afternoon between 2 and 4 PM. The standard smoking cessation treatment provided at the treatment centre follows the treatment programme set out by the National Centre for Smoking Cessation and Training (NCSCT)[27] and The National Institute for Health and Care Excellence (NICE) guidelines for smoking cessation.[28] This treatment combines manualised behavioural support to stop smoking with NRT and takes place over 6 weeks with one session per week. In the context of drug addiction treatment, service users are sometimes offered treatment over a slightly longer period of time. In the first meeting, the service user's readiness and ability to quit is assessed, information for the remainder of the treatment programme is given and a quit date for the next week is set. For the remaining 5 weeks, clients attend the clinic to receive behavioural support and have their abstinence biochemically verified. In the study clinic, NRT is available free of charge to all individuals engaged with smoking cessation treatment, in the form of nicotine patches, gum, inhalators, mouth or oral spray and oral strips. At the time of the study, the clinic is also additionally offering (on a trial basis) e-cigarettes, which have a nicotine content of 18 mg/ml. These e-cigarettes are disposable and securely sealed, initially designed for use in high-security environments such as prisons.[29] The smoking cessation treatment provided at the treatment centre does not include treatment with bupropion.

During the 6 weeks of treatment, service users are given a week's supply of NRT or e-cigarettes at a time. At the end of the 6 weeks, service users are given a further 2-week supply of NRT or e-cigarettes before exiting the treatment. The type of NRT received is decided by clients with guidance from the cessation worker, and can constitute a single form of NRT or a combination of different types. Clients' breath carbon monoxide (CO) levels are measured using a Bedfont piCO+ Smokerlyzer breath CO monitor. Measurements are taken at the initial visit and at each subsequent visit over the next 5 weeks, to biochemically verify self-reported abstinence from smoking (CO<10 ppm[30]). NRT and e-cigarette use is recorded throughout treatment. Participants are made aware of these procedures in the participant information sheet that they are given prior to signing consent to the study (see online supplementary appendix 1).

CM intervention

The CM intervention will run as an adjunct to the normal smoking cessation treatment, and follows an escalating with reset schedule. In escalating with reset CM, rewards increase in a set increment value for each successive verified display of the desired behaviour. When the desired behaviour is not observed, no reward is given, and the reward value for the next verified display of the desired behaviour is reset to that of the initial reward. Reward values then begin to rise again in the same way as before. The CM intervention will run for 5 weeks in total, starting in week 2 of the standard stop smoking services treatment and ending in week 6 (table 1). Randomisation will be performed after collection of demographics following taking of consent. Participants will be rewarded for smoking abstinence in the experimental condition, or for attending the smoking cessation clinic in the control condition. Smoking abstinence will be defined as a breath CO reading of <10 ppm, and attendance will be defined as attending the smoking cessation treatment at the

Table 1 Reward schedule

Smoking cessation treatment week No	1	2	3	4	5	6
CM week No		1	2	3	4	5
Reward value	£0.00	£5.00	£10.00	£20.00	£40.00	£40.00

Reward schedule for a participant that remains abstinent and/or attends all smoking cessation treatment meetings (dependent on condition) for the duration of the intervention. Maximum total reward: £115.
CM, contingency management.

clinic that week. After each smoking cessation treatment session, the cessation worker will fill out a slip that records each participant's individual participant number and his or her breath CO for that day. The cessation worker will give these slips to the PI who will sit in an adjacent room and administer rewards where appropriate. All participant data will be recorded using participant numbers ensuring that no identifiable data leave the clinic, and will be stored in an encrypted file, separate to a sheet matching participant names to IDs which will be kept in a locked office at the treatment centre. Due to the nature of the CM intervention, it is not possible to blind participants to treatment allocation. Cessation workers will not be made aware of treatment allocation; however, they cannot be considered to be blinded to treatment allocation as it is possible that clients may discuss this with them.

Reward values will be the same in both conditions and begin at £5, doubling each time the incentivised behaviour is recorded to a maximum of £40. All rewards will be given as 'Love2Shop' vouchers. Over the course of the whole intervention, participants will be able to earn a maximum of £115 (table 1). At the end of the CM intervention, participants will be asked to complete a client satisfaction and well-being survey, which was previously used to assess client satisfaction of stop smoking services treatment.[31]

Measures

Outcome measures

The primary outcome will be assessed by recording the number of participants completing the 5 weeks of the intervention in each condition. Success will be defined as 60% or more of participants completing treatment.

The secondary objectives of the study are to gather preliminary findings regarding the effects of the CM intervention on smoking in this group, and any possible effects the intervention may have on opioid addiction treatment outcomes. Smoking abstinence will be recorded as point prevalence and biochemically verified with abstinence defined as a breath CO reading of under 10 ppm[30]. Participants were informed that smoking cannabis would increase CO levels.

