Investigating the potential cognitive-behavioural mechanism of change underlying abstinence from cannabis use amongst young people with a history of psychosis and problematic cannabis use

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PhD
Declaration

I, Luke Sheridan Rains confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Signed:

30/06/2019
Acknowledgments

I would like to thank my supervisors, Professor Sonia Johnson and Dr Oliver Mason for all their input throughout my PhD. I would also like to thank Dr Mark Hinton for his feedback on my draft thesis and Dr Louise Marston for her comments on my draft statistical analysis plan (chapter 4).

I am also grateful to the CIRCLE trial group and trial researchers. Much of the research presented in this thesis was conducted in the context of CIRCLE, and the trial methods and results are presented in chapters 3 and 5. The CIRCLE trial management group and research staff are responsible for the successful completion of the trial, and both groups contributed to the write up the trial protocol and results for publication. Portions of those publications are presented in chapters 3 and 5.

I am also indebted to those in the Division of Psychiatry who contributed to my thesis: Thomas Steare (TS) for being the second rater for my systematic review (chapter 2). Laura Curran Middleton (LCM) and Dr Nicola Morant (NM) for being the second rater and for supervising my two qualitative studies (chapters 7 and 9) respectively.

Finally, I would like to thank my family and Tanya for all their support.
Abstract

Cannabis use in psychosis is associated with poorer clinical and functional outcomes. To date there is little evidence of any effective treatments for this cohort. Contingency management (CM) involves reinforcing substance abstinence using rewards. CIRCLE was the first trial of CM focused on cannabis use in people with psychosis (n=551). The aim of this thesis was to conduct a process evaluation of CIRCLE and to consider how to improve treatment for this cohort.

It includes five studies: 1) A systematic review of whether CM treatment is improved by combining it with another formal, evidence-based psychotherapy. 2 and 3) A process evaluation of CIRCLE. A quantitative study (n=353) tested the cognitive-behavioural mechanism of action of the CM intervention. A qualitative study (n=20) explored participants’ experiences and views of the trial. 4) A quantitative study (n=353) explored participants’ reasons for quitting and predictors of cannabis use status. 5) A qualitative study (n=20) explored the process of change underlying quitting in this cohort.

The systematic review found no evidence that adding another psychotherapy to CM improved outcomes. In the CIRCLE process evaluation, there was no evidence of a benefit from CM. Participants reported that CM motivated them to engage with treatment but did not enough to quit. Negative use expectancies, including impact on mental health, ‘self-concept’, and financial concerns were participants’ main reasons for wanting to quit. Frequency of urges was the most important predictor of abstinence by follow-up. Peer support was the most positively viewed form of support.

There is limited evidence that CM is an effective treatment in this cohort. Reasons why psychotherapies often fail in this group are likely related to the multiple disadvantages faced by this population. Supporting people in this population may require a more complex and intensive intervention, which addresses a range of clinical and functional domains.
Impact statement

Cannabis is the most commonly used illicit substance amongst people with psychosis. Its use is associated with poorer clinical and functional outcomes, such as more severe psychotic symptoms or lower engagement in work or education. However, to date there is little evidence of any psychotherapy being effective for treating cannabis use in psychosis.

CIRCLE was the first randomised-controlled trial of Contingency Management (CM) for cannabis use in people with psychosis. One of the programs of work included in this thesis is a process evaluation of CIRCLE. The results suggest that while the CIRCLE CM treatment encouraged participants to engage with treatment, quitting or maintaining their abstinence from cannabis was too difficult. CM is now often understood as an intervention to enhance motivation. In this sense, it seems that the CIRCLE CM treatment did not motivate participants enough to quit. It may be that outcomes could be improved with a different reward programme, such as with more frequent sessions, a longer treatment duration, or higher reward values. Alternatively, it may be that a different approach is required.

The consistent failure of treatments in this cohort highlights the difficulty of supporting people with psychosis change their cannabis use. More needs to be done to consider how to adapt existing therapies or developing novel treatments to this cohort. Evidence regarding the characteristics of this cohort is important in this regard. However, young people with a history of psychosis and problematic cannabis use are a relatively poorly examined cohort, perhaps in part due to them being difficult to engage. A second component of this thesis explores some of the characteristics of this cohort, including what are participants’ reasons for wanting to quit cannabis and what cognitive-behavioural factors predict cannabis use by treatment end? Furthermore, what are patients’ views and experiences of quitting cannabis and what types of support they found helpful?
The results suggest that common reasons for quitting include self-concept (such as ‘to feel better about myself’), negative use expectancies, mental health concerns, and financial concerns. Meanwhile, negative use expectancies, mental health concerns, motivation, self-efficacy, and urges at baseline all predicted cannabis use status at treatment end. Many participants viewed family and social relationships involving cannabis to a major barrier to quitting, and when discussing the support that they had received, participants viewed peer support from people with lived experience of quitting cannabis most positively.

Overall, taken together with previous research, the results of this thesis suggest that a more intensive and complex form of treatment may be required, which supports people across a range of domains such as improving social networks, as well as more conventional topics such as strategies for Relapse Prevention. Peer support may be a beneficial component of such treatment. However, to date there is little evidence in this cohort. While future trials are certainly required in this group, more work is also needed that examines this cohort with the aim of improving our understanding of how to develop potentially effective interventions that meet the needs of this cohort.
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<td>CBT</td>
<td>Cognitive Behavioural Therapy</td>
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<td>CM</td>
<td>Contingency Management</td>
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<td>CMHT</td>
<td>Community Mental Health Team</td>
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<td>CTO</td>
<td>Community Treatment Order</td>
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<td>EIP</td>
<td>Early Intervention in Psychosis service</td>
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<td>EM</td>
<td>Extrinsic Motivation</td>
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<td>HLS</td>
<td>Human Laboratory Study</td>
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<td>IM</td>
<td>Intrinsic Motivation</td>
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<td>MET</td>
<td>Motivational Enhancement Therapy</td>
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<td>Motivational Interviewing</td>
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Chapter 1 – Introduction

1.1 – Introduction to cannabis use and psychosis

Cannabis is the most widely used illicit substance in first episode psychosis (FEP) (Duke et al., 2001; Fowler et al., 1998; Menezes et al., 1996). It is estimated that approximately 33.7% of people with FEP use cannabis (Myles et al., 2015). This compares to 7.2% of 16 to 59-year-olds self-reporting using cannabis in the last year in England and Wales (Lader & Kyriacou, 2016). High rates of use are a significant clinical concern. A substantial body of evidence now exists showing that heavy cannabis use significantly increases the risk of developing a psychotic illness, particularly in younger adults and adolescents (Buchy et al., 2015). Amongst those who have experienced psychosis in the past, heavy use is associated with having more severe psychotic symptoms (Quattrone et al., 2019), and an approximately threefold increase in acute relapse and hospital admission rates (Wade et al., 2006; Linszen et al., 1994). Cannabis use amongst those with psychosis is associated with higher rates of suicidal behaviour, violence, and homelessness (Lambert et al., 2005; Linszen et al., 1994; Verdoux et al., 2001), as well as lower engagement in work and education (Walsh, Buchanan, & Fahy, 2002; Kooymans et al., 2007; Marwaha et al., 2007). It is also associated with increased comorbidity with other psychiatric conditions, such as severe depression or anxiety (Patton, 2002; Curran et al., 2016).

Although still debated, there is now compelling evidence that this association is at least partially attributable to cannabis causing or exacerbating psychosis. As such, treatments for cannabis use in this population have the potential not only to help improve functional outcomes, such as engagement in work or education, but also to help improve clinical outcomes, such as improving symptom severity or reducing the number of acute episodes of psychosis experienced by patients.
1.1.1 – The causal model of cannabis in psychosis

This causal model has now been explored by a very substantial body of research and a wide variety of study designs have been employed to examine this issue. Some of the most compelling evidence comes from prospective longitudinal population studies, observational studies of people with psychosis, and Human Laboratory Studies (HLS).

1.1.1.1 – Longitudinal population studies

The incidence of psychotic illness is fairly low in the population (approximately 31.7 per 100,000 person-years in England Public Health England, 2016)). While it is estimated that using cannabis increases the odds of developing psychosis by as much as 3.9 (95% CI 2.84-5.34) compared to non-users (Hall and Lynskey, 2016), most people who use cannabis do not develop a psychotic disorder (Colizzi and Murray, 2018). Indeed, in a recent review Curran and colleagues (2016) estimate that cannabis users are approximately 9 times more likely to develop cannabis dependence than psychosis. As such, examining the effects of cannabis use in the general population on subsequently developing psychosis is challenging. The opportunity to perform large cohort studies is fairly limited by the availability of suitable datasets. However, there have been several prospective longitudinal studies performed over the last 30 years.

The first of these studies was that of Andréasson and colleagues (1987), who examined a cohort of 45,570 conscripts to the Swedish army. The authors found that amongst high consumers of cannabis (more than 50 occasions in the past), the risk of subsequently developing psychosis was approximately 6 times (95% CI 4.0 - 8.9) that of non-users. Since then, according to a systematic review by Gage and colleagues (2016) at least 10 further studies (n=591 to 50,087) have been performed, which followed-up participants to 30 years after baseline. Seven of these found that the risk of subsequently developing psychosis was significantly higher amongst cannabis users compared to never users, ranging from 1.2
(Odds Ratio; 95% CI 1.1, 1.3) to 8.2 (5.1, 13.1). The other three studies found a positive, but non-statistically significant association. Gage and colleagues report that the pooled risk of experiencing any psychotic outcome amongst cannabis users is 50% higher than non-users (OR=1.46; 95% CI 1.24, 1.72). These studies either excluded people with psychotic symptoms or controlled for severity of symptoms at baseline. In this way, these studies mitigate the possibility that increased cannabis use at baseline is attributable to already having a psychotic illness (reverse causation), rather than developing psychotic illness as a consequence of cannabis use. Another common trend in these studies was that dose-dependent relationship between cannabis and psychosis was found, such that more frequent cannabis use or using more potent strains was associated with worse psychotic outcomes, such as developing psychosis or having more severe symptoms (Gage, Hickman, & Zammit, 2016; Kraan et al., 2015).

1.1.1.2 – Observational studies

Observational studies of people who have already developed psychosis are another valuable source of evidence. In a recent systematic review, Schoeler and colleagues (2016) identified 24 cohort studies (n=16,565 patients) that investigated the effects of continued versus discontinued cannabis use amongst people with a history of psychotic illness. They found that continued use over the previous six months was associated with greater risk of relapse compared to both patients with no history of use (Cohen’s d=0.36, 95% CI 0.22 to 0.50) and discontinued users (d=0.28, 95% CI 0.12 to 0.44), as well as longer hospital admissions than non-users (d=0.36, 95% CI 0.13 to 0.58). Unlike discontinued use, continued cannabis use was also associated with more severe positive psychotic symptoms and poorer global functioning. In one study (Bianconi et al., 2015), cannabis use in patients with first episode of psychosis (FEP) (n=252) was compared to use in controls representing the catchment area population (n=217). They found that while using cannabis, FEP...
participants reported greater symptoms, including feeling more nervous, feeling that they were ‘going mad’, feeling suspicious, hearing voices, and feeling ‘full of plans’.

As with epidemiological studies, there is also evidence of a dose-dependent relationship between cannabis and the risk of experiencing psychosis. A review of 10 studies (n=66,816) reported a dose-dependent relation between cannabis use and psychosis outcomes (Marconi et al., 2016). The meta-analysis found that the risk of having psychotic illness was approximately triple (OR = 3.40 95% CI =2.55 – 4.54) amongst very frequent cannabis users (top 20% of the sample) compared to non-cannabis users. In a case-control study conducted in the UK, Di Forti and colleagues (2015) (n=410) found that the risk of experiencing psychosis amongst people who used high potency cannabis, such as skunk, daily was approximately five times higher compared to non-users.

However, one of the challenges faced by both study designs is that they cannot fully eliminate the possibility that people use cannabis due to their psychotic illness or its prodromal state, rather than cannabis causing their illness. Secondly, the effect of cannabis on psychotic illness is likely to vary with the type or potency of cannabis used. Although many studies report that more potent forms of cannabis increase the risk of developing psychosis, measuring the potency of cannabis used is typically done by self-report and estimation by the authors. For example, in a recent paper by Di Forti and colleagues (2019), the authors asked participants for the colloquial name of the cannabis they typically used (e.g. skunk, hash, weed). The authors then categorised the cannabis as high or low potency based on the European Monitoring Centre for Drugs and Drug Addiction 2016 report, which surveyed the potency of different cannabis types across Europe.

1.1.1.3 – Human Laboratory Studies

These problems are addressed to a degree by HLS’s. Although typically small, they involve administering herbal cannabis or specific cannabis derivatives to participants under
laboratory conditions. Thus, they can fully account for the temporality of association (i.e. whether cannabis use causes psychotic-like symptoms or the reverse) and the dose and type of cannabis or its derivatives received. These studies are often randomised, placebo controlled, and double-blinded. As such, they offer some of the most compelling evidence of the causal association between cannabis and psychosis.

Many of these studies have now been conducted, with one recent literature review (Sherif et al., 2016) identifying 68 studies. A significant majority of the studies identified by Sherif and colleagues (2016) found that administration of cannabis or its derivatives induced transient positive and negative psychotic symptoms as well as psychosis-like cognitive deficits.

Furthermore, HLS’s have been able to examine which cannabinoids are most likely to be responsible for the causal association between psychosis and cannabis. There have been at least 113 cannabinoids derived from the cannabis plant (Aizpurua-Olaizola et al., 2016). One of the outcomes of this work has been to provide solid evidence that delta-9-tetrahydrocannabinol (THC) is the cannabinoid most responsible for increasing the risk of psychosis. THC is the principle psychoactive compound of cannabis and is responsible for its intoxicating effects (ScienceDirect Topics, 2019). HLS’s studies have consistently demonstrated that orally or intravenously administered THC induces psychotic symptoms. One of the larger HLS’s (Bhattacharyya et al., 2015) tested the effects of 10mg of orally administered THC using a cross-over, double blind, placebo-controlled design (n=36). During the experimental phase, participants presented with transient positive psychotic-like symptoms and increased anxiety.

Secondly, they have also found that other cannabinoids appear to have different and potentially beneficial effects on mental health. While THC has been identified as the cannabinoid likely to be primarily responsible for the negative impact of cannabis on
several domains of mental health, including psychotic, depressive and anxiety symptoms, another psychoactive cannabinoid, cannabidiol (CBD) is thought potentially to have antipsychotic and anxiolytic benefits (e.g. McGuire et al., 2018; Wall et al., 2019). A few of the studies in the review by Sheriff and colleagues (2016) followed the THC experimental phase with administering CBD. In those studies, CBD was associated with a reduction in THC induced positive symptoms and other psychiatric symptoms. Beyond HLS’s, there have now been three published randomised controlled trials of CBD as an antipsychotic treatment in patients with psychotic illness (Boggs et al., 2018; Leweke et al., 2012; McGuire et al., 2018). These trials have generally shown a beneficial, albeit sometimes modest, effect on positive psychotic symptoms, with one trial demonstrating similar effects to conventional antipsychotic treatment (Leweke et al., 2012). However, it should be noted that both McGuire and colleagues and Boggs and colleagues delivered CBD as an adjunct to stable antipsychotic treatment, which may have limited the detectable benefit of the treatment to psychotic symptoms. As such, evidence now clearly points to the psychotic effects of cannabis resulting from THC, while CBD appears to ameliorate these effects and may in fact have antipsychotic and anxiolytic effects.

However, almost all HLS’s use participants without a psychiatric history. While the cognitive and neuroimaging evidence from these studies is typically consistent with functional psychoses, it may be that cannabis induced psychosis-like experiences may have distinct neurobiological and phenomenological characteristics to those of functional psychoses. To date only one HLS has administered THC to people with schizophrenia (n=13) (D’Souza et al., 2005), which found that THC transiently exacerbated positive and negative symptoms as well as cognitive deficits. Although the evidence from this study is fairly compelling, the sample size is small and it has never been replicated, perhaps at least partially due to ethical considerations. Furthermore, it arguably does not fully address the possibility that cannabis induced psychotic-like symptoms may be only superficially similar to those in
functional psychosis. Nevertheless, arguably HLS’s offer some of the best evidence for the causal role of THC in psychosis.

Overall, the evidence base that cannabis causes psychosis and exacerbates illness severity is considerable. Epidemiological evidence indicates that in the general population, this association precedes the onset of psychosis, and early cannabis use is associated with an increased likelihood of subsequently developing psychosis. Meanwhile, evidence from HLS’s and observational studies indicates that cannabis use, and specifically THC, is causally related to severity of psychotic symptoms and poorer clinical and functional outcomes. Furthermore, the association between cannabis and psychosis exhibits a dose-dependent relationship in laboratory and population studies, such that higher doses of THC (particularly in proportion to CBD) are particularly strongly associated with psychotic illness. Use high potency cannabis, such as skunk, is especially associated with poorer outcomes (Di Forti et al., 2014). The growing prevalence of skunk cannabis and highly potent synthetic cannabinoids in the UK is probably having damaging consequences in this cohort as well as the general population.

1.1.2 – Patterns of cannabis use

Over the last 30 years, use of forms of cannabis high in THC, such as skunk, has increased in prevalence in the general-public in the UK (Hardwick & King, 2008; King, Carpenter, & Griffiths, 2004; Potter, Clark, & Brown, 2008), and skunk is now by far the most commonly used type of cannabis in FEP (Curran et al., 2016). While the average THC content of cannabis in the 1960’s was 3%, due to selective breeding to increase potency high potency cannabis varieties now available in England average over 16% and 20% in the Netherlands (Murray & Di Forti, 2016). Moreover, while concentrations of THC have risen, concentrations of CBD have stayed low or reduced, such that it is now often present at only negligible levels (Curran et al., 2016). The increased ratio of THC to potentially therapeutic...
compounds such as CBD in cannabis is thought to be especially problematic for mental health and may be the key to understanding skunk’s negative effects on psychosis and other psychiatric illness (Curran et al., 2016).

Freeman and Winstock (2015) report that the use of high-potency cannabis is associated with increased risk of dependency, particularly amongst frequent users. Despite the decline in the number of people using cannabis over the last 20 years, the number of people receiving treatment for cannabis dependence has grown over that period. This is also despite a decline in funding for treatment services during that time (Hamilton et al., 2014). In one of the few papers to look at this issue, Hamilton (2014) suggests that this may be, at least partially, because the increasing prevalence of skunk in the UK is driving a rise in the rate of people experiencing cannabis dependency. Secondly, Freeman and Winstock (2015) found that younger people were especially vulnerable to forming dependence on high potency cannabis. The risk of developing FEP is present throughout adolescence and adulthood but is highest amongst those aged 15 to 35 (Kessler et al., 2007). As such, younger people are both more likely to become dependent on high potency cannabis as well as develop psychosis for the first time. Dependency from using high potency cannabis may be especially problematic in people with FEP. Some of the best evidence of this comes from Di Forti and colleagues (2015; 2019) who found that people with FEP are much more likely to be using skunk daily compared to healthy controls.

In recent years, the increasing use of synthetic cannabinoids has become an additional concern in this group. So far little is known about synthetic cannabinoids. There are many different brands available and a very wide range of distinct synthetic cannabinoids. Since 2008, at least 200 synthetic cannabinoid receptor agonists have been found in herbal mixtures on the market and the list is still growing (van Amsterdam, Brunt, & van den Brink, 2015). Each brand may contain different constituents, and many brands are known to
change their constituents in response to changing legislation or changing market demands, so any analysis of one brand provides little information about the others. However, it is known that concentrations of THC and CBD vary widely, with some types having very high concentrations of THC (van Amsterdam, Brunt, & van den Brink, 2015). Meanwhile, other brands may have low levels or no THC, but have high concentrations of other cannabinoids that are, like THC, cannabinoid type 1 (CB1) receptor agonists (Murray & Di Forti, 2016), which may be equally or perhaps more dangerous than THC for mental health (Murray et al., 2017; van Amsterdam, Brunt, & van den Brink, 2015). Use of synthetic cannabinoids, like high-potency cannabis, is also often associated with psychotic-like symptoms including hallucinations, paranoia, and anxiety. However, they are also thought to create tolerance in users much faster than cannabis and have a relatively high abuse and dependency liability (van Amsterdam, Brunt, & van den Brink, 2015). Synthetic cannabinoid products therefore pose a significant issue for drug misuse treatment services, as there is a need for expertise and a lack of clarity around the composition of such products (Monaghan et al., 2015).

1.1.3 – Difficulties of the causal model

1.1.3.1 – Increasing prevalence of high potency cannabis

While the evidence for a causal relationship between cannabis (and specifically THC) and psychotic illness is now substantial, there remains some uncertainties in our understanding of how cannabis causes psychosis. Some experts have argued that we still cannot be certain of a causal role beyond a reasonable doubt (Hall & Degenhardt, 2015). One potential difficulty for the causal model is that while the prevalence of high-potency cannabis has increased, there does not appear to have been a corresponding increase in the incidence of psychotic illness. If the potency of cannabis is increasing, and cannabis causes psychosis, then one would expect psychosis to become more prevalent. However, in a systematic review of literature reporting incidence rates for psychotic illness in England since the 1950’s, Kirkbride and colleagues (2012) found that rates have been largely stable over that
period (31.7 per 100,000 person-years, 95% CI 24.6 to 40.9). Furthermore, Boydell and colleagues (2006) found that between 1965 and 1999, the prevalence of cannabis use amongst people with schizophrenia rose substantially and disproportionately compared to other psychiatric disorders. Again, this would suggest that there should be a rise in the incidence of psychotic illness. Potentially these seemingly incongruent findings represent a difficulty in the consistency of evidence supporting the causal model.

One potential explanation for this is that although the prevalence of skunk use has increased, the patterns of cannabis use have changed in the UK over the last 20 years. Data from the Crime Survey of England and Wales (Office of National Statistics, 2019) indicate that amongst 16 to 24-year olds, cannabis use has declined from around 25% self-reporting use in the previous year in 1996 to 15.8% in 2016 (Lader & Kyriacou, 2016). This decline made up a large proportion of the fall in use across the working age population (16 to 59-year olds) from 9.4% to 7.2%. It may be that the increasing potency of cannabis has been compensated for, to some degree, by cannabis use falling in this vulnerable demographic. In support of this, in an international cross-sectional study Di Forti and colleagues (2019) found that the odds of having psychosis were five times higher amongst daily high-potency cannabis users compared to never users. Another possibility is that cannabis is only one component cause of psychosis, and may not account for a large proportion of its incidence, so variations in the pattern of the use of cannabis in the population may not have large, easily detectable effects on the prevalence of psychosis.

1.1.3.2 – Biological plausibility

Finally, the exact neurobiological mechanism by which exposure to cannabis causes or exacerbates psychosis is so far unclear (Radhakrishnan, Wilson, & D'Souza, 2014). One of the substantial difficulties with identifying the mechanism of action is that the neurobiology of psychosis itself is currently poorly understood (Kesby et al., 2018).
However, there is growing evidence that cannabinoids appear to modulate dopaminergic, glutaminergic, and gamma-aminobutyric acid activity in brain regions that are broadly consistent with current neurobiological models of psychosis (Radhakrishnan, Wilson, & D’Souza, 2014). As such, while there is still much to do on this topic, our understanding of how cannabis or specific cannabinoids cause psychosis is improving and is broadly consistent with our current understanding of the neurobiology of psychosis.

1.1.4 – Alternative hypotheses of the association between cannabis and psychosis: reverse causation and shared liability

1.1.4.1 – Reverse causation

While there is solid evidence for cannabis having a causal role, there are other explanations that may also contribute to explaining why rates of cannabis misuse in severe mental illness are as high as they are. Reverse causation is the hypothesis that experiencing psychosis increases the likelihood of using cannabis. Some evidence has emerged for reverse causation from Mendelian randomization studies of genetic risk. In one such study, Gage and colleagues (2017) performed a bi-directional two-sample analysis using genome wide data, focusing on genetic variants associated with cannabis initiation and schizophrenia. They found some evidence of a causal effect of cannabis initiation on risk of schizophrenia, but strong evidence consistent with a causal effect of schizophrenia risk on likelihood of cannabis initiation. However, so far there is little evidence exploring this possibility. However, other studies have found evidence consistent with cannabis having a causal effect on psychotic illness (Vaucher et al., 2017).

There are several potential mechanisms for this including that patients may self-medicate or that the symptoms of psychosis, including the cognitive deficits such as impulsivity or anhedonia, may increase the risk of cannabis use (Katz et al., 2017). Of these, self-medication is one of the most well explored, and includes that patients may use to alleviate
negative affective states (such as low mood, boredom or anxiety) or to reduce the positive, negative, or cognitive symptoms of psychosis. One potential objection to this is that increased cannabis use often precedes the onset of psychotic illness in patients. However, reverse causation could still explain, at least partially, the association between using cannabis and subsequently developing psychosis if the prodrome of psychosis increases the likelihood of use.

The self-medication hypothesis is of particular interest because, if valid, it may offer a potential therapeutic target for helping patients reduce their cannabis use. If negative moods, psychotic symptoms, or medication side effects could instead be alleviated through medication or therapy, it may help patients reduce their use. Kolliakou and colleagues (2011) performed the largest literature review to date of the reasons for cannabis use in people with psychosis. They found that the most common reasons were similar to those of the general population, including: ‘to get high’, relax, and to have fun. Social reasons (i.e. that using cannabis is common in their social network) were also frequently reported. Self-medication reasons were reported, but much less frequently than hedonic or social ones. Moreover, self-medication reasons tended to be to alleviate dysphoria, including boredom or anxiety. There was minimal evidence of people using to alleviate the symptoms of psychosis, such as hallucinations or delusions, or medication side effects. Overall, then, it provides evidence that people use for hedonic reasons and to alleviate negative affective states, but not to alleviate psychotic symptoms per se. Such dysphoria is common in psychosis (Hafner et al., 2005) and can be severe. It is also often endorsed more in this population as a reason for using more than non-psychiatric groups. Addressing reasons for dysphoria in psychosis could help alleviate cannabis use.
1.1.4.2 – Shared liability

Another possibility is that psychosis and cannabis use have common causes. These have been suggested to include shared genetic risk factors (Polimanti, Agrawai, & Gelemter, 2017; Power et al., 2014); as well as shared psychological or environmental risk factors (Kolliakou et al., 2011). Shared environmental risk factors include a history of childhood abuse, poorer socioeconomic status, or living in urban environments (van Os, Kenis, & Rutten, 2010). The evidence base that there are shared risk factors is now fairly substantial. For example, several studies have found evidence that a history of childhood abuse increases the risk of both cannabis use and psychosis in later life (Duncan et al., 2008; Houston et al., 2011; Sideli et al., 2015). In some of these studies, evidence of a synergistic interaction between early cannabis use and experiencing childhood abuse was found, such that the combination of the two factors resulted in a greater risk of developing psychosis than the simple addition of their individual risks of developing the disorder (Houston et al., 2011; Sideli et al., 2015).

Treating shared liability factors may be more challenging than some other models of association. However, intervening to reduce exposure to abuse in childhood or alleviating relative or absolute poverty may help mitigate the risk, in addition to the benefits such measures have for people’s mental wellbeing more generally.

1.1.5 – Summary

Overall, there is strong and consistent evidence that psychosis is associated with increased use of cannabis. While, it is likely that, at least part of this association is attributable to factors such as reverse causation or shared liability, current evidence suggests that much of the association can likely be explained in terms of cannabis, and specifically THC, causing and exacerbating psychotic illness. Thus, the increasing prevalence of high potency cannabis and synthetic cannabinoids, and with them the increasing concentrations of THC
and similar CB1 receptor agonists compared to other cannabinoids (such as CBD), likely mean that the risks posed by using cannabis and related substances by people with psychosis is becoming worse. Furthermore, cannabis use in this cohort is likely to have negative effects beyond increasing the likelihood of developing psychosis or making symptoms more severe. As Priester and colleagues (2016) suggest, people with psychosis appear to be especially vulnerable to developing substance misuse disorders because their substance use often worsens mental health symptoms, creates psychological and social instability, lowers motivation, and decreases their ability to seek and access treatment. Continued cannabis use is associated with lower engagement in work or education and higher receipt of state welfare, as well as suicidal behaviour, violence, and homelessness (Hanna et al., 2016; Karila et al., 2014; Lambert et al., 2005; Linszen et al., 1994; Marwaha et al., 2007; Patel et al., 2015; Radhakrishnan et al., 2014; Schoeler et al., 2016; Verdoux et al., 2001; Wade et al., 2006; Walsh et al., 2002). In this sense, looking for effective treatments in this cohort is an important clinical need. Given the poorer social, functional, and clinical outcomes associated with cannabis use in psychosis, identifying clinically and cost-effective treatments has the potential to substantially improve the wellbeing and quality of life of patients.

1.3 – Current evidence regarding treatments for cannabis misuse in the general population

Common treatments for cannabis use disorders include pharmaceutical and psychotherapeutic interventions. However, currently evidence regarding their effectiveness is mixed, and is largely negative in populations with severe mental illness.

1.3.1 – Pharmaceutical treatments

In a Cochrane review of current evidence of pharmacological treatments for cannabis use disorders in non-psychiatric populations, Marshall and colleagues (2014) conclude that
evidence is currently some way from supporting any particular treatment and that the quality of the evidence so far is very poor due to small sizes and risk of bias. Similar conclusions were drawn by Copeland and Pokorski (2016), who identified 56 trials of pharmacological treatments. However, so far the treatments that show greatest promise are cannabinoid-based medications. These include Nabiximols (Sativex), Nabilone, and Dronabinol, all of which contain THC or a synthetic version, and only Nabiximols also containing CBD. Higher doses of Sativex were found to be effective in the treatment of cannabis withdrawal symptoms, but not cravings, compared to placebo in a fairly recently published randomised controlled trial of 54 participants (Trigo et al., 2016). There is growing evidence that substitution therapy with these medications can help with withdrawal symptoms in cannabis use disorders (Copeland and Pokorski, 2016). However, none of the evidence is drawn from populations with psychosis. Secondly, these pharmaceutical products contain THC, and therefore most may not be appropriate for use in psychosis. If they are used as treatments, most are likely, at best, to reduce potential harms of cannabis in psychosis rather than eliminating them. Furthermore, even if substitution therapy may help with withdrawal symptoms, there are many other barriers to abstinence, as discussed below. As such, even if pharmaceutical treatments do have a role, it is likely to be within a broader programme of treatment that includes psychotherapy.

1.3.2 – Psychotherapy

Currently the evidence base for psychotherapy in cannabis use disorders is more substantial. There is fairly good evidence now supporting the effectiveness of certain evidence-based psychosocial interventions for cannabis use disorder in general populations. In a recent Cochrane review of psychosocial interventions for cannabis use disorder, Gates and colleagues (2016) identified 23 randomised controlled trials (N=4,045) that met inclusion criteria. These trials included a range of interventions including CBT, Motivational Interviewing/Motivational Enhancement Therapy (MI/MET), social support
(which involves elements of CBT and MET), drug counselling and/or education, Contingency Management (CM), mindfulness-based meditation, and/or a combination of these. The authors conclude that there is good quality evidence that CBT, MI/MET, or a combination of the two each significantly reduced frequency of cannabis use and severity of dependence at or soon after treatment end. Other reviews have come to similar conclusions (Davis et al., 2016). Meanwhile, there is evidence that CM is particularly effective. In another review of randomised controlled trials (Cooper et al., 2015), CM, CBT, and MI/MET were all found to be more effective than a wait list and other similar no intervention control treatments.

1.4 – Treating cannabis misuse in psychosis

In contrast to the clear benefit in populations without comorbidity, in psychosis there is currently very limited evidence for any intervention being more effective than Treatment-As-Usual. In a systematic review of psychotherapy for cannabis use, Cooper and colleagues (2015) identified 26 studies in non-psychiatric populations and found good evidence that longer courses of CBT (4-14 sessions) especially benefited patients compared to Treatment-As-Usual. However, the authors failed to find similar evidence in the seven studies they identified targeting psychiatric populations. Randomised controlled trials delivering CBT compared to either Treatment-As-Usual or a brief motivational interviewing treatment to populations with comorbid severe mental illness or major depressive disorder all failed to find a beneficial effect on substance use outcomes in psychiatric populations.

Similar results were found by a Cochrane review (Hunt et al., 2013) of randomised controlled trials of interventions for substance misuse in severe mental illness, last updated in 2013. It identified 32 trials (n=3165), which included a range of psychosocial interventions including CBT, motivational interviewing, and skills training, as well as intensive case management and long-term integrated care. The authors conclude that
there is little evidence supporting any particular intervention over Treatment-As-Usual.

Other systematic reviews have produced similar conclusions (Jeffrey et al., 2004; Rygaard Hjorthøj et al., 2014; Bradizza, Stasiewicz, & Dermen, 2014).

Two of the larger trials conducted to date were performed in the UK by Barrowclough and colleagues (2010; 2014). The first of these (MIDAS; 2010) (N=327) tested CBT and MI with standard care compared to standard care alone. The experimental group received up to 26 therapy sessions over one year. The treatment sought to ‘build motivation’ early in treatment through selectively eliciting and reinforcing ‘change talk’ using MI. This phase of treatment had three goals: to engage patients, to identify and understand their life goals, and thirdly to explore their perspectives on both their substance misuse and mental health in relation to those goals. But despite a fairly intensive and lengthy intervention, no improvement was found on most clinical outcomes including frequency of use, perceived negative consequences of use, or severity of psychotic illness and global functioning. Although there was a slight reduction in the quantity used on cannabis using days, and improved readiness-to-change. The second trial (2014) delivered a similar intervention targeting FEP, and again demonstrated little benefit.

The evidence that psychosocial interventions are effective for cannabis misuse in non-comorbid populations, but not ones with severe mental illness highlights the relative difficulty of treating misuse in this cohort. In their systematic review, Bradizza and colleagues (2014) point to this difficulty and argue that it may be that devising an effective intervention for substance misuse in severe mental illness will require tailoring treatment to the cognitive-behavioural characteristics of that population. They argue that CM may be effective where other interventions are not due to it being less cognitively demanding. Equally, it may help address the motivational ambivalence that appears to often be a
barrier for this cohort. Some studies have tested CM, and so far it is unusual in demonstrating a treatment effect.

1.5 – Contingency Management as a psychological treatment for cannabis use

1.5.1 – Background and principles

CM is a psychotherapy in which abstinence from substance use is reinforced using incentives. In most cases, CM treatment involves the delivery of a financial reward such as a voucher or cash. However, some CM interventions have employed punishments. For example, the patient may be required to risk their own money, which is lost each time they are found to have used substances. CM was originally developed based on operant-conditioning principles. Operant conditioning is a form of behaviorism, along with classical conditioning, and was originally developed by B. F. Skinner. In both classical and operant conditioning models, behaviour is conceptualised in terms of a stimulus-response model, which does not posit internal or psychological states. As the classical behaviorist John Watson said: ‘Psychology as the behaviorist views it is a purely objective experimental branch of natural science. Its theoretical goal is the prediction and control of behaviour.’ (Watson, 1913).

In classical models of conditioning, the animal or person was viewed as a passive agent, subject to the influence of its environment. In a series of famous experiments, Pavlov (1960) demonstrated that dogs could be conditioned to have a desired response to a neutral stimulus, i.e. one that that would not typically elicit that response. In the experiments, researchers would ring a bell whenever they fed the dogs being studied. Over time, the dogs would salivate whenever they heard the bell being rung. In this sense, the dogs were conditioned to give a desired response (salivation) to a neutral stimulus (the sound of the bell), which would normally only have been elicited by a potent stimulus (food).
By contrast, in operant conditioning the subject is viewed as an active agent who interacts with their environment (Schacter, Gilbert, & Wegner, 2011). Through positive or negative reinforcers, behaviours are increased and strengthened, or decreased and eventually extinguished. To demonstrate these effects, Skinner proposed an experimental chamber (named the Skinner box), which typically featured levers or bars that produce a stimulus when activated. A rat or pigeon in this chamber would learn from interacting with its environment that activating the lever would produce a response, which was either positive (e.g. food) or negative (e.g. an electric shock). These stimuli would condition the animal either to repeat its behaviour (positive reinforcer) or stop (negative reinforcer).

The Skinner box allowed researchers to study closely how operant conditioning shaped behaviour. One of the main phenomena Skinner studied was how different reinforcement schedules affected learning (Ferster and Skinner, 1957). He found that continuous reinforcement (the reinforcement is delivered every time the lever is pressed) tended to produce relatively rapid learning, but also led to quick extinction (the behaviour stopping) once reinforcement was halted. A schedule that varied the ratio (the number of lever presses required for the reinforcer) or interval (period of time between reinforcer) tended to produce fast learning times, but also slower extinction rates.

In the 1960’s, these principles were adapted for treatment of substance misuse by developing CM. The earliest research into the benefits of CM addressed alcohol use and adherence to treatment (Gallant et al., 1968). However, since then a broad range of substances and other health related behaviours have been targeted (Higgins & Petry, 1999). As a form of operant conditioning, it was conceptualised as featuring a three-term contingency (Ardila, 2015):

1) The antecedent or discriminative stimulus: the participant is enrolled into a CM treatment and provided with a copy of its rules.
2) The operant behaviour: the participant demonstrates abstinence from substance use, normally biometrically.

3) Its consequent reinforcer: the participant is given the financial reward or punishment.

1.5.2 – Evidence supporting Contingency Management

Since its development in the 1960’s, a significant evidence base has been amassed demonstrating the effectiveness of CM across a variety of cohorts and behaviours (Giles et al., 2014; Cooper et al., 2015). Given the evidence base in relation to substance misuse, the National Institute for Health and Care Excellence (NICE) (2007) has recommended that drug services introduce CM programmes to treat substance use and promote engagement since their 2008 guidance. In their supporting systematic review, CM was found to be more effective than control or CBT for reducing use for all substances considered during the treatment period, but was no better than CBT at follow-up. Included in the review were 14 studies, of which three were related to cannabis use. Other drugs targeted by studies in the review included cocaine, opiates, and methamphetamine.

Other systematic reviews of CM typically find similar results (Hjorthøj, Fohlmann, & Nordentoft, 2009; Dutra et al., 2008). Since the NICE (2007) guidelines were released, a number of trials of CM for substance misuse have been published. Davis and colleagues (2016) identified 69 trials published between 2009 and 2014. 59 of those studies reported significant treatment effects for CM for substance misuse during the intervention period. Substances included tobacco, alcohol, cocaine, methamphetamine, cannabis, and opioids. Studies featured a broad range of populations, including people with substance dependence, pregnant women, mental illness, and sexual minorities amongst others. Since the end of 2014, numerous further trials of CM have been published, which have targeted a range of behaviours including abstinence in alcohol use disorders (Barnett et al., 2017);
cocaine (Carroll et al., 2016; Miguel et al., 2016); cocaine use in opiate dependency (Blanken et al., 2016); cannabis use disorders (Budney et al., 2015; Schuster et al., 2016); tobacco in adolescents (Morean et al., 2015; Reynolds et al., 2015; Stanger et al., 2015), homeless populations (Carpenter et al., 2015), and alcohol dependency (Cooney et al., 2017); polysubstance use (Rash et al., 2017); as well as engagement with substance misuse treatment (Fitzsimmons et al., 2015; Rash et al., 2017) and cognitive remediation training (Kiluk et al., 2017). Of these studies, all reported significant benefits associated with CM treatment, either as a standalone intervention or as an adjunct to other treatment, often psychotherapy (e.g. CBT) or medication. In a recent meta-analysis of CM for non-prescribed substance use during opiate treatment (Ainscough et al., 2017), 22 studies were included featuring 2,333 participants in total. CM treatment was associated with a substantially higher proportion of cannabis negative urines compared to Treatment-As-Usual by intervention cessation when the effect was pooled across all substances targeted including cocaine, opiates, tobacco, and poly-substance use (standardised mean difference = 0.41, 95% CI 0.28, 0.54).

1.5.3 – Contingency Management in psychosis

Compared to the substantial evidence base for CM in other populations, there have been relatively few randomised controlled trials of CM for health-related outcomes in psychosis. However, there is currently some evidence for CM having a beneficial effect in psychosis on smoking rates (Roll et al., 1998; Tidey et al., 2011; Gallagher et al., 2007; Bennett et al., 2015; Bradizza, Stasiewicz, & Dermen, 2014); alcohol use (Tracy et al., 2007) and screening rates (Khadjesari et al., 2016); treatment adherence including to antipsychotic medication (Priebe et al., 2013) and psychotherapy/counselling (Drebing et al., 2005); exercise (Thyrer & Irvine, 1984); and substance use (Tracy et al., 2007; Messina, Farabee, & Rawson, 2003; McDonell et al., 2013; Roll, Chermack, & Chudzynski, 2004; Shaner et al., 1997; Bradizza, Stasiewicz, & Dermen, 2014). In one relatively large, UK based trial (FIAT), Priebe and
colleagues (2009; 2013) conducted a cluster randomised controlled trial (N=141) of CM compared to Treatment-As-Usual for adherence to depot antipsychotic treatment. In the experimental group, adherence rose from 67% to 85%, with an adjusted effect estimate of 11.5%. In another trial (McDonell et al, 2017), CM for alcohol use in psychosis was compared to CM for study participation. However, the sample size was fairly small (n=79). The authors report a significant effect for CM for abstinence. Of the randomised controlled trials that have been conducted, none have focused on cannabis in psychosis.

There have been a few studies that have targeted cannabis use to some extent. Bellack and colleagues (2006) performed a randomised controlled trial (n=129) in the US of CM combined with MI for substance dependence in people with severe mental illness and major affective disorders. The results of the study showed an increase in drug free urines and quality of life, as well as a reduction in hospital admissions. However, participants used a variety of substances, which included cannabis (7%) as well as opioids (24.6%) and cocaine (68.6%), and only 38.3% of participants had schizophrenia or schizoaffective disorder while 54.9% had affective disorders. So overall it offers very little evidence that CM is effective for cannabis use in psychosis. The only other studies were not randomised controlled trials. These include two small feasibility studies (Sigmon et al., 2000; Sigmon & Higgins, 2006). Both used a crossover (A-B-A) design and featured a treatment period of either 12 or 15 weeks. However, between them they only included 25 participants. Although small, both studies reported that CM significantly reduced cannabis use during the treatment phase. Beyond these three, no other published studies of CM for cannabis use in psychosis could be identified from literature searches.

The present thesis was conducted in the context of the CIRCLE trial. CIRCLE was a randomised controlled trial testing the clinical and cost effectiveness of CM for problematic cannabis use in Early Intervention in Psychosis (EIP) service users (the protocol of the study
is presented in Johnson et al., 2016, contained in appendix 3.1). In it, CM was delivered alongside an optimised version of treatment as usual that comprised a structured psychoeducational package. The control group received the Treatment-As-Usual package only. The CM intervention comprised 12 once weekly sessions, during which participants were asked to submit samples for urinalysis to demonstrate that they had not used cannabis in the previous week. Chapter 3 presents the study design and methods of the CIRCLE trial, and chapter 5 presents its results.

1.6 – Motivation and the cognitive-behavioural mechanism underlying substance misuse

Relapse Prevention is a cognitive-behavioural approach to understanding and reducing the likelihood and severity of relapse following cessation or reduction of substance misuse behaviours (Hendershot et al., 2011). It has been a mainstay of addictions theory and treatment since its introduction almost four decades ago when Marlatt’s model of Relapse Prevention (Marlatt & Gordon, 1980) was introduced. Marlatt published an updated model (figure 1.1) in 2004 (Witkiewitz & Marlatt, 2004), reflecting developments in Relapse Prevention literature since the original. This model proposes tonic (stable) and phasic (transient) processes. Tonic processes include distal risks, which are stable background factors related to relapse, such as family history, social or peer support, and dependence severity. Other tonic processes include relatively stable cognitive factors, including motivation, self-efficacy, use expectancies, and withdrawal severity. Phasic processes are momentary or proximal responses to one’s environment and other factors. These include transient cognitive and affective processes, such as urges and cravings, or fluctuations in mood, outcome expectancies, self-efficacy, and motivation. Other phasic processes include the coping strategies used to avoid relapsing when other processes significantly increase the likelihood of doing so, such as resolving negative affective states without using.
Immediate consequences of substance use, such as impaired decision-making, are additional phasic processes that occur immediately following a lapse. In summary, while tonic processes can determine who is vulnerable for relapse, phasic processes largely determine when relapse occurs.

Figure 1.1 - Witkiewitz and Marlatt’s (2004) cognitive-behavioural model of relapse

A key feature of this model is its emphasis on the interactions between tonic and phasic processes being nonlinear and dynamic (Hendershot et al., 2011). Distal risks, for example, may influence relapse either directly or indirectly via phasic processes, so the influence of a phasic factor may vary based on the presence and severity of distal factors. Feedback loops are also possible, for example if someone relapses because of transient cognitive or affective states, this can have reciprocal effects on the same cognitive or affective factors, further altering the likelihood of future use. Thus the model postulates that relapses are the result of complex relationships between a range of cognitive-behavioural, as well as genetic, physiological, environmental, and social factors. Within this, paths to relapse can take various forms. Momentary and unpredictable influences can cascade and result in a
sudden and unexpected return to use. Alternatively, relapse can occur through a deliberative and conscious decision (Hendershot et al., 2011).

Of these domains, cognitive processes are the most important component for this thesis. Amongst those included in the model, some of the best investigated are motivational factors. Reducing ambivalence or improving Intrinsic Motivation (IM) to abstain is a central component of a number of psychotherapeutic interventions for substance use, such as MI and MET. Other cognitive factors include self-efficacy, readiness-to-change, cravings, and drug use outcome expectancies (Hendershot et al., 2011). The following sections will discuss the evidence for the role of each of these factors in understanding substance misuse and abstinence.

1.6.1 – Motivation

There is emerging evidence that self-reported motivation to quit at baseline is significantly associated with smokers making a quit attempt (Smit et al., 2014), and with whether a smoking cessation attempt is successful (Caponnetto & Polosa, 2008). There is also good evidence that initial motivation to quit is associated with abstinence both during and after treatment (Mushtaq, Boeckman, & Beebe, 2015; Pineiro et al., 2016; Thomas et al., 2015). A systematic review of factors associated with quitting cigarette smoking (Vangeli et al., 2011), found that motivational factors were the most important predictors of making a quit attempt.

Meanwhile, two specific components of motivation are often identified. Extrinsic motivation (EM) is conceptualised as originating from a source external to the target behaviour. In the case of substance use abstinence, types of EM include quitting due to pressure from one’s family or peers or because of concerns about legal repercussions. In both cases, the person is abstaining for reasons that are indirectly related to (or are external to) their substance use (e.g. to avoid legal problems) rather than for reasons
intrinsic to substance use itself. In the context of CM, behaviour change is motivated by financial rewards rather than the negative consequences arising from the patient’s substance use itself (DiClemente, 1999).

EM is contrasted with IM. IM is the form of motivation that is internal to the individual. In one particularly influential paper by Ryan and Deci (2000), it is defined as the ‘natural inclination toward assimilation, mastery, spontaneous interest, and exploration that is so essential to cognitive and social development and that represents a principal source of enjoyment and vitality throughout life.’ It refers to motivation that originates directly in relation to the desired object or goal: to situations in which a person is motivated to achieve a goal or complete a task for its own sake. For many people, this will be using substances, performing tasks, playing games, or engaging in hobbies because they enjoy them. In the context of abstinence from substance use, a person is intrinsically motivated to abstain if the direct consequences of doing so incentives them. Such situations can include if the person wants to quit because they have negative use expectancies (for example, that they do not enjoy the intoxicating effects of the substance), that it will help them feel more in control of their use, or it will improve their self-esteem.

In a review of predictors of successful abstinence from smoking, Caponnetto and Polosa (2008) found that both IM and EM may be enough to initiate behaviour change. However, they also found that IM has been associated with sustained changes in health behaviours, including involvement in addiction treatment. Longitudinal studies found that higher levels of IM relative to EM predict smoking cessation among self-selected, volunteer samples of smokers seeking assistance in quitting and in a general population sample of smokers. Moreover, there is evidence that a high IM relative to EM being associated with more sustained quit attempts. In a paper reporting on 98 students receiving treatment for cannabis abuse, greater IM to use cannabis (measured as positive use expectancies) was
associated with substantially lower levels of abstinence by treatment end (Buckner, Walukevich, Lemke & Jeffries, 2018). However, these studies primarily contain data from objective measures of IM, namely substance use post-treatment, which are much more widely available (Promberger & Marteau, 2013).

A small but growing body of literature provides data on the association between self-reported measures of IM and outcomes of psychotherapy for substance use or mental health conditions. Shamloo and Cox (2010) reported that in a study of university students (n=94) who drank alcohol (but were not dependent), greater self-reported IM to abstain was associated with lower alcohol consumption in the week prior to assessment. Furthermore, IM at treatment end was associated with lower future use (Curry et al., 2001). This effect has been found across a range of substances, including cannabis (Chauchard et al., 2013), as well as alcohol (Shamloo & Cox, 2010), and tobacco (Moadel et al., 2012; Thomas et al., 2015).

There is now also good evidence that that higher self-reported IM at baseline is associated with higher adherence to treatment (Ryan, Plant, & O’Malley, 1995; Moadel et al, 2012; Gaitan-Sierra & Dempster, 2016), lower during-treatment use (Chauchard et al., 2013; Ryan, Plant, & O’Malley, 1995; Curry et al., 2001; Moadel et al., 2012; Shamloo & Cox, 2010), as well as post-treatment abstinence (Thomas et al., 2015). In two other studies of patients without severe mental illness, IM predicted treatment adherence (Alfonsson, Olsson, & Hursti, 2016) as well as abstinence at 3 months post-treatment, while EM predicted urinalysis outcomes for cannabis at treatment end and at 3 months (Alfonsson, Olsson, & Hursti, 2016). IM factors, including self-image and health concerns, are some of the most strongly predictive of treatment uptake (Aschbrenner et al., 2015; Guimond et al., 2016; Laudet & Stanick, 2010) and successful abstinence (Hughes et al., 2015). Beyond these, other specific motivational factors found to significantly predict successful quit
attempts include financial concerns (Hughes et al., 2015), social acceptability (Twyman et al., 2014), and social/peer influence (Aschbrenner et al., 2015; Hughes et al., 2015).

1.6.2 – Self-efficacy

Self-efficacy (the perceived ability to achieve and maintain a target behaviour) has been demonstrated to be a predictor of treatment outcome. In a systematic review of evidence related to self-efficacy, Kadden and Litt (2011) concluded that there was good evidence that it predicted the quantity and frequency of use. Meanwhile, participants’ self-efficacy has been found to be lower on the day before a lapse and that lower self-efficacy in the days following a lapse predicts progression to relapse (Shiffman, 2000), while self-efficacy rose during periods of abstinence, likely reflecting increasing confidence as abstinence was maintained (Gwaltney, Shiffman, & Sayette, 2005). These findings suggest that, consistent with Bandura (1977) seminal paper, there is a close relationship between self-efficacy and actual use. In this paper, Bandura proposed a model of addiction that suggested four kinds of self-efficacy: enactive mastery, verbal persuasion, vicarious experience, or physiological state (i.e. one’s monitoring of one’s own internal state in stressful situations). Of these, the model suggests that substance misuse treatment is effective and durable to the extent that it increases expectations of personal efficacy, which occurs when patients have successful coping experiences (Litt, Kadden, & Petry, 2013).

1.6.3 – Readiness-to-change

Another important construct in the treatment of substance use disorders, and which has a substantial evidence base, is readiness-to-change, or the degree to which an individual is motivated to change problematic behaviour patterns (Carey et al., 1999). DiClemente and Prochaska (1998) provided a model of readiness-to-change that offers a framework for understanding the cognitive-behavioural stages involved in engendering change. Many structured psychosocial interventions, including MI and MET, support patients’ progression
through the stages of the readiness-to-change model as a central component (Rollnick & Miller, 1995). In the context of substance use, greater readiness-to-change has been found to be associated with being more likely to quit; users in early stages in the model, such as the pre-contemplation stage, are substantially less likely to make an attempt to quit than users in the later stages, such as preparation or contemplation stages (Martinez et al., 2015; Smit et al., 2014). Readiness-to-change has also been found to be significantly related to current substance use (Gossop, Stewart, & Marsden, 2007), and treatment outcomes in a systematic review of 39 studies (Norcross, Krebs, & Prochaska, 2010). Furthermore, in a population with schizophrenia, readiness-to-change was associated with smoking reduction in schizophrenia (Wu & Lan, 2015).

1.6.4 – Social support

Although not a cognitive process, a person’s social environment is an important component of relapse, and one that a patient may look to change as part of substance use therapy. The initiation, maintenance, and cessation of smoking is strongly associated with social environment. Social pressure, particularly from people whose opinion they value, is often strongly associated with desire to quit and making a quit attempt. Having good social support, especially from family members, makes a quit attempt more likely to be successful, but the number of smokers in the household has a negative relationship with likelihood of success (Norberg et al., 2016). Amongst cannabis users, environmental cues, such as exposure to peers using cannabis, were the most important factor identified in a systematic review of predictors of relapse (Norberg et al., 2016). Use amongst peers has also been identified as a strong predictor of initiation of cannabis use (Miller & Miller, 1997), as well as incident use (i.e. not associated with use disorders) (Galea, Nandi, & Vlahov, 2004).
1.6.5 – Cravings

Finally, frequency and severity of cravings were associated with current use status in several studies, both during and following treatment (Hartz, Frederick-Osborne, & Galloway, 2001; Pombo et al., 2016; Witkiewitz & Bowen, 2010). In a recent study, Zvolensky and colleagues (2018) explored barriers to quitting amongst cannabis users. They found that greater perceived barriers for quitting cannabis were uniquely associated with cannabis use problems, greater withdrawal symptoms, and lower self-efficacy for quitting. The authors conclude that perceived barriers for cannabis cessation may help in better understanding an array of clinically significant cannabis use processes. Amongst smokers, Gökbayrak and colleagues (2015) found that habit strength (severity of smoking) predicted whether patients would relapse, but stage of change did not. There is a growing body of evidence indicating that cravings and urges are associated with relapse (Smit et al., 2014; Riaz et al., 2016), and instances of substance use were found to be predicted by a rise in cravings in the hours before (Hopper et al., 2006). Increase in cravings is also associated with a number of possible cues, including media messages or exposure to use amongst peers (Hagger et al., 2013).

1.6.6 – The cognitive-behavioural characteristics of populations with psychosis and their relationship with substance misuse

The previous sections discussed the literature regarding factors associated with relapse in substance misuse in the general population. However, psychotherapy is generally much less effective in populations with psychosis than in non-psychiatric ones. Reasons for this are currently unclear. But as suggested by Bradizza and colleagues (2014) and DiClemente and colleagues (2008), it could be due, at least partially, to this population having distinct characteristics compared to other, more treatment responsive groups that limit the success of therapy. As such, when considering how to improve substance misuse treatment in this
cohort, it is important to consider how this cohort differs from the general population and how that may affect treatment outcomes.

Bradizza and colleagues (2014) point to research that explores the therapeutic processes associated with effective MI. They state that it is currently not known whether those can be successfully replicated in a population with severe mental illness and substance misuse problems. An example of this is, they say, that MI should lead to increased change talk. However, it is unclear whether this happens with patients with comorbid severe mental illness, or whether increased readiness-to-change is associated with them then reducing their substance use. These are crucial components of MI. If psychotherapy fails to impact them, it perhaps suggests a more fundamental problem of delivering such treatment to this population.

1.6.6.1 – Cognitive functioning

Bradizza and colleagues (2014) also argue that this failure of treatment may be at least partially attributable to the deficits in cognitive functioning associated with schizophrenia, such as poorer episodic memory and processing speed amongst other areas. These deficits may affect the extent to which patients can benefit from psychotherapy, and especially relatively complex therapies such as MI and CBT. DiClemente and colleagues (2008) also suggest that the limited successes of psychotherapy could be attributable to the nature of psychotic symptoms and the cognitive deficits sometimes present in the condition. These they argue may affect the process of behavioural change in this population, as such change requires decision-making, intentionality, commitment, planning, and self-evaluation (including self-efficacy). But in severe mental illness, these may be more difficult to achieve. Bergman and colleagues (2014) meanwhile report that there is evidence that this cohort, compared to non-comorbid populations, tend to employ less adaptive coping strategies and have poorer overall social functioning (Bergman et al., 2014; Boden & Moos,

Such factors may mean that participants with severe mental illness find it more challenging to engage with interventions, to engender behavioural change, have poorer social support to help them achieve their goals, or be less likely to use coping, Relapse Prevention, and harm reduction strategies effectively.

However, cognitive function deficits also appear to limit the successfulness of psychotherapy by impoverishing adherence to treatment in the population. In a systematic review (n=122 papers) of predictors of adherence to addiction treatment, Brorson and colleagues (2013) found that the presence of cognitive function deficits, comorbid personality disorders, and younger age were important predictors of dropping out of treatment. A total of 11 (9%) of the included papers explored the relationship between cognitive function and drop-out, and all reported evidence of an association between the two variables, with lower cognitive functioning always resulting in higher dropout.

1.6.6.2 – Motivation and functioning

Another concern is the relatively poor motivation and functioning in this population. DiClemente and colleagues (2008) and Priester and colleagues (2016), both suggest that greater disorganisation, poorer social interaction skills, and lower motivation and energy levels (perhaps partially attributable to medication) are common in this group and are likely to pose significant barriers to psychosocial intervention for substance misuse being effective. Motivational deficits have long been associated with psychotic illness, having first been identified as part of the disorder by Bleuler and Kraepelin (Luther et al., 2015).

Currently, there is evidence that amotivation in psychosis is strongly associated with poorer global functioning (Fulford et al., 2017) and is particularly diminished in patients with greater negative symptoms (Luther et al., 2015). Deficits in motivation are associated with reduced autonomy, self-efficacy, relatedness (feeling of connectedness with others), and
goal-directed behaviour (Luther et al., 2015; Fulford et al., 2017). Consequences of this include reduced engagement in work and education, and poorer social functioning (Fulford et al., 2017). Moreover, in a systematic review of barriers to smoking cessation, Twyman and colleagues (2014) found that people with Severe Mental Illness (SMI) had poorer motivation to quit, and that people with lower levels of motivation to quit were more likely to have poorer treatment outcomes.

Furthermore, the problem of amotivation in people with psychosis limiting the effectiveness of therapy is likely to be made worse by heavy cannabis use. Long-term, heavy cannabis use is also known to reduce motivation, as well as negatively affecting users’ ability to learn and maintain attention (Volkow et al., 2016). Likely mediated by these effects, heavy cannabis use has been associated with poorer educational and functional outcomes. Poorer motivation and educational or functional outcomes are thought to be attributable both to the neurobiological effects of cannabis (particularly THC), and to using cannabis becoming a major motivator for patients, such that patients use instead of engaging in other activities (Volkow et al., 2016).

IM is believed to be especially problematic in psychosis. There is good evidence that it can be substantially poorer in people with psychosis, and its diminishment has been strongly associated with overall amotivation and severity of negative symptoms (Kremen et al., 2016). As such, some believe that reduced IM is the primary component driving poorer overall motivation in the illness (Kremen et al., 2016; Luther et al., 2015). Furthermore, while in non-psychiatric populations IM is an important predictor of abstinence, this relationship appears not to be as robust in populations with severe mental illness; although the availability of data is limited. In a study involving a smoking cessation programme for people with schizophrenia, post-treatment tobacco use was not predicted by self-reported IM, self-efficacy, or overall motivation (Mann-Wrobel et al., 2011).
Evidence regarding the cognitive functioning, functional, and motivational deficits in psychosis can plausibly explain (at least partially) the lack of success in this group of otherwise effective psychotherapies. Furthermore, these deficits are likely to be further exacerbated by heavy cannabis use (DeRosse et al., 2010). Of particular concern is the lack of a relationship between IM and substance use abstinence, which suggests that IM plays a much less important role in treatment outcomes in this population than non-psychiatric ones. It may be that more needs to be done to adapt current formal psychosocial treatments to this cohort, or perhaps new treatments are required that are more tailored to the cohort’s unique characteristics.

1.7 – The cognitive-behavioural model for Contingency Management

As discussed in chapter 1.5, CM was originally developed based on operant conditioning principles (Higgins & Petry, 1999). Operant conditioning paradigms include only directly observable phenomena and do not posit psychological states (Watson 1913). As such, CM has traditionally been conceptualised in terms of a purely behavioural model. More recently, CM has been conceptualised in terms of a cognitive-behavioural paradigm, and as a method of enhancing motivation. As Budney and colleagues (2006) describe: ‘[CM] is a method to enhance and maintain initial motivation to abstain from [substance] use by providing a structure (weekly urine testing) and incentive (vouchers) for doing so’. These models typically view CM as a form of EM as patients are encouraged to quit for a financial incentive rather than for reasons intrinsic to the substance itself. This contrasts with many other structured psychotherapies, such as MI or MET (Rubak et al., 2005). A central aim of these treatments is to improve patients’ IM to change substance use by exploring and resolving patients’ ambivalence around their substance use and building commitment to abstain (Miller & Rollnick, 2002). These therapies focus on evoking the client’s own IM to change their substance use, including their desires, reasons, or needs. Examples of this
include negative experiences of using, health related concerns, or that substance use no longer fits who they want to be.

1.7.1 – A possible limitation of Contingency Management: Does it undermine Intrinsic Motivation?

1.7.2 – Self Determination Theory

Although CM has a strong evidence base, some have argued that any effects are likely to be short-lived, and that the use of financial incentives may reduce patient’s IM to abstain (Petry, 2010).

Deci (1971) argued that if an individual is encouraged to perform a particular behaviour with financial incentives, their IM to perform that behaviour will be undermined. In the context of substance misuse, this would likely result in very short maintenance of abstinence or an increase in substance use following treatment cessation (Petry, 2010). In support of this view Deci and colleagues (1999) published a meta-analysis of 128 studies of the effect of tangible rewards on participants’ IM to perform a study task. For the most part, study tasks were simple, such as completing puzzles or drawing pictures. They conclude that receiving rewards reduced the likelihood that participants would continue performing the task during a ‘free choice’ period following cessation of the rewards. They argue that this is because rewards make participants feel like they are being externally controlled, which reduces their sense of autonomy. Deci and Ryan (2008) argue that CM type interventions are likely to produce only short-lived behavioural change, and that they may undermine any motivation the patient had pre-treatment to adopt healthier behaviours. If correct, even if CM is effective at reducing cannabis use during treatment, its clinical benefits will be limited if it has little impact on long term cannabis use or actually reduces any pre-treatment motivation the patient has to abstain.
However, since the Deci and colleagues (1999) review focused on study tasks like puzzles or drawing, it may be that the finding does not apply to substance abstinence or adopting healthier behaviours. Secondly, another meta-analysis by Cameron and Pierce (1994) of 124 studies (of similar simple tasks to the Deci and colleagues’ (1999) review), found limited, but mixed, evidence that CM undermines IM. In this review, authors considered whether study design mattered: whether the rewards were expected versus unexpected, or whether rewards were offered for attendance to study sessions versus successfully completing the task. Or if reward type was important: verbal versus tangible. The authors found that tangible rewards, whether they were unexpected or performance related, had no effect on the time participants spent on a task once the reward was withdrawn. Meanwhile verbal rewards resulted in participants spending longer on the task after rewards ceased. However, negative effects were found for rewards that were non-contingent upon successful performance. In this case, individuals were found to spend less time on the task than controls once rewards ended.

1.7.3 – An alternative model (Cognitive Evaluation Theory)

An alternative explanation for the effect of CM on IM is proposed by Cognitive Evaluation Theory (Deci & Ryan, 1986). Cognitive Evaluation Theory suggests that rewards only reduce IM when they are perceived as controlling or diminish the patient’s sense of autonomy and could rather improve IM if they increase the individual’s sense of competency or barrier self-efficacy. Barrier self-efficacy, also named self-regulatory efficacy, refers to the patients’ belief in being able to abstain while overcoming barriers to abstinence.

In theory, part of this process may be that CM raises overall motivation to abstain during treatment and does so sufficiently to resist or change certain barriers to abstinence, including urges or cravings, withdrawal symptoms, or social cues. For example, amongst cigarette smokers, the Center for Disease Control and Prevention (CDC) estimates that
around 70% of smokers want to quit, but that only 6% are successful during a particular quit attempt (CDC, 2017), and that smokers will make over 6 quit attempts on average before being successful (Chaiton et al., 2016). Amongst cannabis users, Curran and colleagues (2016) found that 50% of people who met the criteria for cannabis dependency reported withdrawal symptoms such as craving, sleep problems, nightmares, anger, irritability, dysphoria and nausea (Gates, Albertella, & Copeland, 2016; Lee et al., 2013; Levin et al., 2010). Around 40% of those with withdrawal symptoms reported using to avoid those symptoms (Coffey et al., 2002; Levin et al., 2010). CM may benefit recently abstinent individuals by providing short term EM (Budney et al., 2006). Given a sufficiently long period of treatment, it may be that these other barriers to abstinence will diminish. This may potentially either have no substantial impact on IM or could improve patients’ confidence in being able to remain abstinent (their self-efficacy) and thereby help bolster IM to abstain. There is evidence of this effect in relation to health, where self-efficacy has been found to mediate the relationship between IM and physical activity, as well as predict IM (Sweet et al., 2012).

1.8 – Evidence regarding the effects of CM for health-related behaviours on IM and its limitations

In a review of literature related to CM for health-related behaviours, Promberger and Marteau (2013) conclude that there is very little evidence that CM undermines IM in such contexts. They found strong evidence in psychological and economic literature for an undermining effect for certain tasks, such as simple tasks like those used in studies reviewed by Deci and colleagues (1999). However, the situation was different for health behaviours. Promberger and Marteau’s (2013) review found that there was no evidence of an undermining effect in studies of financial incentives for cigarette smoking, weight loss, attending screening appointments for sexually transmitted diseases, or blood donations.
While they say there was mixed evidence regarding whether CM encourages long-term behaviour change post-treatment, there was no evidence that CM decreased the likelihood of participants abstaining post-treatment compared to controls. The authors conclude that there is no evidence that CM for health-related behaviours undermines IM.

However, most of the evidence regarding the impact of CM on IM in this review is inferred participants’ behaviour after the rewards end. As described by Marteau and Promberger, in Cognitive Evaluation Theory literature (2013), IM is defined and operationalised as the difference between post-treatment behaviour amongst those who received CM compared to those who did not. This is typically measured as time continuing the behaviour post-treatment. For example, in the case of substance misuse, this is normally measured as time before relapse to substance use. The Deci and Ryan (2008), Cameron and Pierce (1994), and Promberger and Marteau (2013) reviews all measured IM primarily by examining post-treatment behaviour, either in the context of how long participants continued drawing/solving puzzles, or continued the health-related behaviours, such as abstinence. Only the Promberger and Marteau (2013) review assessed the self-reported motivation literature. They report just one paper (Ledgerwood & Petry, 2006) that provides a self-report measure of motivation, which was based on the stages of change model. The authors argue that since there was no measured change in motivation, there was no evidence that IM was undermined.

One difficulty with using post-treatment behaviour to infer IM is that CM trials have historically tended not to have long follow-up periods post-cessation, making assessing the long-term benefit of CM or its effect on IM more challenging. Prendergast and colleagues (2006) suggest that this could be because historically there has been an assumption amongst many researchers that CM alone will only provide benefit during the period of the intervention. As such, evidence is only inconsistently available.
Secondly, by focusing on post-treatment behaviour, researchers may be missing changes to IM caused by CM that are not identifiable in behaviour changes at follow-up assessment. Follow-up assessments are typically up to six months post-treatment cessation, and changes to IM may occur during treatment that are not substantial enough to be reflected in substance use behaviour, or that are not maintained until the follow-up assessment. Alternatively, it may be that changes in behaviour by follow-up are not attributable to CM, but instead are the product of confounding effects from other factors. This issue arises, at least partially, because self-reported measures of IM in CM studies are rare. This is despite several self-reported measures for IM now existing (e.g. McBride et al., 1994). In one of the few studies that has featured such a measure, Tevyaw and colleagues (2009) trialled CM for tobacco use (N=110) and measured self-reported interest in quitting. They found that tobacco use was significantly lower at treatment end in the CM group compared to controls, and that self-reported IM at treatment end was correspondingly higher in the CM group (d=0.44). However, these results did not translate to higher quit rates at 6 months post-treatment, which were no different from controls. Thus, IM may be increased by CM, even if this effect does not last to study follow-up, which are often 6 months or more following treatment for health interventions. Another difficulty with this literature is that much of it comes from CM for tobacco use, and it may not be generalisable to other substances.

The evidence collected to date regarding the long-term benefits of CM has been mixed. The FIAT trial (Priebe, Bremner, & Pavlickova, 2016) found a beneficial effect from CM on antipsychotic medication adherence during the intervention period, but not 6 months or 24 months following treatment cessation. Similar drop offs in effectiveness following treatment have been also reported elsewhere (Kadden, Litt, & Kabela-Cormier, 2007; Litt et al., 2008). However, evidence is mixed, with some studies finding a benefit at 6 months or more post-treatment (Prendergast et al., 2006; Kadden, Litt, & Kabela-Cormier, 2007;
At best, if CM does produce significant benefits following treatment cessation, it is inconsistent and appears to be present in only a minority of trials. In the 69 trials Davis and colleagues (2016) reviewed, 28 included at least one follow-up assessment post treatment. Of these, only eight found a lasting benefit of CM. This could be attributable to IM being undermined during treatment, but it could also be other factors. It may be that IM is not undermined so much as just not improved. Alternatively, as demonstrated by Tevyaw and colleagues (2009), it may be that CM does improve IM, but that this does not translate into abstinence by post-treatment follow-up due to patients failing to maintain abstinence. This may be due to IM not being raised sufficiently to result in improved substance use outcomes by post-treatment follow-up. Alternatively it may be that CM fails to capitalise on this compared to other psychotherapies by not providing patients with the skills to prevent relapse or cope with high risk situations.

1.9 – The present thesis

This thesis contains two programmes of work. It uses a mixed-methods research approach, incorporating both quantitative and qualitative data.

The first programme of research is a process evaluation of the CIRCLE trial. Process evaluation studies aim to understand the functioning of an intervention by examining implementation, mechanisms of impact, and contextual factors (Medical Research Council, 2015). The main focus of this study is the cognitive-behavioural mechanism of impact of the CIRCLE CM treatment. The primary outcome is whether CM improves IM by treatment end. Its secondary aims are to test whether CM improves motivation, self-efficacy, readiness-to-change and other cognitive-behavioural factors. The qualitative component of this study aims to explore what participants’ experiences of CIRCLE and its treatments are.
The second programme of work addresses the question of how to improve treatment for cannabis use in this cohort. Its specific aims are to examine:

1) whether adding another psychotherapy to CM improves substance use outcomes,

2) what participants’ reasons for wanting to quit cannabis are and what cognitive-behavioural factors predict cannabis use at treatment end.

3) participants’ experiences of and perspectives on quitting cannabis, including the barriers and facilitators of quitting, as well as their main motivations for quitting.

Contained in this thesis is a systematic review, two quantitative studies, and two qualitative studies:

1.9.1 – Chapter 2

Chapter 2 presents the systematic review, which evaluates whether there is a synergistic relationship between CM and other formal structured psychotherapies, such as CBT, as has been hypothesised by some authors (e.g. by Litt et al., 2008; Litt, Kadden, & Petry, 2013; Carroll et al., 2012). It is expected that the combination of the two will result in lower substance use outcomes, both at treatment end and at post-treatment follow-up, than either intervention alone. This is expected to occur because CM is effective at encouraging engagement with treatment and motivation to abstain during treatment by incentivising these behaviours. Meanwhile, interventions such as CBT or MET are better at facilitating long-term abstinence by providing patients with greater motivation to change and by giving them the tools to cope with the affective, cognitive, and environmental cues to relapse. Thereby the two intervention types offer complementary mechanisms of action that when combined provide a more effective intervention than either standalone treatment. Several studies have now been published that have compared CM as a standalone intervention to CM combined with another psychotherapy, typically CBT or MI. However, so far there have
been no systematic reviews focused on whether combining CM for substance misuse with another psychotherapy is better than CM alone.

1.9.2 – Chapters 3 and 5

Chapter 3 presents the study design and methods of the CIRCLE trial. This provides context to subsequent chapters by briefly presenting details of the CIRCLE trial. As the cognitive-behavioural process evaluation was designed during the CIRCLE trial, the methods and study design of that study are described in chapter 4. The results of the CIRCLE trial are presented in chapter 5.

1.9.3 – Chapters 4 and 6

Chapter 4 presents the study design and methods of a quantitative study investigating a hypothesised mechanism of action of the CIRCLE CM treatment. The results of this study are presented in chapter 6. Along with the qualitative study presented in chapter 7, this study is the process evaluation of the CIRCLE trial.

A number of key cognitive-behavioural constructs were considered, including: intrinsic and extrinsic motivation, self-efficacy, readiness-to-change, urges, and exposure to cannabis using peers. The primary analysis examined the effect of CM on IM, which, as described in chapter 1.7, some have argued is either not impacted or may perhaps be undermined by CM, and consequently CM is unlikely to have a long-term beneficial impact on behaviour. The aim of this study is to explore whether this hypothesis is true in the context of substance use in psychosis. It is hypothesised that the CM intervention will increase participants’ IM to abstain by treatment cessation (3 months post-study inclusion).

Secondary analyses considered the effect of CM on other dimensions of motivation, including EM and self-efficacy, as well as readiness-to-change, the frequency and severity of cannabis use urges, and exposure to social cues (i.e. cannabis using peers). The aim of the secondary analyses is to explore the mechanism of action of CM, and so help develop a
model of CM and its impact on behaviour and motivation to abstain in psychosis and comorbid cannabis use. As mentioned, some have suggested that CM will undermine IM to abstain. However, others (chapter 1.7) have suggested that CM may rather improve IM by increasing participants’ self-efficacy in being able to abstain and/or by helping to reduce participants’ ambivalence about substance use. The analysis in this chapter will help explore these possibilities. Its aims are to test whether, by treatment end, CM: 1) increases participants’ IM to abstain from cannabis (primary outcome); 2) increases EM; 3) reduces frequency and severity of cravings; 4) reduces exposure to cannabis use by family members and peers; 5) increases readiness-to-change; and 6) increases overall motivation and self-efficacy. Secondly, it will consider these same outcomes at 18 months post-randomisation.

1.9.4 – Chapter 7

Chapter 7 presents a qualitative study that explores participants’ experiences of the CIRCLE CM and control treatments. This is a complimentary analysis to chapter 4 and helps to explore how participants view the benefits or negatives of CM as well as its cognitive-behavioural mechanism of action. The aims of this work include to explore the perceived impact of the CM on participants’ cannabis use, what in the treatments was helpful or unhelpful, and how participants felt they affected their motivation and other barriers and facilitators for abstaining (such as spending time with cannabis using peers). Secondly, to consider the acceptability of it as a treatment, and thirdly to consider whether it is more beneficial to receive CM as a standalone treatment or in conjunction with another psychotherapy.

1.9.5 – Chapter 8

Chapter 8 presents quantitative data investigating participants’ reasons for wanting to quit cannabis and predictors of cannabis use. There is currently a body of published research on why people with psychosis use cannabis, but very little on their reasons for wanting to quit.
The aim is to explore what the reasons for wanting to quit cannabis are amongst people with psychosis. Secondly, this study investigates baseline predictors of cannabis use at treatment end to explore potentially effective therapeutic cognitive-behavioural targets in this group. The aim is to identify potential therapeutic targets for treatment by exploring baseline cognitive-behavioural predictors of cannabis use at treatment end. Hypotheses include that mental health concerns (Copersino et al., 2006) and the prospect of receiving the financial rewards (due to the CIRCLE CM intervention) are hypothesised to be the primary reasons participants give for wanting to quit in this group. Secondly, that higher motivation, including intrinsic and extrinsic measures, readiness-to-change, cannabis urges, and exposure to cannabis use will predict cannabis use at treatment end.

1.9.6 – Chapter 9

Chapter 9 presents qualitative data exploring participants’ experiences and perspectives on quitting cannabis. Its aims are to explore participants’ views of effective treatment for cannabis use, reflecting on what was helpful and unhelpful about the treatments they have received in the past. Secondly, to explore the barriers and facilitators to quitting cannabis, in terms of support from friends and family, cognitive-behavioural factors (such as motivation and cravings), as well as other topics participants felt were important. Thirdly, to examine participants’ attitudes towards cannabis, including extent and patterns of use and changes to motivation, social relationships, and lifestyle during the treatment period and since treatment cessation.
Summary of research aims:

1) To conduct a systematic review of whether combining CM with another formal psychotherapy improves substance use outcomes by either treatment end or follow-up compared to CM alone (chapter 2).

2) To investigate a hypothesised cognitive-behavioural mechanism of action for the CIRCLE CM treatment with quantitative data.
   a. The primary analysis investigates whether the CIRCLE CM intervention improves IM compared to controls by treatment end.
   b. Secondary analyses include whether at treatment end or post-treatment follow-up, CM: 1) increases EM to abstain from cannabis; 2) increases overall motivation and self-efficacy; 3) increases readiness-to-change; 4) reduces exposure to cannabis use by family members and peers; and 5) reduces frequency and severity of urges (chapters 4 and 6).

3) To perform a qualitative process evaluation of the CIRCLE trial from the perspective of participants who were allocated to the experimental (receiving CM) group. This will explore participants’ views of the CM and psychoeducation treatments, including the acceptability and efficacy of the treatments (chapter 7).

4) To investigate the process of cognitive-behavioural change underlying abstinence from cannabis in a cohort with early psychosis. This will firstly explore participants’ reasons for wanting to quit cannabis, and secondly aim to identify baseline predictors of cannabis use status at treatment end and at post-treatment follow-up. It is hypothesised that:
   a. The most important reasons for quitting in this cohort are mental health concerns and cannabis use expectancies.
   b. Higher intrinsic motivation, self-efficacy, and readiness-to-change, as well as less severe (frequency and strength) cravings and less time spent with other cannabis users will each be associated with a greater likelihood of being abstinent at treatment end (chapter 8).

5) To explore the process of change associated with quitting cannabis in this cohort using qualitative data. It will be done by eliciting participants’ experiences of quitting cannabis, their reasons for wanting to quit, and what approaches or treatments they have found helpful outside of CIRCLE (chapter 9).
Chapter 2 – Systematic review of whether combining contingency management with another psychotherapy improves substance use outcomes

2.1 – Introduction

2.1.1 – Background

Many structured evidence-based psychotherapy interventions, such as CBT and MET, are intended to evoke and strengthen the patient’s own motivation for change and assist the individual in developing effective coping and harm reduction strategies (Thombs & Osborn, 2013). As discussed in chapter 1.3, there is good evidence that these interventions provide clinical benefit and help improve abstinence in substance misuse during the treatment phase (Gates, Albertella, & Copeland, 2016). However, when delivered as a standalone intervention, they are typically found to be less effective than CM alone. In a systematic review of the during-treatment benefit of CM for substance use disorders, Dutra and colleagues (2008) found that CM was more effective at reducing use than CBT or Relapse Prevention treatments, but CM in combination with CBT was more effective than either CM or CBT alone. In relation to cannabis specifically, Carroll and colleagues (2006) and Kadden and colleagues (2007) both tested CM and CBT/MET, each as standalone treatments and in combination, alongside a control. They both found that CM was more effective than CBT/MET at reducing cannabis use during the treatment period. CM was also found to improve engagement with treatment and study retention. However, at post-treatment follow-up there was no main effect for CM, while CBT/MET was found to reduce cannabis use compared to control. Similarly, a recent Cochrane review by Minozzi and colleagues (2016) of psychosocial interventions for psychostimulant use amongst people without
psychiatric illness, CM resulted in the clearest evidence of significant reduction in use by treatment end. However, at longest follow-up, CM produced no benefit compared to Treatment-As-Usual. CBT meanwhile was associated with significant reductions in use (risk ratio = 1.89, 95% CI 1.18, 3.02). As such, it appears that while CM is more effective during treatment, there is evidence that the benefit from other evidence-based psychotherapies appears to have less of a drop-off post-treatment. Potentially combining the two will offer the best short-term and long-term outcomes.