Participant medical records will be accessed after completion of the intervention to ascertain participants' opioid addiction treatment, including treatment adherence, drug types (methadone, Subutex, so on), dosage and schedule (daily supervised pickup, weekly pickup, so on) as well as illicit drug use throughout the period of the trial.

Follow-up measures

At the 6-month follow-up (see below for follow-up procedures), the following measures will be recorded:

Point prevalence smoking abstinence: Self-reported smoking abstinence for 7-days before follow-up and exhaled air CO<10 ppm.[30]

Continuous abstinence: Self-reported smoking abstinence since end of treatment and exhaled air CO<10 ppm. Participants smoking five or fewer cigarettes during the 6-month follow-up will be considered self-reported quitters.[30]

Illicit drug use, collected at the end of the study from participants' medical records.

All those lost to follow-up will be treated as smoking.[30]

Other measures

At the first stop smoking treatment session, a number of demographic and smoking behaviour variables will be recorded. The collection form for this information is shown in online supplementary appendix 2. As many contact details as possible will also be taken for the participants in order to increase the probability of participants being able to be followed-up. This will include the details of relevant friends and family members. Participants will also complete a satisfaction questionnaire on the last day of their participation in the trial, which will assess a number of satisfaction criteria including the value of incentives received (see online supplementary appendix 3).

Follow-up procedures

Six months after their set quit date, participants will be contacted by the PI to ascertain their self-reported smoking status. The main purpose of this follow-up is to ascertain whether participants can be successfully followed-up for 6 months, and no group differences are expected to be found between the different conditions. To test the optimal follow-up method, participants will be pseudo-randomised by recruitment order to be contacted by text and phone call, or email and phone call. All participants will also be asked to return to the clinic in order to have their breath CO levels tested to verify abstinence. Once this is done, participants will have completed their participation in the study. Participants will receive a £10 voucher for completing the follow-up procedure.

Planned analysis

As the primary objective of the intervention does not entail any hypothesis testing, the only statistics reported for this will be descriptive, namely means and SD for the number of participants retained at the end of treatment in each condition. Baseline demographics will be compared between conditions using t-tests for continuous and χ^2 test for categorical data to ensure that any differences in these are not driving any potential differences in retention.

For the secondary objectives, differences between the groups in smoking cessation will be investigated using χ^2 test, differences between conditions on opioid use and opioid treatment during the intervention will be compared using t-tests and χ^2 tests dependent on data and any questionnaire data will be reported using descriptive

statistics. All statistics will be performed as two-tailed tests using an alpha value of 0.05.

DISCUSSION

The addition of contingent incentives to standard evidence-based smoking cessation treatment in opiate addiction clients will be an innovative approach, having never been attempted before in the UK.

The current trial has a number of limitations that should be improved in future studies. First, the value and frequency of rewards in this study are comparatively lower than those of previous trials and should, therefore, be increased to encourage the cessation. The use of breath CO only in measuring abstinence is not the most rigorous method available for testing, due to the relatively short period of time it takes for breath CO levels to return to levels considered as those of a non-smoker. Urine cotinine levels provide a more rigorous measure of abstinence; however, they are confounded by the use of NRT, therefore necessitating the measurement of anabasine instead. The measurements of both cotinine and anabasine were beyond the scope of the current intervention. Furthermore, provision of incentives to participants in the attendance group should come before breath CO levels are measures to avoid the risk of these participants thinking their incentives are linked to CO levels.

However, the intervention has a number of potential strengths. If feasible, the intervention will be easily disseminated, and it has the potential to be an effective intervention for smoking in this client group. Pilot studies are an imperative step in the development of complex interventions, and form the first step on the road to full-scale RCT and potentially implementation.[32 33] If successful, this programme paves the way for the development of a full-scale RCT of CM for smoking in opiate addiction treatment, which would include an economic evaluation, and potential trials for smokers in other drug addiction treatment.

Contributors TSA was responsible for the design of the study with input from AM, LSB and JS. TSA is responsible for the recruitment of participants and for the collection, and analysis of participant data with input from AM and LSB.