In chapter 1.7, the cognitive-behavioural mechanism of CM was discussed. CM is now generally viewed as a method of enhancing motivation to abstain using extrinsic rewards. This method may undermine IM to abstain (self-determination theory) or enhance self-efficacy and thereby improve IM (cognitive evaluation theory). Other psychotherapies, such as CBT or MET, meanwhile, focus more on enhancing the patient’s IM to abstain. It has been argued (e.g. by Litt et al., 2008; Litt, Kadden, & Petry, 2013; Carroll et al., 2012) that integrating treatments could result in improved treatment compared to treatment individually. As Sherman and McRae-Clark (2016) suggest: ‘abstinence-based CM leads to longer periods of continuous abstinence during treatment and CBT works to enhance abstinence durability following treatment.’ One explanation for the increased benefit of CM and MET/CBT combined is that each intervention is likely to address different factors influencing relapse. CM appears to be effective by increasing retention in treatment and reducing use during treatment compared to MET/CBT alone (Carroll et al., 2012; Litt, Kadden, & Petry, 2013). Thereby it may also be effective in terms of reducing cravings and other symptoms of withdrawal by treatment end. MET/CBT interventions meanwhile typically include aims such as (Thombs & Osborn, 2013): to provide educational materials on the likely consequences of continued use; to evoke and strengthen the patient’s own motivation for change; to assist the individual in developing effective coping strategies and harm reduction strategies ‘to deal with the affective, cognitive and environmental cues that
trigger drug use, and/or lack the skills to maintain abstinence’ (Litt et al., 2008). These aims, if successful could aid participants with maintaining abstinence post-treatment. A CM plus MET/CBT intervention may therefore improve long term treatment outcomes partially through the potentially complimentary benefits of CM and MET/CBT as standalone treatments, but secondly through combinatory effects, such as CM improving engagement with MET/CBT treatments compared to MET/CBT alone.

2.1.2 – Aims

To evaluate whether substance use outcomes are better for CM in combination with another formal, evidence-based psychotherapy, such as CBT, compared to CM alone. Substance use outcomes will be measured using point prevalence abstinence (PPA) and self-reported use, which will be evaluated at both treatment end and at post-treatment follow-up. The primary outcome is PPA at treatment end.
2.2 – Methods

2.2.1 – Design

The protocol for this review was developed in 2017, and the database searches were performed on the 19th and 21st December 2017. The review protocol was registered on PROSPERO (number CRD42017025625) on 16th December 2017 and is presented in appendix 2.1. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement was followed.

A search of the Cochrane Database of Systematic Reviews (CDSR), the Centre for Reviews and Dissemination’s (CRD) database of reviews, and PROSPERO found no published systematic reviews or protocols of planned reviews that were similar.

Study inclusion criteria were:

1) Only randomised controlled trials.

2) Studies that included adult participants (18-65-year old) only.

3) Study designs needed to feature at least one experimental arm in which participants received combined CM and a structured evidence-based psychotherapeutic intervention (PS), and an arm in which participants receive CM alone. Studies featuring more than these 2 groups will also be included if the main comparison (CM plus psychotherapy compared to CM only) can be extracted from the data. Suitable psychotherapies are those listed in the International Standards for the Treatment of Drug Use Disorders (2016) by the United Nations Office on Drugs and Crime (UNODC). These are: cognitive behavioural therapy (CBT), couples’ therapy, psychodynamic therapy, behavioural therapies, social network therapy, and motivational interventions including MI and MET, and twelve-step facilitation for alcohol dependence.

4) Studies needed to target illicit substances, alcohol, or tobacco misuse. Although
financial rewards have been trialled for a range of behaviours and cohorts, there is some evidence that they affect motivation in different ways between target behaviours (Promberger & Marteau, 2013). Thus, for the purposes of this review, studies were limited to CM for substance use.

5) Studies needed to measure substance use either by a biometrically verified or self-reported measure of substance use at treatment end.

Any treatment or work setting was included. There were no restrictions on study publication dates. Articles were excluded if they could not be translated into English. Publications reporting interim results or pilot studies reporting data later included in another article of the completed trial, the pilot phase/interim publication were excluded.

2.2.2 – Search and study selection

Studies were identified by performing a keyword and subject search of the following electronic bibliographic databases: MEDLINE, PsycINFO, and EMBASE using Ovid SP, as well as Scopus (Elsevier), Web of Science (WoS), and Cumulative Index to Nursing and Allied Health Literature (CINAHL). Databases of clinical trials were searched for completed and ongoing trials, which were: Cochrane Central Register of Controlled Trials (CENTRAL), International Standard Randomised Controlled Trial Number Register (ISCTN registry), ClinicalTrials.gov (US National Institutes of Health), the NIHR UK Clinical Trials Gateway, and the WHO’s International Clinical Trials Registry Platform (ICTRP). Grey literature was searched through the British Library’s e-thesis online service (EThoS) and the APA’s PsycEXTRA database. Reference lists for related systematic reviews and included publications were hand searched. Databases were searched from inception to December 2017. The following search terms were used: contingency management; prize*; behavio* contract*; token econom*; (financ* or voucher* or mone*) [proximity operator] (reward*
or incentiv* or reinfo* or pay*) AND substance*; drug [proximity operator] ("use*" or "misuse*" or "abuse*" or “abstinence*”); addict*; alcohol*; cannab*; *cannabinol; marijuana; narcotic*; cocaine*; crack; opioid*; opiat*; opium; heroin; stimulant*; tobacco; nicotine; smok*; sedative*; inhalant*; hallucin*; hypnotic*; methylenedioxymethamphetamine; mdma; *amphetamine; crystal meth*; legal high*; khat; methadone; ketamine; codeine; PCP; Phencyclidine; Psilocybin; mescaline; LSD; Lysergic acid diethylamide; Peyote. The full search strategy for OVID SP is included in appendix 2.2. Search results were managed using reference management software.

Studies were reviewed for inclusion by two independent reviewers. The first reviewer (LSR) removed duplicates and processed all titles and abstracts. A second reviewer (TS – see Acknowledgements, p.5) sifted a random sample of 10% of unique references and checked all studies identified by the first reviewer. Disagreements were resolved by discussion between the two reviewers. Based on Cochrane guidelines (Higgins & Green, 2008), if there had of been disagreement of >5%, further training would have been provided and screening restarted.

2.2.3 – Data extraction and risk of bias assessment

Data were extracted by two reviewers (LSR and TS) independently using an extraction table designed for the study and disagreements were resolved through discussion. The primary outcome was Point Prevalence Abstinence (PPA) of the substance being targeted by the intervention at treatment end in the CM and the CM plus psychotherapy groups. PPA is a measure of abstinence from substance use measured using biometrics including urinalysis, saliva cotinine, or other appropriate methods. Secondary outcomes include PPA at follow-up at least 3 months following treatment cessation and self-reported days of substance use at treatment end and follow-up. Other secondary outcomes were PPA at treatment end for treatment as usual and psychotherapy only trial arms. Data was only extracted for suitable
Treatment-As-Usual conditions. Trials with active control interventions were not included in this secondary analysis.

For PPA outcomes, the number of substance negative samples and the total number of samples were extracted. Self-reported substance use was extracted as the mean number of substance using days. Where necessary, outcome data were calculated from the reported number of substance positive urines or the proportion of positive/negative samples. Where data could not be extracted from the published report, the authors were contacted where possible.

Studies were evaluated for risk of bias in relation to sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other biases using the Cochrane bias risk tool (Higgins et al., 2011). Overall quality of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) (BMJ, 2019) approach. GRADE assesses the quality of evidence based on five domains: 1) risk of bias; 2) imprecision (the risk of random error); 3) inconsistency (certainty in a body of evidence is highest when there are several studies that show consistent effects); 4) indirectness (evidence is most certain when studies directly compare the interventions of interest in the population of interest, and report outcome of greatest clinical interest); 5) publication bias.

Bias and quality of evidence assessment was performed by two reviewers (LSR and TS) independently and disagreements resolved through discussion. If the disagreement could not be resolved in this way, one of the supervisors of this thesis would make the decision. Funnel plots were generated to assess risk of publication bias.

2.2.4 – Data analyses

Meta-analyses were conducted using Review Manager 5.3. Data analyses used an inverse variance with random effects (Dersimonian and Laird) method throughout to compare the
effectiveness of interventions between groups. For the primary analysis and secondary analyses with PPA outcomes, risk ratios were calculated (BMJ, 2014). For self-reported days of substance use, standardised mean differences were calculated. Random effects analyses were used due to heterogeneity in the interventions between research reports. Due to heterogeneity in the psychotherapeutic interventions used in conjunction with CM, a sensitivity analysis was performed in the primary analysis that included only studies delivering a CBT and/or MET intervention. Statistical heterogeneity was assessed using the $I^2$ statistic and by visually inspecting forest plots.
2.3 – Results

2.3.1 – Study selection and description

14,692 records were identified during the initial search, yielding 12 studies that met inclusion criteria (Carrico et al., 2015; Carroll et al., 2001; Carroll et al., 2012; Epstein et al., 2003; Kadden et al., 2007; Milby et al., 2008; Ondersma et al., 2012; Rawson et al., 2002; Rawson et al., 2006; Rowan-Szal et al., 2005; Shoptaw et al., 2005; Tevyaw et al., 2009). Study characteristics are presented in table 2.1. For the primary outcome, 10 studies included PPA outcomes at treatment end. Six studies included PPA outcomes at post-treatment follow-up. Six reported self-reported use data at treatment end and four at follow-up. Seven studies featured a suitable treatment as usual arm, of which five reported PPA outcomes at treatment end. Eight studies featured psychotherapy only groups and seven reported PPA outcomes at treatment end. Four studies included both psychotherapy only and TAU groups and reported PPA outcomes.

Included studies had a combined subject pool of 1,654 participants. The average age was 34.28 and 1,123 (68%) were male. Eight studies had four experimental arms, two had three arms, and two had two arms. Only data from suitable arms were extracted for a total subject pool of 974.

All studies were conducted in the USA, with 6 being recruited to and delivered via community-based substance misuse treatment centres, including four methadone clinics, one via universities, one via an agency serving homeless people, one from prenatal care clinics, and three recruited using public focused advertising and delivered via a research clinic or university. Three studies targeted cocaine, two cannabis, two methamphetamine, one cocaine or methamphetamine, one cocaine or opioids, two tobacco, and one polysubstance use. In five studies, all trial participants were also receiving opioid substitution therapy (four methadone and one naltrexone).
Intervention characteristics are described in table 2.3 (p.40). The duration of the intervention period varied from three to 24 weeks. The number of CM sessions varied from five to 48, and the maximum reward that participants could receive was between $25 and $1,277.50. Nine studies used a variable reward schedule in which the value of the rewards rose as more sessions were passed, two studies featured a fixed reward, and the other offered a prize draw for rewards of various values for each negative result.

Figure 2.1 – Flow diagram

The type of psychotherapies varied quite widely: seven included CBT and/or MET, and the other five were structured psychotherapeutic packages targeting substance use. These were:
1) Affect Regulation Treatment to Enhance Methamphetamine Intervention Success (ARTEMIS) (Carrico et al., 2015), an individual tailored intervention targeting positive affect;

2) Significant other or family counselling (Carroll et al., 2001);

3) Manualised behavioural treatment (Milby et al., 2008);

4) A brief, computer-delivered intervention (Ondersma et al., 2011);

5) One-to-one counselling (Rowan-Szal et al., 2005).

The duration of the psychotherapies varied from five to 64 sessions. The CBT and/or MET studies featured between nine to 48 sessions of treatment over 3 to 16 weeks.

Seven studies featured follow-up assessments after the end of treatment, varying from one month to one year. For the post-treatment PPA secondary outcome, data from six months were included from six studies, and from one year from the other. Retention rates by treatment end were between 39% and 99% (median 80%), and 65% and 95% (median 83%) at post-treatment follow-up.

2.3.2 – Risk of bias and quality of evidence assessment

Table 2.1 summarises the risk of bias table for the included studies. None of the included trials could blind participants or personnel to allocation. Seven studies (Carrico et al., 2015; Carroll et al., 2001; Carroll et al., 2012; Kadden et al., 2007; Ondersma et al., 2012; Rawson et al., 2006; Shoptaw et al., 2005) had low risk of bias from random sequence generation, with the risk in the other five considered unclear due to insufficient detail provided. Six studies (Carrico et al., 2015; Carroll et al., 2001; Carroll et al., 2012; Kadden et al., 2007; Rawson et al., 2006; Shoptaw et al., 2005) had a low risk of allocation concealment bias, while the other six had an unclear risk due to insufficient detail. In 10 studies, it was unclear whether outcome assessors were blinded to allocation due to insufficient detail, low in one (Ondersma et al., 2012) and high in the other (Tevyaw et al., 2009) due to the
assessors not being blinded to allocation. Three studies (Ondersma et al., 2012, Rawson et al., 2006, Shoptaw et al., 2005) had a high risk of attrition bias due to poor retention rates and missingness mechanism not being explored. The risk of attrition bias in two others (Rawson et al., 2002; Rowan-Szal et al., 2005) was unclear due to insufficient detail, and low in the other seven. Risk of selective reporting was low in 11 studies, and unclear in the remaining one study (Rawson et al., 2002). There was a low risk of bias from the source of funding or the vested interests of researchers across all the studies. A funnel plot was generated and did not indicate publication basis (appendix 2.3)

Table 2.1 – Risk of bias summary
Overall, the quality of evidence was rated as moderate using GRADE due to the possibility of bias. Risk of bias varied widely between papers, with several considered to have high risk of bias in some domains. Meanwhile, none could blind participants to allocation.

2.3.3 – Data synthesis and meta-analyses

For the primary analysis, 10 studies reported biometrically verified (PPA) data at treatment end, including a total of 774 participants. Overall, in the primary outcome there was no benefit on PPA substance use outcomes from adding psychotherapy to CM (Relative Risk (RR) 0.97, 95% CI 0.85, 1.09; p=0.58) (figure 2.3). There was no evidence of statistical heterogeneity ($I^2=0\%$) in the included trials. Figure 2.3 shows the effect sizes of individual studies. The other two studies reported self-reported substance use measures only. At treatment end, neither reported an effect for CM plus psychotherapy compared to CM only. Overall, one out of 12 studies reported a significant treatment effect for CM plus psychotherapy compared to CM by treatment end, favouring CM only, and one at post-treatment follow-up that favoured CM plus psychotherapy. Due to wide variability in the types of psychotherapy used across trials, a sensitivity analysis was performed for the six trials delivering CBT and/or MET. Results were similar to the primary analysis and indicated no effect (RR 0.93; 95% CI 0.79, 1.08; p = 0.33). As before, there was no evidence of heterogeneity in study results ($I^2=0\%$).

PPA outcomes at post-treatment follow-up, like at treatment end, showed no treatment effect for CM plus psychotherapy compared to CM alone (RR 0.98 95% CI 0.80, 1.21, p = 0.86). Self-reported measures of substance use at treatment end also found no benefit for CM plus psychotherapy compared to CM alone (SMD = 0.2, 95% CI -0.4, 0.35, p = 0.10) or post-treatment follow-up (SMD = -0.18, 95% CI -0.68, 0.32, p=0.47). There was evidence of heterogeneity in the PPA results at post-treatment follow-up ($I^2 = 34\%$), and of moderate
heterogeneity in self-report at treatment end ($I^2 = 37\%$) and high at post-treatment follow-up ($I^2 = 77\%$).

Figure 2.3 – PPA outcomes at treatment end

Amongst studies reporting PPA outcomes, CM was more effective than Treatment-As-Usual by treatment end (RR 0.44 95% CI 0.28, 0.69, p<0.01) ($I^2$=0\%). CM plus psychotherapy (RR 0.44, 95% CI 0.28 0.69, p<0.01) ($I^2$=0\%) and psychotherapy only (RR 1.92, 95% CI 1.01 3.68, p=0.05) ($I^2$=0\%) were also more effective than Treatment-As-Usual. There was no significant difference between psychotherapy only and CM only (RR 0.64, 95% CI 0.35 1.19, p=0.16) or CM plus psychotherapy (RR 0.88, 95% CI 0.52 1.50, p=0.64) groups. Although there was moderate heterogeneity in results ($I^2$= 54\% and 42\% respectively). Five of seven studies reported CM only was more effective than psychotherapy only.
2.4 – Discussion

2.4.1 – Main findings

This review evaluated whether there was a synergistic effect of combining CM for substance use with a structured evidence-based psychotherapy. 12 randomised controlled trials were identified that featured at least one group receiving CM only and another receiving CM plus psychotherapy. The primary outcome was whether combining CM with psychotherapy reduced substance use (PPA) at treatment end compared to CM alone. Secondary outcomes included whether CM plus another psychotherapy compared to CM only improved: 1) substance use (PPA) by post-treatment follow-up, or self-reported substance use at either 2) treatment end or 3) post-treatment follow-up.

Studies targeting illicit substance, alcohol, or tobacco use were included. In total, 12 studies met inclusion criteria, and of these 10 reported PPA at treatment end and were included in the primary analysis. Overall, there was no treatment benefit for CM and psychotherapy compared to CM alone at treatment end (RR 0.97, 95% CI 0.85, 1.09; p=0.58) or at post-treatment follow-up (RR 0.98 95% CI 0.80, 1.21, p = 0.86). Types of psychotherapy included CBT with or without MET, MET alone, counselling, family therapy, manualised or computerised behavioural treatment, and intervention aimed at improving affect. Due to the heterogeneity in treatment types, a sensitivity analysis was performed that included only the six trials with CBT and/or MET. PPA outcomes were similar and indicated no effect (RR 0.93; 95% CI 0.79, 1.08; p = 0.33) at treatment end.

Other secondary analyses found that CM provided a substantial benefit compared to treatment as usual and was associated with a 56% increase in likelihood of participants being abstinent by treatment end. Similarly, both CM plus psychotherapy and psychotherapy only groups were both more effective than TAU, but active treatment conditions did not significantly differ when compared to each other. Overall these patterns
of results are consistent with previous literature, which strongly supports the view that behavioural treatments in general are more effective than Treatment-As-Usual. However, the primary result of this review indicates that there is no synergistic benefit to combining CM with another psychotherapy by treatment end. However, since CM plus psychotherapy was no better than CM alone, there appears to be a ceiling effect in the effectiveness of these treatments, such that treatment outcomes for CM cannot be improved by adding in another treatment. This perhaps implies that both types of treatment have a similar mechanism of action. It may be that, as suggested by Davies and colleagues (2014) that the nature of the treatment is less important than receiving a formal, well designed treatment programme.

2.4.2 – Implications

A common criticism of CM is that while the intervention reduces substance use during treatment, it fails to induce IM to maintain behavioural change post-treatment and consequently any treatment effect seems to drop off more rapidly compared to other interventions (Petry, 2010). It has been hypothesised by a number of authors, including Carroll and colleagues (2012) and Litt and colleagues (2008), that there may be an additive benefit of combining CM with another formal psychotherapy intervention such as CBT, which are generally more focused on enhancing IM. The results of the present study demonstrate that this does not appear to be the case, and this negative result was found both across all psychotherapy and in the CBT sub-group.

This is the first systematic review to focus on the treatment benefit of combining CM with another psychotherapy. However, at least one other review has assessed this question as one of its outcomes. Dutra and colleagues (2008), analysed effectiveness by treatment end, and unlike this study they found a benefit compared to CM only. However, they identified only two CM plus CBT trials and so caution against drawing conclusions based on this
result. The present study presents stronger evidence, drawn from a wider range of interventions and a larger number of trials, and found no clear benefit. To the best of the authors’ knowledge, no systematic reviews have examined post-treatment effectiveness.

2.4.3 – Limitations

Many studies did not provide enough detail to assess bias across all dimensions. Secondly, no study could blind clinician to group allocation and there are other methodological concerns with some of the trials included. Overall, the quality of evidence was moderate. The quality of evidence could be improved by more large, high quality, and well reported trials.

Secondly, only a relatively small number of trials were identified, and often the trials had multiple trial arms, so the number of participants included in this review is relatively low. As such caution should be taken when drawing conclusions from these results. However, to date the evidence indicates no overall combinatory benefit from the interventions under test.

There was quite high heterogeneity across the non-CM psychotherapy interventions. Although several studies included CBT or MET interventions, the number of sessions varied from 12 to 48 sessions and the contents of the different CBT interventions is often unclear. However, the sensitivity analysis of CBT or MET only trials was performed to address this issue, and also found no significant effect. Unfortunately, there were too few studies included in the sensitivity analysis to control for the potential moderating effects of number of treatment sessions and total reward value of the CM treatment across trials (Higgins & Green, 2008). Doing so would help clarify the treatment benefits of the interventions. Other possible confounding effects include whether the benefits of CM or psychotherapy vary across substances or cohorts. With more trials a moderator analysis could be performed, which would help elucidate the relationship.
For the meta-analyses, confirmed PPA data were used. However, all studies experienced attrition and it may be that some participants who were not followed up were in fact abstinent. While attrition does not appear to have differed substantially between the groups of interest in individual studies, it is possible that participant drop out may have biased the results of this review.

Finally, a range of substances were targeted by treatment, including opiates, cocaine, methamphetamine, cannabis, and tobacco. Cohorts were predominately patients with dependence on the target substance or cigarette smokers. Ideally meta-analyses would explore the potentially confounding effect of differing levels of use and types of substance. However, not enough trials are currently published.

2.4.4 – Conclusion

Due to the heterogeneity of the evidence base, further high-quality research is required before definitive conclusions can be made regarding the potential benefits of combining CM and another psychotherapy for specific cohorts, as effects may vary significantly across degrees of severity of misuse or across substances. However, based on current evidence, adding another psychotherapy to CM does not improve abstinence rates at either treatment end or follow-up. The different types of therapy thus do not provide synergistic effects and suggests that they do not have complimentary mechanism of action.

The results of this chapter are important for considering how to improve the substance use outcomes of CM treatment. The lack of an effect suggest they are not improved with the addition of another psychotherapy. In the next five chapters, a process evaluation of the CIRCLE trial is presented, which delivered a CM intervention targeting cannabis use in people with early psychosis. The first two chapters describe the study design and methods of the CIRCLE trial and an evaluation of a hypothesis of the cognitive-behavioural mechanism of action of the CM intervention in the CIRCLE trial. The results of these studies
are presented in chapters 5 and 6. Chapter 7 presents a qualitative study exploring
participants’ experiences and views of the CM and control treatments of the CIRCLE trial.
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Total randomized (N)</th>
<th>Study arms</th>
<th>N in each arm</th>
<th>Male (N)</th>
<th>Age - mean (SD)</th>
<th>Substance of misuse</th>
<th>Additional treatment</th>
<th>Populati</th>
<th>Substance use at baseline</th>
<th>Timing of follow ups</th>
<th>Substance use outcomes</th>
<th>Number included in follow-up analyses in each arm at each point</th>
<th>Treatment end substance use outcomes (n/N or mean (sd))</th>
<th>Follow-up substance use outcomes</th>
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<td>Carrico et al.</td>
<td>2015</td>
<td>21</td>
<td>CM, CM plus PS</td>
<td>CM+PS = 12, CM only = 9</td>
<td>21</td>
<td>41.1 (9)</td>
<td>Methamphetamine</td>
<td>None</td>
<td>Methamphetamine-using men who have sex with men</td>
<td>At least weekly use.</td>
<td>3 months (treatment end); 6 months</td>
<td>Urinalysis PPA and self-reported days of use</td>
<td>19 at 3 months and 18 at 6 months</td>
<td>PPA: CM + PS = 8/12; CM = 8/9. Self-reported days: CM+PS 4.4 (7.5); CM = 0.1 (0.4)</td>
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<td>2001</td>
<td>127</td>
<td>control, CM, CM+PS</td>
<td>CM+PS= 48, CM only = 35, control = 44</td>
<td>96</td>
<td>32.4 (8.1)</td>
<td>Opioids or Naltrexone</td>
<td>Recently detoxified opioid-dependent individuals</td>
<td>20.6 (6.9) days (max = 28)</td>
<td>3 months (treatment end)</td>
<td>Self-reported days of use</td>
<td>PS + CM = 23, CM only = 15, control = 11</td>
<td>Self-reported days: CM+PS 11 (20.3); CM = 12.5 (20.9)</td>
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<td></td>
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<tr>
<td>Author</td>
<td>Year</td>
<td>Total randomized (N)</td>
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<td>N in each arm</td>
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<td>Age - mean (SD)</td>
<td>Substance of misuse</td>
<td>Additional treatment</td>
<td>Populati</td>
<td>Substance use at baseline</td>
<td>Timing of follow ups</td>
<td>Substance use outcomes</td>
<td>Number included in follow-up analyses in each arm at each point</td>
<td>Treatment end substance use outcomes</td>
<td>Follow-up substance use outcomes</td>
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<td>Carroll et al.</td>
<td>2012</td>
<td>127</td>
<td>CM alone, PS alone, CM+PS, CM for PS attendance</td>
<td>CM only=27, PS only=36, CM (att)=32, CM+PS=32</td>
<td>107</td>
<td>25.7 (7.1)</td>
<td>Cannabis</td>
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<td>Treatment-seeking young adults with cannabis dependence</td>
<td>17.9 (12.9) days (max = 28)</td>
<td>Treatment end, every 3 months for 6 months</td>
<td>rinalysis PPA and self-reported days of use</td>
<td>CM only = 25, PS only = 23, CM+PS = 27, and PS+CM(adherence)=26</td>
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<td>2003</td>
<td>193</td>
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<td>110</td>
<td>39 (6.8)</td>
<td>Cocaine</td>
<td>Methadone</td>
<td>Cocaine-using methadone-maintained outpatients</td>
<td>18.3 (10.1) days (max=30)</td>
<td>Treatment end, and 6 and 12 months post-treatment</td>
<td>Urinalysis PPA and self-reported days of use</td>
<td>3, 6, and 12 months: control n=38, 35, 35; CM only n=32, 34, 37; CBT only n=32, 30, 30; CM+CBT n=30, 26, 31</td>
<td>PPA: CM + PS = 15/49; CM = 12/48</td>
<td>Self-reported days: CM+PS 0.34 (0.44); CM = 0.22 (0.24)</td>
</tr>
<tr>
<td>Author</td>
<td>Year</td>
<td>Total randomized (N)</td>
<td>Study arms</td>
<td>Male (N)</td>
<td>Age - mean (SD)</td>
<td>Substance of misuse</td>
<td>Additional treatments</td>
<td>Populati on</td>
<td>Substance use at baseline</td>
<td>Timing of follow ups</td>
<td>Substance use outcomes</td>
<td>Number included in follow-up analyses in each arm at each point</td>
<td>Treatment end substance use outcomes</td>
<td>Follow-up substance use outcomes</td>
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<tr>
<td>Kadden et al.</td>
<td>2007</td>
<td>240</td>
<td>PS only, PS+CM, CM only, control</td>
<td>170</td>
<td>32.7 (9.6)</td>
<td>Cannabis</td>
<td>None</td>
<td>Marijuan a dependent participa nts</td>
<td>80 (13.5) days (max=90)</td>
<td>9 weeks (treatment end), every 3 months for 1 year</td>
<td>Self-reported days of use</td>
<td>9 weeks and 1 year: CM = 54, 52; PS = 55, 49; CM=50, 48; PS+CM=59,51</td>
<td>Self-reported days: CM+PS 0.45 (0.43); CM = 0.32 (0.35)</td>
<td>Self-reported days: CM+PS 0.29 (0.4); CM = 0.6 (0.37)</td>
<td></td>
</tr>
<tr>
<td>Milby et al.</td>
<td>2008</td>
<td>206</td>
<td>CM+PS and CM only</td>
<td>150</td>
<td>40 (7.1)</td>
<td>Polysubstance</td>
<td>None</td>
<td>Cocaine dependent, homeless people</td>
<td>at least once in last 2 weeks</td>
<td>Treatment end (24 weeks) and 1 year.</td>
<td>Urinalysis PPA</td>
<td>6 weeks: CM=57, CM+=62</td>
<td>PPA: CM + PS = 63/103; CM = 53/103</td>
<td>PPA: CM + PS = 41/103; CM = 28/103</td>
<td></td>
</tr>
<tr>
<td>Ondersma et al.</td>
<td>2012</td>
<td>110</td>
<td>PS only, PS+CM, CM only, control</td>
<td>110</td>
<td>27.9 (6.4)</td>
<td>Tobacco</td>
<td>None</td>
<td>Pregnant women smokers</td>
<td>8 (8.2) per day</td>
<td>Treatment end (10 weeks)</td>
<td>Cotinine PPA</td>
<td>PS=23, CM=22, CM+PS=26, control=23</td>
<td>PPA: CM + PS = 4/30; CM = 3/28</td>
<td>N/A</td>
<td></td>
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<tr>
<td>Author</td>
<td>Year</td>
<td>Total randomised (N)</td>
<td>Study arms</td>
<td>N in each arm</td>
<td>Male (N)</td>
<td>Age - mean (SD)</td>
<td>Substance of misuse</td>
<td>Additional treatment(s)</td>
<td>Populaton</td>
<td>Substance use at baseline</td>
<td>Timing of follow ups</td>
<td>Substance use outcomes</td>
<td>Number included in follow-up analyses in each arm at each point</td>
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<tr>
<td>Rawson et al.</td>
<td>2002</td>
<td>120</td>
<td>CM only, PS only, CM+PS, control</td>
<td>CM only = 30, PS only = 30, CM+PS=30, methadone main=30</td>
<td>67</td>
<td>43</td>
<td>Cocaine</td>
<td>Methadone</td>
<td>Cocaine dependent people with or without Antisocial personality disorder and who are receiving methadone maintenance</td>
<td>all used in last 30 days</td>
<td>Treatment end (17 weeks), 6 months, and 1 year</td>
<td>Urinalysis PPA</td>
<td>17 weeks, 26 weeks, 52 weeks: n=108, 100, 100</td>
<td>PPA: CM + PS = 14/30; CM = 16/30</td>
<td>PPA: CM + PS = 11/30; CM = 14/30</td>
</tr>
<tr>
<td>Rawson et al.</td>
<td>2006</td>
<td>177</td>
<td>CM, CBT+PS only</td>
<td>CM=60, PS=58, CM+PS=59</td>
<td>135</td>
<td>36.2</td>
<td>Methamphetamine or cocaine</td>
<td>None</td>
<td>Stimulant-dependent individuals</td>
<td>cocaine used at least once in last 2 weeks</td>
<td>Treatment end (17 weeks), 6 months, and 1 year</td>
<td>Urinalysis PPA</td>
<td>17 weeks, 26 weeks, 52 weeks: CM n=45, 46, 45; PS n=47, 44, 45; CM+PS=46, 49, 48</td>
<td>PPA: CM + PS = 36/59; CM = 36/60</td>
<td>PPA: CM + PS = 34/59; CM = 34/60</td>
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<tr>
<td>Author</td>
<td>Year</td>
<td>Total randomised (N)</td>
<td>Study arms</td>
<td>N in each arm</td>
<td>Male (N)</td>
<td>Age - mean (SD)</td>
<td>Substance of misuse</td>
<td>Additional treatments</td>
<td>Populati on</td>
<td>Substance use at baseline</td>
<td>Timing of follow ups</td>
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<td>Number included in follow-up analyses in each arm at each point</td>
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<tr>
<td>Rowan-Szal et al.</td>
<td>2005</td>
<td>61</td>
<td>PS only, PS+CM, CM only, treatment as usual</td>
<td>CM=13, control=15, CM+PS=17, PS=16</td>
<td>38</td>
<td>33</td>
<td>Cocaine</td>
<td>Methadone</td>
<td>Cocaine dependent methadone using patients</td>
<td>unclear</td>
<td>16 weeks</td>
<td>Urinalysis PPA</td>
<td>CM only =9, control =11, PS+CM=15, PS only=14</td>
<td>PPA: CM + PS = 6/17; CM = 9/13</td>
<td>N/A</td>
</tr>
<tr>
<td>Shoptaw et al.</td>
<td>2005</td>
<td>162</td>
<td>CM, CM+PS, PS</td>
<td>PS=40, CM=42, CM+PS=40, control=40</td>
<td>162</td>
<td>37.2</td>
<td>Methamphetamine</td>
<td>Methadone</td>
<td>Methamphetamine dependent gay and bisexual men</td>
<td>16.7 days (max 30)</td>
<td>Treatment end (16 weeks), 6 months, and 12 months</td>
<td>Urinalysis PPA</td>
<td>week 16 =116, week 26=127, week 52=123</td>
<td>PPA: CM + PS = 31/40; CM = 35/42</td>
<td>Self-reported days: CM+PS 1.7 (5.1); CM = 2.7 (4.6)</td>
</tr>
<tr>
<td>Author</td>
<td>Year</td>
<td>Total randomised (N)</td>
<td>Study arms</td>
<td>N in each arm</td>
<td>Male (N)</td>
<td>Age - mean (SD)</td>
<td>Substance of misuse</td>
<td>Additional treatments</td>
<td>Populati on</td>
<td>Substance use at baseline</td>
<td>Timing of follow ups</td>
<td>Substance use outcomes</td>
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<tr>
<td>Tevyaw et al.</td>
<td>2009</td>
<td>110</td>
<td>PS plus non-contingent CM, PS+CM, CM and weekly relaxation sessions, non-contingent CM</td>
<td>68</td>
<td>19.7 (15)</td>
<td>Tobacco</td>
<td>None</td>
<td>Participants non-treatment seeking daily smokers</td>
<td>12.3 (6.8) per day</td>
<td>1 month, 3 months, 6 months</td>
<td>CM+PS=28, CM only=27, PS only=27, control=28</td>
<td>1 month, 3 months, 6 months: CM+PS=28, CM=27, PS=26, control=28; control=28</td>
<td>N/A</td>
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</tbody>
</table>
Table 2.3 – Intervention characteristics

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Intervention length (weeks)</th>
<th>Details of other psychotherapy</th>
<th>Details of CM intervention</th>
<th>Average number of treatment sessions attended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carrico et al.</td>
<td>2015</td>
<td>12</td>
<td>5 sessions of ARTEMIS: a positive affect intervention for recently diagnosed HIV-positive persons</td>
<td>12 sessions of escalating rewards-based CM. $330 maximum value.</td>
<td>unclear</td>
</tr>
<tr>
<td>Carroll et al.</td>
<td>2001</td>
<td>12</td>
<td>6 sessions of significant other involvement (SO) counselling</td>
<td>12 sessions of escalating rewards-based CM for naltrexone treatment adherence and opioid free urines. $561 maximum value.</td>
<td>control = 5.6 (4.5), CM = 7.4 (4.4), CM + PS = 7.4 (5.1)</td>
</tr>
<tr>
<td>Carroll et al.</td>
<td>2012</td>
<td>12</td>
<td>12 sessions of CBT</td>
<td>12 sessions of prize-based CM. Expected maximum earnings of $250</td>
<td>PS sessions = 5.9, CM = unclear</td>
</tr>
<tr>
<td>Epstein et al.</td>
<td>2003</td>
<td>12</td>
<td>12 sessions of group CBT treatment</td>
<td>12 sessions of escalating rewards-based CM. Maximum value $1155</td>
<td>unclear</td>
</tr>
<tr>
<td>Kadden et al.</td>
<td>2007</td>
<td>9</td>
<td>9 sessions of motivational enhancement therapy plus cognitive behavioural therapy (MET+CBT)</td>
<td>48 sessions of escalating rewards-based CM. Maximum value = $385</td>
<td>5.2 across groups. No difference between groups</td>
</tr>
<tr>
<td>Milby et al.</td>
<td>2008</td>
<td>24</td>
<td>72 sessions of group treatment including emotional support and processing meetings, drug and alcohol education group, and relapse prevention</td>
<td>72 sessions of escalating rewards-based CM. Maximum value is unclear</td>
<td>20 weeks completed</td>
</tr>
<tr>
<td>Ondersma et al.</td>
<td>2012</td>
<td>10</td>
<td>CD-SAs: A computer delivered brief intervention including video materials, psychoeducation, relapse prevention, and harm minimisation</td>
<td>up to 5 fixed reward-based CM-Lite sessions. Maximum value = $250</td>
<td>3.7 CM sessions. PS unclear</td>
</tr>
<tr>
<td>Rawson et al.</td>
<td>2002</td>
<td>16</td>
<td>48 sessions per week of group CBT</td>
<td>48 sessions of escalating rewards-based CM. Maximum value = $1277.50</td>
<td>14.7 weeks in treatment</td>
</tr>
</tbody>
</table>

93
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Sessions</th>
<th>Intervention</th>
<th>Sessions of Escalating Rewards-Based CM</th>
<th>Maximum Value</th>
<th>CM+PS=26.5, PS=19, CM unclear</th>
<th>CM only=19.6 sessions, CM+PS=35.4 sessions, control =26.8 sessions. CM unclear</th>
<th>PS=2.9, CM unclear</th>
<th>CM=33, PS=2.73</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rawson et al.</td>
<td>2006</td>
<td>16</td>
<td>48 sessions of group CBT</td>
<td>48 sessions of escalating rewards-based CM. Maximum value = $960</td>
<td></td>
<td>CM+PS=26.5, PS=19, CM unclear</td>
<td>PS only=19.6 sessions, CM+PS=35.4 sessions, control =26.8 sessions. CM unclear</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rowan-Szal et al.</td>
<td>2005</td>
<td>8</td>
<td>manualised one-to-one counselling for Cocaine Abuse.</td>
<td>8 sessions of fixed value-based CM. Maximum value = $25.</td>
<td></td>
<td>PS=2.9, CM unclear</td>
<td></td>
<td></td>
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<tr>
<td>Shoptaw et al.</td>
<td>2005</td>
<td>16</td>
<td>48 sessions per week of group CBT</td>
<td>48 sessions of escalating rewards-based CM. Maximum value = $1277.50</td>
<td></td>
<td>CM+PS=26.5, PS=19, CM unclear</td>
<td>PS only=19.6 sessions, CM+PS=35.4 sessions, control =26.8 sessions. CM unclear</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tevyaw et al.</td>
<td>2009</td>
<td>3</td>
<td>9 MET sessions</td>
<td>42 sessions of escalating rewards-based CM. Maximum value = $523.50</td>
<td></td>
<td>CM+PS=26.5, PS=19, CM unclear</td>
<td></td>
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</table>
Chapter 3 - Overview of the CIRCLE trial: methods and study design

3.1 – Introduction

3.1.1 – Background

The research presented in subsequent chapters was conducted in the context of the CIRCLE trial, a randomised controlled trial investigating the clinical and cost-effectiveness of CM for cannabis use in EIP service users. The protocol of the CIRCLE trial is published in Johnson and colleagues (2016) (appendix 3.1), and the results of the study are reported in (Sheridan-Rains et al., 2019). As such, CIRCLE is described here only in brief. Portions of the methods section of this chapter have been reproduced from Johnson and colleagues (2016) and Sheridan-Rains and colleagues (2019).

CIRCLE was the first randomised controlled trial of CM that focused on treating cannabis use in psychosis, it was also one of the largest trials (n=551) of CM for health-related outcomes in people with severe mental illness. It recruited across the Midlands and the Southeast of England, and so represented a wide range of geographical regions and demographic characteristics.

In this chapter, the study design and methods of CIRCLE are described. This provides the context of a cognitive-behavioural process evaluation of the CIRCLE trial, which is presented in chapter 4. This process evaluation was conducted alongside the CIRCLE trial. Chapters 5 and 6 present the results of CIRCLE and the process evaluation.

3.1.2 – Aims

The main aim of CIRCLE was to conduct a randomised controlled trial of a pragmatic CM intervention for cannabis use in people with a history of psychosis. CIRCLE evaluated the cost and clinical effectiveness of the CM intervention.
3.2 – Methods

3.2.1 – Study design

CIRCLE was a randomised controlled trial of a CM intervention in EIP service users. Recruitment to the trial occurred between 2012 and 2016, and follow-up data collection completed in late 2017. Potential participants were identified through discussion with clinicians in EIP services throughout the Midlands and Southeast of England.

EIP teams have been set up across England following the 2000 NHS Plan (Department of Health, 2000). EIP services accept individuals who have developed psychotic illness for the first time and aim to treat the initial episode early and effectively, minimise relapse, and optimise clinical and social recovery. EIP services offer intensive treatment during the first three years after first developing a psychotic illness. They are multidisciplinary Mental Health services that focus on delivery of evidence-based, individually tailored interventions to service users and their families NHS England, 2016). The aim is to support patients with the challenges of avoiding future relapses of their psychotic illness, forming a stable identity, improving their peer network, and engaging in vocational activities (McGorry, Killackey, & Yung, 2013).

CIRCLE featured two arms: the experimental group received a 12-week CM intervention in which participants were rewarded with a shopping voucher if urinalysis indicated that they had not used cannabis in the previous week. They also received an optimised Treatment-As-Usual intervention, which was a psychoeducational intervention targeting cannabis use. The control group received the psychoeducation only.

3.2.2 – Inclusion criteria

CIRCLE inclusion criteria were:

1) currently being on an EIP service caseload
2) having used cannabis at least once in 12 out of the previous 24 weeks
3) being aged 18-36
4) having stable accommodation
5) speaking enough English to be able to understand fully and answer the assessment instruments
6) being able to give informed consent to participate in the study
7) not being subject to a compulsory community treatment or court order requiring urine testing for cannabis
8) not currently receiving treatment for cannabis use from another agency
9) not currently being compulsorily detained in hospital, or in prison

3.2.3 – Randomisation

Following consent, a baseline assessment interview was performed by a CIRCLE researcher. Following this, participants were randomised with a 1:1 ratio, stratified on severity of cannabis use (1-3 uses per week, >3 uses per week) to one of the two experimental groups.

3.2.4 – Primary and secondary outcomes

The treatment phase lasted for 12 weeks, after which a follow-up assessment interview was performed. A second, and final, follow-up interview assessment was performed at 18 months following consent. The primary outcome was time to relapse, operationalised as admission to an acute mental health service (including psychiatric hospital, crisis resolution team or crisis house, or other acute mental health service intended as an equivalent to hospital), which was collected from patient records at 18 months. Secondary outcomes were between group differences at follow-up for:

1) Severity of positive symptoms of psychosis.
2) Social-functioning based on self-reports of engagement in work or study.
3) Self-reported number of days cannabis use in the previous 3 months at 3-month follow-up, or the previous six months at 18 months.

4) Proportion of cannabis-free urines at assessment.

5) Number of admissions over 18 months follow-up.

6) Quality Adjusted Life Years (QALYs) (SF-12 and EQ-5D) and service use (CSRI) were used in the cost-effectiveness analyses.

Baseline and secondary outcome data were collected primarily during assessment interviews. Some secondary outcome data were checked or collected using electronic patient records at each assessment.

3.2.5 – Outcome measures

The following measures were performed at all assessment interviews:

- Demographics, including standard demographics (age, gender, vocational status etc.), most recent diagnosis and social information. Where feasible, data were checked using patient records.

Cannabis use

- The Time Line Follow Back (TLFB) (Sobell L & Sobell M., 1992) was used to record self-reported substance use, including cannabis, other illicit substances, and alcohol, over the previous 6 months at baseline and 18 months, and over the previous 3 months at the 3-month follow-up assessment interview. The TLFB is a retrospective calendar-based measure of daily substance use. It has shown to have good test-retest reliability for cannabis (Robinson et al., 2014).

- Structured Clinical Interview for DSM IV (SCID) part E was used to assess history of alcohol and substance misuse disorders.

- Urinalysis for cannabis, performed using a commercially available
immunoassay test for metabolites of the cannabinoid Tetrahydrocannabinol (THC) using the standard cut-off of 50 ng/ml (National Drug Court Institute, 2006).

Psychotic symptoms:

- The positive and negative symptom subscales of Positive and Negative Syndrome Scale (PANSS) (Kay, Fiszbein, & Opler, 1987). The PANSS is a well-established measure of psychotic symptoms, with strong psychometric properties in terms of validity, reliability, and sensitivity (Leucht et al., 2005).

Service use and health economic analysis:

- Client Service Receipt Inventory (CSRI) (Beecham & Knapp, 2001) was used to record clinical service use, medication use, receipt of state welfare benefits, and use of other state funded services including the criminal justice system. Data were collected for the previous 6 months at baseline and 18-month, and for the preceding 3 months at 3-month assessment. Data were collected at assessment interview and checked using patient records. To minimise attrition, at 18 months data were collected from patient records for a subset of the resources deemed most likely to contribute to higher costs and that feasibly could be collected. Patient record data were collected were feasible for all patients still in the trial.

- 12-Item Short Form Survey (SF-12) (Brazier & Roberts, 2004) and the EQ-5D (McCrone et al., 2009) were used to derive quality adjusted life years (QALYs).

Details were collected of the participant’s referral to the EIP service, their history of admissions to acute Mental Health services, and their time spent on a Community Treatment Order (CTO) in the last 6 months at baseline. At 3 months and 18 months,
history of admission to acute Mental Health services and time spent on CTO were recorded since study inclusion. At 18 months, data were collected using patient records where feasible.

3.2.6 – Treatments

All participants in the CIRCLE were offered a psychoeducation package (intended to be an optimised version of Treatment-As-Usual), while those allocated to the experimental group were also offered a 12-week CM package.

Both treatments were delivered by staff in EIP services recruiting to the trial supported by CIRCLE researchers who provided training, responded to clinician questions regarding the treatments, and occasionally delivered individual treatment sessions. In the pilot phase of the trial, the treatments were delivered primarily by care coordinators. But during this period, it became clear that care coordinators often struggled to find the time.

Furthermore, as discussed in the results of the pilot qualitative study (appendix 7.2), some care coordinators were concerned that delivering the CM sessions themselves could negatively affect their relationship with their client if they failed the CM urinalysis sessions. Care coordinators said that this meant that they were sometimes reluctant to refer their clients to the CIRCLE research team. As such, teams were given greater scope in the main trial to identify who would deliver the treatments within their team. In some cases, this was care coordinators. But more often this was support workers or assistant psychologists. Therefore there was fairly wide variation in the knowledge and experience of those delivering the interventions.

Staff delivering the treatments were given training by a member of the CIRCLE research team, which lasted up to a full day.
3.2.6.1 – The CM scheme

The CM intervention was adapted from Budney and colleagues (2000; 2006), who trialled a voucher-based CM intervention to treat cannabis dependence in a non-comorbid population. The CIRCLE CM involved offering voucher rewards contingent on urinalysis results indicating the participant had abstained from cannabis over the previous week. Participants were offered 12 once-weekly urinalysis sessions, which were delivered by EIP clinicians and were performed either in EIP services or in the participant’s home. In the first week, participants received a £5 voucher for attending and providing a urine sample independent of the urinalysis result, which provided a ‘baseline’ for subsequent weeks. From week 2 to week 12, voucher rewards increased by £5 every 2 weeks they passed, and participants would receive £240 overall if they passed all the sessions. Since for heavy users it can take 30-60 days for urinary cannabis concentration to fall below the threshold for detection (50 ng/ml) (Goodwin et al., 2008), a drop in urinary concentration from the previous week was taken as evidence of abstinence until urinary THC concentration dropped below detectable levels. After then, any rise above the detectable threshold was taken as evidence of cannabis use. Urinalysis was performed using a portable benchtop analyser that could give immediate urinary THC concentration readings.

If a participant provided a urine sample indicating cannabis use since the previous session, they received £5 for providing a sample. At the next session, a clean urine sample was rewarded with a £10 voucher. If they provided a second clean sample in the subsequent session, they would return to the highest previous level of reward they had attained. If a participant failed to attend a session, it would count as a fail and they would not receive a voucher as they had not provided a sample.
3.2.6.2 – The psychoeducation package

The psychoeducation package was offered to both arms of the trial and was intended to reflect a standardised version of an optimised ‘Treatment-As-Usual’. A training manual and other supporting materials were also made available to them.

The CIRCLE psychoeducation consisted for 6 modules, each lasting approximately 30 minutes. The package included a pdf, video material, short quizzes, audio files, online content, and further information, all of which were delivered using a standard PC. Participants were given written materials to keep after the sessions. The package was designed to be an individually tailored psychoeducational approach to cannabis use. It was developed by the research team through an iterative process, with frequent input from service users. It drew on the psychoeducational package offered in the control arm of a previous Melbourne pilot study of psychological intervention for cannabis use, the Cannabis and Psychosis trial (Edwards et al., 2006). The content was based on MI principles, Relapse Prevention, and harm reduction strategies. It provided information about cannabis use in terms of its impact on seven areas: family, finance, activity/engagement in work or education, mental health, physical health, legality, and social groups/friendships. The materials explored the potential advantages and disadvantages of cannabis use and of cannabis abstinence. Finally, staff discussed setting goals regarding the participant’s future use of cannabis and strategies for achieving those goals and avoiding relapse. It was intended to help the participant make a decision about their cannabis use and help them in achieving those goals through strengthening their motivation to abstain and working with them to develop effective coping and harm reduction strategies. Its main aim was harm minimisation, with an acknowledgement that in a young person with psychosis, cannabis abstinence may be required to ensure that no harm is done.
3.2.7 – Sample size, statistical analyses, and health economic analyses

The sample size calculation, the statistical analysis methods, and health economic analysis methods are described in Johnson and colleagues (2016) (appendix 3.1). They are described here only in brief.

The sample size for the trial was 544. This was based on data suggesting a usual acute psychiatric admission rate of around 50% over the study timeframe in cannabis users (Linszen et al., 1994; Wade et al., 2006). A 15% decrease in this relapse rate due to the intervention was considered to be clinically beneficial. Using a power of 90% and a significance level of 5%, a total sample size of 460 subjects was determined to be required. This sample size was based on an analysis of time to relapse acute psychiatric admission and allowed a 37% decrease in the hazard of psychiatric admission relapse (hazard ratio of 0.63) in the intervention group to be detected using a Cox proportional hazards model. The sample size was inflated by a factor of 1.06, which assumed that each clinician delivering the intervention would see an average of four trial participants, and an intraclass correlation coefficient of 0.02 for clinician clustering, which gave a total sample size of 488. Finally, the sample size was inflated by 10% to account for attrition for the primary outcome, giving a total sample size of 544.

All statistical analyses were carried out comparing CM and control group as randomised using all available data. Logistic regression was used to determine baseline predictors of missingness. A Cox proportional hazards model was used to compare the primary outcome in the intervention and control groups, adjusting for severity of cannabis use (the stratification variable; 1 to 3 times a week versus 4 or more times a week) at baseline and whether the participant was part of the pilot trial. The assumption of proportional hazards was checked using Schoenfeld residuals (Collett, 2014). Several supportive analyses were conducted that adjusted for: baseline predictors of missingness, participants who had no
secondary outcome data (for 12 weeks and 18 months separately), whether they were part of the pilot trial, number of psychoeducation sessions attended number of admissions in the six months prior to baseline, and clustering by EI service instead of clinician.

Secondary outcomes were analysed separately at 3 and 18 months. Models were adjusted for severity of cannabis use at baseline and whether the participant was part of the pilot trial. For the dichotomous outcomes (cannabis positive urine, engaged in work or study), logistic regression was used. The residuals for the positive and negative symptoms from PANSS outcomes were not normally distributed and were therefore log transformed and analysed using linear regression models. Zero inflated Poisson regression was used for count outcomes including number of cannabis days and number of admissions over follow-up, as there were excess zeros in these outcomes. The number of cannabis days at 3 months was analysed using Poisson regression. All secondary outcomes were also analysed after adjusting for predictors of missingness. An additional supportive analysis for number of admissions was to include all those who were discharged from psychiatric services within 18 months and assuming they did not have any admissions over 18 months Robust standard errors were used in all regression models to account for clustering by clinician delivering the CM in the analyses (White, 1980).

The health economic or cost-effectiveness analysis was conducted from an NHS/social care perspective over 18 months. Costs of the CM intervention and psychoeducation were calculated based on NHS and study resource use data collected from CIRCLE intervention records, CSRI assessment, and electronic NHS patient records. Costs were compared between arms at 18-month follow-.

Quality adjusted life years (QALYs) were derived from the EQ-5D-3L and SF12 (McCrone et al., 2009; Brazier et al., 2004).
3.3 – Conclusion

The results of the CIRCLE trial are presented in Chapter 5. In the next chapter, the study methods of an evaluation of a hypothesised mechanism of action of the CIRCLE CM are described. In chapter 7, a qualitative process evaluation of the CIRCLE trial is presented.
Chapter 4 – Evaluation of a potential cognitive-behavioural mechanism of change underlying the CIRCLE CM intervention: methods and study design

4.1 – Introduction

4.1.1 – Background

The primary aim of this chapter is to investigate a hypothesised cognitive-behavioural model of the mechanism of action of the CIRCLE CM intervention. This work was planned and initiated in the early 2014, during the recruitment phase of CIRCLE. The focus of this chapter is to assess whether the CIRCLE CM intervention positively impacted IM and other commonly identified factors associated with abstinence from substance use or relapse in substance use. The aim is to facilitate understanding of the outcomes of the main trial by evaluating CM as a treatment in this cohort in terms of common cognitive-behavioural targets for psychotherapy. The factors examined in this chapter include overall motivation, intrinsic and EM, self-efficacy, readiness-to-change, urges, and exposure to cannabis using peers. A fairly large body of evidence (Najt, Fusar-Poli, & Brambilla, 2011) now exists that demonstrates the value of such cognitive, social, and affective factors for predicting relapse, and as offering potentially effective targets for therapy. The role of cognitive processes and social factors are discussed in the chapter 1.6.

In psychosis, as discussed in chapter 1.6.6, overall motivation can be diminished, and amotivation is a recognised negative symptom of the disorder. In particular, IM for engaging in activities, work, or education appears to be reduced. In substance use, it is less strongly associated with abstinence outcomes than in the general population. This appears to be further impacted by heavy cannabis use. IM amongst heavy cannabis users have been found to be substantially lower, with greater apathy in situations involving reward driven
task completion (Volkow et al., 2016). Like in non-psychiatric populations, there is some
evidence that motivation predicts abstinence from tobacco use in this population. In a
study of 224 patients who smoked cigarettes, Prochaska and colleagues (2014) found that
overall motivation predicted abstinence by the end of treatment.

Beyond motivation, the literature on cognitive-behavioural processes in relation to
substance use in psychosis is very limited. In one of the few identified studies, Vancampfort
and colleagues (2014) found that readiness-to-change predicted whether patients engaged
in physical activity by follow-up. Similarly, there little or no evidence regarding the
effectiveness of competency, cravings, and time spent with substance using peers for
predicting abstinence. However, there is evidence that cravings are high in people with
psychosis compared to non-psychiatric populations (Schnell et al., 2013).

4.1.2 – The hypothesised cognitive-behavioural model of CM

Based on both the literature discussed in chapter 1.6 and 1.7, which is principally obtained
from non-psychiatric populations, a hypothesised model for the CIRCLE CM was developed
(figure 4.1). According to Cognitive Evaluation Theory (Deci, 1971), CM provides a form of
EM that enhances participants’ overall motivation to quit cannabis. If they then manage to
abstain from cannabis use, their self-efficacy in abstaining improves and thereby so does
their IM to abstain. Into this basic model several other cognitive-behavioural variables have
been included: readiness-to-change, urges, exposure to cannabis using peers, and
compliance with the psychoeducation treatment. These cognitive and behavioural variables
were included because there is solid evidence of their importance in predicting relapse and
so may mediate or moderate the relationship between CM, cannabis use, and IM.
Secondly, it was speculated that most would be impacted by the CIRCLE psychoeducation.
The model was developed to be broadly consistent with other models in the literature,
such as Carey and colleagues (2001) who proposed a model of behavioural change in relation to a motivation-based treatment for substance use in people with psychosis.

Engagement with the CIRCLE psychoeducation treatment may have impacted many of the cognitive-behavioural variables directly or may have moderated their inter-relationships. The aims of the CIRCLE psychoeducation included to reduce ambivalence about using and encourage participants to consider their cannabis use and make a decision about whether or not to quit. In this way, it was speculated that it may affect participants’ IM to abstain. Secondly, it provided people with coping skills and Relapse Prevention strategies, including how to cope with urges or other cannabis use cues, as well as encourage people to avoid high risk situations for relapse, such as spending time with cannabis using peers. This was hypothesised to improve self-efficacy and reduce environmental exposure to cannabis use, as well as potentially improve extrinsic mediation to abstain related to social pressure not to use. Thirdly, it provided information on the legal and health implications of using cannabis, and so may improve motivation related to legal (EM) and health concerns (IM). Meanwhile, increased adherence with the CIRCLE psychoeducation is speculated to result in less time spent with cannabis using peers. Since the psychoeducation was modular and each session had a specific topic, it is expected that some of these effects will only be present if participants attend each session. In this sense, it is expected that the impact of the psychoeducation will depend on the number of sessions attended. When examining the cognitive-behavioural effect of the CIRCLE CM, it is important that the number of psychoeducation sessions attended is controlled for.

These hypothesised effects are depicted in figure 4.1. Positive associations between variables are depicted with (+) and negative associations with (-). For example, if EM is increased due to the CIRCLE CM, then overall motivation and in turn readiness-to-change
should both increase too. However, it is likely that the relationships between individual components of the model are complex and are not fully captured in figure 4.1.

Figure 4.1 - the hypothesised cognitive-behavioural mechanism of action of the CIRCLE CM intervention

4.1.3 – The present study

The present study was conducted in the context of the CIRCLE trial. The overall aim was to examine the hypothesised model of the cognitive-behavioural mechanism of action of the CIRCLE CM treatment. It tested whether CM had the predicted cognitive-behavioural effects (figure 4.1) by treatment end or by post-treatment follow-up. It did this by comparing change in self-reported measures of cognitive-behavioural the experimental (CM) group with the control group by treatment end and at 18 months post-treatment initiation.

4.1.3.1 – Aims

4.1.3.1.1 – Primary objective

To investigate whether CM increases participants’ IM to abstain by treatment cessation (3 months post-study inclusion). Based on Cognitive Evaluation Theory (Deci, 1971), it was
hypothesised that IM will be higher in the experimental group compared to the control group by treatment end.

4.1.3.1.2 – Secondary objectives

To investigate the hypothesised cognitive-behavioural mechanism underlying CM.

Compared to controls, CM therapy will:

1) Reduce frequency and severity of cravings, measured by the Mood and Physical Symptoms scale (MPSS) (West & Hajek, 2004) cravings subscale (2 items).
2) Result in participants avoiding exposure to peer/social cannabis use, measured with The Wisconsin Predicting Patients’ Relapse questionnaire (WI-PREPARE) (Bolt et al., 2009) environmental use subscale only (1 item in total).
3) Increase self-reported overall motivation and self-efficacy to abstain, which will be assessed using a three-item motivation measure (Chung et al., 2011).
4) Increase readiness-to-change, which will be measured with the single item measure Readiness Ruler (Heather, Smailes, & Cassidy, 2008).
5) Increase EM and overall motivation as measured by the RFQ.
6) Increase IM at 18 months following consent.

4.2 – Method

4.2.1 – Design

This study was conducted in the context of the CIRCLE trial, and the protocol for the present study was developed in the first half of 2014 before the results of the CIRCLE trial were known (the protocol is presented in appendix 4.2). Data for the present study were collected from all participants randomised into CIRCLE (both experimental groups) at all three assessment interviews once ethical approval for the study was obtained. Study inclusion and exclusion criteria were the same as the CIRCLE trial (chapter 3.2). Ethical
approval was received as part of substantial amendment no.5 to the CIRCLE trial dated 10th June 2014. Participants were informed of the aims of this study as part of the consent process for the CIRCLE trial. A Gantt chart of the schedule of events is presented in appendix 4.1.

4.2.1.1 – Outcome measures

A SPIRIT diagram of when outcomes measures were collected is presented in table 4.1. Some of the data used in this study were collected via a ‘cognitive-behavioural’ questionnaire, which was introduced to all three CIRCLE assessment interviews for this study. The questionnaire is presented in appendix 4.3. The questionnaire contained the following items, each of which were rated with a Likert type scale:

1) Intrinsic (IM) and Extrinsic Motivation (EM):
   a) Reasons for Quitting in Marijuana (RFQ) (McBride et al., 1994). The RFQ is a 20-item questionnaire assessing participants’ motivations for quitting cannabis. Respondents are asked to indicate how strongly each item applies to them using a 5-point Likert scale, which ranges from not at all true (0) to extremely true (4). The RFQ includes four dimensions: health concerns, self-control, social pressure, and legal concerns. The first two subscales measure IM and the latter two EM. The RFQ has good internal consistency (McBride et al., 1994), and predictive validity (Curry et al., 1990; Foster et al., 2015; Pokhrel & Herzog, 2015). The four-dimensional model has been evidenced across diverse substances and samples (e.g. Curry et al., 1990; McBride, 1994; McBride et al., 2001; Zvolensky et al., 2007).
   b) Based on previous research (Kolliakou et al., 2011), it was speculated that other motivations to quit may also be important to this cohort, but these
are not measured by the RFQ. These topics were: the impact of cannabis on mental health, the cost of using cannabis, and negative use expectancies associated with cannabis. 7 additional items were included: 1) Concerned that mental health already impacted by cannabis; 2) Cannot afford to use cannabis; 3) Cannabis not enjoyable; 4) Cannabis causes nausea/panic; 5) Concerned about cannabis impact on future MH; 6) Cannabis makes it hard to accomplish things/think clearly; 7) Because of the reward scheme (asked at baseline only). Endorsement for each item was measured using the same Likert-scale as the RFQ. Mean scores were calculated individually for items related to mental health concerns (items 1, 5) and negative use expectancies (items 3, 4, 6).

2) Motivation and self-efficacy: Chung and colleagues (2011) validated a 3-item measure of motivation to abstain, perceived difficulty of abstaining, and self-efficacy in being able to abstain. The original measure targeted cigarette smoking and was adapted for the present study by changing references to cigarette smoking to cannabis use. These measures have been demonstrated to have good concurrent and predictive validity of number of cigarettes smoked (both at baseline and 6 months post-baseline) (Chung et al., 2011).

3) Readiness-to-change: Readiness Ruler (Heather, Smailes, & Cassidy, 2008) is a single item measure of readiness-to-change. The original measure targeted alcohol use, and as above the measure was adapted for the present sub-study by changing references to alcohol use to cannabis use. The Readiness Ruler has been demonstrated to have good concurrent validity with widely used Readiness-to-change Questionnaire (RCQ) (Rollnick et al., 1992). It also has good predictive validity with both treatment adherence and outcomes (Dean et al., 2016).

4) Urges/Cravings: Mood and physical symptoms scale (MPSS) (West and Hajek, 2004)
cravings subscale only (2 items). These items were adapted to refer to cannabis use instead of cigarette smoking. The scale features 6 items ranging from ‘not at all’ to ‘all the time’. These will be numbered and treated as ordinal data. The MPSS has good test-retest reliability and concurrent validity (West & Ussher, 2010).

5) Environmental/social cues: The Wisconsin Predicting Patients’ Relapse questionnaire (WI-PREPARE) (Bolt et al., 2009) environmental use subscale only (1 item in total), which was adapted to refer to cannabis use instead of cigarette smoking. The WI-PREPARE has good predictive validity and good external validity across cohorts (Bolt et al., 2009).

The following measures were collected for CIRCLE and were used in this study:

1) Demographic and clinical data, including: 1) positive and negative PANSS sub-scale scores; 2) Diagnosis (most recently available diagnosis at 18 months follow-up).

2) Cannabis use data including: 1) The Timeline Follow Back (TLFB) (Sobell & Sobell, 1992) is a calendar type self-reported measure of substance use; 2) Urinalysis for presence of cannabis.

3) Engagement: Engagement with the interventions is judged based on the number of CIRCLE psychoeducation sessions each participant attends.
Table 4.1 - SPIRIT diagram of the schedule of events. * - outcome measures co-opted from the CIRCLE trial

<table>
<thead>
<tr>
<th>STUDY PERIOD</th>
<th>Enrolment</th>
<th>Allocation</th>
<th>Post-allocation</th>
<th>Close-out</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMEPOINT**</td>
<td>-(t_2)</td>
<td>0</td>
<td>Week 1</td>
<td>Week 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Week ...</td>
<td>Week 12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>18 months</td>
<td></td>
</tr>
</tbody>
</table>

**ENROLMENT:**
- Eligibility screened
- Informed consent
- Allocation

**INTERVENTIONS:**
- CM – Experimental group only
- OTAU – experimental and control groups

**COG-BEH OUTCOME MEASURES:**
- Reasons for quitting (RFQ)
- Chung et al.
- Readiness Ruler
- Mood and physical symptoms scale (MPSS)
- The Wisconsin Predicting Patients’ Relapse questionnaire (WI-PREPARE)

**CIRCLE**:
- Demographics
- TLFB
- Urinalysis for cannabis

* - outcome measures co-opted from the CIRCLE trial.
4.2.2 – Statistical analyses

Summary statistics of demographic, clinical, cognitive-behavioural, and compliance with the psychoeducation treatment variables were performed. For numeric variables, mean and standard deviation statistics are presented where appropriate. For numeric measures with non-parametric distributions, the median and inter-quartile range were calculated. For categorical variables, frequencies and percentages are given.

4.2.2.1 – Missing data

The missing data mechanism was explored through analysis of baseline variables (both cognitive-behavioural and CIRCLE variables) and by considering potential reasons for missing data. Predictors of missingness were identified using logistic regression analyses using dummy variables for follow-up at 3 months and 18 months. It was planned that multiple imputation would have been used if appropriate. However, few baseline variables predicted follow-up at 3 months and those that did showed only weak associations. It was judged that multiple imputation was unlikely to contribute much to the analysis. Rates of attrition at 18 months were very high (50%), making multiple imputation inappropriate (Jakobsen et al., 2017). As such, a sensitivity analysis was performed for the primary and secondary analyses that adjusted for predictors of missingness alongside the other variables discussed in the primary and secondary analyses methods chapters.

4.2.2.2 – Validating the Reasons for Quitting marijuana questionnaire

The first version of the RFQ questionnaire was aimed at tobacco users (Curry, Wagner, & Grothaus, 1990). It had four subscales: self-concept, social, health, legal. Subsequently, there are two published validations of the RFQ for Marijuana (McBride et al., 1994; Downey, Rosengren & Donovan, 2001). In each publication, the authors performed a confirmatory factor analysis to identify whether the factor structure of the original RFQ for tobacco questionnaire was valid in a cannabis using cohort. They performed a factor
analysis with a four-factor solution. They then identified the questionnaire items that met the following inclusion criteria: questionnaire items must load on the subscale it was intended to, with a factor score of 0.30 or greater, and with a difference of at least 0.25 between the first and second highest loadings. The authors each identified 14 questionnaire items meeting the inclusion criteria, but difference items were included in each paper.

However, both publications were conducted in the United States with cohorts without comorbid severe mental illness. For the present study, there was a concern that using the RFQ in a UK based cohort with psychosis may lack validity. Firstly, some of the questionnaire items were speculated to be more relevant to a US cohort. For example, item 18: ‘Because there is a drug testing policy where I work’ is likely to be more relevant to a US population than a UK one, as drug testing at work is uncommon in the UK. Secondly, reasons for wanting to quit cannabis are likely to be complex and it is plausible that they may differ significantly in a cohort with psychosis. There is some, albeit limited evidence of this. Few studies have compared reasons for quitting cannabis in a cohort with psychosis and a non-psychiatric cohort. However, in a study that used the RFQ in tobacco questionnaire, Zvolensky and colleagues (2007) found that reasons for wanting to quit cigarettes in a cohort with psychosis differed quite substantially from non-psychiatric controls. Specifically, the cohort with psychosis reported higher levels of motivation on the social influence and self-concept subscales. For the present study, it was thought that substantial differences in reasons for wanting to quit cannabis may potentially limit the validity of a questionnaire only validated in populations without comorbid psychosis.

As a first step in revalidating the RFQ in this cohort, a confirmatory factor analysis was performed to test whether the factor structure proposed in the original validation paper (McBride et al., 1994) was a good fit for the data from this cohort. Based on McBride and
colleagues (1994), the RFQ was hypothesised to include 4 latent variables: self-concept, social influence, legal, and physical health. Covariance terms between all 4 latent variables were included. To test the goodness-of-fit of the model, the Root Mean Square Error of Approximation (RMSEA), comparative fit index, and Tucker-Lewis index were calculated (Hu & Bentler, 1999). The confirmatory factor analysis was performed using the structural equation modelling module (SEM Builder) of STATA version 14.0.

Based on the results of this analysis, an exploratory factor analysis was performed. A principal components factor analysis (PCA) was performed, which initially extracted factors with eigenvalues over 1. A rotation was performed to make interpretation of the loadings easier. Given the covariance between factors in the confirmatory factor analysis, a promax oblique rotation solution was used to allow factors to correlate. A parallel analysis plot was generated to confirm the number of factors. The criteria for including items in each of the subscale was taken from McBride and colleagues (1994). These were that 1) the item should load on the factor it was intended to, 2) that it should load on a factor with a score of .30 or greater, and 3) have a difference of at least .25 from the first to the second highest loading. Cronbach’s alphas were calculated for the resulting factors.

4.2.2.3 – Sample size

The proposed sample size for the CIRCLE trial was 544. The present process evaluation study was introduced to the CIRCLE trial in June 2014, by which time 198 participants had already been recruited into CIRCLE. As such, the expected sample size was 346. Based on a commonly used guideline, 10-20 observations are required per predictor (Harrell, 2015). Therefore, the sample size was expected to be more than sufficient for the primary analysis.
4.2.2.4 – Primary analysis

The primary analysis investigated whether participants in the experimental group showed higher IM to abstain by treatment end compared to controls. The primary outcome was change in IM by treatment end, which was calculated by subtracting IM at baseline from IM at treatment end (3-month CIRCLE assessment). The relationship between treatment group and change in IM was hypothesised to be moderated by compliance with the CIRCLE treatment. An initial univariate linear regression analysis was performed to test the effect of treatment group on change in IM by 3 months. Subsequently, the primary analysis was performed, which adjusted for compliance with treatment (measured as the number of psychoeducation treatment attended), and predictors of missingness. This measure of compliance was chosen as both groups were offered the psychoeducation.

Model assumptions and potential outliers were checked using standard methods (appendix 4.4). Complete cases were used initially. Predictors of missingness were included in the primary analysis.

4.2.2.5 – Secondary analysis

The cognitive-behavioural mechanism underlying CM was investigated by testing the change in:

- The strength and frequency of cravings,
- Time spent with peers using cannabis,
- Readiness-to-change,
- Perceived difficulty in quitting and confidence in quitting,
- Overall motivation to quit.

These variables were investigated for evidence of improvement by treatment end and by 18 months post-treatment in the CM group compared to controls. Motivation was measured as overall motivation, as well as intrinsic and EM. A change variable was
calculated for each outcome measure by subtracting baseline values from 3-month values. For each variable, as with the primary outcome, an initial simple linear regression analysis was performed to test the effect of treatment group on the outcome variable. Subsequently, an analysis was performed to adjust for compliance with treatment, measured as the number of psychoeducation treatment attended, and predictors of missingness. The same model diagnostics were then performed as for the primary outcome.

4.2.3 – Next chapter

In the next chapter the results of the CIRCLE trial are presented. These provide the context for this process evaluation of the CIRCLE CM’s cognitive-behavioural mechanism of action. The results of this evaluation are presented in chapter 6. A qualitative study evaluating the CIRCLE trial is presented in chapter 7.
Chapter 5 – Results of the CIRCLE trial

5.1 – Introduction

This chapter presents the results of the CIRCLE trial. Portions of the results and discussion sections of this chapter have been replicated from Sheridan Rains and colleagues (2019). The study design and methods were described in chapter 3. In brief, CIRCLE was a randomised controlled trial assessing the clinical and cost-effectiveness of a 12-week CM intervention for cannabis use. Trial participants were EIP service users with problematic cannabis use. The experimental group was offered the CM treatment as well as a 6-module psychoeducation treatment. The control group received the psychoeducation only. There were follow-up interview assessments at 3 months (treatment end) and 18 months post-study initiation. The primary outcome was time to psychiatric relapse to an acute psychiatric service, which was collected from patient records at 18 months. Secondary outcomes include clinical, functional, and health economic outcomes, which were primarily assessed at follow-up interview assessment.
5.2 – Results

5.2.1 – Demographics

At baseline, most characteristics were similar between the two groups (table 5.1). Over 85% of participants were male, with a mean age of around 25 (SD 4). 72% were using cannabis more than three times a week and reported using on 111 days on average in the previous 6 months. Around a third of participants were diagnosed with schizophrenia or schizoaffective disorder and half had diagnoses of other types of psychosis. A quarter of participants were currently engaged in some form of work or education, but a large majority (over 80%) had held open market employment at some point. Median PANSS positive symptom score was 12 (IQR 9, 17) in the control group and 13 (IQR 9, 16) in the CM group. Lifetime rates of alcohol misuse or dependence were high (e.g. 36% of control and 32% of intervention group members met criteria for alcohol dependence. Reports of using substances other than cannabis were also high (e.g. 47% of control and 52% of intervention group members reported using cocaine) (able 5.1). In the six months prior to baseline, median days of substance use other than cannabis were low (0) in the CM group (IQR 0,4) and in the control group (0; IQR 0,1). Median alcohol using days was 6 in both the CM (IQR 0,26) and control groups (IQR 0,26).

5.2.2 – Participation in CIRCLE treatment (CM and psychoeducation) and attrition by follow-up

Participants in the CM group (n=278) obtained a mean of £64 (std dev = 69.5) (out of a maximum of £240) in voucher rewards and attended a median number of 9 (IQR 3, 12) (maximum of 12) CM sessions. 46 participants declined the CM intervention or did not attend any sessions. Participants attended a median of 6 and 4 (maximum of 6) psychoeducation sessions in the CM and control groups (n=273) respectively. However, 86
participants in the control group and 63 in the CM group declined the psychoeducation or did not attend any sessions.

At follow-up, primary outcome data were collected from electronic patient records for 530 (96%) participants. Assessment interviews, during which secondary outcome data were collected, were performed for 371 participants (67%) at 3-month follow-up, and 278 participants (50%) at 18-month follow-up.

5.2.3 – Primary and secondary outcomes

For the primary outcome, there was no statistically significant difference in time to admission to an acute mental health service between the randomised groups (hazard ratio (HR) 1.03, 95% CI 0.76, 1.40) (Table 5.2). Approximately a third of participants experienced at least one acute admission to a mental health service, including hospital alternatives such as crisis teams and crisis houses, by 18 months in both the CM (90/272) and control group (85/259) (OR 1.02, 95% CI 0.70, 1.48). Amongst those who relapsed, the median number of days until relapse was 245 (IQR 99, 382) in the control group and 196 (IQR 82, 364) in the CM group.

Most results from the secondary analyses, including cannabis positive urine, cannabis using days, days of use of other illicit substances or alcohol, being in paid work or study, and severity of negative psychotic symptoms, were not statistically significant at either 3 and 18-month. Positive psychotic symptoms at three months were slightly lower in the CM group than the control group (β=-0.07, 95% CI -14%, -0%, p=0.04).

A post-hoc analysis was performed to help understand the results in the context of whether people had received psychoeducation as planned. Attending at least four of the six psychoeducation sessions planned was selected as the measure of compliance with the CIRCLE psychoeducation package. There were no marked differences in demographic, social, or clinical baseline characteristics between compliers and non-compliers between
A Cox model with robust standard errors was conducted. The primary outcome of the trial (time to psychiatric relapse) was used as the dependent variable in the analysis. A dichotomous variable indicating compliance was created. Randomisation group, compliance with the psychoeducation, severity of cannabis use at baseline and whether the participant was part of the pilot trial were included as covariates and an interaction term between compliance and randomisation group was used. The analysis was statistically significant ($p = 0.016$), which suggests that CM might be effective in participants who receive sufficient psychoeducation. This may be because, amongst those who engage with treatment, CM is effective at motivating people to quit.

5.2.4 – Health economics

Health economic analysis suggested that the CM was likely to be cost-effective compared to the Treatment-As-Usual (psychoeducation) package. There was a small, but not statistically significant, cost difference between the experimental groups, with the CM (experimental) group costing slightly less (£1,625 per person) than the controls. Quality Adjusted Life Years (QALYs) were slightly better for people in the CM group than for controls (1.2218 compared to 1.1855). However, it should be noted that due to attrition at 18-month follow-up and missing data, service use costs were collected for 42% of the total CIRCLE sample (231/551). Meanwhile, the E5-QD and SF-12 (used to calculate the QALYS) were collected for 50% of the CIRCLE sample (273/551). Health economic analyses (cost differences and QALYs for each group) were performed following multiple imputation based on these data.

Overall, the CM group had lower costs and better QALYs than controls, and so ‘dominated’. Based on a standard threshold of £20,000 (for cost-effectiveness (McCabe, Claxton, & Culyer, 2008), there was an 80% chance of the CM intervention being more cost-effective than the Treatment-As-Usual (psychoeducation).
Table 5.1 – baseline demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control</th>
<th>Experimental</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N or median or utility score</td>
<td>%, SD, or IQR</td>
</tr>
<tr>
<td>Male</td>
<td>240/273</td>
<td>238/278</td>
</tr>
<tr>
<td>Age mean (SD)</td>
<td>25</td>
<td>24</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>144/273</td>
<td>148/277</td>
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<tr>
<td>Black</td>
<td>62/273</td>
<td>65/277</td>
</tr>
<tr>
<td>Asian</td>
<td>30/273</td>
<td>29/277</td>
</tr>
<tr>
<td>Other</td>
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<td>35/277</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
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<td>259/278</td>
</tr>
<tr>
<td>Married or cohabiting</td>
<td>14/273</td>
<td>17/278</td>
</tr>
<tr>
<td>Other</td>
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<td>2/278</td>
</tr>
<tr>
<td>Educational attainment</td>
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</tr>
<tr>
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<td>133/277</td>
</tr>
<tr>
<td>A level or equivalent</td>
<td>67/273</td>
<td>58/277</td>
</tr>
<tr>
<td>Post 18 education (including HND, trade, degree)</td>
<td>54/273</td>
<td>43/277</td>
</tr>
<tr>
<td>Ever had open market employment</td>
<td>223/273</td>
<td>240/278</td>
</tr>
<tr>
<td>Any current work or study</td>
<td>67/273</td>
<td>73/278</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Control</td>
<td>Experimental</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>---------</td>
<td>--------------</td>
</tr>
<tr>
<td></td>
<td>n/N, Median</td>
<td>n/N, Median</td>
</tr>
<tr>
<td>Schizophrenia or schizo-affective disorder</td>
<td>80/256</td>
<td>90/268</td>
</tr>
<tr>
<td>Bipolar affective disorder</td>
<td>26/256</td>
<td>19/268</td>
</tr>
<tr>
<td>Depression with psychotic symptoms</td>
<td>11/256</td>
<td>5/268</td>
</tr>
<tr>
<td>Other psychosis</td>
<td>139/256</td>
<td>154/268</td>
</tr>
<tr>
<td>Cannabis use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3 times a week</td>
<td>77/273</td>
<td>78/278</td>
</tr>
<tr>
<td>More than 3 times a week</td>
<td>196/273</td>
<td>200/278</td>
</tr>
<tr>
<td>Cannabis positive urine</td>
<td>210/262</td>
<td>214/272</td>
</tr>
<tr>
<td>Number of days using cannabis*</td>
<td>108</td>
<td>(67, 156)</td>
</tr>
<tr>
<td>History of cannabis dependence</td>
<td>238/273</td>
<td>236/278</td>
</tr>
<tr>
<td>Current cannabis dependence</td>
<td>183/238</td>
<td>185/236</td>
</tr>
<tr>
<td>PANSS positive symptoms median (IQR)</td>
<td>12</td>
<td>(9, 17)</td>
</tr>
<tr>
<td>PANSS negative symptoms median (IQR)</td>
<td>14</td>
<td>(11, 19)</td>
</tr>
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</table>

Table 5.2 - outcomes at 3 months (treatment end) and 18 months

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Experimental</th>
<th>Difference between groups</th>
</tr>
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<tr>
<td></td>
<td>n/N, Median</td>
<td>n/N, Median</td>
<td>Estimate†</td>
</tr>
<tr>
<td>Time to relapse</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any work or study currently</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>58/183</td>
<td>58/189</td>
<td>32</td>
</tr>
<tr>
<td>18 months</td>
<td>45/135</td>
<td>42/145</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>3 months</td>
<td>18 months</td>
<td>6 months</td>
</tr>
<tr>
<td>--------------------------</td>
<td>----------</td>
<td>-----------</td>
<td>----------</td>
</tr>
<tr>
<td>Cannabis positive urine</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>122/170</td>
<td>61</td>
<td>72</td>
</tr>
<tr>
<td>18 months</td>
<td>76/124</td>
<td>77/136</td>
<td>57</td>
</tr>
<tr>
<td>Number of days using cannabis* (median)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>30 (3, 84)</td>
<td>26 (1, 67)</td>
<td>0.88</td>
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<tr>
<td>18 months</td>
<td>26 (1, 142)</td>
<td>26 (0, 118)</td>
<td>1.08</td>
</tr>
<tr>
<td>PANSS positive symptoms (median)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>11 (8, 16)</td>
<td>10 (8, 14)</td>
<td>-0.07</td>
</tr>
<tr>
<td>18 months</td>
<td>10 (8, 15)</td>
<td>11 (8, 13)</td>
<td>-0.04</td>
</tr>
<tr>
<td>PANSS negative symptoms (median)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 months</td>
<td>14 (10, 18)</td>
<td>12 (9, 17)</td>
<td>-0.08</td>
</tr>
<tr>
<td>18 months</td>
<td>12 (8, 17)</td>
<td>12 (9, 17)</td>
<td>0.02</td>
</tr>
<tr>
<td>Number of psychoeducation sessions attended (median)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 (0, 6)</td>
<td>6 (1, 6)</td>
<td></td>
</tr>
<tr>
<td>Number of contingency management sessions attended (median)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9 (3, 12)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*at 3 months this was for the previous 12 weeks/84 days. At 18 months this was for the previous 168 days. CI – confidence interval
† Estimate of hazard ratio, odds ratio, incident rate ratio as appropriate. Adjusted for level of cannabis use at baseline and whether in the pilot study adjusting for baseline predictors of missingness. These were:

- Time to admission, number of admissions, at least one admission: any work or study
- Urine positive 3m, PANSS positive 3m, PANSS negative 3m, any work or study 3m, number of days cannabis use 3m: exempt from work due to disability
- Urine positive 18m: any work or study
- PANSS positive 18m, PANSS negative 18m, any work or study 18m, number of days cannabis use 18m: voluntary work
5.3 – Discussion

5.3.1 – Main findings

There was no evidence that the CM treatment improved time to relapse (the primary outcome) or most secondary outcomes, including cannabis use, engagement in work or education, and negative psychotic symptoms. However, there was weak evidence of a very slight improvement to positive psychotic symptoms ($\beta=-0.07$, 95% CI -0.14, 0.00, $p=0.04$).