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Competing interests JS has contributed to UK guidelines which include consideration of the potential role of contingency management in the management of addiction problems (NICE, 2007; chaired by JS), and JS also chaired the broader-scope pan-UK working group preparing the 2007 and 2017 editions of the 'Orange Book' ('Guidelines on the Management of Drug Misuse & Dependence') for the UK Departments of Health, providing guidance on management and treatment of drug dependence and misuse, which include guidance on possible inclusion of contingency management. JS's institution has received support and funding from the Department of Health (England) and National Treatment Agency (England), and JS and JS's institution have provided funded consultancy advice on possible novel addiction treatments, products and formulations to a range of pharmaceutical companies but these do not have any connection to the intervention being investigated in this paper. JS's employer (King's College London) has registered intellectual property on a novel buccal naloxone with which JS is involved, and JS has been named in a patent registration by a pharmaceutical company as inventor of a potential novel concentrated nasal spray, but these do not have any connection to the work being reported in this paper. A fuller account of JS's interests is at http://www.kcl.ac.uk/ioppn/depts/addictions/people/hod.aspx.JS is supported by the National Institute for Health Research (NIHR) Biomedical Research Centre for Mental Health at South London and Maudsley NHS Foundation Trust and King's College London and is an NIHR Senior Investigator.

Ethics approval London—city and east.

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Contingency management for tobacco smoking during opioid addiction treatment: a randomised pilot study

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Appendix 5: Baseline Data Collection Forms from Pilot Study

Demographics	
Participant ID	
Gender	Male, Female, Not reported
Pregnant	Yes, No, Not reported
Breastfeeding	Yes, No, Not reported
Eligible for free prescriptions?	Yes, No, Not reported
Ethnic Group	White British, White Irish, White Other, Mixed White & Black Caribbean, Mixed White & Black African, Mixed White & Asian, Mixed Other, Asia/Asian Brit – Indian, Asia/Asian Brit – Pakistani, Asia/Asian Brit – Bangladeshi, Asia/Asian Brit – Other, Black/Black Brit - Caribbean Black/Black Brit – African, Black/Black Brit – Other, Chinese, Any other ethnic group
Employment Status	Full time student, Never Worked/Unemployed for over 1 year, Retired, Sick/Disabled/Unable to return to work, Home carer (unpaid), Managerial/Professional, Intermediate occupation (e.g. clerical worker), Routine & Manual occupation (e.g. electrician) Other
How did you hear about the service?	GP , Practice nurse, Pharmacist, Other Professional, NHS National smoking helpline, Internet, Family/Friends, Previous user of the service, Newspaper or magazine, TV, Poster/leaflet, Other

Quitting Data			
Quitting confidence	1 (Not at all) – 10 (Very)		
Quitting importance	1 (Not at all) – 10 (Very)		
Quitting Readiness	1 (Not at all) – 10 (Very)		
Tried to stop smoking before?	Yes / No	# Times:	
# weeks since last quit attempt			
Longest period of abstinence			
Have you tried NRT?	Yes / No	Types:	
		How long used for	
Ever tried Zyban/Champix?	Yes / No	How long used for	
Have you used other stop smoking aids?	Yes / No	Please Specify	

Smoking Behaviour	
What type of tobacco do you smoke?	Cigarettes, Roll-ups, Cigars, Oral
How many cig. Do you smoke per day? (if hand rolled, how many ounces per week - 0.5 oz is 12.5g, or 20 cigs)	
How soon after waking do you have your first cig.?	Less than 5 mins, 5-15 mins, 15-30 mins, 30-60 mins, 1-2 hours, More than 2 hours
How many years have you smoked?	
Age started smoking	
Live with a smoker?	

Appendix 6: Participant Information Sheet and Consent Form from Pilot Study

Study title: Addition of contingency management to stop smoking services for in-treatment opiate addicts: a randomised controlled pilot study

Participant Information Sheet

V1 14/03/2016
IRAS ID: 171709

South London and Maudsley NHS Foundation Trust

Smoking Cessation Study

King's College London Institute of Psychiatry, Psychology & Neuroscience

We invite you to take part in a research study

- Before deciding to take part in the study, it is important for you to understand why the research is being done and what taking part will involve
- Please take time to read the following information carefully and discuss it with friends and relatives if you wish
- You are free to decide whether or not to take part in this study. If you choose not to take part this will not affect the care that you receive at Lorraine Hewitt House or anywhere else
- If there is anything that is not clear or you would like more information, then please ask

Important things you need to know

- Tobacco smoking is very common amongst opiate and methadone users. This makes them likely to experience negative health effects.
- Stopping smoking is one of the best things you can do for your health. It can also reduce the discomfort resulting from opiate use treatment.
- Rewards are one way of helping people stop smoking. This is sometimes called contingency management.
- Contingency management has been shown to work well in changing lots of different behaviours. We want to see whether it could help opiate use patients to stop smoking.
- The aim of this study, is to see whether or not it would be possible to test this treatment in a larger trial
- If you take part in the study, you are free to withdraw from the study at any time, **without giving any reason**. If requested, any data that we have collected from you will be destroyed.
- We might ask you to fill out a small questionnaire if you do decide to withdraw from the study, to help us improve our interventions in the future. There is no obligation to complete this questionnaire though.