The relapse rate was lower than anticipated in the trial as a whole. Only around a third in each group required admission to acute care, while for the sample size calculation it was expected, based on previous literature, that half would relapse (Linszen, Dingemans, and Lenior, 1994; Wade et al., 2006). This suggests that a comparatively stable group of patients was recruited to trial, and/or that the psychoeducation and/or the extra attention of being in a research study had a beneficial impact. Although the majority still had cannabis-positive urine, the number of reported cannabis-using days in the previous six months fell from over 100 to 26 in each group by 18-months follow-up, indicating that cannabis use declined in both groups over this period. This could be due to the psychoeducation intervention, the normal progression of use in this group, regression to the mean, or to a combination of these factors including more frequent rewards or higher reward values.

A post-hoc analysis examined whether participants who had complied with the psychoeducation sessions benefited from being in the CM group compared to controls. The results indicate that, amongst those who were compliant with the CIRCLE psychoeducation package, receiving the CM was associated with a statistically significant longer time to relapse. This may be because CM was beneficial amongst those who engaged with treatment. This pattern of results is complex. It may be that there was some benefit from the CM, but that it was not substantial enough to be detected in the intention-to-treat
analysis. This could be partially due to engagement rates. Around one third did not attend any psychoeducation or CM sessions, and it might be that if engagement was better, then the CM would have been more clinically beneficial. Further work needs to be performed to explore whether CM could be effective in this group. One possibility is that a different design would have been more effective, such as having more frequent reward sessions or higher reward values.

5.3.2 – Implications

Evidence in support of CM for substance misuse is mixed in people with comorbid severe mental illness. Bradizza and colleagues (2014) and Hunt and colleagues (2013) each performed systematic reviews of the literature. They identified four studies between them. Both authors conclude that the current evidence does not clearly support the efficacy of CM for treating substance abuse in comorbid severe mental illness. However, the results of all the trials found that substance use in the CM group was lower, although it was fairly often a small effect that disappeared once treatment ended. Overall, it appears that evidence for CM is much more mixed in populations with comorbid severe mental illness and substance misuse than non-psychiatric populations. Where a benefit is found to substance use outcomes, it seems to be generally smaller and may be more transient. It appears then that CM has a reduced effect in this population compared to the general populations. Based on CIRCLE, it may also be that CM for some substances, such as cannabis, is less effective in populations with psychosis than for other substances. Reasons for this, however, are uncertain based on the literature to date.

5.3.3 – Limitations

CIRCLE had several limitations: Firstly, a higher reward or more frequent reward sessions may have been more clinically effective, even if not cost-effective. The CIRCLE reward value was intended to be substantial enough to incentivise abstinence without being viewed as
coercive and thus ethically problematic, and was supported by clinicians, service users via the patient and public involvement consultation, and experts in the field. However, further work with stakeholders and experts in the field could be done to explore this issue.

Secondly, engagement with the interventions was quite good, with people attending a median of four TAU intervention sessions in the control group and six in the experimental group. Secondly, data on delivery of the intervention suggested that those delivering it did adhere well to the intended protocols. However, a high proportion of people (around one third of people in the control group and one quarter in the experimental group) declined the intervention or did not attend any sessions. The compliance with the psychoeducation analysis indicates that the CM intervention had a beneficial clinical effect amongst compliers. It may be that a more treatment seeking population would have benefited to a greater extent from the intervention.

Thirdly, cannabis dependence was high in this sample (around three-quarters of participants at baseline), and those with dependence may find it harder to change their behaviour compared to those with less severe problematic cannabis use. However, in the two trials by Budney et al. (2000; 2006) and Bellack et al. (2006) all participants were dependent, and so it is unlikely that the CM intervention failed to provide a benefit because of high rates of dependence. An alternative explanation is that participants may have been using more highly potent forms of the cannabis, and consequently may have found it more difficult to abstain than those using less potent forms. There is good evidence that this cohort typically uses more potent forms of cannabis than non-psychiatric groups (Di Forti et al., 2014), and that high potency cannabis use is relatively prevalent in London, where much of the CIRCLE sample was recruited (Di Forti et al., 2019). It is therefore plausible that use of highly potent types of cannabis may have been relatively
widespread in the sample. However, we did not systematically record the type of cannabis participants were using, making further exploration of this possibility difficult.

Fourthly, in CIRCLE, cannabis use (measured with urinalysis) fell substantially from 80% at baseline to 71% at 3 months and 59% at 18 months. The fall in cannabis use across the sample could be partially the consequence of attrition (one third were not followed up at 3 months and a half at 18 months) and it may be that heavier cannabis users were harder to follow-up. It may also be the result of natural progression in this cohort. Across the general population, there is a pattern of people generally reducing their use as they become older (Lader et al., 2016). However, this reduction may also be partially the result of CIRCLE being delivered in the context of EIP services or because of the psychoeducation treatment.

Current evidence that CM for cannabis use works in this population comes from Bellack and colleagues (2006), in which only 7% of participants were misusing cannabis, and two small feasibility studies by Sigmon and colleagues (2000; 2006). In all studies, participants were recruited from community based mental health teams in the USA. However, it is unclear what the exact nature of these services were, and what level of support they provided to service users. EIP aims to support patients with the challenges of forming a stable identity, peer network, and engaging in vocational activities (McGorry, Killackey, & Yung, 2013), and there is good evidence that EIP is effective at improving clinical and functional outcomes in this population (NHS England, 2016). There is some, albeit currently weak, evidence that being in EIP helps reduce cannabis. Archie and colleagues (2007) performed a cohort study of 200 patients in EIP services in Canada (compared to the general population). They found that in the first 12 months of EIP treatment, cannabis use fell substantially.

Originally the CM and psychoeducation treatments were intended to be delivered by care coordinators (the nurses, occupational therapist or social workers with primary
responsibility for keeping in touch with patients and organising their care). However, few care coordinators were prepared to deliver the interventions, largely due to concerns regarding time pressures and potential disruption to therapeutic relationships. Instead, they were generally delivered by other clinical staff, such as support workers or assistant psychologists. The main reason for this was the pressure on care coordinator time making it impractical to learn and deliver an additional intervention. As such, the CIRCLE treatments were not fully integrated into EIP care, which may have limited the benefits of this treatment on cannabis use. However, it is possible that even without being fully integrated in EIP care, this context may have had some impact on participants’ cannabis use. One potential explanation for this reduction is that it is an indirect result of improving clinical and functional outcomes for patients, perhaps because of being in work or having improved social networks. As such, it may be that treatment effects from the CIRCLE CM would be easier to detect if patients are recruited from community-based clinics in the USA if the level of support patients typically receive is poorer than from EIP services in the UK.

Another possibility is that the psychoeducation package, which was delivered to both the control and experimental groups, was too well designed to be a control and resulted in the CM intervention not producing a detectable effect. Consistent with this possibility, there was evidence that amongst those who complied with treatment, that CM plus psychoeducation was more effective than the psychoeducation alone (Sheridan Rains et al., 2019). While it was intended to be a standardised form of Treatment-As-Usual, it became apparent that it was a much better developed and more ambitious psychoeducational intervention than was otherwise available in many of the participating EIP teams. As such the psychoeducation package could be viewed as an active control and may have conferred a benefit to participants. Again, it is possible that the psychoeducation could have made it more difficult to detect any benefit from the CM treatment.
Fifthly, as discussed, the CIRCLE treatments were intended to be integrated into EIP care. However, typically it was not care coordinators that delivered the treatments, but rather other EIP staff or CIRCLE staff. It has already been discussed that the EIP context may have made it harder to detect beneficial effects from the CM treatment. But it is also possible that greater integration into routine appointments would have improved the effectiveness of the CM intervention. Doing so may have made better use of the EIP service context as more senior EIP clinical staff who already have a good therapeutic relationship with patients may have been able to improve delivery of the treatments.

Sixthly, although medication data were collected as part of the CSRI, which was conducted as part of the CIRCLE assessment, these data were only analysed as part of the CIRCLE cost-effectiveness analysis. Given that antipsychotic medications are potent sedatives, it may be that the use of such medication may make it more difficult for patients to engage with treatment and could potentially contribute to the lack of any benefit from the CM treatment. Further analysis could help explore this possibility.

Finally, while the follow-up rate for the primary outcome was very high, attrition was greater than anticipated on the interview measures, potentially introducing bias. The most common reason for participants being lost to follow-up (approximately 70% of participants) was that they could not be contacted by CIRCLE researchers (see chapter 6.2.3). This was despite CIRCLE researchers collecting contact details of family members from friends from participants were possible to minimise attrition. Reasons for this may be partially related to CIRCLE outcomes, such as heavier cannabis use perhaps making participants more apathetic and harder to contact, but could also be partially attributable to unrelated reasons such as patients changing their phone numbers. Few baseline measures predicted missingness at either follow-up. In the comparison of unadjusted outcomes and outcomes
adjusted for predictors of missingness, there was little evidence in the CIRCLE results of systematic bias from attrition (Sheridan Rains et al., 2019).

5.3.4 – Summary

Overall, the intention-to-treat analyses provide no evidence that CM treatment benefited participants. However, the post-hoc analysis suggest that for some CM may have had a benefit amongst those who engaged well with treatment. One possibility is that a different CM design, such as higher reward values or more frequent sessions, would improve effectiveness. But it may also be that a substantially different approach is required to address the significant clinical problem of cannabis use in people with psychosis. The aim of the next two chapters is to explore the cognitive-behavioural mechanism underlying the CM intervention, which will help investigate these possibilities.
Chapter 6 – Cognitive-behavioural process evaluation: results

6.1 – Introduction

This chapter presents the results of a process evaluation of the hypothesised cognitive-behavioural mechanism of action of the CIRCLE trial. The study design and methods were described in chapter 4.

In brief, the primary aim was to investigate whether participants in the CM (experimental) group showed higher IM to abstain by treatment end compared to controls. Secondary aims included exploring whether the strength and frequency of cravings, time spent with peers using cannabis, readiness-to-change, self-efficacy, and overall or EM to quit improved in the CM group compared to the control group by follow-up. The overall objective was to explore a hypothesised cognitive-behavioural mechanism of action of CM in this cohort.
6.2 – Results

6.2.1 – Descriptive statistics

In total, 551 participants were recruited for CIRCLE. Recruitment for CIRCLE took place between June 2012 and April 2016. 70 EIP services across 23 trusts in the Midlands and the South East of England were included in CIRCLE. Of these, 353 participants were recruited after June 2014 and were included in this study. Figure 6.1 shows the flow of participants through the study. At 3 months, 237 participants were followed-up (67.14%), and 188 at 18 months (53.26%). Table 4.1 provides demographic, clinical, cannabis use, and cognitive-behavioural measures at baseline for both the present sample and of the CIRCLE sample. Both demographic and clinical characteristics for the present sample were very similar to the CIRCLE sample, with no measures showing much difference between the two samples. As such, the present sample is representative of the CIRCLE sample. Baseline characteristics also did not differ between the experimental (CM) and control groups in the present study (appendix 6.1).

At baseline, participants in this sample were aged 18-36 (mean 23.95), 84.4% were male, and over half were white and one quarter were black (table 6.1). 41% had completed GCSEs, 24% had completed A-levels, and 19% had attained some education or training after school. 31% were currently in employment or education, 45% were unemployed, and 26% were exempt due to disability. Mean PANSS positive sub-scale score was 13 and negative sub-scale score was 15. 88.6% had a lifetime history of cannabis dependency, with 76.9% being currently dependent. Participants had used cannabis on an average of 112.8 days in the last 6 months, and 78.6% tested positive for cannabis. While other clinical variables were collected at baseline, diagnosis information was collected at 18 months. 27% had received a diagnosis of schizophrenia, 12% bipolar or depression with psychotic illness, and 61% another psychotic illness.
6.2.2 – Participation in treatment (CM and psychoeducation)

In the experimental group, the median number of CM sessions attended was nine and five psychoeducation sessions. In the control group, the median number of psychoeducation sessions attended was four (table 6.1). These figures were very similar in the whole CIRCLE sample.

6.2.3 – Missing data

Most missing data at both follow-ups were missing due to participants not being followed up for the CIRCLE follow-up interview assessment (figure 6.1). 116 participants (32.86%) were not followed up at 3 months and 165 at 18 months (46.74%). In the main trial (chapter 5.2.2), a similar proportion were not followed up at 3 months (180/551, 32.7%) and at 18 months (273/551, 49.5%). In CIRCLE, most people not followed up were lost to contact (130/180 at 3 months; 202/273 at 18 months), and a minority declined or withdrew (43/180 at 3 months; 69/273 at 18 months) or were too unwell (7/180 at 3 months; 2/273 at 18 months). Baseline predictors of missingness at 3 months included having a history of cannabis dependence (Odds Ratio (OR)=2.27, CI 95% 1.17,4.42, p=0.02), current dependence (OR=0.52, CI 95% 0.28,0.98, p=0.04), and being unemployed (OR=0.6, 95% CI 0.36, 0.99, p=0.05). No other baseline measures predicted follow-up at 3 months. Where analyses adjusted for predictors of missingness, current cannabis dependence and being unemployed at baseline were included in the analyses. History of cannabis dependence was omitted due to collinearity with current cannabis dependence. No baseline measures predicted follow-up at 18 months. Amongst those followed up at 3 months, incomplete questionnaires meant that primary outcome was missing for 5 participants (1.4%).
Figure 6.1 – consort diagram of participants in the study

Table 6.1 - Sample Characteristics at baseline (N=353)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Present study (n=353)</th>
<th>CIRCLE trial overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N, Mean, or median</td>
<td>% or (SD) or (IQR)</td>
</tr>
<tr>
<td>Age (mean)</td>
<td>23.9 (4.2)</td>
<td>24.5 (4.0)</td>
</tr>
<tr>
<td>Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experimental</td>
<td>175/353</td>
<td>49.6</td>
</tr>
<tr>
<td>Gender</td>
<td>298/353</td>
<td>84.4</td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>325/353</td>
<td>92.0</td>
</tr>
<tr>
<td>Married or cohabiting</td>
<td>23/353</td>
<td>6.5</td>
</tr>
<tr>
<td>Other</td>
<td>5/353</td>
<td>1.5</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>178/353</td>
<td>50.4</td>
</tr>
<tr>
<td>Black</td>
<td>91/353</td>
<td>25.8</td>
</tr>
<tr>
<td>Asian</td>
<td>37/353</td>
<td>10.5</td>
</tr>
<tr>
<td>Other</td>
<td>47/353</td>
<td>13.3</td>
</tr>
<tr>
<td>Highest education level attained</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Qualifications</td>
<td>57/352</td>
<td>16.1</td>
</tr>
<tr>
<td>GCSE or equivalent</td>
<td>145/352</td>
<td>41.1</td>
</tr>
<tr>
<td>A-level or equivalent</td>
<td>83/352</td>
<td>23.5</td>
</tr>
<tr>
<td>Post-18 education (university, HND, etc.)</td>
<td>67/352</td>
<td>19.0</td>
</tr>
<tr>
<td>Living arrangements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lives alone</td>
<td>82/353</td>
<td>23.2</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>--------</td>
<td>------</td>
</tr>
<tr>
<td>Lives with parents</td>
<td>160/353</td>
<td>45.3</td>
</tr>
<tr>
<td>Lives with other adults (with or without children)</td>
<td>106/353</td>
<td>30.0</td>
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<tr>
<td>Other</td>
<td>5/353</td>
<td>1.42</td>
</tr>
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</table>

**Housing**

<table>
<thead>
<tr>
<th>Independent accommodation</th>
<th>285/353</th>
<th>80.7</th>
<th>419/548</th>
<th>74.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supported accommodation</td>
<td>49/353</td>
<td>13.9</td>
<td>88/548</td>
<td>16.0</td>
</tr>
<tr>
<td>Other</td>
<td>19/353</td>
<td>5.4</td>
<td>41/548</td>
<td>7.5</td>
</tr>
<tr>
<td>Have a job now or have had in the past</td>
<td>291/353</td>
<td>82.4</td>
<td>463/551</td>
<td>84.0</td>
</tr>
<tr>
<td>Currently in work or education</td>
<td>119/353</td>
<td>33.7</td>
<td>140/551</td>
<td>25.4</td>
</tr>
</tbody>
</table>

**Cannabis use**

<table>
<thead>
<tr>
<th>Self-reported days of cannabis use in the last 6 months (mean)</th>
<th>112.8 (49.0)</th>
<th>107.8 (49.6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinalysis positive for cannabis</td>
<td>269/342</td>
<td>78.6</td>
</tr>
</tbody>
</table>

**Cannabis dependence**

| Lifetime history of dependence | 311/353 | 88.6 | 475/548 | 86.7 |
| Current prevalence of dependence | 239/353 | 76.9 | 369/475 | 77.7 |

**Severity of cannabis dependence for those currently dependent**

| Mild | 64/239 | 26.8 | 86/369 | 23.3 |
| Moderate | 111/239 | 46.4 | 183/369 | 50.0 |
| Severe | 64/239 | 26.8 | 100/369 | 27.1 |

**Symptom severity**

<table>
<thead>
<tr>
<th>PANSS Positive sub-scale (max value = 49) (median)</th>
<th>12 (9, 16)</th>
<th>12 (9, 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PANSS Negative sub-scale (max value = 49) (median)</td>
<td>14 (10, 19)</td>
<td>14 (10, 19)</td>
</tr>
</tbody>
</table>

**Diagnosis (collected at 18 months)**

| Schizophrenia or schizoaffective disorders | 92/339 | 27.1 | 170/524 | 32.4 |
| bipolar disorder | 32/339 | 9.44 | 45/524 | 8.6 |
| Depression with psychotic symptoms | 8/339 | 2.36 | 16/524 | 3.1 |
| Other psychosis | 207/339 | 61.1 | 293/524 | 55.9 |

**Compliance with CIRCLE treatment**

| Psychoeducation sessions attended by experimental group (max value = 6) (median and IQR) | 5 (0, 6) | 6 (1, 6) |
| Psychoeducation sessions attended by control group (max value = 6) (median and IQR) | 4 (0, 6) | 4 (0, 6) |
| Contingency management sessions attended (max = 12) (median and IQR) | 9 (0, 12) | 9 (3,12) |

**Cognitive-behavioural measures**

| Intrinsic Motivation Baseline (max value = 4) (mean) | 2.22 (0.8) | NA | NA |
| Extrinsic Motivation Baseline (max value = 4) (mean) | 1.80 (0.9) | NA | NA |
| Self-concept (intrinsic motivation) (mean) | 2.62 (1.04) | NA | NA |
| Legal (extrinsic motivation) (mean) | 1.76 (1.13) | NA | NA |
| Social (extrinsic motivation) (mean) | 1.83 (0.97) | NA | NA |
| Health (intrinsic motivation) (mean) | 0.71 (0.50) | NA | NA |
| Mental health concerns (mean) | 2.47 (1.26) | NA | NA |
| Negative use expectancies (mean) | 1.99 (1.07) | NA | NA |
| Financial (mean) | 2.09 (1.42) | NA | NA |
| Readiness-to-change (max value = 5) (mean) | 3.64 (1.3) | NA | NA |
| Overall motivation at baseline (max value = 10) (mean) | 6.78 (2.54) | NA | NA |
Confidence in quitting at baseline (max value = 10) (mean) 6.39 (2.53) NA NA
Perceived difficulty of quitting at baseline (max value = 10) (mean) 6.48 (2.78) NA NA
Frequency of urges at baseline (max value = 6) (mean) 3.66 (1.48) NA NA
Strength of urges at baseline (max value = 6) (mean) 3.57 (1.43) NA NA
Exposure to peers using cannabis at baseline (max value = 10) (mean) 6.54 (3.0) NA NA

6.2.4 – Validation of the RFQ for marijuana in a UK cohort with psychosis

A summary of the RFQ scores at baseline are presented in table 6.2. A discussion of the endorsement of each item by participants as a reason for quitting is presented in chapter 8.

The original paper (Curry, Wagner, & Grothaus, 1990) proposed two structural models for the RFQ: Firstly, a model with four hypothesised factors: 1) whether being a cannabis user fits with their self-image or concept (self-concept); 2) concerns about the impact of cannabis on their physical health (health); 3) concerns about the legal repercussions of cannabis use (legal); 4) social pressure, especially from peers, family, or significant others (social). The second structural model featured two hypothesised factors: IM and EM. Items loading on the self-concept and health factors were believed also to be components of IM, and the items hypothesised to load on the legal and social factors were thought to also be components of EM.

Table 6.2 - RFQ item characteristics (N=353)
5. So that I can get praise from people I am close to. Social 1.67 1.37
6. Because using cannabis does not fit who I want to be. Self-concept 2.14 1.41
7. Because using cannabis is becoming less socially acceptable. Social 1.61 1.39
8. Because someone gave me an ultimatum. Social 1.44 1.41
9. Because I am concerned that I will suffer from a serious illness if I don’t quit. Health 2.22 1.45
10. Because people I am close to will be upset with me if I don’t quit. Social 2.07 1.38
11. Because I have physical health symptoms related to smoking cannabis (such as lung/chest problems). Health 1.51 1.35
12. Because I want to save the money that I spend on cannabis. Social 2.71 1.36
13. Because of legal problems related to cannabis. Legal 1.70 1.40
14. Because I know people who have suffered from serious illnesses caused by cannabis. Health 1.60 1.42
15. To prove to myself that I am not addicted to cannabis. Self-concept 2.34 1.39
16. To avoid being arrested or receiving a conviction. Legal 1.83 1.51
17. Because I want to avoid involvement in anything illegal. Legal 1.9 1.50
18. Because there is a drug testing policy where I work. Legal 0.05 0.23
19. Because I won’t have to leave social functions or other people's houses. Social 1.30 1.01
20. Because I am concerned that smoking cannabis will shorten my life. Health 1.32 1.07

6.2.4.1 – Confirmatory Factor Analysis

Appendix 6.2 shows the structural equation model used for the confirmatory factor analysis. The confirmatory factor analysis was performed as a complete case analysis, which included 345 participants. 8 were excluded due to incomplete data. The sample size meets the suggested minimum (N=300) for performing a confirmatory factor analysis (Myers, Ahn, & Jin, 2011). In the results from the confirmatory factor analysis, all loadings were statistically significant except item 18 (‘Because there is a drug testing policy where I work’) (appendix 6.2). Covariance terms between latent variables indicated that all factors moderately correlated with one another. Goodness of fit statistics indicated that the model fitted the data poorly (root mean squared error of approximation (RMSEA) = 0.09;
Comparative fit index = 0.77; Tucker-Lewis index = 0.74). The confirmatory factor analysis was run again excluding item 18, however goodness of fit diagnostic metrics still indicated a poor fit for the model.

6.2.4.2 – Exploratory Factor Analysis

Due to the poor model fit and high covariance in results of the confirmatory factor analysis, an exploratory factor analysis was performed. The aim was to examine the factor structure of the RFQ in this cohort and identify how to use the questionnaire to measure intrinsic and EM. The poor model fit and high covariance suggested that the hypothesised factor structure, or measurement model, did not fit the data from this cohort. As such, a new model was sought. The factorability of the RFQ in this cohort was initially examined. Tests of the assumptions of the exploratory factor analysis indicated that factor analysis would be appropriate in this circumstance (appendix 6.3, table appendix 2).

The PCA found five components with Eigenvalues over 1. Since dimensions were correlated, an oblique rotation was used. Table 6.3 shows the final results of the PCA. More results are presented in appendix 6.3 (table appendix 3-6). There was low to moderate levels of association between the five factors.

Table 6.3 - Promax oblique rotated solution

<table>
<thead>
<tr>
<th>Item number</th>
<th>Factor1 (Legal)</th>
<th>Factor2 (Self)</th>
<th>Factor3 (Social)</th>
<th>Factor4 (Health)</th>
<th>Factor5 (drug testing)</th>
<th>Uniqueness</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. To show myself that I can quit if I want to.</td>
<td>0.04</td>
<td>0.69*</td>
<td>0.12</td>
<td>-0.04</td>
<td>0.25</td>
<td>0.40</td>
</tr>
<tr>
<td>2. Because I will feel better about myself if I quit.</td>
<td>-0.17</td>
<td>0.83*</td>
<td>0.07</td>
<td>0.10</td>
<td>-0.08</td>
<td>0.31</td>
</tr>
<tr>
<td>3. So that I can feel in control of my life.</td>
<td>-0.12</td>
<td>0.72*</td>
<td>0.21</td>
<td>-0.01</td>
<td>-0.23</td>
<td>0.39</td>
</tr>
<tr>
<td>4. Because my family or someone else I am close to will stop nagging me about using cannabis if I quit.</td>
<td>-0.08</td>
<td>0.17</td>
<td>0.76*</td>
<td>-0.02</td>
<td>-0.06</td>
<td>0.41</td>
</tr>
<tr>
<td>5. So that I can get praise from people I am close to.</td>
<td>0.18</td>
<td>-0.04</td>
<td>0.66*</td>
<td>-0.02</td>
<td>0.03</td>
<td>0.46</td>
</tr>
<tr>
<td>6. Because using cannabis does not fit who I want to be.</td>
<td>0.37</td>
<td>0.46</td>
<td>-0.03</td>
<td>0.10</td>
<td>-0.12</td>
<td>0.51</td>
</tr>
<tr>
<td>Item</td>
<td>Factor 1</td>
<td>Factor 2</td>
<td>Factor 3</td>
<td>Factor 4</td>
<td>Factor 5</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
<td></td>
</tr>
<tr>
<td>7. Because using cannabis is becoming less socially acceptable.</td>
<td>0.58</td>
<td>-0.17</td>
<td>0.21</td>
<td>0.09</td>
<td>0.06</td>
<td>0.52</td>
</tr>
<tr>
<td>8. Because someone gave me an ultimatum.</td>
<td>0.24</td>
<td>-0.30</td>
<td>0.46</td>
<td>0.14</td>
<td>-0.16</td>
<td>0.54</td>
</tr>
<tr>
<td>9. Because I am concerned that I will suffer from a serious illness if I don't quit.</td>
<td>0.15</td>
<td>0.42</td>
<td>-0.10</td>
<td>0.51</td>
<td>0.01</td>
<td>0.45</td>
</tr>
<tr>
<td>10. Because people I am close to will be upset with me if I don't quit.</td>
<td>0.09</td>
<td>0.12</td>
<td>0.64*</td>
<td>-0.03</td>
<td>-0.22</td>
<td>0.43</td>
</tr>
<tr>
<td>11. Because I have physical health symptoms related to smoking cannabis (such as lung/chest problems).</td>
<td>-0.17</td>
<td>0.03</td>
<td>0.10</td>
<td>0.76*</td>
<td>0.04</td>
<td>0.44</td>
</tr>
<tr>
<td>12. Because I want to save the money that I spend on cannabis.</td>
<td>0.13</td>
<td>0.72*</td>
<td>-0.17</td>
<td>-0.01</td>
<td>-0.04</td>
<td>0.44</td>
</tr>
<tr>
<td>13. Because of legal problems related to cannabis.</td>
<td>0.39</td>
<td>-0.12</td>
<td>0.02</td>
<td>0.53</td>
<td>0.02</td>
<td>0.47</td>
</tr>
<tr>
<td>14. Because I know people who have suffered from serious illnesses caused by cannabis.</td>
<td>0.88</td>
<td>-0.16</td>
<td>-0.01</td>
<td>-0.08</td>
<td>0.01</td>
<td>0.32</td>
</tr>
<tr>
<td>15. To prove to myself that I am not addicted to cannabis.</td>
<td>0.34</td>
<td>0.48</td>
<td>0.11</td>
<td>-0.14</td>
<td>0.18</td>
<td>0.51</td>
</tr>
<tr>
<td>16. To avoid being arrested or receiving a conviction.</td>
<td>0.79*</td>
<td>0.11</td>
<td>0.04</td>
<td>-0.08</td>
<td>0.01</td>
<td>0.32</td>
</tr>
<tr>
<td>17. Because I want to avoid involvement in anything illegal.</td>
<td>0.76*</td>
<td>0.23</td>
<td>-0.09</td>
<td>-0.03</td>
<td>-0.02</td>
<td>0.34</td>
</tr>
<tr>
<td>18. Because there is a drug testing policy where I work.</td>
<td>0.02</td>
<td>-0.09</td>
<td>-0.02</td>
<td>0.08</td>
<td>0.85*</td>
<td>0.29</td>
</tr>
<tr>
<td>19. Because I won't have to leave social functions or other people's houses.</td>
<td>-0.12</td>
<td>0.10</td>
<td>0.69*</td>
<td>0.01</td>
<td>0.38</td>
<td>0.43</td>
</tr>
<tr>
<td>20. Because I am concerned that smoking cannabis will shorten my life.</td>
<td>-0.10</td>
<td>0.04</td>
<td>-0.07</td>
<td>0.80*</td>
<td>0.05</td>
<td>0.41</td>
</tr>
</tbody>
</table>

* Items meeting threshold for inclusion on that factor

Parallel analysis (Franklin et al., 1995) for principal components analysis was performed, taking the average of 10 replications of the random dataset (appendix 6.3, figure appendix 3). The plot indicated that four dimensions should be retained. The fifth factor had only one questionnaire item (item 18) loading on it and so was dropped. Based on the criteria for inclusion adopted by McBride and colleagues (1994), the resulting four dimensions were:

1) Self-concept: items 1, 2, 3, and 12
2) Health: items 11 and 20
3) Legal: items 16, and 17
4) Social: items 4, 5, 10, and 19

Cronbach’s alpha tests (table 6.4) indicated that the four dimensions had reasonable to good internal consistency. The correlational matrix indicates weak to moderate associations between dimensions, with legal and social dimensions correlating most strongly (0.43), which are both conceptualised as together comprising EM.

IM and EM measures were produced by taking the mean of the dimensions hypothesised to comprise them. For IM, these were the health and self-concept dimensions, and the legal and social dimensions for EM. Summary statistics for the factors are in table 6.4.

Participants’ endorsement of each factor is discussed in chapter 8.3.1.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Number of questionnaire items</th>
<th>mean</th>
<th>SD</th>
<th>Cronbach’s α</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor 2: self</td>
<td>4</td>
<td>2.62</td>
<td>1.04</td>
<td>0.78</td>
</tr>
<tr>
<td>Factor 4: health</td>
<td>2</td>
<td>1.41</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Factor 1: legal</td>
<td>2</td>
<td>1.86</td>
<td>1.13</td>
<td>0.79</td>
</tr>
<tr>
<td>Factor 3: social</td>
<td>4</td>
<td>1.83</td>
<td>0.97</td>
<td>0.71</td>
</tr>
<tr>
<td>Factor 2&amp;4: IM</td>
<td>6</td>
<td>2.02</td>
<td>0.76</td>
<td>0.67</td>
</tr>
<tr>
<td>Factor 1&amp;3: EM</td>
<td>6</td>
<td>1.77</td>
<td>0.9</td>
<td>0.8</td>
</tr>
</tbody>
</table>

6.2.5 – Primary analysis: does CM for cannabis in psychosis improve intrinsic motivation to abstain?

Results are shown in table 6.6. Univariate linear regression analyses showed very weak evidence of association between group allocation and IM at 3 months, with the experimental (CM) group showing very slightly lower IM compared to the control group (β=-0.19, 95% CI -0.41 to 0.03, p=0.08). In this analysis, IM in the control group rose very slightly (0.07), while it fell in the experimental (CM) group (-0.12), implying that CM may have had a slight negative (but non-significant) effect on IM.

However, in the primary analysis, which adjusted for predictors of missingness and number of psychoeducation sessions attended, there was no evidence that the CM impacted IM by treatment end (β= -0.07, 95% CI = -0.32, 0.18, p=0.59).
Post-analysis diagnostic tests were performed for the adjusted model (appendix 6.4). There was no evidence of heteroscedasticity (Breusch-Pagan test: p=0.91). Residual plots overall indicated that normality assumptions were met (appendix 6.4, figure appendix 4-6). Variance Inflation Factors (VIF’s) indicated no collinearity between variables (mean vif = 1.02). Outliers were checked for, and although some influential points were identified, added-variable plots and scatter plots of the individual predictor variables against the outcome variable together suggested that removing influential points likely would not improve the model (appendix 6.4). No data points were removed.

6.2.6 – Secondary analyses: examining the impact of CM on other cognitive-behavioural measures

Descriptive statistics of the cognitive-behavioural variables at follow-up are presented in table 6.5. All change measures indicated minimal difference by either follow-up, with virtually all values being under ± 1. However, by treatment end, in the experimental group, both IM and EM had decreased very slightly (mean=-0.12, SD=0.81; -0.12, 0.81 respectively), but rose by a similar amount in the control group (0.07, 0.88; 0.07, 0.79 respectively). Concerns about the impact of cannabis on mental health and concerns about the cost of cannabis had also fallen slightly in the experimental group (-0.10, 1.28; -0.31, 1.44) but rose slightly in the controls (0.12, 1.23; 0.06, 1.70). Meanwhile, overall motivation (0.16, 3.2), readiness-to-change (0.23, 1.89), and negative cannabis use expectancies (0.06, 1.06) all increased in the experimental group and decreased or remained flat in controls (-0.29, 3.41; 0.01, 1.81; -0.05, 1.21). Confidence in quitting, time spent with cannabis using peers (exposure to cannabis use), and frequency and strength of urges all decreased in both experimental (-0.06, 2.99; -0.63, 3.55; -0.77, 1.69; -0.62, 1.56) and control groups (-0.09, 3.50; -0.43, 3.61; -0.51, 1.55; -0.42, 1.57). Overall, this pattern of results suggests that in general there was a minimal effect from the CIRCLE treatment, especially on IM and EM. However, there was some evidence of improvements in self-efficacy (lower perceived
difficulty in quitting), decreased urges, and motivating participants to spend less time with cannabis using peers during the CIRCLE treatments.

CM had little effect by 3-month or 18-month follow-up (table 6.6) on any cognitive-behavioural measure in univariate linear regression analyses. After adjusting for predictors of missingness and number of psychoeducation sessions attended, at 3-month follow-up only frequency of urges differed significantly between groups, with the experimental group experiencing urges less frequently than controls ($\beta = -0.50$, 95% CI -0.97, -0.03, p=0.04). At 18 months, IM and physical health concerns differed slightly by group, with results showing that the experimental group had lower of both (IM: $\beta = -0.30$, 95% CI -0.6 0, p=0.05; physical health concerns: -0.20, 95% CI -0.40, -0.01, p=0.04). No other measures showed any evidence of an effect from the intervention.

Table 6.5 - average change in outcomes measures by follow-up

<table>
<thead>
<tr>
<th>Variable</th>
<th>Change at 3 months by group</th>
<th>Change at 18 months by group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Experimental group Mean (SD)</td>
<td>Control group Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>Experimental group Mean (SD)</td>
<td>Control group Mean (SD)</td>
</tr>
<tr>
<td>IM* (max =)</td>
<td>-0.12 (0.81)</td>
<td>0.07 (0.88)</td>
</tr>
<tr>
<td>EM (max =)</td>
<td>-0.12 (0.81)</td>
<td>0.07 (0.79)</td>
</tr>
<tr>
<td>Self (max =)</td>
<td>-0.17 (0.96)</td>
<td>0.05 (1.13)</td>
</tr>
<tr>
<td>Legal (max =)</td>
<td>-0.12 (0.91)</td>
<td>0.10 (1.01)</td>
</tr>
<tr>
<td>Social (max =)</td>
<td>0.18 (1.00)</td>
<td>0.16 (0.85)</td>
</tr>
<tr>
<td>Health (max =)</td>
<td>0.01 (0.58)</td>
<td>0.05 (0.65)</td>
</tr>
<tr>
<td>Mental health concerns (max =)</td>
<td>-0.10 (1.28)</td>
<td>0.12 (1.23)</td>
</tr>
<tr>
<td>Can’t afford to use cannabis (max =)</td>
<td>-0.31 (1.44)</td>
<td>0.06 (1.70)</td>
</tr>
<tr>
<td>Negative cannabis use expectancies (max =)</td>
<td>0.06 (1.06)</td>
<td>-0.05 (1.21)</td>
</tr>
<tr>
<td>Overall motivation (max =)</td>
<td>0.16 (3.20)</td>
<td>-0.29 (3.41)</td>
</tr>
<tr>
<td>Confidence in quitting (max =)</td>
<td>-0.06 (2.99)</td>
<td>-0.09 (3.50)</td>
</tr>
<tr>
<td>Perceived difficulty (max =)</td>
<td>-1.07 (4.13)</td>
<td>-0.79 (3.66)</td>
</tr>
<tr>
<td>Readiness-to-change (max =)</td>
<td>0.23 (1.89)</td>
<td>0.01 (1.81)</td>
</tr>
<tr>
<td>Exposure to cannabis using peers (max =)</td>
<td>-0.63 (3.55)</td>
<td>-0.43 (3.61)</td>
</tr>
<tr>
<td>Frequency of urges (max =)</td>
<td>-0.77 (1.69)</td>
<td>-0.51 (1.55)</td>
</tr>
</tbody>
</table>
**Table 6.6 - linear regression estimates of cognitive-behavioural change measures by group at follow-up**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unadjusted</th>
<th>Adjusted†</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimate*</td>
<td>95% CI</td>
</tr>
<tr>
<td><strong>Primary Outcome:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IM (3 months)</td>
<td>-0.19</td>
<td>-0.41, 0.03</td>
</tr>
<tr>
<td><strong>Secondary Outcomes:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IM (18 months)</td>
<td>-0.30</td>
<td>-0.60, 0.00</td>
</tr>
<tr>
<td>EM (3 months)</td>
<td>-0.05</td>
<td>-0.25, 0.15</td>
</tr>
<tr>
<td>EM (18 months)</td>
<td>-0.06</td>
<td>-0.40, 0.28</td>
</tr>
<tr>
<td>Self (3 months)</td>
<td>-0.22</td>
<td>-0.49, 0.05</td>
</tr>
<tr>
<td>Self (18 months)</td>
<td>-0.25</td>
<td>-0.65, 0.16</td>
</tr>
<tr>
<td>Legal (3 months)</td>
<td>-0.21</td>
<td>-0.46, 0.04</td>
</tr>
<tr>
<td>Legal (18 months)</td>
<td>0.01</td>
<td>-0.40, 0.41</td>
</tr>
<tr>
<td>Social (3 months)</td>
<td>0.02</td>
<td>-0.22, 0.25</td>
</tr>
<tr>
<td>Social (18 months)</td>
<td>-0.06</td>
<td>-0.42, 0.29</td>
</tr>
<tr>
<td>Health (3 months)</td>
<td>-0.04</td>
<td>-0.20, 0.12</td>
</tr>
<tr>
<td>Health (18 months)</td>
<td>-0.19</td>
<td>-0.39, 0.00</td>
</tr>
<tr>
<td>Mental health concerns (3 months)</td>
<td>-0.22</td>
<td>-0.54, 0.10</td>
</tr>
<tr>
<td>Mental health concerns (18 months)</td>
<td>-0.31</td>
<td>-0.79, 0.18</td>
</tr>
<tr>
<td>Can’t afford to use cannabis (3 months)</td>
<td>-0.37</td>
<td>-0.78, 0.03</td>
</tr>
<tr>
<td>Can’t afford to use cannabis (18 months)</td>
<td>0.08</td>
<td>-0.47, 0.63</td>
</tr>
<tr>
<td>Negative cannabis use expectancies (3 months)</td>
<td>0.10</td>
<td>-0.19, 0.39</td>
</tr>
<tr>
<td>Negative cannabis use expectancies (18 months)</td>
<td>-0.04</td>
<td>-0.41, 0.34</td>
</tr>
<tr>
<td>Overall motivation (3 months)</td>
<td>0.45</td>
<td>-0.41, 1.3</td>
</tr>
<tr>
<td></td>
<td>Estimate</td>
<td>95% CI</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>----------</td>
<td>----------------</td>
</tr>
<tr>
<td><strong>Overall motivation</strong> (18 months)</td>
<td>-0.92</td>
<td>-1.99, 0.16</td>
</tr>
<tr>
<td><strong>Confidence in quitting</strong> (3 months)</td>
<td>0.04</td>
<td>-0.80, 0.88</td>
</tr>
<tr>
<td><strong>Confidence in quitting</strong> (18 months)</td>
<td>-0.87</td>
<td>-1.91, 0.17</td>
</tr>
<tr>
<td><strong>Perceived difficulty</strong> (3 months)</td>
<td>-0.28</td>
<td>-1.28, 0.73</td>
</tr>
<tr>
<td><strong>Perceived difficulty</strong> (18 months)</td>
<td>0.18</td>
<td>-1.06, 1.42</td>
</tr>
<tr>
<td><strong>Readiness-to-change</strong> (3 months)</td>
<td>0.22</td>
<td>-0.26, 0.71</td>
</tr>
<tr>
<td><strong>Readiness-to-change</strong> (18 months)</td>
<td>0.10</td>
<td>-0.47, 0.67</td>
</tr>
<tr>
<td><strong>Exposure to cannabis using peers</strong> (3 months)</td>
<td>-0.20</td>
<td>-1.13, 0.72</td>
</tr>
<tr>
<td><strong>Exposure to cannabis using peers</strong> (18 months)</td>
<td>-0.56</td>
<td>-1.67, 0.55</td>
</tr>
<tr>
<td><strong>Frequency of urges</strong> (3 months)</td>
<td>-0.25</td>
<td>-0.68, 0.17</td>
</tr>
<tr>
<td><strong>Frequency of urges</strong> (18 months)</td>
<td>0.02</td>
<td>-0.53, 0.58</td>
</tr>
<tr>
<td><strong>Strength of urges</strong> (3 months)</td>
<td>-0.20</td>
<td>-0.61, 0.21</td>
</tr>
<tr>
<td><strong>Strength of urges</strong> (18 months)</td>
<td>0.25</td>
<td>-0.30, 0.81</td>
</tr>
</tbody>
</table>

* - Estimate of the regression β coefficient (mean difference in outcome variable in the experimental (CM) group compared to controls). † - adjusted for psychoeducation sessions attended and predictors of missingness (being unemployed at baseline, having current dependence at baseline)
6.3 – Discussion

6.3.1 – Main findings

This chapter presents the results of an analysis of a hypothesised cognitive-behavioural mechanism underlying CIRCLE CM intervention. Although outcomes in the intention-to-treat analysis in CIRCLE showed no evidence of improvement in cannabis use and other clinical outcomes, there was some evidence of an effect amongst those who complied with treatment. Thus, prior to conducting the analysis in this chapter, it was supposed that CM could have improved motivation even if this did not translate into behavioural change across the whole group (but was detectable amongst those who complied with treatment).

The process evaluation of the cognitive-behavioural mechanism of change presented in this chapter and chapter 4 considered: 1) intrinsic, extrinsic, and overall motivation, 2) self-efficacy, 3) readiness-to-change, 4) strength and frequency of cravings, and 5) exposure to cannabis using peers. Intrinsic and EM were measured using the RFQ questionnaire (McBride et al., 1994).

As the RFQ had never been validated in a cohort of people with psychosis and cannabis use, nor in a UK based population, the first step of the analysis was to validate the measure in this cohort. The initial confirmatory factor analysis failed to validate the hypothesised factor structure. However, the subsequent exploratory factor analysis found a broadly similar factor structure to the one originally proposed by McBride and colleagues (1994) for cannabis users, with most items loading on the expected factors. However, slightly different questionnaire items met inclusion criteria compared to the original validation of the RFQ in tobacco users (Curry, Wagner, & Grothaus, 1990) or in cannabis users (McBride et al., 1994). In both papers, the same items loaded on the self-factor. However, in addition to items 11 and 20, which both loaded on the health factor in the present analysis, in McBride and colleagues (1994) items 9 (‘Because I am concerned that I will suffer from a
serious illness if I don’t quit’) and 14 (‘Because I know people who have suffered from serious illnesses caused by cannabis’) also loaded on it. The social factor differed slightly, with the same two items (4 and 10) being included in the factor in both papers. However, in the present paper, items 19 or 5 also loaded on the factor, while in McBride and colleagues (1994) item 8 (‘Because someone gave me an ultimatum’) loaded instead. Finally, the same two items (16 and 17) again loaded on the legal factor in both analyses, while in McBride and colleagues (1994) item 13 (‘Because of legal problems related to cannabis’) and 18 also loaded on the factor. Overall, the similarities between analyses suggest few substantial differences between reasons for quitting in this cohort compared to the McBride and colleagues (1994) cohort (participants receiving treatment for cannabis misuse in the USA). The only exception to this is item 18, which is probably attributable to differences in the prevalence of drug testing in the work-place in the UK compared to the USA, and the relatively low rates of employment in this cohort. A discussion of the degree of endorsement of individual items in the RFQ is presented in chapter 8.

Across the whole sample, there was little change in any cognitive-behavioural measures by follow-up. The mean change at both 3 months and 18 months for almost all variables was less than ± 1. Overall, these results suggest that the CIRCLE CM intervention had a minimal cognitive-behavioural impact by either treatment end or by 18-month follow-up. So while there was a high level of dependency in the sample recruited (chapter 3), there was also a fairly low degree of self-reported motivation to quit. This is despite the psychoeducation package providing information about the impact of using cannabis on health, potential legal repercussions, and its aim of reducing motivational ambivalence about quitting cannabis.

The primary and secondary analyses explored the cognitive-behavioural mechanism of action of the CIRCLE CM intervention. Overall, there was a lack of a clear effect from the
CM in the present analysis. In the primary analysis, there was no evidence of CM impacting IM by treatment end. Similar results were found for most secondary outcomes. However, compared to controls, there was weak evidence of the CM group having reduced frequency of urges slightly at 3-month ($\beta = -0.50$, 95% CI -0.97, -0.03, $p=0.04$), but not at 18-month follow-up. This result may potentially suggest that CM may have had some benefit, but that a different CM scheme design may be required.

The CM group also reported reduced IM and physical health concerns at 18 months (IM: $\beta = -0.30$, 95% CI -0.60, $p=0.05$; physical health concerns: -0.20, 95% CI -0.40, -0.01, $p=0.04$). As physical health concerns are one of the two subscales used to measure IM, and that the other subscale (self-concept) did not differ between groups, it is likely that the difference in IM is driven by physical health concerns. In both cases, the evidence of an effect is weak, and the effect size is small. It may be that physical health concerns were impacted slightly by the PE, which experimental participants engaged with better than controls.

However, given the lack of impact on other cognitive-behavioural measures, and the lack of change in cannabis use at either 3 or 18 months (chapter 3), CM did not appear to have any clear benefit. While it appears that CM impacted IM by 18 months, since there was no effect at 3-months it is unclear if this effect was due to the CM treatment. Overall, there was limited evidence of an impact from the CM intervention on any cognitive-behavioural measure. As no post-hoc corrections for multiple-comparison were made and results were mixed, with no clear rationale for happening, any weak evidence of small effects should be treated with caution.

Compliance with treatment in CIRCLE was generally quite high (median of nine sessions attended out of maximum of 12), but around one fifth of participants failed to attend any CM or psychoeducation sessions at all. A compliance analysis in CIRCLE suggested that those who engaged with treatment appeared to benefit from receiving the CM. However,
controlling for compliance with the CIRCLE treatment in this study failed to find any cognitive-behavioural benefit for the CM. As such, evidence is mixed about whether CM benefitted participants who engaged with the treatment. Again, this perhaps suggests that the CM treatment may have had some effect, but it appears to be minimal and did not clearly improve trial or cognitive-behavioural outcomes, even amongst those who complied with treatment. Perhaps if there was an effect from CM, it might be strengthened by a different design of scheme, such as higher or more frequent rewards.

Since the CM intervention did not appear to impact cannabis use or cognitive-behavioural outcomes in the CIRCLE trial, and there was little evidence of any cognitive-behavioural variable changing much during treatment, no further analysis was conducted of whether the hypothesised model (figure 4.1) fitted the data. If there had been evidence of an effect from the CM intervention, such an analysis would have helped understand the cognitive-behavioural mechanism of action of CM in this cohort.

6.3.2 – Limitations

There were a number of limitations to this study. Firstly, the post-hoc analysis in the CIRCLE trial used a measure of compliance with the CIRCLE treatment of attending at least four psychoeducation sessions. However, in the present study compliance was adjusted for by including the number of attended psychoeducation sessions as a covariate in regression analyses, as this was the planned analysis method. It is conceivable that this difference in approach meant that an effect from the CM was not identified in this study, despite one being found in the main trial.

Secondly, although the number of psychoeducation sessions participants attended was adjusted for, it is likely that the skills and experience of clinicians varied, as did the quality of the relationship between clinicians and participants. Given that the psychoeducation relied heavily on the skills and experience of clinicians, and the mix of backgrounds of those
clinicians (as described in chapter 3.2.6) who could be cases care coordinators, support workers, or assistant psychologists, this variation was potentially quite large. It may be that the quality of the therapeutic alliance between clinicians and their clients, as well as the backgrounds of clinicians, could both have affected the cognitive and behavioural impact of the psychoeducation treatment especially on participants. As such, they may moderate the relationship between the treatments and the cognitive-behavioural outcomes measured in this study. Unfortunately, information about clinicians’ skills and experience level was not collected. Equally, the quality of the therapeutic alliance was not measured. As such, it was not possible to explore this possibility in the analysis.

A third limitation is that the present study featured a sub-sample (approximately two-thirds) of the main trial. Although the demographic and clinical characteristics of sample in this study closely resembled the CIRCLE sample in general (table 6.1), the smaller sample size may have meant that small effects from the CM intervention were missed. This is another potential explanation for why an effect was identified in the main trial when controlling for treatment compliance but not in the present study.

Fourthly, change in cognitive-behavioural measures was used as the outcome variable in the analysis, calculated by subtracting baseline values from those at follow-up. This was chosen as it was the outcome of interest, and so the results were more intuitive. An alternative method would have been to include cognitive-behavioural values at follow-up as the outcome and baseline values as a covariate in the model. Such an approach may have led to slightly more precise estimates of the effect of CM treatment on the outcome measures.

Fifthly, it was planned that a third follow-up assessment would be conducted at six months post-treatment (nine months post-consent) to record participants’ cannabis use. Doing so would have offered more data on the course of cannabis use following treatment and
allowed the longevity of any effect from the CM intervention to be tested better.

Unfortunately, given the substantial pressures of conducting the CIRCLE trial, it soon became apparent once this data collection had begun that it was not feasible. As such, it was decided to stop collecting data at this time point.

Sixthly, while there is evidence that IM measured using the RFQ questionnaire has good predictive value of current and future cigarette use status (Foster et al., 2015; Pokhrel & Herzog, 2015), there is less evidence in cannabis using populations. In a study of 500 non-treatment seeking cannabis users, Chauchard and colleagues (2013) found no evidence of an association between baseline intrinsic or EM measured by the RFQ and cannabis use at follow-up. It may be that a better developed measure of IM would have had greater validity. However, the RFQ is currently one of the better and more widely used measures of IM in substance misuse, and one of the few to have been validated in cannabis using populations.

In addition, there were several limitations of to the CIRCLE study that are relevant to this study (chapter 5.3.2). These include that attrition in the present study, as in CIRCLE, was fairly high. Across CIRCLE, as well as this study, around a third of participants were not followed up by assessment interview at 3 months, and one half were not followed up at 18 months. At each follow-up point, around three-quarters of participants who were not followed-up could not be contacted by researchers. Around one fifth declined or withdrew, and a small number were too unwell. Few baseline measures predicted loss to follow-up, which meant that imputing missing values was unlikely to be useful. Instead, predictors of missingness were adjusted for in the analyses. However, it is plausible that data were not missing at random and that the factors driving missingness were not measured in this study. As such, it is difficult to know how attrition may have biased the results of the study.
Secondly, it is possible that a different CM intervention design or integrating it more into clinical care may have benefited this population more. For example, a higher reward value may have had a greater cognitive-behavioural effect.

Thirdly, while engagement with the interventions overall was quite good, and the analyses controlled for compliance with the CIRCLE treatments, it may be that the intervention would have had more of an impact on a more treatment seeking population.

Fourthly, it was suggested (chapter 5.3.3) that the psychoeducation package should be viewed as an active control, which could make it more difficult to interpret the impact of the CM. Specifically, in the context of the present study, it may be that any cognitive-behavioural impact of the CM is difficult to detect if the psychoeducation package has a substantial effect itself. However, the overall results, which suggest that there was minimal cognitive-behavioural change by treatment end across both groups, perhaps indicate that this is unlikely.

6.3.3 – Summary

Overall, the present analysis explored the cognitive-behavioural mechanism underlying the CIRCLE intervention, a CM programme for people with early psychosis and problematic cannabis use. The intention-to-treat analysis in the main CIRCLE trial showed no clinical benefit from the treatment. The results of the present study suggest that CM has a very limited impact either cognitively or behaviourally, but that there may have been some small impact on cravings. No effect from the intervention was found on motivation, readiness-to-change, self-efficacy, or exposure to cannabis using peers. Meanwhile, in CIRCLE there was evidence of a benefit from the CM treatment amongst those who complied with treatment, but no benefit was found in this study when adjusting for treatment adherence. Overall, these results do not provide clear evidence of a clear benefit from the CM treatment.
The next chapter presents a qualitative process evaluation of the CIRCLE trial. It explores participants’ experiences of the trial, their reasons for wanting to take part, and their views of the acceptability of CM treatment.
Chapter 7 – A qualitative study of participants’ experiences of the CIRCLE trial

7.1 – Introduction

7.1.1 – Background

As discussed in chapter 1.5, there is good evidence of CM being effective in a range of cohorts and behaviours (Giles et al., 2014). It is perhaps surprising then that only limited evidence of a clinical benefit from the CIRCLE CM intervention was found, either in the main CIRCLE trial or in the cognitive-behavioural analysis in chapter 4. In this chapter, a qualitative study is presented the aim of which is to explore participants’ views and experiences of the CIRCLE trial and both of its interventions. This study was performed alongside CIRCLE, and the data were collected before the results of the CIRCLE trial were known and they were analysed after the CIRCLE analysis had completed. As reported in chapters 3 and 4, no evidence was found for a benefit from the CIRCLE CM intervention on either cannabis use or the cognitive-behavioural factors investigated in the present thesis. The overall aim of this chapter is to explore patients’ own experiences of the CIRCLE trial.

In the past, limited qualitative data have been published exploring service user experiences of CM. A literature search using Medline and Google Scholar identified just one publication that has been published in the last 20 years. Neale, Tompkins, and Strang (2015) report a study of 20 service users in an injectable opioid treatment (IOT) clinic and who received a CM-like programme that incentivised patients to reduce their use of IOT. The authors report a process evaluation of the intervention in which they identify the barriers and facilitators of engaging with and benefiting from the treatment, as well as patients’ views of the intervention itself.
Neale, Tompkins, and Strang (2015) found that most patients were highly motivated, and that this was an important factor in them deciding to take part in, as well as engage with, treatment. Another important facilitator was their relationship with their care coordinator, and whether their clinician thought it was a good idea for them to take part. Many participants thought that it was important that the intervention had clear rules and being given the opportunity to ask questions about the treatment. This helped participants engage with treatment and benefit from taking part in the study. Meanwhile, low motivation to quit substance misuse was associated with poorer substance use outcomes and greater reluctance to take part. Another reason some patients gave for being reluctant to engage was that they were sceptical about the voucher scheme as it seemed ‘too good to be true’. They were unsure what the purpose of the intervention was or why it had been introduced.

In the present study, patients’ views of the CIRCLE CM and psychoeducation treatments will be elicited. It will build on previous work by focusing on a CM treatment for reducing substance use, which is a novel topic for qualitative research. Furthermore, the CIRCLE CM intervention was delivered alongside a psychoeducation package and therefore had a context that is also unique for this type of research.

7.1.2 – Aims

The overall aim of present qualitative analysis is to explore participants’ experiences of and perspectives on the CIRCLE trial. Specifically, the views of participants in the CIRCLE experimental (CM) group were elicited regarding the acceptability of CM as a treatment for cannabis use, both ethically and in terms of its appropriateness as a treatment. Secondly, participants’ views of the efficacy and the cognitive-behavioural impact of the CIRCLE CM and psychoeducation treatments were explored. This looked to elicit participants’ views on whether the CIRCLE treatments impact factors such as motivation and social relationships,
and whether it encourages long-term abstinence. Finally, it considers participants’ opinions of CM as an intervention to be delivered alongside other treatments, such as the psychoeducation treatment in CIRCLE, or whether it would be better as a stand-alone treatment.
7.2 – Methods

In the present study, participants’ experiences of and perspectives on the CIRCLE trial and its interventions are explored. Participants were recruited from the experimental arm (CM arm) of CIRCLE. Participants were approached following completion of the final follow-up assessment for CIRCLE at 18-months post-consent to avoid introducing bias to the main trial. Participants were interviewed in one-to-one interviews by a single researcher, and interviews were expected to last around 30-45 minutes. Thematic analysis was used to analyse the interview transcripts.

7.2.1 – Sample

It was planned that 20 participants would be included at first and then that the data collection would be reviewed. This sample size is in line with guidelines for medium sized studies of participant-generated data, analysed using thematic analysis (Braun & Clarke, 2013; Fugard & Potts, 2015; Ritchie et al., 2014). If it was thought that saturation had not been achieved, then more participants would be sampled. Saturation here means that, during interviews, participants were bringing up similar concepts or ideas to other interviewees, with little novel being elicited (Ando, Cousins, & Young, 2014). As the main focus of this work was the CIRCLE trial, it was intended that saturation should be achieved for participants’ views of the trial and its interventions.

Only participants in experimental group of the CIRCLE trial were included. Purposive sampling was used to obtain a heterogeneous group that reflected the diversity of the CIRCLE CM cohort. Sampling methods aimed to obtain a mix of: 1) genders, 2) ages, 3) ethnicities, 4) whether they were engaged in work or education, 5) levels of education attained, 6) psychotic illness severities, 7) cannabis use frequencies, 8) living circumstances, 9) geographical areas: rural and urban; in London and outside, and 10) those who quit cannabis use during the CIRCLE intervention period and those who did not.
Demographic and clinical data obtained for the sample included: age, gender, ethnicity, living arrangements, relationship status, employment status, self-reported cannabis use and cannabis urinalysis result, current polysubstance use, history of cannabis dependency, severity of psychotic symptoms, and diagnosis. Engagement with both the CIRCLE CM and psychoeducation treatments was also obtained. Demographic, clinical, and treatment engagement data for the participants were co-opted from the main CIRCLE trial.

7.2.2 – Ethical considerations

Ethical approval was received as part of a substantial amendment (no. 6) to the CIRCLE trial, reviewed by the London – South East NRES committee (REC reference 11/LO/1939) (the protocol is presented in appendix 7.1). Approval was given on the 22nd November 2016. The participant information sheet, consent form, and topic guide were amongst approved documents included in the amendment (appendix 7.1).

Participants had already taken part in the CIRCLE trial and had recently been followed up for the CIRCLE 18-month assessment interview. Prior to consenting to be in the study, participants were provided with a participant information sheet that explained all aspects of the qualitative study, including their right to refuse or withdrawal from the study without it affecting their involvement in the main trial. Participants had the opportunity to discuss the study with a researcher when initially informed of the study/given the participant information sheet and at the time of consent. Participants were given at least 24 hours to decide whether to proceed before consent was taken. All data were anonymised and stored securely in University College London. Participants without capacity to consent were not included.

7.2.3 – Interviews

One-to-one, semi-structured interviews were conducted by LSR and took place in EIP service centres participating in the CIRCLE trial or in participants’ homes. All interviews took
place between March and November 2017. Due to concerns about introducing bias to CIRCLE outcomes, participant interviews were arranged for after the final CIRCLE assessment interview at 18 months. Interviews were conducted as soon after the assessment as feasible. Memory aids were given to participants during interviews, including a handout of the CIRCLE study design and some materials from the psychoeducation package. Interviews were digitally recorded and were expected to last approximately 30-45 minutes, and participants could take breaks as required or split the interview over two sessions if preferred, although none requested to. Participants were thanked for their time with a shopping voucher for a major supermarket worth £20.

7.2.3.1 – CIRCLE pilot qualitative study

The interview schedule was based on qualitative work performed following the pilot phase of the CIRCLE trial. This qualitative study was conducted to explore outcomes from the pilot and inform development of the main trial. In it, 10 participants allocated to the CIRCLE experimental group were recruited and interviewed one-to-one by LSR or one other CIRCLE researcher between March and April 2013. The interviews were performed following the CIRCLE 3-month follow-up assessment.

One-to-one interviews with participants were semi-structured. Initial topic guides for that qualitative data collection were developed by the CIRCLE research team and refined in collaboration with service user and carer steering groups. Topic guides were then piloted and finalised by the research team. Topics covered by the interview schedule included service user perceptions of the CIRCLE trial overall and of its treatments, their views regarding acceptability of the CM treatment, and suggestions for improvements.

The results of this study informed changes made to the main phase of the CIRCLE trial and are presented in appendix 7.2. These include changes to the reward schedule in the CM intervention as well as the content and supporting materials featured in the
psychoeducation. Based on feedback, the CM reward schedule was simplified, but the total reward amount remained the same (£240). Also, a temperature strip was added to the urine sample cups to make it more difficult for participants to provide tampered samples. Meanwhile, more information about the connection between cannabis and mental health was included in the psychoeducation, and several relatively small changes were made to make it less repetitive. A manual for clinicians delivering the psychoeducation and paper materials for participants were also developed. As such, views of the interventions are likely to differ slightly amongst participants in the main trial compared to those in the pilot study.

The results also informed the interview schedule for the present study. This interview schedule looked to explore many of the same topics as the pilot qualitative study. However, one of the main focuses of the interview schedule in the pilot study was to elicit views on how to improve the CIRCLE interventions ahead of the main trial, and so those were changed as they were no longer helpful. Secondly, some of the questions were refined or merged, as similar responses were often given to several of questions in the pilot phase.

7.2.3.2 – The present qualitative study

In addition to the topics covered in the pilot interview schedule, in the present study the interview schedule (appendix 7.1.2) was developed further to include participants’ views of: 1) the long-term benefits of the CM and psychoeducation treatments; 2) Quit attempts they have made outside of CIRCLE; 3) Treatments or strategies they have used/received (beyond CIRCLE) to change their cannabis use behaviour and if they found them to be helpful. Overall, the topic guide used for the present study considered service users’ views of the short and long-term effects of the CM and psychoeducation interventions, as well as
the impact of receiving them in combination. Specifically, the interview schedule (appendix 7.1.2) considered:

- Why participants took part in the trial or wanted to quit cannabis, and their previous experiences of trying to quit.
- How participants’ cannabis use had changed since they were enrolled in CIRCLE.
- Whether they have quit/reduced their use in the past.
  - What strategies they have used in the past or treatments they have received.
  - What did they find helpful or unhelpful.
- Participants’ views of CIRCLE overall, including:
  - The positive and negatives of trial, including both the CM and psychoeducation treatments and how they could be improved.
  - If CIRCLE encouraged them to abstain both during the intervention period and post-treatment.
- Participants’ views of the CM intervention, including:
  - How they felt if they passed or did not pass the CM urinalysis sessions.
  - The acceptability of the CM treatment, both in terms of whether it is an ethical treatment and an appropriate treatment for cannabis use.
  - The appropriateness of CM both as a standalone intervention and as delivered in combination with another therapy.
- Participants’ views of the psychoeducation package, including:
  - If it was beneficial to participants, and how it impacted their behaviour and attitudes related to cannabis. For example, whether participants viewed cannabis as more problematic for their mental health because of the PE.
- How participants spend their spare time or how their lifestyle has changed since taking part in CIRCLE or changing their cannabis use.
• How taking part in CIRCLE or changing their cannabis use has affected their social relationships with friends and family.
• What their EIP care coordinator thought about them taking part in CIRCLE and if they would recommend it to a friend.

7.2.4 – Analysis

Demographic, clinical, and CIRCLE treatment data were summarised as means and standard deviations, medians and interquartile ranges, or frequencies and percentages where appropriate. Interviews were digitally recorded and transcribed by a professional transcription service (WayWithWords). Transcripts were checked for accuracy against the original audio recordings by LSR. Quantitative analyses were performed with STATA v14. Qualitative analyses were performed using NVivo version 11 and Microsoft Word for Office 365.

7.2.4.1 – Theoretical approach

Ontologically and epistemologically, the researchers adopted a generally positivist approach as this was thought to fit the research aims and data best. This overall approach was considered most appropriate as researchers were looking to evaluate the CIRCLE treatments and explore participants’ own experiences of quitting cannabis. The researchers adopted a strongly inductive approach that grounded the results firmly in the data and provided a systematic and comprehensive coverage of the dataset.

7.2.4.2 – Researchers

The analysis was performed as a collaborative process between three researchers: LSR, LCM, and NM (see acknowledgements p.5). It is acknowledged that the background of the researcher will influence their approach to the data and how they analyse it. I (LSR) am the CI of the present study and the present author. At the time of the interviews, I was the trial
manager of the CIRCLE trial and had been so for five years. As the CIRCLE trial ended shortly after completing data collection, I became a Research Associate in the NIHR Mental Health Policy Research Unit before starting the analysis. Both posts were based in the Division of Psychiatry, UCL. Prior to this analysis, my previous experience of qualitative research had come primarily from the CIRCLE pilot qualitative work as well as a number of qualitative research training events.

LCM had been an MSc student in the Division of Psychiatry, UCL, and at the time of the analysis she was working as an assistant psychologist in Great Ormond Street Hospital. She had written their dissertation on an evaluation of the feasibility and acceptability of implementing CM interventions in EIP services. This study was also performed in the context of the CIRCLE trial. For it, she had conducted focus groups with EIP clinicians, and one-to-one interviews with key informants. LSR and NM had contributed to analysing the data for that study. NM is an associate professor in the Division of Psychiatry, UCL, and a qualitative methodology specialist.

7.2.4.3 – Procedure

Transcripts were analysed using a thematic approach as described by Braun and Clarke (2006). This approach offers a systematic method for identifying concepts or patterns in the data set. The analysis followed six key stages as described by Braun and Clarke (2006):

1) Initially each transcript was reviewed by LSR and one third were reviewed by LCM independently of one another to familiarise themselves with the data and make notes on the data.

2) Initial codes were then generated. Every line of the transcripts was coded (line-by-line coding), which is a practice that facilitates deep analysis of the data and is suited to an inductive approach (Maguire, & Delahunt, 2017). As an example of coding, the following quote was given in response to the question: ‘How did it feel passing [the CIRCLE CM
sessions] each week?’ It contains sections coded as: ‘set goal of quitting during CIRCLE’, ‘successfully quit during CIRCLE’, ‘happy about quitting’, ‘achievement/accomplishment from passing CM’, and ‘used vouchers to buy a PlayStation’:

‘I set myself a goal to stop by the time the CIRCLE trial had finished and I did it within the first couple of weeks. So, that really made me... that made me really happy and I saved the vouchers up and I bought myself a PlayStation with them. Accomplishment, yes, and achievement.’

Participant_09

3) Themes were then searched for by examining codes and by arranging them into potential themes. A theme is ‘a pattern that captures something significant or interesting about the data’ (Maguire, & Delahunt, 2017). Themes were developed by looking for similarities between codes and by grouping them based on which ones fitted together. Examples of initial themes include: ‘How they felt passing or failing the CM sessions’, ‘When and taking decision to quit cannabis’, and ‘Reasons for taking part in CIRCLE’.

4) These potential themes were arranged into an initial thematic framework. To facilitate development of a thematic framework, a conceptual model of this framework was developed (appendix 7.3). This initial framework was then reviewed by LSR and LCM. Through an iterative process over three meetings, LSR and LCM refined the framework through discussion of potential amendments. At each stage, all the codes relevant to the themes were identified and gathered. During this process, several questions were asked:

1) Do the themes make sense?
2) Does the data support the themes?
3) Are the themes too small or large?
4) Do the themes overlap?
5) Are there unidentified themes or sub-themes?

6) Do the themes address the research aims? (Maguire & Delahunt, 2017).

From this process, a final thematic framework was drafted. This framework was then reviewed by NM and further amendments and inconsistencies debated. The thematic framework was then finalised (appendix 7.4).

5) LSR then defined the themes and looked to ‘identify the “essence” of what each theme was about’ (Braun & Clarke, 2006).

6) Lastly, LSR wrote the final report of the results.
7.3 – Results

Once the 20 initially planned interviews had been conducted, it was believed that saturation had been achieved, so no further participants were recruited. The average length of interviews was approximately 30 minutes.

7.3.1 – Sample characteristics

Sample characteristics (demographic, clinical, substance use, and number of CIRCLE treatment sessions attended) are presented in table 7.1. They were broadly similar to those of the whole CIRLCLE CM group at 18 months. In both groups, the proportion of male participants was around 90%, with similar mean age (26), severity of psychotic symptoms (PANSS positive symptoms were around 10, PANSS negative symptoms were around 12), history of cannabis dependence (around 90% of both samples), history of use of other substances (polysubstance use) (35% in both groups) and approximately half were in employment or education. However, there were differences. A larger proportion of the present sample were Black or mixed ethnicity (55% compared to 32% in CIRCLE) and lived with other adults or family members (80% compared to 55%). The present cohort had more education (60% A-Level or higher compared to 26%) and a lower proportion was diagnosed with schizophrenia (20% compared to 26%). They also reported using cannabis on more days in the last six months (58 compared to 26) but had slightly fewer cannabis positive urines (50% compared to 57%). In terms of treatment adherence, the median number of CM sessions attended by this sample was 10 and six psychoeducation sessions, which were very similar to the whole CIRCLE CM arm (nine CM sessions and six psychoeducation sessions). The mean amount received in the CM intervention was £85 (max £240), which was slightly higher than in CIRCLE (£64).
Table 7.1 – baseline characteristics of participants in this study and the CIRCLE trial

<table>
<thead>
<tr>
<th></th>
<th>Participants in the present study</th>
<th>CIRCLE trial CM group at 18 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD), Median (IQR), or n/N (%)</td>
<td>Mean (SD), Median (IQR), or n/N (%)</td>
</tr>
<tr>
<td>Age (mean, sd)</td>
<td>26.1 (3.63)</td>
<td>26 (4)</td>
</tr>
<tr>
<td>Male</td>
<td>18/20 (90%)</td>
<td>127/145 (88%)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>6/20 (30%)</td>
<td>78/144 (54%)</td>
</tr>
<tr>
<td>Black</td>
<td>7/20 (35%)</td>
<td>29/144 (20%)</td>
</tr>
<tr>
<td>Asian</td>
<td>3/20 (15%)</td>
<td>20/144 (14%)</td>
</tr>
<tr>
<td>Mixed</td>
<td>4/20 (20%)</td>
<td>17/144 (12%)</td>
</tr>
<tr>
<td>Living arrangements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lives alone</td>
<td>4/20 (20%)</td>
<td>50/143 (35%)</td>
</tr>
<tr>
<td>Lives with other adults</td>
<td>5/20 (25%)</td>
<td>25/143 (38%)</td>
</tr>
<tr>
<td>Lives with family/partner</td>
<td>11/20 (55%)</td>
<td>55/143 (17%)</td>
</tr>
<tr>
<td>Other</td>
<td>0/20 (0%)</td>
<td>13/143 (9%)</td>
</tr>
<tr>
<td>Relationship status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>18/20 (90%)</td>
<td>129/144 (90%)</td>
</tr>
<tr>
<td>Married/cohabiting</td>
<td>2/20 (10%)</td>
<td>14/144 (10%)</td>
</tr>
<tr>
<td>Other</td>
<td>0/20 (0%)</td>
<td>1/144 (1%)</td>
</tr>
<tr>
<td>Highest education achieved</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No qualifications</td>
<td>2/20 (10%)</td>
<td>22/143 (35%)</td>
</tr>
<tr>
<td>GCSE or equivalent</td>
<td>6/20 (30%)</td>
<td>57/143 (38%)</td>
</tr>
<tr>
<td>A Level or equivalent</td>
<td>6/20 (30%)</td>
<td>31/143 (17%)</td>
</tr>
<tr>
<td>Post 18 education (including HND, trade, degree)</td>
<td>6/20 (30%)</td>
<td>33/143 (9%)</td>
</tr>
<tr>
<td>Employed, in education, full-time carer, or exempt due to disability</td>
<td>12/20 (50%)</td>
<td>66/145 (46%)</td>
</tr>
<tr>
<td>Urinalysis positive for cannabis</td>
<td>10/20 (50%)</td>
<td>77/136 (57%)</td>
</tr>
<tr>
<td>Number of days of cannabis use in previous 6 months (max =168) (median, IQR)</td>
<td>58.5 (0.75, 102)</td>
<td>26 (0, 118)</td>
</tr>
<tr>
<td>History of cannabis misuse</td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of cannabis dependence</td>
<td>18/20 (90%)</td>
<td>129/145 (89%)</td>
</tr>
<tr>
<td>Current cannabis dependence</td>
<td>8/20 (40%)</td>
<td>65/145 (45%)</td>
</tr>
<tr>
<td>History of polysubstance use</td>
<td>7/20 (35%)</td>
<td>49/143 (34%)</td>
</tr>
<tr>
<td>Severity of psychotic symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive symptoms (PANSS) (median, IQR)</td>
<td>9.5 (7.25, 12.75)</td>
<td>11 (8, 13)</td>
</tr>
<tr>
<td>Negative symptoms (PANSS) (median, IQR)</td>
<td>12 (9, 15)</td>
<td>12 (9, 17)</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>------------</td>
<td>------------</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizophrenia or schizoaffective disorder</td>
<td>4/20 (20%)</td>
<td>38/145 (26%)</td>
</tr>
<tr>
<td>Bipolar affective disorder</td>
<td>1/20 (5%)</td>
<td>10/145 (7%)</td>
</tr>
<tr>
<td>Depression with psychotic symptoms</td>
<td>0/20 (0%)</td>
<td>3/145 (2%)</td>
</tr>
<tr>
<td>Other psychosis</td>
<td>15/20 (75%)</td>
<td>94/145 (65%)</td>
</tr>
<tr>
<td>Treatment engagement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CM sessions attended (max=12) (median, IQR)</td>
<td>10 (7, 11.25)</td>
<td>9 (3, 12)</td>
</tr>
<tr>
<td>Psychoeducation sessions attended (max=6) (median, IQR)</td>
<td>6 (3.5, 6)</td>
<td>6 (1, 6)</td>
</tr>
</tbody>
</table>

7.3.2 – Interview results

The results were divided into two domains:

1) The CIRCLE trial. This domain explores participants’ cannabis use prior to taking part in CIRCLE, which provided context to their participation in the trial. Secondly, it examines participants’ experiences and views of the CIRCLE trial, primarily focusing on its interventions.

2) Quitting cannabis and support outside of the CIRCLE trial. This domain contains material related to participants’ reasons for wanting to quit cannabis. Secondly, their experiences outside of CIRCLE of trying to change their cannabis use behaviour, including the treatment or support that they received or strategies they used.

The first domain (the CIRCLE trial) is presented in this chapter. The other domain is discussed in chapter 9.

The CIRCLE trial

In general, participants were positive about the trial overall. Despite this, a minority of participants reported quitting because of the CIRCLE CM intervention, and only one of
these had not relapsed since. In this chapter, participants’ experiences of using cannabis are discussed first. These data provide context to the other themes, which examine the CIRCLE trial and include: views of CIRCLE overall, their experiences of the CM and psychoeducation treatments, and if it helped them quit cannabis and why. Four themes are discussed: 1) History and patterns of cannabis use; 2) Motivation; 3) Knowledge; 4) Support.

7.3.3 – Theme 1: history and patterns of cannabis use

This theme discusses participants’ history of cannabis use before taking part in the CIRCLE trial. This theme is divided into two sub-themes: 1) how they started using cannabis, and 2) cannabis use prior to CIRCLE.

Sub-themes:

7.3.3.1 – How they started using cannabis

Virtually all participants started smoking with friends. But there were other reasons alongside this. Some reported curiosity. Others reported using all substances, including alcohol and cannabis, more following a significant negative life event, such as bereavement.

‘Mainly I suppose, half curiosity, half because everybody else was doing it. I never felt any real pressure to do it at that time, no-one was forcing it on me. But it was, I suppose, fear of being left out and I would be the only person in that group who wasn’t doing it and I ended up liking it. And it went from there I suppose.’

Participant_17

‘I got in with the wrong crowd and then just started smoking it every day... I was smoking all the time then when [CIRCLE started].’

Participant_09

Although almost all participants started using cannabis with friends, many smoked by themselves as well. Several participants said that while cannabis is something they do with
friends, it is less sociable than alcohol. As such, it is something most participants did by themselves at least some of the times they used.

‘I started smoking when I was younger with two or three friends. Within six months of starting smoking, I smoked on my own. And ever since then, the only people I sort of share with is my fiancée or [friend] or someone like that, which is a good friend, and so on. Or my brother… Purely for the fact that I only have to find the money for myself.’

Participant_14

‘Drinking is more social and cannabis is a bit more personal… A bit more, but it’s still a social thing.’

Participant_03

7.3.3.2 – Cannabis use prior to CIRCLE

Cannabis use outcomes from the CIRCLE quantitative interview assessments are presented in table 7.1. During the qualitative interviews. Participants reported having used cannabis for between approximately two to 15 years before taking part in the trial. Most participants reported using heavily before taking part in the trial. Three-quarters of participants reported daily or almost daily use.

‘I was smoking loads…two spliffs, three spliffs a day.’

Participant_07

‘The majority of my time was spent smoking weed and getting high.’

Participant_05

Some participants reported very heavy cannabis use, with a few saying that they spent all day every day smoking.

‘I was smoking £60 a day when, just before I stopped… all day every day…. Wake up, get high on my own and then go out and get high with other people… I was very dependent on smoking, and I literally needed it all day every day.’

Participant_18

‘I smoked a lot… I’ll literally be indoors for a week, and smoke cannabis all week, yes. I used to smoke £40 worth a day.’

Participant_02
Overall, participants in this group were often heavy cannabis users, and had all smoked for many years prior to taking part in CIRCLE. In most cases, they began using cannabis with friends. However, since then, most had progressed to using by themselves as well.