Requirements

In order to take part in the study you need to:

- Be in treatment for opiate addiction
- Smoke at least 10 cigarettes per day
- Be between 18 and 65 years old
- Must **NOT** be in treatment for any other drug addiction
- Must **NOT** be participating in any other research

What will taking part involve?

- This study is for people who want to stop smoking, and will attend the stop smoking clinic at Lorraine Hewitt house.
- You will need to come to Lorraine Hewitt House **once a week** on a Monday, Wednesday or Friday to attend the smoking clinic. You will have to do this for a total of 6 weeks.
- At the first study visit you will be asked questions about your age and work history etc. You will also be asked to plan to quit smoking for the following week.
- Every time you come into the clinic, you will have to blow into a machine that measures chemicals in your breath. This is how we know if you have been smoking or not.
- You will be put into one of two groups at random (e.g. by coin toss). In one group you can earn rewards for attending the stop smoking clinic and not smoking. In the other group you can earn rewards just for attending the clinic.
- Rewards will be 'Love2Shop' vouchers
- The amount of money that you earn each time you meet the criteria for that group (attending the stop smoking clinic and not smoking in one, and just attending the stop smoking clinic in the other) will start at £5 and will double each time you meet the criteria up to £40. The diagram below shows how much you will earn if you meet the criteria for reward for the duration of the study

	SSS Week/Visit Number						
	1	2	3	4	5	6	
	Intervention Week/Visit Number						
		1	2	3	4	5	**Total**
Reward Value	£0.00	£5.00	£10.00	£20.00	£40.00	£40.00	**£115.00**

- If you don't meet the criteria though you won't get paid for that visit to the clinic, and the amount that you get paid for the next time you do will start again at £5, and will increase each time like before.

Benefits of taking part

- You could earn up to £115 just by attending the stop smoking clinic and stopping smoking
- Taking part may help you to stop smoking for good. This will help improve your general health greatly
- By taking part, you will be helping us to better understand how we can help other people to stop smoking

Possible disadvantages of taking part

- Giving up smoking can result in a number of withdrawal symptoms that may cause discomfort. The behavioural support and nicotine replacement therapy that you will receive as part of the normal smoking cessation clinic is designed to help this.

Frequently asked questions and further information

- **What will happen if I don't want to carry on with the study?** If at any point during the study you decide that you no longer want to take part, you can withdraw without giving any reason. All you need to do is tell anyone at the clinic related with the study that this is the case, and you will immediately be withdrawn from the study. You can also request that all of the data collected from you be destroyed.
- **How will my information be kept confidential?** Any data stored about you will be anonymous, and will not contain any data that would allow you to be identified. All information recorded from you will be held on a secure computer system at King's College London, in an encrypted format that can only be accessed the research team involved with the study.
- **What will happen to the results of this study?** The results of this study will be used by the primary researcher Tom Ainscough as part of his doctoral thesis, will be written up as an academic paper to be published, and will help inform the design of future research.
- **What if I want to know the results of the study when it finishes?** If you want to be informed of the results of the study once it has finished, this information will be made freely available at Lorraine Hewitt House. Just ask at the reception.
- **Who is organising and funding this study?** The study is organised through the Institute of Psychology, Psychiatry and Neuroscience, King's College London and the South London and Maudsley NHS Trust, and is funded by the Medical Research Council (http://www.mrc.ac.uk/)
- **Who has reviewed this study?** The study design has been reviewed by both an NHS ethics committee and the Research and Development department of the Institute of Psychology, Psychiatry and Neuroscience, King's College London
- **Where can I find more information about research?** For more general information about research you can visit either http://www.invo.org.uk/ or www.testingtreatments.org
- **Who can I contact for more information about this study?** If you need any further information about the study, please contact Tom Ainscough by emailing thomas.ainscough@kcl.ac.uk or calling 020 7848 5727

Study title: Addition of contingency management to stop smoking services for in-treatment opiate addicts: a randomised controlled pilot study

South London and Maudsley NHS Foundation Trust

King's College London Institute of Psychiatry, Psychology & Neuroscience

Smoking Cessation study

Consent Form

V1 14/04/2016

Centre Number: IRAS ID: 171709

Participant ID:

Name of Researcher: Tom Ainscough

	Initial
1. I confirm that I have read the information sheet dated 28/04/2016 (version 1.1) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	☐
2. I am aware that I am required to attend the stop smoking clinic at Lorraine Hewitt House once a week for a total of weeks (please complete).	☐
3. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	☐
4. I understand that my medical notes about my drug use treatment, the and data collected during the study may be looked at by individuals from The Institute of Psychiatry, Psychology and Neuroscience, King's College London. I give permission for these individuals to have access to my records	☐
5. I agree to take part in the above study.	☐

Name of participant	Date	Signature

Name of person taking consent	Date	Signature