7.3.4 – Theme 2: motivation

This theme explores the topic of motivation in relation to the CIRCLE CM treatment. There are four sub-themes: 1) Motivation to engage with treatment, 2) Motivation to abstain from cannabis use, 3) Participants’ experiences of receiving rewards, 4) Long term benefits of CM.

Sub-themes

7.3.4.1 – Motivation to engage with treatment

The CM voucher incentives motivated participants to engage with treatment, both in terms of taking part in the trial and attending psychoeducation sessions. However, for many it did not provide enough motivation to quit. All the participants said the vouchers were one of the reasons they took part in the trial and a few said they were their main reason.

Meanwhile, several participants said that they would not have engaged with the psychoeducation intervention if it was not for the vouchers. Some viewed the vouchers as not an incentive to quit per se, but instead as an incentive to engage with the psychoeducation treatment. Participants liked that they received a voucher for £5 for attending the CM session even if the result showed that they had used cannabis as this made them feel like they were being paid for their time. Some participants said that this made them feel like their time was valued.

‘Well, I sort of, as soon as I heard about [CIRCLE], I wanted to do it, because I needed help. And it sounded like it was going to help. And it did... I reckon it was all good. Like, the information was definitely important, but the vouchers helped me eat... I don’t know, just the information was good, and it was needed. That was it, really.’

Participant_18
'At first, I probably thought it would be a bit boring with the education thing, but I think the money incentives were what pushed me to start coming... And then afterwards, I thought, it’s not that bad, like, it’s just like a chilled conversation. It’s not like, it’s not too bad, so, yes. It’s something I could cope with for the reward incentive... I knew that if I passed I would’ve got more incentive, but I still thought that even if I didn’t pass I’d still get something, and in the back of my head I was thinking, I’m not really trying to quit anyways. So, in a way, it was kind of good for me, because I got drawn into it, just from the incentive as well. In the back of my head, I was thinking, I don’t really want to quit anyways, I’m just doing it for the, for the reward...

(interviewer) Do you think that if it wasn’t for the incentives, do you think you would have wanted to take part?

I don’t think so.’

Participant_16

7.3.4.2 – Motivation to abstain from cannabis use

Almost every participant reported trying to quit during the intervention and many reported managing to cut down at least a bit. However, most reported not passing the majority of their sessions. So while the intervention had some effect in encouraging and reinforcing abstinence amongst interviewed participants, it did not provide enough motivation to abstain for most participants. Difficulties in abstaining are discussed in more depth in chapter 9, in the second theme.

‘I think for maybe the first three or four weeks. I was still using and then I think there was maybe, like, an eight or nine week stretch where I was just cutting down or stopped completely. I think by the end of the study I had stopped.’

Participant_08

‘[I made] a good effort [to cut down] ... But what I was disappointed about is that I never, I could never get the clean one. I wanted to prove to myself that I could get that one and I found it just a little bit hard to fully quit that. At that time, I could never quit. It wasn’t happening... I wanted to pass it, but I never, so that was a bit of a downfall. But the good thing is you always give your vouchers, so then you don’t mind doing it.’

Participant_13

Of the few participants who did manage to quit during the CM intervention, only one said they have not lapsed since. As such, the CIRCLE intervention was not particularly successful
at encouraging long term abstinence, even amongst people who quit or substantially reduced their use during CIRCLE.

‘Once the study finished and the incentive was gone, I kind of continued using it... And then was pretty much on it, and the only time I stopped was for the study... Then after a certain period I stopped completely. I only have gone back, like, one, one time. In maybe nine months or something.’

Participant_08

While barriers to quitting are discussed in more depth in chapter 9, participants said that they had found quitting during CIRCLE too difficult. Amongst those who did manage to reduce, their initial motivation to quit had often faded by the end of the CM period. Amongst the participants who quit early in the intervention, a few reported that they had relapsed by the end of treatment. Some said that if the CM intervention had been offered to them when they were ready to quit, they may have been more successful.

‘I don’t know, because I did [quit], it was, like, I started to go back into old habits.’

Participant_04

‘I tried to [quit], but didn’t. It just wasn’t the right time. It was very stressful and I had a lot of things going on.’

Participant_14

7.3.4.3 – Participants’ experiences of receiving rewards

Many participants said that passing the CM sessions (giving a clean urine sample) gave them a positive feeling, which was often a sense of accomplishment or being proud.

‘Proud of myself. Said to myself, yes, if I really want to do this I can really do it ... Yes, to do with the sessions, I was more focused on coming in the next week to get a better result, test and stuff to prove to myself I can... [when they failed the urinalysis] I was disappointed... I felt like I had let a lot of people down, my care coordinator and stuff, so quite down, the buzz wasn’t worth that feeling.’

Participant_06

‘I’m proud of myself ... It [CM] helps; motivation.’

Participant_03
Equally, many participants felt disappointed in themselves if they failed, particularly if they were trying to quit. However, others reported feeling ambivalent about the sessions because the outcome was expected, whether they passed or failed, and it was ‘simply part of their life’. This ambivalence was more common though amongst participants who did not quit cannabis during the intervention.

‘I was disappointed... I felt like I had let a lot of people down, my care coordinator and stuff, so quite down, the buzz wasn’t worth that feeling.’

Participant_06

‘It wasn’t good and it wasn’t bad ... No, it was just a neutral thing ... I didn’t see it [CIRCLE] as something which was going to help me stop. Because I didn’t have the, I did want to stop, but I didn’t at the same time.’

Participant_05

7.3.4.4 – Long term benefits of CM

While most participants were positive about the CM overall, a few were pessimistic about the its long-term effectiveness after treatment. They all felt that if someone can quit for vouchers, then they can quit without them. So once the vouchers stopped people would relapse.

‘They might just stop to get the voucher. If they can stop to get the vouchers, they should be able to stop anyway ... I think that it’s not really a long-term solution.’

Participant_15

7.3.5 – Theme 3: knowledge

Most participants reported that learning or gaining knowledge was one of the main benefits of the trial. The psychoeducation package was the principle source of learning. This theme has two sub-themes: 1) Psychoeducation. 2) CM.
Sub-themes

7.3.5.1 – Psychoeducation

Overall, the psychoeducation was generally positively received, and most people felt that they had benefited from taking part. There are two sub-sub-themes: 1) Positives. 2) Negatives

7.3.5.1.1 – Positives

The parts of the psychoeducation that participants remembered the most clearly included the video materials, discussions about how much they were spending on cannabis, the impact of cannabis on mental health, and the Relapse Prevention techniques. Post-treatment, it was the psychoeducation that left the bigger impression and motivation to quit long-term: In some cases, the psychoeducation did not have an immediate impact, but people thought about the material afterwards and later on made the decision to quit or used the strategies they had learnt.

‘I tried using the [PE] information, like, to put my mind on other things, but also I tried stopping hanging around with people I was hanging around with. But that’s pretty hard, because they’re the only people I know. But, like, I shut myself away from them, and, like, yes, now I can be around them. I used the information [I was] given, to, like, activities, like, do things and, like, try to keep my mind off it. It worked.’

Participant_18

‘I didn’t take the [PE] as seriously as I should have. I didn’t take it that serious, but what helped was just like talking about the problems and stuff like that … The education part, like when they teach you about some of the things, back then I didn’t really care. I felt like I knew all kind of things, I was like, I don’t need that, just want to take the pee test and just get the vouchers and go. You know what I mean. But looking back at it now, it’s kind of like it is helpful, you know, because I’m at the stage like where I understand now it’s always good to learn, even if you knew about it before, it’s just to recap and just keep being on like the ball, kind of thing. So yes.’

Participant_11
7.3.5.1.2 – Negatives

There was diversity in opinion about how useful the psychoeducation was. A small proportion viewed it negatively. In some cases, this was because they already knew the material.

‘[I] kind of knew the stuff already, because [when] I hit college, that's when I started doing more research into it and I started to understand more about the drug, started to understand its effects, its compounds and what its uses are and stuff, and that's when I started to understand more about it. It was only when I joined the CIRCLE Study that I started to realise that I knew most of the stuff that they were telling me ... [What] would be beneficial, continue to focus on the aspects which you're focusing on, but also try to bring in aspects that are unknown to people who are researching it, if that makes any sense.’

Participant_05

However, for others already knowing the material was not a problem because the psychoeducation helped to reiterate and remind them of why they wanted to quit in the first place.

‘But for me it was more so I’d already been clean for a long time before. So, it was, kind of, like, just, kind of, yes, reinforcing, reiterating things I already knew. And it kind of... if anything it gave me a reason to want to stay clean. I was like, right, so there is a benefit to this at the moment.’

Participant_10

For others, the problem was the person delivering the package and it could have been improved if someone with experience of quitting cannabis had delivered it instead of a clinician. This was because it felt like the clinician did not understand what it is like to quit cannabis. Furthermore, one person focused on the video materials, which they felt had been made by people who did not really understand cannabis use and addiction. They said that being spoken to by a clinician felt like they were being told off by a teacher.

‘I don’t think it would’ve necessarily have had much of an impact on the incentives, because the psycho-education, for me, wasn’t any incentive to cut down. It was just information. But I think if someone was, I guess, given a similar story or something that mirrored all elements that I could identify, then I would’ve maybe okay, that’s interesting.’
‘Some of the literature that they were giving me and some of the stuff they were showing me to watch actually made me laugh more than anything else. And some of these videos had obviously been made a very long time ago by people who clearly had no idea what they were talking about. Maybe, to me it seemed like the people who were making these videos had never even had cannabis and didn’t understand it. I think that in the future if you are going to be showing these videos and giving this literature to people like me, I think having them made by people like me would be the important thing... I felt like I was just being told off by a teacher. And when you’re being told off by a teacher for smoking in the gates of the school, you pretend you are sorry and then you just carry on doing it regardless. And that’s how I felt in regard to that... I think even now that I’m clear headed and somewhat sober, I think watching those videos now, I would feel exactly the same way. I don’t think that those were the best ones to choose, yes.’

Participant_08

7.3.5.2 – CM

In terms of what participants learnt from the CM treatment, the biggest benefit came from the urinary THC readings. A few participants said that they liked finding out how much THC they had in their system during the CM urinalysis sessions, and for some participants this was the main benefit of taking part in the trial.

‘[CM] was something to try and measure how much cannabis I take because I never knew I could measure really the THC [I] intake... I kept in it because I thought maybe I could try and cut down as well.’

Participant_03

‘If I had bought any, how much I’d bought at the time, and it gave me a more, or it gave me a broader understanding of the amount I was in-taking between the time I would buy some. So, if I was to buy a Q [quarter of an ounce] I would realise how much of that Q I’d be using up throughout the week or the month or so. And if I was a bad score, I’d realise how much I would be taking in.’

Participant_05

7.3.6 – Theme 4: support

Overall, the format was generally well accepted. There were two sub-themes in this section: 1) Design of the interventions; 2) CM as a stand-alone intervention; 3) Support from clinicians.
7.3.6.1 – Design of the interventions

A few participants said that having something focused on cannabis was new to them and very welcome as they wanted help with quitting. A couple of participants specifically commented that they liked the length of the intervention period and frequency of sessions.

‘Well, I sort of, as soon as I heard about it, I wanted to do it, because I needed help. And it sounded like it was going to help. And it did.’

Participant_18

[It] ‘was more helpful than it would have been every month, once a month or something because if it wasn’t... if it was like once a month I’d have more than likely gone back onto the drugs.’

Participant_09

7.3.6.2 – CM as a stand-alone intervention

Virtually all participants thought that receiving just the CM by itself would be worse than receiving it in combination with the psychoeducation package. For many, CM without the psychoeducation would be inferior as it would not provide any rationale for trying to quit or would not provide enough support for quitting.

‘[Without PE] you’re not giving them any information or knowledge about what’s going on or what they’re taking into their system or what it’s all about. You’re just saying pee in this cup. You need the information. You need knowledge. Knowledge is the most useful thing as well and without it, then we’re just mindless apes, running around.’

Participant_05

‘The way I see it, the psychoeducation is a necessity... Because you want to know what you’re inhaling into your lungs. You want to know how it’s going to affect you. The incentives is just a bonus. That knowledge is important, like, if someone just comes and go, I’m going to piss in the cup, get my voucher, and I’m going to smoke a joint. But if you’re doing the psychoeducation ... you read it, and then you start reading into it, and you’re like right, okay. That makes a lot of sense. Like, so now I understand why I have this, why this happens, why that happens. It gives you insight, into a different point of view, a different perspective.

But when it comes to the incentives and that lot, yes, it is nice and it is good, yes you get your little voucher here, your little voucher there. But the psychoeducation is a necessity, I think, personally. Put them together, brilliant!’

Participant_01
'I don’t think it would have helped if I’d just had the vouchers because there’s no support really is there? It’s [CM] not really helping you in a way is it, I mean, you’re just getting vouchers for a urine sample and that’s not what it’s aimed for.’

Participant_09

For some, the CM made them feel like they were being paid for their time. It made them feel like their time was valuable. This, as discussed in theme 1 (sub-theme 1), encouraged them to engage with treatment.

‘Without the vouchers, there wouldn’t be no need of it, isn’t it? The vouchers are what will get you. You think you’re getting paid for your time. And to sit somewhere for an hour or longer, you know how hard that is sometimes? It’s hard. But with a voucher, you think, just do it, at the end you’re going to go shopping with it ... The thing done good is that you need to have understanding. To come in and just piss and that, no one would do it probably. You don’t need it. Because deep down they know they are smoking and you’re coming in to find out you are positive and you’d already smoked the drug, isn’t it?’

Participant_13

7.3.6.3 – Support from clinicians

This sub-theme explores the support participants received from clinicians. It is divided into two sub-sub-themes: 1) Positives; 2) Negatives.

7.3.6.3.1 – Positives

Almost all participants spoke highly about the support they had received from the clinicians delivering the intervention and said they found taking part in the study helpful. Almost all participants said that having an opportunity to talk to someone during the psychoeducation was helpful and many said they liked that the sessions were one-to-one.

‘I don’t think there were any negatives. But the positives were like, she was very... The information she could give me was good, like, how to put my mind on other things, just ways of trying to not think about it.’

Participant_18

‘When I got into CIRCLE Project I was inspired by [the clinician] ... And the [circle researcher], I was very inspired to do something different.’

Participant_06
For some participants, clinician had reflected on their own experiences, and sharing common experiences was very helpful.

‘It's good to share problems and I think [the clinician] kind of bounced back in terms of where he kind of had similar experience as well. And I think that's key, especially because sometimes I may feel like only I have that problem, but there's so many people in the world that may have the same problem you're having. Yes, so it's good.’

Participant_11

7.3.6.3.2 – Negatives

One person gave negative feedback about the support from the clinicians, who felt that the sessions could have been more comforting and feel less like he was being tested. One participant thought that the intervention should have been more positive and focused on the benefits of quitting. Several others said the psychoeducation could have been improved further if peers with similar experiences had delivered the sessions instead of a clinician.

‘I didn’t like watching the videos because it was almost like I was looking at somebody who is probably depressed or going through that and they’re saying how bad it is, how sad it is. At that point I needed motivation, I didn’t need more of something dragging me down about how bad it is, do you see what I mean. It’s my personal experience. Yes, but not just positive of somebody talking positively, but somebody who has been through that. Someone who has been through and you can kind of talk about how they got through it.’

Participant_20
7.4 – Discussion

7.4.1 – Main findings

Overall, participants were positive about the CIRCLE trial as well as its CM and psychoeducation treatments. Many specifically mentioned that they liked having support focused on cannabis as they said they had not otherwise been offered tailored support. The CM intervention was generally well liked, and some commented that the length of the intervention period and frequency of sessions were good. However, while several interviewees cut down or quit during the trial, only one has not relapsed since.

Participants reported that the voucher rewards CM motivated them to engagement with treatment, and several said that they would not have taken part in the trial if the psychoeducation had been offered by itself. Amongst those who were using cannabis when they signed up for the trial, all tried to quit during the intervention, but for most people it was too difficult. Of those who had managed to reduce their use, in many cases their initial motivation to abstain had faded by the end of the treatment phase and they had relapsed. For others, they felt that they were not ready to quit at the time of the trial, and that they would be more successful if the treatment was offered at the right time.

But most did not view the vouchers as an incentive to quit per se, but instead as an incentive to engage with the psychoeducation, which many said they would not otherwise have taken up. For some, the vouchers were seen as a payment for their time to attend the psychoeducation and it made them feel valued. However, few said they would quit solely because they were receiving vouchers to do so.

Instead, for many what they learnt during the trial, including how cannabis use translates into urinary THC concentration, strategies for quitting and coping strategies to avoid relapse, and information about the effects of cannabis were the most useful aspects of taking part in the trial. Participants believed that it was important to combine a CM
intervention with the psychoeducation, as by itself CM would lack any rationale for quitting, such as information about the potential benefits of quitting cannabis. Following cessation of treatment, the psychoeducation left a bigger impression and greater motivation to abstain long-term. For some, the psychoeducation did not have an immediate impact, but following treatment cessation, they decided to quit based on information presented in, or used strategies when quitting that they had learnt from the psychoeducation. Interestingly, some participants thought that the psychoeducation would have been more effective if it had been delivered by someone with lived experience of quitting cannabis. This was because, to them, clinicians did not seem to understand what it is like to quit cannabis and this made the material feel more like a lesson rather than treatment that would help support them quit cannabis.

7.4.2 – Implications

Notably, qualitative data related to participant experiences of treatment for cannabis use is extremely limited. A small number of qualitative studies have been conducted alongside trials of treatments for substance misuse, but seemingly extremely few are in a population with psychosis or cannabis misuse. Consequently, while there have been several negative or inconclusive trials for substance misuse in psychosis, there are little qualitative data exploring participants’ views why treatments have not worked. The findings presented here suggest that participants in general found the intervention beneficial, and several changed their use to some degree because of it, but that it was not enough to help them quit.

Many also said that it was valuable to have an intervention tailored to cannabis use as there is currently very little help available through the Mental Health services. This suggests that the intervention had little effect, but that there is a demand for effective treatments. Many felt that CM was an intervention that should not be delivered alone and needs to be combined with another treatment as it would otherwise lack rationale. However, many
participants viewed CM as not enough by itself to motivate them to stop using cannabis, and that it was best understood as an incentive for engaging with treatment. CM therefore offered a good reason to engage with treatment, which they may not have engaged with otherwise. CM is sometimes criticised for failing to motivate patients to abstain beyond the treatment period as it only provides EM and fails to engender IM. This is arguably supported by participant feedback, with most participants saying that a standalone CM intervention would be inferior to delivery in combination. Combined with other results, this perhaps suggests that cannabis misuse in this cohort is a more intractable problem than can be addressed solely through a reward-based intervention. Arguably as demonstrated by the lack of positive trials in this cohort, the barriers to quitting participants experienced, which are described in chapter 7, are too challenging for many psychosocial interventions targeting cannabis use in isolation. Based on chapter 2, it may be that a combination of CBT/MI and CM would not result in a substantially better outcomes than either treatment alone. Instead, alternative approaches to treatment may be required.

7.4.3 – Limitations

One of the limitations of this study is that the interviews were conducted around 15 months after the treatment ended. Therefore, participants’ recollection of the intervention is likely to be poorer than if they had been interviewed immediately following treatment. However, memory aids were given to the participants to help address this issue. Secondly, participants were recruited towards the end of the follow-up data collection for CIRCLE, and so participants were recruited from the tail-end of the CIRCLE participants and their experiences may have differed to those of participants recruited earlier on in the trial. A sample recruited throughout the CIRCLE trial may have been more representative of the trial overall. However, on the other hand, saturation was achieved in the data collection and there were no significant changes to CIRCLE procedures during the main phase of the trial. This mitigates the possibility of substantial variations in views over the course of the
trial. A third limitation of this study is that it explores participants’ views of the intervention and the cognitive-behavioural mechanism underlying it, but participants may lack insight into those motivational changes or what may be an effective treatment.

Secondly, while the theoretical approach adopted was positivist and strongly inductive, as this was thought to fit the data best, there are limits to such methodologies. No approach should be regarded as purely positivist or inductivist, as wholly value or theory free approaches to data analysis are not achievable. For example, researchers need to be aware that the interview space is not entirely neutral or objective, and that knowledge is to some degree affected by the research process (Ritchie et al., 2014). The interviewee may, at least partially, tailor their answers to tacit inferences they have made about the researcher’s epistemic goals (Norenzayan & Schwarz, 1999). In this sense, a person’s understanding or interpretation of their experiences of the trial may be shaped to a degree by the interview process. Equally the analysis of the data is not wholly value free. Each researcher brings experience of and their own approaches to data analysis, as well as their own perspectives and understandings of the phenomena being discussed (Ritchie et al., 2014). As such each researcher carries their own preconceptions into the data analysis.

7.4.4 – Summary

In conclusion, participants viewed CM as effective for engaging them in treatment, but also said that it did not provide them with enough motivation to support them in abstaining long term. As a standalone intervention, people viewed CM as likely to be unhelpful. However, participants viewed CM in combination with another treatment positively. Based on this data, CM combined with another intervention may be an effective treatment in this group. However, as the results of chapter 2 demonstrate, CM combined with CBT or MI is unlikely to be more effective in this cohort than either intervention alone. Alternative treatments in this group may be required to tackle the challenging, and currently seemingly
intractable, problem of cannabis use in this cohort. Subsequent chapters explore potentially important factors that a treatment in this cohort needs to address. These include participants’ reasons for wanting to quit, the cognitive-behavioural predictors of cannabis use at treatment end, and participants’ own experiences of effective strategies and treatments for quitting cannabis use.
Chapter 8 – Investigating abstinence from cannabis in psychosis: a quantitative evaluation of the predictors of cannabis use status at follow-up and patients’ reasons for quitting

8.1 – Introduction

8.1.1 – Background

Given the lack of clear benefit from the CIRCLE CM intervention, the question of what would be effective arises. Overall, as demonstrated by the lack of success of trials in this population (in contrast to non-comorbid populations, see chapter 1.3), this cohort appears to be quite unresponsive to psychosocial treatment. Reasons for this are currently unclear, but as discussed in chapter 1.6.6, it could be at least partially due to this population having distinct characteristics compared to non-psychiatric groups that may limit the effectiveness of treatment.

There is a need to identify which cognitive-behavioural factors are important therapeutic targets in this group. However, relevant literature is very limited, with very little data published on Relapse Prevention or predictors of relapse in this group (Bradizza, Stasiewicz, & Paas, 2006). Perhaps the most substantial body of work to date has explored patients’ reasons for using. However, as discussed in chapter 1.1, the most commonly cited reasons for cannabis use in people with psychosis are ‘to get high’, relax, to alleviate boredom, and to have fun (Kolliakou et al., 2011). But these are fairly similar to other groups. Self-medicating to alleviate symptoms of psychosis or low mood is generally only reported by a minority of patients. As such, while self-medication is one therapeutic target, beyond this,
reasons for using perhaps do not appear to offer much insight into how treatments could be better adapted.

In terms of reasons for quitting, there is currently very little published for populations with psychosis. In non-psychiatric groups, several papers have reported similar broad categories of reasons. In a paper by Chauchard and colleagues (2013), the main reasons for quitting cannabis included self-image and self-control, health concerns, interpersonal relationship concerns, legal concerns, social acceptability concerns, and self-efficacy. Other studies report similar results (McBride et al., 1994; Curry et al., 2001). Meanwhile there is evidence that amongst these, negative effects on self-image, physical health, and social image are the most important for predicting successful abstinence (Copersino et al., 2006). Beyond reasons for quitting, there is some evidence that motivation and intentions related to substance-use behaviour change also predict abstinence in substance-abusing patients (DiClemente, Nidecker, & Bellack, 2008).

There are only a few papers evaluating how well different reasons for using or quitting predicted cannabis use in psychosis population. Clark and colleagues (2017) conducted one of the largest of these studies to date (n=235). It considered which reasons for smoking predicted quitting by follow-up, which like the present study was conducted in the context of a large randomised controlled trial. They evaluated three domains: 1) smoking to cope, such as: ‘helps to relax’, ‘take a break’, or ‘handle stress’; 2) physiological reasons, such as withdrawal symptoms and cravings; 3) stimulation, such as to help concentration, help weight loss, or feel more alert. They found that amongst these, endorsing stimulation reasons for using was associated with a substantially lower likelihood of being quit by follow-up.
8.1.2 – Aims

The aim of this chapter is to explore participants’ reasons for quitting, and what the predictors are of still using cannabis by treatment end and 18-month follow-up in this group. Doing so will help identify potential therapeutic targets in this population and potentially contribute to developing effective cognitive-behavioural treatments in this cohort.

Specific aims include:

1) Consider the reasons patients have for wanting to quit cannabis and how these change over time. Mental health concerns (Copersino et al., 2006) and the prospect of receiving the financial rewards (due to the CIRCLE CM intervention) are hypothesised to be the primary reasons participants give for wanting to quit in this group.

2) Examine the cognitive-behavioural mechanism underlying quitting cannabis use by investigating predictors of use status at follow-up. It is predicted that higher motivation, including intrinsic and extrinsic measures, readiness-to-change, cannabis urges, and exposure to cannabis use will each decrease the likelihood of testing positive for cannabis.
8.2 – Methods

8.2.1 – Design

The study design, cognitive-behavioural measures, and participant characteristics are described in chapter 4. As described there, data were collected from all three CIRCLE assessment interviews using a cognitive-behavioural questionnaire along with data co-opted from the CIRCLE trial assessments. The sample comprised CIRCLE participants randomised after June 2014. Participants were informed of the aims of this study as part of the consent process for the CIRCLE trial.

1) Intrinsic Motivation (IM) and Extrinsic Motivation (EM):
   a) Reasons for Quitting in Marijuana (RFQ) (McBride et al., 1994).
   b) Seven further reasons for quitting measured using the same Likert-scale as the RFQ: 1) Concerned that mental health already impacted by cannabis. 2) Cannot afford to use cannabis. 3) Cannabis is not enjoyable. 4) Cannabis causes nausea/panic. 5) Concerned about cannabis impact on future mental health. 6) Cannabis makes it hard to accomplish things/think clearly. 7) Because of the reward scheme (asked at baseline only). Mean scores were calculated individually for items related to mental health concerns (items 1, 5) and negative use expectancies (items 3, 4, 6).

2) Motivation and self-efficacy: 3-item measure of motivation to abstain from Chung and colleagues (2011).

3) Readiness-to-change: Readiness Ruler (Heather, Smailes, & Cassidy, 2008).

4) Urges/Cravings: Mood and physical symptoms scale (MPSS) (West & Hajek, 2004) cravings subscale only (2 items).

5) Environmental/social cues: The Wisconsin Predicting Patients’ Relapse questionnaire (WI-PREPARE) (Bolt et al., 2009).
The following measures were collected for CIRCLE and were used in this study:

6) Demographic and clinical data

7) Cannabis use tested using a standard urinalysis test sensitive to 50 ng/ml of urinary THC

8) Engagement: number of CIRCLE psychoeducation sessions each participant attends.

8.2.2 – Statistical analysis

Sample summary statistics for demographic, clinical, cognitive-behavioural, and compliance with treatment variables are presented in chapter 6, table 6.1. The process of exploring the patterns of missingness are also described there.

Descriptive statistics were used to explore participants’ reasons for wanting to quit (objective 1). These tested how strongly different reasons in the RFQ and the other 7 study specific items were endorsed at baseline. The mean and standard deviation for each item were calculated.

Cognitive-behavioural predictors of testing positive for cannabis at 3-month follow-up were investigated (objective 2). Initially, the association between individual cognitive-behavioural measures and urinalysis for cannabis result were analysed at baseline. For this, individual logistic regression analyses were performed for each measure, with urinalysis result as the outcome variable.

Predictors of testing positive for cannabis use at treatment end (3-month follow-up) and post-treatment (18-month follow-up) were examined using logistic regression analyses. Urinalysis result was used at the dependent variable as it offers an objectively valid test of cannabis use status. For each measure, an initial univariate model was performed with
cannabis use status as the outcome. A second logistic regression was then performed that controlled for group allocation, treatment engagement, and predictors of missingness.

A second stage was then performed, in which a logistic regression model was built based on significant predictors of urinalysis outcome and other variables believed to be relevant. Associations between potential predictor variables were tested prior to model inclusion. A guideline of one predictor for every 15 participants in the dataset was used (Harrell, 2015). An initial model was developed that included significant cognitive-behavioural predictors of cannabis use status, predictors of missingness, psychoeducation sessions attended, and group allocation. Backward elimination was performed using Wald tests to identify cognitive-behavioural parameters to be removed. Regression diagnostic tests were subsequently performed on the final model to test model assumptions, including plotting Lowess graph and checking variance inflation factors. Goodness of fit was checked using the Hosmer-Lemeshow’s test.
8.3 – Results

Sample characteristics are described in chapter 6, table 6.1.

8.3.1 – Objective 1: participants’ reasons for quitting

Table 8.1 - summary of RFQ items and additional reasons for quitting at baseline (n=353)

<table>
<thead>
<tr>
<th>Item</th>
<th>Mean*</th>
<th>S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. To show myself that I can quit if I want to.</td>
<td>2.60</td>
<td>1.29</td>
</tr>
<tr>
<td>2. Because I will feel better about myself if I quit.</td>
<td>2.52</td>
<td>1.35</td>
</tr>
<tr>
<td>3. So that I can feel in control of my life.</td>
<td>2.67</td>
<td>1.35</td>
</tr>
<tr>
<td>4. Because my family or someone else I am close to will stop nagging me about using cannabis if I quit.</td>
<td>2.27</td>
<td>1.51</td>
</tr>
<tr>
<td>5. So that I can get praise from people I am close to.</td>
<td>1.67</td>
<td>1.37</td>
</tr>
<tr>
<td>6. Because using cannabis does not fit who I want to be.</td>
<td>2.14</td>
<td>1.41</td>
</tr>
<tr>
<td>7. Because using cannabis is becoming less socially acceptable.</td>
<td>1.61</td>
<td>1.39</td>
</tr>
<tr>
<td>8. Because someone gave me an ultimatum.</td>
<td>1.44</td>
<td>1.41</td>
</tr>
<tr>
<td>9. Because I am concerned that I will suffer from a serious illness if I don’t quit.</td>
<td>2.22</td>
<td>1.45</td>
</tr>
<tr>
<td>10. Because people I am close to will be upset with me if I don’t quit.</td>
<td>2.07</td>
<td>1.38</td>
</tr>
<tr>
<td>11. Because I have physical health symptoms related to smoking cannabis (such as lung/chest problems).</td>
<td>1.51</td>
<td>1.35</td>
</tr>
<tr>
<td>12. Because I want to save the money that I spend on cannabis.</td>
<td>2.71</td>
<td>1.36</td>
</tr>
<tr>
<td>13. Because of legal problems related to cannabis.</td>
<td>1.70</td>
<td>1.40</td>
</tr>
<tr>
<td>14. Because I know people who have suffered from serious illnesses caused by cannabis.</td>
<td>1.60</td>
<td>1.42</td>
</tr>
<tr>
<td>15. To prove to myself that I am not addicted to cannabis.</td>
<td>2.35</td>
<td>1.39</td>
</tr>
<tr>
<td>16. To avoid being arrested or receiving a conviction.</td>
<td>1.83</td>
<td>1.51</td>
</tr>
<tr>
<td>17. Because I want to avoid involvement in anything illegal.</td>
<td>1.92</td>
<td>1.50</td>
</tr>
<tr>
<td>18. Because there is a drug testing policy where I work.</td>
<td>0.05</td>
<td>0.23</td>
</tr>
<tr>
<td>19. Because I won’t have to leave social functions or other people’s houses.</td>
<td>1.70</td>
<td>1.01</td>
</tr>
<tr>
<td>20. Because I am concerned that smoking cannabis will shorten my life.</td>
<td>1.52</td>
<td>1.07</td>
</tr>
<tr>
<td>21. Because I believe that my mental illness was partly the result of using cannabis.</td>
<td>2.38</td>
<td>1.40</td>
</tr>
<tr>
<td>22. Because I can’t afford to smoke.</td>
<td>2.09</td>
<td>1.42</td>
</tr>
<tr>
<td>23. Because using cannabis isn’t enjoyable any more.</td>
<td>1.89</td>
<td>1.39</td>
</tr>
<tr>
<td>24. Because cannabis makes me feel nauseous or panicky.</td>
<td>1.81</td>
<td>1.40</td>
</tr>
<tr>
<td>25. Because I am worried about the impact of cannabis on my mental health.</td>
<td>2.55</td>
<td>1.40</td>
</tr>
</tbody>
</table>
26. Because cannabis prevents me from being able to do other things/think clearly. 2.25 1.41
27. Because of the reward scheme. 1.74 1.35

* - The mean endorsement of each item (min = 0, max = 4)

Summary statistics for participants’ endorsement of all 27 items reasons for quitting included in the cognitive-behavioural questionnaire are presented in table 8.1. Items loading on the self-concept factor in the RFQ (item 1, 2, 3, and 12), were amongst the most strongly endorsed indicating the relative importance of self-image for this cohort (mean = 2.60, 2.52, 2.67, and 2.71 respectively). The two items targeting mental health concerns (items 21 and 25) were also strongly endorsed (mean = 2.38 and 2.55 respectively) and were more strongly endorsed than most of the RFQ items, demonstrating the importance of mental health concerns in this cohort. Physical health items were amongst the least endorsed, which may be due to the relatively young age of the cohort or may reflect a relative lack of knowledge of the potential physical harms of smoking cannabis. Item 18, which targeted concerns about drug testing at work, was the weakest endorsed RFQ item (mean = 0.05, sd = 0.23), likely reflecting the low levels of employment in the cohort and the relative infrequency of workplace testing for cannabis in the UK. Overall, self-concept, financial concerns, and mental health concerns about cannabis were the most important for participants at baseline.

8.3.2 – Objective 2: predicting cannabis use status at treatment end

8.3.2.1 – Association between cognitive-behavioural measures and smoking status

8.3.2.2 – Treatment end (3-month follow-up)

Urinalysis results at both follow-up assessments were similar between groups. At 3 months, 69.3% of participants in the experimental group and 71.3% in the control group tested positive for cannabis. There was no evidence of a between group difference in the
proportion testing positive at either follow-up assessment ($\chi^2=0.11, p=0.75$ at 3 months).

At baseline, analyses between cognitive-behavioural measures and concurrent cannabis use status at baseline were performed to identify which measures were associated with each of the measures. Analyses results are presented in full in appendix 8.1. Cannabis use status was measured as the baseline urinalysis result (threshold for testing positive was 50 ng/ml). They found statistically significant relationships between concurrent use status (testing positive for cannabis) and motivation to quit (self-efficacy) (odds ratio=0.73; 95% CI 0.64, 0.83; p<0.01), confidence in being able to quit (self-efficacy) (OR=0.68; 95% CI 0.59, 0.77; p<0.01), and perceived difficulty (self-efficacy) in quitting (OR=1.12; 95% CI 1.02, 1.23; p=0.02), as well as frequency (OR=2.11; 95% CI 1.68, 2.67; p<0.01) and strength (OR=1.77; 95% CI 1.43, 2.20; p<0.01) of urges, and having negative use expectancies (OR=0.73; 95% CI 0.57, 0.93; p=0.01) and mental health concerns (OR=0.73; 95% CI 0.57, 0.93; p=0.01). No evidence of an association was found for the other cognitive-behavioural measures.

Results of the logistic regression analyses exploring predictors of cannabis use status at 3-month follow-up are presented in table 8.2. Analyses were initially performed for each cognitive-behavioural variable individual, using urinalysis result at 3-month follow-up as the outcome. Subsequently, analyses were performed again controlling for group allocation, psychoeducation sessions attended, and predictors of missingness at baseline (engagement in work or education and cannabis dependence status).

Results from adjusted analyses show that, at baseline, greater physical health concerns, lower overall motivation to quit, lower confidence in quitting, and greater strength and frequency of urges each statistically significantly predicted testing positive for cannabis at 3-month follow-up. In univariate analyses, mental health concerns, negative cannabis use expectancies, and self-concept reasons for quitting also predicted cannabis use status. However, they were not significant in adjusted analyses.
Table 8.2 - predictors of cannabis use at 3 months. Cognitive-behavioural measures collected at baseline

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unadjusted</th>
<th>Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR‡</td>
<td>95% CI</td>
</tr>
<tr>
<td>Self-concept concern†</td>
<td>0.74</td>
<td>0.55, 0.99</td>
</tr>
<tr>
<td>Physical health concern†</td>
<td>1.65</td>
<td>0.93, 2.93</td>
</tr>
<tr>
<td>Social influence concern</td>
<td>0.96</td>
<td>0.71, 1.29</td>
</tr>
<tr>
<td>Legal concern</td>
<td>0.85</td>
<td>0.66, 1.10</td>
</tr>
<tr>
<td>Intrinsic motivation</td>
<td>0.82</td>
<td>0.58, 1.17</td>
</tr>
<tr>
<td>Extrinsic motivation</td>
<td>0.87</td>
<td>0.63, 1.19</td>
</tr>
<tr>
<td>Mental health concerns †</td>
<td>0.78</td>
<td>0.62, 0.99</td>
</tr>
<tr>
<td>Can’t afford to use cannabis</td>
<td>0.90</td>
<td>0.73, 1.10</td>
</tr>
<tr>
<td>Negative cannabis use expectancies †</td>
<td>0.65</td>
<td>0.49, 0.86</td>
</tr>
<tr>
<td>Because of the reward scheme</td>
<td>0.91</td>
<td>0.73, 1.13</td>
</tr>
<tr>
<td>Motivation to quit †</td>
<td>0.77</td>
<td>0.68, 0.88</td>
</tr>
<tr>
<td>Confidence in being able to quit †</td>
<td>0.76</td>
<td>0.67, 0.87</td>
</tr>
<tr>
<td>Perceived difficulty in quitting</td>
<td>1.08</td>
<td>0.97, 1.20</td>
</tr>
<tr>
<td>Readiness-to-change</td>
<td>0.91</td>
<td>0.72, 1.14</td>
</tr>
<tr>
<td>Exposure to cannabis use †</td>
<td>1.1</td>
<td>1.00, 1.21</td>
</tr>
<tr>
<td>Frequency of urges †</td>
<td>1.85</td>
<td>1.45, 2.36</td>
</tr>
<tr>
<td>Strength of urges †</td>
<td>1.47</td>
<td>1.18, 1.85</td>
</tr>
</tbody>
</table>

† - variables initially included as predictors in logistic regression model * - adjusted for group allocation, number of psychoeducation sessions attended, and baseline predictors of missingness at 3 months (being cannabis dependent and being unemployed). ‡ - Odds ratio of testing positive for cannabis at 3-month follow-up.

8.3.2.2.1 – Model selection

Variables that predicted testing positive for cannabis use at treatment end in adjusted analyses were put into an initial logistic model (Table 8.2 indicates these variables). The initial model also included CIRCLE experimental group allocation, psychoeducation sessions attended, and predictors of missingness (unemployment status and currently being dependent on cannabis). Associations between these variables were explored (appendix 8.2). There were significant associations between strength and frequency of urges (r = 0.70, p<0.01) and motivation to quit and confidence in being able to quit (r = 0.64, p<0.01).

Consequently, both strength of urges and confidence in being able to quit were dropped from the model. Backwards manual selection resulted in the final model presented in table 8.3. Number of psychoeducation sessions, group allocation, and predictors of missingness were kept in the model as these were thought to potentially mediate or moderate the
relationship between cognitive-behavioural measures and cannabis use status at follow-up.

The only cognitive-behavioural variable left in the model was frequency of urges.

Table 8.3 - Final prediction model of cannabis use status

<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of urges at baseline</td>
<td>1.75</td>
<td>1.31, 2.33</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Psychoeducation sessions attended</td>
<td>0.91</td>
<td>0.78, 1.05</td>
<td>0.19</td>
</tr>
<tr>
<td>Group (CM compared to control)</td>
<td>1.08</td>
<td>0.54, 2.19</td>
<td>0.82</td>
</tr>
<tr>
<td>Current dependence at baseline</td>
<td>2.36</td>
<td>1.07, 5.20</td>
<td>0.03</td>
</tr>
<tr>
<td>Engaged in work or education at baseline</td>
<td>0.91</td>
<td>0.78, 1.06</td>
<td>0.19</td>
</tr>
<tr>
<td>Constant</td>
<td>0.25</td>
<td>0.07, 0.91</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Model overall: N=194, Log likelihood= -97.62, $R^2=0.16$, p<0.01

Hosmer-Lemeshow’s test ($Chi^2=7.08$, p=0.53) indicated a good fit for the model. Variance inflation factors (VIF) were all close to 1, indicating little collinearity between predictors. A Lowess graph between predicted and observed values for the model (appendix 8.3) indicated that the model fitted the data.

8.3.2.3 –18-month follow-up

Urinalysis at 18 months were again similar between groups, with 63.6% and 59.8% testing positive in the experimental (CM) and control groups respectively. There was no evidence of a between group difference ($Chi^2=0.67$, p=0.60 at 18 months). Results of the logistic regression analyses exploring predictors of being positive for cannabis use at 18-month follow-up are presented in table 8.4. As at 3 months, analyses were initially performed for cognitive-behavioural variables at baseline. Urinalysis result at 18-month follow-up was used as the outcome. Subsequently, analyses were performed controlling for group allocation, psychoeducation sessions attended, and predictors at baseline of missingness at 18-month follow-up (engagement in work or education).
Adjusted and unadjusted results both suggest that physical health concerns and urges at baseline predicted cannabis use status at 18 months. Compared to 3 months, both physical health concern and urges predicted cannabis use status at both follow-up points. However, overall motivation and confidence in quitting did not predict cannabis use status at 18 months but did at 3 months.

Table 8.4 - predictors of cannabis use at 18 months. Cognitive-behavioural measures collected at baseline

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unadjusted</th>
<th>Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR‡</td>
<td>95% CI</td>
</tr>
<tr>
<td>Self-concept concern</td>
<td>0.92</td>
<td>0.68, 1.24</td>
</tr>
<tr>
<td>Physical health concern†</td>
<td>1.45</td>
<td>1.04, 2.01</td>
</tr>
<tr>
<td>Social influence concern</td>
<td>0.86</td>
<td>0.62, 1.19</td>
</tr>
<tr>
<td>Legal concern</td>
<td>1.10</td>
<td>0.83, 1.46</td>
</tr>
<tr>
<td>Intrinsic motivation</td>
<td>1.25</td>
<td>0.83, 1.87</td>
</tr>
<tr>
<td>Extrinsic motivation</td>
<td>0.99</td>
<td>0.69, 1.42</td>
</tr>
<tr>
<td>Mental health concerns</td>
<td>1.10</td>
<td>0.86, 1.40</td>
</tr>
<tr>
<td>Can’t afford to use cannabis</td>
<td>1.01</td>
<td>0.81, 1.26</td>
</tr>
<tr>
<td>Negative cannabis use      †</td>
<td>1.10</td>
<td>0.82, 1.48</td>
</tr>
<tr>
<td>Because of the reward scheme</td>
<td>0.95</td>
<td>0.75, 1.21</td>
</tr>
<tr>
<td>Motivation to quit</td>
<td>0.96</td>
<td>0.84, 1.1</td>
</tr>
<tr>
<td>Confidence in being able to quit</td>
<td>0.87</td>
<td>0.76, 0.99</td>
</tr>
<tr>
<td>Perceived difficulty in quitting</td>
<td>1.11</td>
<td>0.99, 1.26</td>
</tr>
<tr>
<td>Readiness-to-change</td>
<td>1.02</td>
<td>0.88, 1.04</td>
</tr>
<tr>
<td>Exposure to cannabis use</td>
<td>0.94</td>
<td>0.84, 1.14</td>
</tr>
<tr>
<td>Frequency of urges†</td>
<td>1.27</td>
<td>0.05, 1.01</td>
</tr>
<tr>
<td>Strength of urges†</td>
<td>1.26</td>
<td>0.99, 1.59</td>
</tr>
</tbody>
</table>

† - variables initially included as predictors in logistic regression model * - adjusted for group allocation, number of psychoeducation sessions attended, and baseline predictors of missingness at 18 months (not being engaged in work or education). ‡ - Odds ratio of testing positive for cannabis at 3-month follow-up.

8.3.2.3.1 – Model selection

As at 3 months, the variables that predicted cannabis use status in adjusted analyses were put into an initial logistic model (Table 8.4 indicates these variables). The initial model also included CIRCLE experimental group allocation, psychoeducation sessions attended, and
predictors of missingness (unemployment status and currently being dependent on cannabis). As before, strength of urges was not included in the model due to collinearity with frequency of urges. Backwards manual selection resulted in the model in table 8.5. As before, the only cognitive-behavioural variable left in the final model was frequency of urges. But the overall model was not significant.

Table 8.5 – Final model of predictors of using cannabis at 18-month follow-up.

<table>
<thead>
<tr>
<th>Predictor variables</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of urges</td>
<td>1.30</td>
<td>1.03, 1.65</td>
<td>0.03</td>
</tr>
<tr>
<td>Psychoeducation sessions attended</td>
<td>1.03</td>
<td>0.90, 1.17</td>
<td>0.66</td>
</tr>
<tr>
<td>Group (CM compared to control)</td>
<td>1.07</td>
<td>0.56, 2.04</td>
<td>0.84</td>
</tr>
<tr>
<td>Engaged in work or education</td>
<td>1.73</td>
<td>0.90, 3.33</td>
<td>0.10</td>
</tr>
<tr>
<td>Constant</td>
<td>0.41</td>
<td>0.12, 1.36</td>
<td>0.15</td>
</tr>
</tbody>
</table>

Model overall: N=164, Log likelihood= -105.05, R²=0.03, p=0.12
8.4 – Discussion

This chapter examined two questions: 1) What are participants’ reasons for wanting to quit? 2) What cognitive-behavioural indicators predict cannabis use status at treatment end and at post-treatment follow-up?

8.4.1 – Reasons for quitting

8.4.1.1 – Main findings

The most subjectively important reasons for wanting to quit cannabis were to save money, because of concerns about mental illness, and to have more control over their cannabis use and feel better about themselves. The single most strongly endorsed reason for wanting to quit at baseline was financial (‘Because I want to save the money that I spend on cannabis’). Although, in chapter 7 many participants had said that the voucher scheme was an important reason for taking part in the CIRCLE trial, ‘because of the reward scheme’ was not one of the most strongly endorsed items and was far less important than saving money. At baseline, participants in this cohort reported using 49% of days in the last six months on average, and rates of current dependence were high (76.9%). These results perhaps suggest that participants may have been spending more on cannabis each week than they received from the reward scheme by abstaining. In this case, it may be that the CIRCLE CM reward amount was actually less important than other factors in motivating participants to quit.

Other reasons that were also strongly endorsed included those related to self-image (“To show myself that I can quit if I want to”, “Because I will feel better about myself if I quit”, “So that I can feel in control of my life”) and secondly to concerns regarding their mental health (“Because I am worried about the impact of cannabis on my mental health”).
8.4.1.2 – Implications

Given the characteristics of this cohort, some of these reasons may reflect the concerns and pressures that may be greater on this cohort than the general population. For example, around two thirds of participants were not in paid employment. As such, they may have financial concerns or found it more difficult to afford using cannabis. Meanwhile, all participants had a history of psychosis, and had their first psychotic episode within the last 3 years. Having a psychotic episode is a traumatic experience for many (Rodrigues & Anderson, 2017), and something many patients are concerned about experiencing again in the future (chapter 9.3.1). Believing that cannabis increases the risk of having future episodes is likely an important factor in participants wanting to quit cannabis.

There is a lack of data regarding reasons for quitting in this population and very little evidence more widely. In other populations, endorsed factors were broadly similar to the results of this study, with self-concept as one of the most strongly endorsed factor at baseline (for example Chauchard et al., 2013) However, endorsed factors can vary quite widely across populations. Martz and colleagues (2018) found that the most strongly endorsed factors by high school seniors included concerns about becoming addicted, use being against one’s beliefs, not liking cannabis users, and not having friends who use cannabis, and that not enjoying cannabis use was the most important predictor of use at 1 year follow-up. Overall, reasons for wanting to quit cannabis in this group are similar to other groups but reflect some of the concerns that are particularly relevant to this cohort, such as mental illness.

8.4.2 – Predicting cannabis use status

8.4.2.1 – Main findings: at baseline

At baseline, greater negative use expectancies and mental health concerns were both associated with participants being more likely to be concurrently cannabis free (provided
negative urinalysis results at baseline). These are both components of IM, indicating the association between intrinsic motivations for abstinence and cannabis use. However, IM measured with the RFQ questionnaire were not associated with use, unlike in other populations. In a study of 200 treatment seeking smokers, Foster and colleagues (2015) found evidence of weak correlations between nicotine dependence and intrinsic motivational factors. By follow-up, motivation measured with the RFQ was associated with quitting both alcohol and smoking. Similar results were found by Pokhrel and Herzog (2015) in 1988 daily cigarette smokers, who found evidence of weak negative correlations between nicotine dependence and intrinsic motivational factors (i.e. health concerns and self-concept reasons for quitting). That the RFQ is not associated with cannabis use status in the present population suggests that the relationship between IM or EM (as measured by the RFQ) and use status is different to that amongst smokers. There are many potential reasons for this, but it arguably indicates that the relationship is mediated or moderated by other domains, and that these limit the strength of the association. This is discussed further in chapter 10.2.

Amongst reasons for wanting to quit cannabis, mental health concerns and negative use expectancies were both significantly associated with cannabis use status. There was also very weak evidence of an association between self-concept reasons for wanting to quit and use status. Overall, these point to some dimensions of IM being the most important for understanding use status.

Meanwhile, there was good evidence that overall motivation, self-efficacy, and cravings were associated with cannabis use status. There was also very weak evidence of an association between cannabis use with readiness-to-change and time spent with cannabis using peers.
8.4.2.2 – Predicting cannabis use at treatment end (3 months) and post-treatment (18 months)

After adjusting for group, number of psychoeducation sessions attended, and predictors of missingness, frequency of urges emerged as the most important cognitive-behavioural predictor of cannabis use at follow-up. It was the only cognitive-behavioural measure included in the final model developed to predict cannabis use at treatment end (3 months). It also predicted cannabis use at 18 months in adjusted analyses. However, the model was not significant overall. There was also evidence in adjusted analyses that physical health concerns also predicted cannabis use at both follow-up points, as did overall motivation and self-efficacy at treatment end (3 months) but not at 18 months.

Physical health items were amongst the most weakly endorsed on the RFQ. Meanwhile, in the qualitative work discussed in chapter 9.3.1, some people said they stopped using cannabis because they had experienced chest problems, which was targeted by the RFQ. However, most people who quit cannabis for physical health reasons did so because it was incompatible with exercise related hobbies, like playing football. But physical health concerns related to exercise were not targeted by the RFQ questionnaire. In short, the weak endorsement of the physical health items is likely due to the relatively young age of this cohort, and that few had yet experienced any physical health problems arising from their use. That physical health concerns were associated with abstinence by treatment end likely reflects a relatively small group of people who have experienced physical health difficulties, such as chest or lung problems, or who are now significantly concerned about their use.

Initial univariate analyses identified several other predictors of cannabis use at treatment end, which did not predict cannabis use in adjusted analyses. These included greater endorsement of some reasons for quitting: self-concept reasons, mental health concerns,
and negative cannabis use expectancies. It also included spending less time with other cannabis users. There was very limited evidence that extrinsic motivational reasons for quitting predicted cannabis use. Meanwhile, there was no evidence that social factors were predictive of abstinence, which was also the case for physical health concerns in initial, univariate analysis. However, after controlling for predictors of missingness, physical health concerns predicted cannabis use.

Overall, these results suggest that in this group, urges were the strongest predictor of abstinence by treatment end. This arguably suggests that a replacement therapy, similar to nicotine replacement therapy (NRT), such as nicotine gum or nicotine patches may offer an effective intervention in this group. However, as discussed in chapter 1.3, a product that contains THC may need to be viewed as harm reduction in this cohort rather than eliminating the potential harms of cannabis use. However, a form of replacement therapy in this group may be an effective short-term strategy to help patients reduce their cannabis use, ideally with a view to tapering dose and eventually achieving abstinence.

The results also provide some, albeit weak, evidence that amongst reasons for quitting, intrinsic factors are amongst the most important factors for someone being able to abstain from cannabis. These include how participants see themselves, expecting cannabis use to be unpleasant, and worries around their mental health. However, given how the results differ between analyses before and after controlling for predictors of missingness, these results are inconclusive as they may be confounded by attrition at follow-up.

8.4.2.3 – Implications

This suggests that targeting cravings directly may be the most effective method of treating cannabis use in this cohort, although this evidence is arguably quite weak by itself. Furthermore, targeting ambivalence around using cannabis and fostering a sense of being able to quit cannabis may also be beneficial.
Given these results, it is perhaps surprising that treatments so far have not proven effective. CIRCLE, a trial of a financial reward-based treatment, found no effect despite finances being the most strongly endorsed reason for wanting to quit. Meanwhile, improving motivation and self-efficacy are two goals of MI and CBT, and to date none of the trials of these therapies have been positive. Explanations for this may be that underlying factors, such as severity or frequency of urges, may be greater in this population, making it less likely that treatment will work. Secondly, it may be that motivation to quit and/or self-efficacy is lower in people in this cohort, and/or they may be less amenable to therapy. It may be that the form of psychosocial treatment is in principle effective, for example, that a more intensive or thorough programme of treatment, or CM at a different reward level, may be more effective.

8.4.3 – Limitations

One of the key limitations of the present study was also reported for the study described in chapter 4. Namely, the high rate of attrition by follow-up (at both 3 months and 18 months). While patterns of missingness were explored and predictors of not being followed-up were controlled for, it may be that there were reasons for attrition that were not considered. Moreover, controlling for missingness substantially changed the results of the analyses, suggesting bias from attrition. Therefore, interpretation of the results needs to take this into account.

Another limitation is that this study was conducted in the context of a trial. While group allocation was controlled for, and there was no evidence of an effect from the CM on cognitive-behavioural predictors (see chapter 4), it may be that taking part in the trial confounded the results. Some likely effects of taking part in the trial include that participants in the experimental (CM) group received more time with clinical staff and engaged with the psychoeducation more. Meanwhile, the psychoeducation, despite being
intended as an optimised Treatment-As-Usual, should perhaps be seen as an active control, as acknowledged in chapter 5.3. These effects may confound the analysis of baseline predictors of cannabis use.

8.4.4 – Summary

In conclusion, the reasons for wanting to quit amongst people with psychosis and problematic cannabis use include financial and mental health concerns, as well as wanting to have more control over their use, and cannabis no longer fitting who they want to be. Meanwhile, cravings were the cognitive-behavioural construct that was most associated with cannabis use at follow-up. It may be that future therapies would benefit from being tailored to target these issues most effectively.

The next chapter presents qualitative data that explores participants’ experiences of quitting cannabis. This includes their reasons for wanting to quit, their history of making quit attempts, and any barriers or facilitators to quitting that they experienced. This includes the strategies that they have adopted or support they have received or been offered. It aims to consider what more can be done to help support this population with quitting cannabis.
Chapter 9 – Exploring participants’ perspectives of abstaining from cannabis use in dual diagnosis: a qualitative study

9.1 – Introduction

9.1.1 – Background

As described in chapter 1.4, previous published studies indicate that there is currently a lack of evidence supporting any formal psychotherapies, such as CBT or MET, as effective for cannabis use disorders in psychosis (Gates, Albertella, & Copeland, 2016). As described in chapter 5, CIRCLE also found limited evidence that CM is an effective intervention in this group. This lack of evidence contrasts with the relative success of trials of psychotherapy in populations without comorbid psychotic illness. There is thus a need to understand why this is better, and what the cognitive-behavioural process underlying quitting and abstaining from cannabis is in this cohort. In this chapter, CIRCLE participants’ experiences of quitting cannabis are explored, both in terms of the barriers and facilitators of abstinence, and their views of treatment for cannabis use are discussed. The aim of this chapter is to explore, using qualitative data, the cognitive-behavioural process of change underlying quitting cannabis in this cohort, and to identify the strategies and types of support service users have found beneficial in helping them quit.

Currently, there is only a very small body of qualitative evidence on the experiences of patients with psychosis of quitting cannabis. Meanwhile, there is very little published on what types of support patients have received to help support them quit cannabis through the Mental Health services in the UK; or what in their view is (or would be) helpful in supporting them to quit. Of the papers that have been published, perhaps the most relevant is by Lobban and colleagues (2010), which reported a qualitative study that
included 19 EIP service users with current substance misuse. All participants had been cannabis users, and for 68% of the sample cannabis was the primary drug of use. The key reason given by participants for wanting to quit substances was a change in personal life goals, which were often an increase in the perceived value of health, disposable income, and close family relationships. This was particularly true for older participants. Many meanwhile cited social relationships, and specifically peer relationships, as a key reason for starting their use, but it was also a key reason for stopping their use. Participants’ own use was often consistent with the perceived norms of their peer groups or of those that they aspired to belong to, whether that meant starting or stopping cannabis use. Older participants referred to wanting to have a normal social life, which typically excluded illicit substance use, while younger participants still saw illicit substances as a normal part of their social life. Changes in drug use behaviour were often accompanied by positive social relationships that supported their change. However, in a minority of cases, behavioural change was provoked by major life event, including having children. Some participants felt that substance use made their mental health worse or had a negative causal effect on their mental health, but others reporting using to help alleviate mental health issues, such as anxiety. However, several participants believed that there was no link between cannabis use and psychosis.

Lobban and colleagues (2010) was the only identified qualitative paper looking at the experiences of quitting cannabis in an EIP cohort. But there is a small body of literature reporting on the views and experiences of other groups with psychosis. In many cases, the results of the studies are broadly similar to Lobban and colleagues (2010). In cohorts of people with psychosis and problematic cannabis use, qualitative studies from various countries report to have found that reasons for quitting include concerns about mental health, its incompatibility with current responsibilities or with future life goals, social or family relationships, ‘self-image’ reasons, and wanting to feel more in control of their use.
and being concerned about tolerance and dependence (Laudet & White, 2010; Pettersen, 2014; Rebgetz et al., 2016). The negative impact of cannabis on mental health is typically related to concerns about psychosis, needing to take medication, and being concerned about returning to hospital. However, recognising that cannabis exacerbated emotional difficulties was another important factor. Some of the most common life goals patients give include having a relationship or a family and getting back into work or education. Amongst people who already have these, cannabis is seen as incompatible with those relationships and responsibilities. However, amongst those still using substances, ambivalence about their use was high, and motivation to change was low. Changing use was something many planned to do at some point in the future when their circumstances changed, such as when they wanted to start a family, but many felt that it was not immediately important.

In terms of strategies for quitting that patients have found helpful, patients in this cohort (Laudet & White, 2010; Pettersen, 2014; Rebgetz et al., 2016) report focusing on their reasons for quitting to stay motivated. For example, some report focusing on negative use expectancies, such as unpleasant effects of acute intoxication from cannabis and its impact on their mental health, such as paranoia, to help sustain their motivation to abstain. Others report staying motivated by not wanting to disappoint or let down family members (Pettersen, 2014; Rebgetz et al., 2016). Secondly, patients report engaging in activities, like playing video games, physical exercise, or work, to distract themselves from thinking about cannabis, and engaging in meaningful relationships that did not involve using cannabis. A third, and associated methods was, changing their social networks to help themselves stay in control. Associated with this, some patients report spending more time with supportive friends and family, who do not use cannabis (Pettersen, 2014). Participants who relapsed to cannabis use cited being around cannabis using peers, and to alleviate negative moods or anxiety, in some cases related to difficulties in close relationships with partners or family members (Rebgetz et al., 2016).
However, while this literature explores participants’ reasons for wanting to quit, and briefly considers their strategies for quitting, there is a gap in the literature regarding service user experiences of therapy in the UK. Mental health service models differ substantially between countries, but it is unclear which, if any, are effective. There is a need to consider what models of service delivery currently exist in the UK, and if or how these can be improved. The present chapter explores participants’ own experiences of quitting cannabis, their reasons for doing so, and what therapies, types of support, and relapse prevention and coping strategies they have been offered and which they found effective.

9.1.2 – Aims

In this chapter, participants’ perspectives on their cannabis use and how they have tried to reduce their use outside of the CIRCLE trial are discussed. Specific aims include to explore participants’ reasons for wanting to quit cannabis and the attempts they have made in the past. Secondly, it explores participants’ views of the barriers to reducing their use. Thirdly, it considers the strategies participants report adopting or treatments that they received from the Mental Health services or voluntary sector, and how helpful they were. This work is intended to help generate potential strategies for supporting people with psychosis with reducing their cannabis use.

9.2 – Methods

The present data collection was conducted as part of the study described in chapter 5 and is summarised here only in brief.

20 participants from the experimental arm of CIRCLE were recruited following the final follow-up assessment for the trial (18 months post-consent). Participants were purposively sampled to include a range of demographic and clinical characteristics. Participants were interviewed one-to-one by LSR using a semi-structured interview guide. Development of the interview guide is described in chapter 5. The interview guide explored participants’
reasons for wanting to quit cannabis and their experiences of doing so. It investigated the barriers and facilitators of quitting cannabis, which included factors that made quitting more difficult, such as participants’ experiences of withdrawal symptoms, and strategies participants found helpful to support them quit, such as changing their social relationships. It also considered what treatments participants had received in the past, and what they found helpful or unhelpful.

9.2.1 – Analysis

Data were analysed as part of the same analysis reported in chapter 7, and so the methods were identical. In the final thematic framework of that analysis, themes were divided into two domains: 1) an evaluation of the CIRCLE trial, and 2) participants’ reasons for quitting cannabis, and their attempts/approaches taken outside of CIRCLE to change their cannabis use. Here the second domain is presented.

9.3 – Results

Demographic and clinical characteristics of the sample are presented in chapter 7, table 7.1.

Three themes were identified: 1) Reasons for quitting. 2) Difficulties or barriers to quitting. 3) Support and strategies for quitting.

9.3.1 – Theme 1: reasons for quitting

All participants reported that they have had periods when they did not use cannabis in the past. However, the most common reason for making a quit attempt had been that there was change in the person’s life that made it more difficult or inconvenient to use cannabis. Examples of this included being in hospital, living with parents, or going abroad. However, these were not planned efforts to quit.

‘I went through phases of going on and coming off [cannabis], going on and coming off, but it wasn’t that I was trying to stop. It was more or less like ... during
that period of time I'd be doing certain things and I'd be, like, oh okay, I can't use this anymore throughout that period, and I would just stop and I would go through months without having any, then I'd go back again.’

Participant_05

Overall, participants all reported having made at least one deliberate attempt to cut down or quit, which in many cases has only happened since enrolling in the CIRCLE trial.

However, most participants report that their previous attempts to cut down or quit have been unsuccessful, with some relapsing within hours, reflecting the difficulty many participants have experienced when trying to quit. Only a few participants reported having quit for at least the previous six months at the time of the interview:

(Interviewer) ‘How many times did you try to quit before you finally did?
Plenty times, plenty times. Like I would say I’m quitting, then maybe a week later, two, a couple days later even, or even today, the next night, back on it again, so it’s, it’s hard to quit. It’s quite addictive. The feeling as well, like, the buzz and everything.’

Participant_16

Deliberate decisions to quit were often complex, with few having a single reason when making a quit attempt. However, some reasons were clearly more common or important amongst participants. These are discussed in three sub-themes: 1) using cannabis no longer being compatible with who they want to be, 2) problems associated with cannabis use or negative events due to cannabis use, and 3) no longer enjoying cannabis. Amongst those who had not used cannabis for at least 6 months by the time of the interview, only two reported that CIRCLE had played a key role in them abstaining. As such, CIRCLE was a relatively uncommon reason for abstaining long term amongst participants.

Sub-themes

9.3.1.1 – Not compatible with self-image

One of the most important factors for participants was that cannabis did not fit who they wanted to be, or that it prevented them from achieving their life goals, which was reported
by several participants. Examples of this included that many participants felt like they had outgrown cannabis and that it was something you do when you are young. In most cases, participants felt that they wanted a different lifestyle now, which was not compatible with using cannabis. Most common goals included wanting to have a job and a career, wanting to be more productive, or wanting to have a relationship. Many participants found that cannabis made them feel ‘sluggish’ or unmotivated, and because of this, it made engaging in work or education difficult. As such, cannabis made many participants feel ‘unproductive’. These participants often felt better about themselves when they quit cannabis, not least because they were able to work or study. One participant described quitting cannabis because of this as being ‘kind’ to themselves.

‘So it just came down to giving myself a lot, a bit more love, you see what I mean. If I'm doing so well then understanding that taking cannabis prevents me from doing what I want to do, like I've gone to uni after that. I started going to the gym, I'm taking care of myself, I'm working part-time now, studying full-time. Stopping [cannabis] was a stepping stone to getting to where I got to. Cannabis is just one of the things that is going to get in the way or progress in life and whatever you want to do.’

Participant_20

For other participants, they saw using cannabis as incompatible with other life goals, such as having a relationship. In most such cases, participants wanted to have a relationship in the future, and believed that quitting now was important for achieving that.

However, cannabis was not universally viewed as incompatible with these goals. For some, cannabis was viewed as a mild drug, and something you use in an evening and still get up for work in the morning. However, in general, participants with more severe cannabis use tended to see more of a problem with their use. Equally, some participants had relationships in which their cannabis use was accepted by their partner. But again, these participants tended not to be amongst the most severe users.
Some participants said that their main reason for quitting originally was that cannabis made them feel ‘bad tempered’ and ‘unpleasant’ to be around. In such cases, it was typically that they had a dependency on cannabis and they would become angry or irritable when they were not using:

‘With [cannabis] I’m a version of myself which isn’t savoury, it’s not nice. Very kind of short, aggressive, kind of, like, I don’t know I guess it’s kind of the fact of… it’s just not a side of me that I like. So, without it I feel like a better person especially, you know, if you want to be... this is my own personal opinion if you want to be a functioning, responsible person you can’t do... you can’t do the whole smoke weed everyday thing.’

Participant_10

In most cases, it was conflict with their parents or family member that made them aware of how cannabis was affecting them. In this respect, this sub-theme overlaps with another sub-theme (chapter 9.3.1.3.3) in which conflicts with friends and family is identified as another motivation that participants gave for wanting to quit:

‘[I had] a very big problem … I’d go round [my mum’s], and if I didn’t have money I’d beg her and beg her for money, and she was like, look, this is getting out of hand. Like, I’m not very proud of you anymore. And that sort of hit me.’

Participant_18

Another reason in this sub-theme was that participants wanted greater control over their use. Many participants viewed their cannabis use as being problematic, and some viewed it as having a significantly negative impact on their life. Participants often wanted to quit to have more control over their use and not feel the urge to use:

‘There are millions of individuals out there with different perceptions and ideas and a lot of people who smoke weed really believe that it’s a good thing for them... But you’ve got to understand that recreational use becomes a habitual thing and then you become to abuse it, you come to use it as if it’s just like cigarettes, you smoke it 24/7..., it’s not benefiting you because you’re abusing it.’

Participant_05

Other participants felt that cannabis was incompatible with their spiritual beliefs or how they saw themselves. Some participants reported making big changes in their lifestyle
because they wanted to be healthier or ‘cleaner’, typically as part of improving how they saw themselves or as an ethical choice. Quitting cannabis had been a part of this. In one case, the participant had become a vegan, stopped drinking alcohol, stopped smoking cigarettes, and made other changes. Meanwhile, in a minority of cases, participant’s spiritual beliefs had led them to see cannabis as something ‘evil’ or sinful. This was for them an important reason to quit.

9.3.1.2 – No longer enjoyed cannabis or had negative use expectancies associated with cannabis

Just under half of participants reported that they no longer enjoyed the intoxicating or acute effects of cannabis, or no longer found it worthwhile. In some cases, participants said that their experiences of using cannabis have changed, often since developing psychosis. Whereas they used to find using cannabis pleasurable, since first developing psychosis, they now find smoking cannabis unpleasant:

‘I think once the, once the whole episode happened, going into hospital and everything, like, it hasn’t been the same since, the effects that it has on me... It kind of tends to speed up thoughts and make more anxious thoughts rather than being able to relax.’

Participant_08

For others, they came to view cannabis as unhelpful or counterproductive, such as finding it easier to get things done when they are not smoking, or preferring not to rely on a substance to give them peace or facilitate social situations. This tends not to be accompanied by a change in their experience of cannabis per se, so much as a change in whether they enjoy using cannabis. As discussed in the self-image sub-theme above (chapter 9.3.1.1), some participants felt that they had outgrown cannabis or that their priorities were now different and were no longer compatible with using cannabis:

‘Just, I notice that if I smoke, I don’t really like going out and stuff... So, I don’t get much done during the day, I just end up smoking and chilling around, getting lazy
and stuff. Yes, so, yes. But I’ve realised that when I smoke it kind of has a negative effect on me, I become lazy, I become tired.’

Participant_16

Associated with this, all participants who had successfully quit or wanted to quit viewed cannabis more negatively than previously. No participant in the study had a purely positive opinion of cannabis. However, many participants viewed cannabis very negatively. Such views of cannabis were important for understanding why people wanted to quit. But in many cases, they were not enough to motivate participants to quit or reduce use. As such, while reasons for wanting to quit were important for understanding participants’ motivations, strongly negative views were not always associated with abstinence. Rather, the relationship between reasons for quitting with their cannabis use was complex.

Participants rarely held positive views of cannabis, and almost all wanted to quit or had quit. But some found it too difficult to abstain:

‘No one can make you quit. You can only quit yourself. But some people need it all their life. But now I have got to the stage it’s just, it’s nothing. I wish I had never started, mate.’

Participant_13

9.3.1.3 – Negative life consequences of using cannabis

Almost all the participants who had not used cannabis for at least six months by the time of the interviews believed that they had previously had a ‘serious problem’ with cannabis. In the whole sample, almost all participants said that cannabis had caused problems in their lives. These are divided into 4 sub-sub-themes: a) mental health concerns, b) physical health concerns, c) conflict with family members, and 4) the cost of using cannabis.

9.3.1.3.1 – Mental health concerns

The impact of cannabis on participants’ mental health was an important topic, and it was something that they had discussed at some length during the CIRCLE psychoeducation.

Most had previously discussed the connection between cannabis and psychosis with a
clinician prior to taking part in CIRCLE. However, for many the information that they had received previously had been quite limited, and most participants reported that the CIRCLE psychoeducation had been a good and useful opportunity to learn more about the relationship (see chapter 7.3).

Three-quarters of participants believed that cannabis had played a role in them developing psychosis either as an indirect or direct cause. An example of an indirect cause was making them more socially isolated or depressed, and thereby contributing to the circumstances in which they became unwell:

‘What led up to going to hospital? This is a bit of a double whammy I will say. [Cannabis was] the main reason according to the [mental health] team... In my opinion it did not play a significant role... What cannabis I feel did, was further isolate me from the world... Depressed, withdraw, isolated and then one of the things... It was literature with an extremist point of view that meant I ended up in hospital.’

Participant_20

Amongst those who saw cannabis as a direct cause, only a small minority said that they had been unwell wholly because of using cannabis. One of these participants believed that their cannabis may have been laced with stimulants and did not think cannabis by itself would have made them ill. Most participants thought cannabis was a contributor to their illness, but that other factors may have been more important, such as stress or other drug use. However, participants were ambiguous about what exactly these causes were in most cases, and said they did not know exactly why they had become unwell:

‘I think there’s a variety of factors, but maybe weed is a part of the issue, or could have provoked it, or kind of just been that final thing to draw you, kind of, over the edge.’

Participant_16

Several participants reported that they had self-medicated with cannabis in the past to help with boredom, anxiety, and other concerns. But a majority of these participants said that they now think that cannabis only helps short-term, and that long-term heavy use causes
problems. Three participants said that they now believe cannabis exacerbated or caused depression or anxiety, and that was a factor in why they wanted to quit:

‘I was using cannabis to suppress the short-term symptoms. If I was, for example, having a panic attack or if I felt particularly depressed I would smoke in that instance and it would make me feel better in that short period of time. But I suppose I just noticed that certain symptoms were worsened at times that I was smoking a lot more. Like general anxiety and I suppose paranoia as well would come into that.’

Participant_17

Around half of the sample reported that mental health concerns were partly or wholly responsible for their decision to quit. In most cases, participants were concerned about experiencing future psychotic episodes or going back to hospital. In others, participants felt that even if cannabis was not primarily responsible, it was not worth risking more mental health problems by smoking:

‘I came home to London where I am right now, and I saw my mum… and [she] noticed that I was starting to show symptoms of another episode. And she said she was worried about me and she said that it looked like things were going the same way as they did two years ago… Those words, the ones that prompted me to think about my life and the only thing that has happened in my life recently that is, kind of, an anomaly was the cannabis and I thought this time it’s clear that it does have a link. Yes, and I just, I’m just quite terrified of going back into the hospital. I don’t want that to happen, I don’t want to put my family and friends through that again. So I’m doing it for them as much as myself really.’

Participant_17

9.3.1.3.2 – Physical health

Although not widespread, a few participants mentioned physical health concerns as an important factor to them. When these reasons were discussed, they were often the participant’s main reason for wanting to quit. For the most part, these participants played sports as a hobby, and saw cannabis use as hindering their fitness.

‘So that’s when I started the football team. And the football team was like quite good, so I didn’t smoke that much … I think the only thing that motivates me to stop smoking is sports. Football and sports.’

Participant_11
However, one participant reported using cannabis very heavily and experiencing problems with their chest:

‘I coughed up loads of blood, yes, and I was just like, no, this has got to stop.’

Participant_18

9.3.1.3.3 – Relationships with family or friends

A third of participants reported partly or wholly quitting in the past because of cannabis causing problems with family or friends, and half of these said it was the main reason for deciding to quit. Often this had involved a parent or partner showing their concern or disapproval related to the participant’s cannabis use. Participants gave several examples of this, including that their mother had expressed concern that they were becoming unwell again, or that they would not give them any more money for cannabis. This sub-theme overlaps to a degree with other reasons for quitting, such as the self-concept theme (chapter 9.3.1.3.1). In most cases this conflict led participants to feel that they did not much like themselves when they were using cannabis:

‘On a Sunday night... I’d begged my brother for a joint, and he got, you know, arsey with me, and give me, like, three joints worth of bud, which is all he had, and he was, like, fucking take it, smoke it, you’ll never get any more out of me. And I thought, fuck, if I pushed you to that... because he’d help me with anything, do you know what I mean? And I thought, fuck, I’ve pushed you to a limit. So I rolled all three joints, smoked the spliff. I noticed it was nearly 12 o’clock, and I thought, well, that’s it. I won’t touch it.’

Participant_14

As such, family or friend relationships are frequently intimately bound up with the person’s self-image. It was also through these relationships that participants came to view their own behaviour as problematic or see themselves negatively, including being bad tempered or irritable, because of cannabis (as discussed in theme 9.3.1.3.1). It was often conflict with family members, and typically with parents or partners, that led participants to believe that they had a problem with cannabis and needed to change their use. While disapproval from,
or conflict with, partners and family members was frequently ignored at first by participants, in many cases it became an important main reason for wanting to quit. This change was often precipitated by a moment or short period of relatively intense conflict in which the participant came to see their use as problematic. This often involved the participant recognising that they did not have control over their use, did not like who they were, or recognised that cannabis was having a negative effect on their mental health. Moreover, as discussed in a subsequent theme, when they come to change their use, it is often those family members that participants seek support from to help them quit.

9.3.1.3.4 – Money

A third of participants reported that the cost of using cannabis was an important factor in their decision to quit, which was often a feeling that the money could be better spent on other things or was being wasted. This was often tied to other sub-themes and was particularly problematic for severe users or participants who were unemployed. Not only would cannabis cost often a lot of money, but participants viewed it as making it more difficult to engage with work. As such, it was financially problematic for two reasons. For many participants, thinking about the amount of money they spent on cannabis and what they could otherwise be using that money for was an important source of motivation to help them quit:

‘And I was realising the amount of money that was going down the drain, you know, the amount of money I was spending on weed I could’ve been spending on something else, you know. I could’ve been spending it on bills, spending it on food, clothing, whatever, you know. Or I was putting it aside to save up for a holiday.’

Participant_04

9.3.2 – Theme 2: difficulties in quitting

Most participants found quitting difficult and they cited many barriers to quitting, although some could not really say why it was challenging. Several participants who were still using
said they wanted to quit but found it extremely difficult. In one case, a participant said that although they had reduced their use, they wanted to quit completely. But they find it too difficult and they feel like they are letting themselves down:

(Interviewer) ‘Now that you have very much reduced the amount that you smoked, how do you feel when you do smoke?

I still feel let down, like I don’t quite... like I’m just half way there.’

Participant_06

The three most common barriers to quitting are described as sub-themes: 1) family and friends, 2) withdrawal symptoms, and 3) cannabis use is enjoyable or helpful. Only a few participants said that they find quitting quite easy and that they experience few or no withdrawal symptoms.

9.3.2.1 – Friends and family

As discussed in the previous theme (chapter 9.3.1.3.3), conflict with or disapproval from partners, parents, and other family members was one of the main reasons for wanting to quit (chapter 9.3.1.3.3). Wanting to start a family or have a relationship was another key motivation (chapter 9.3.1.1). However, the role of friends and family in participants’ cannabis use was complex. Virtually all participants started smoking with friends or family members, and in amongst those still smoking cannabis, many see most or all of their friendships as revolving around cannabis to some degree. Moreover, about a quarter of participants reported that their family, most often siblings, used cannabis, and it was often them that that they had started using cannabis with:

‘All my friendships have been made because of cannabis, and if I hadn’t smoked cannabis I would not have any friends.’

Participant_17

Overall then, for most participants, friends and family divided between those who used cannabis and those who did not:
‘A couple of my family was like encouraging me to stop, but then the other half [friends] that’s encouraging me to continue is like angel and devil, you know, so it was like, yes, what do you choose?’

Participant_11

In most cases, participants saw their relationships with cannabis using friends and family as barriers to quitting. For some, this was due to pressure being put on the participant to use by their cannabis using peers. This ranged in nature as well as degree: in some cases, participants reported that their friends would explicitly encourage them to use cannabis as well:

‘When I first [quit], I still stayed with the same friends who smoked. I just didn’t smoke while they were smoking. I think they kind like tried to put peer pressure a bit, yes.’

Participant_11

While in other cases, it was more tacit, perhaps due to lack of conscientiousness on the part of their friends and family members, or due to an ambivalence or subtle disapproval towards the participants’ efforts to quit:

‘All my mates smoke, and they still smoke ... I [have to] say no to everyone... It’s got easy now, it’s been so long. But I had a mate’s funeral on Monday, Tuesday, and all of the people that went smoke ... and every single person had a spliff on them and every single one of them said, here, bruv, here, bruv and I’m like, mate, I told you already, I don’t smoke anymore. Because I was such a big... I was a bigger smoker than all of them [friends], and they probably just forget. I’ve got one friend, a really good friend, and I sit next to him when he’s smoking, and he doesn’t offer me or nothing.’

Participant_18

However, it was often more complex than pressure to use cannabis per se. Even if participants reported that their friends were supportive of their efforts to quit and avoided using in their presence, some participants still viewed those relationships as problematic. In one case, rather than being pressured by their friends to use, the participant felt that knowing their friends were avoiding using around them made them uncomfortable. They would prefer either to use with their friends or avoid being around their friends altogether.
As such, being around cannabis using peers was a barrier for participants. In some cases, this was true even if those peers were explicitly trying to avoid pressuring them to use.

As such, the relationships participants had with their friends and family were key for understanding their motivations around their cannabis use. One the one hand, these relationships were important motivators to quit for many participants, and often facilitated the participant in changing how they saw themselves and their views of cannabis. This was particularly true of their relationships with their parents or partners, whom they typically felt responsibility to or in some sense understood themselves through (such as knowing when they are becoming unwell or unpleasant to be around). On the other hand, relationships with cannabis using friends and family were a substantial barrier to quitting for all participants. This barrier was particularly severe amongst those who felt unsupported by friends and family, and in some cases made people question their friendships and decide not to see those friends anymore. But in virtually all cases, as discussed below (chapter 9.3.3.3.1), participants reported needing to change these relationships, at least temporarily during the initial stages of quitting cannabis.

9.3.2.2 – Withdrawal symptoms

Around half of participants said they found quitting difficult because they experienced withdrawal symptoms, including sleeplessness, changes in mood, and anxiety. For these participants, withdrawal symptoms along with cravings and urges were amongst the most important reasons why they had relapsed in the past:

[When they quit] ‘I do feel worse. Because it’s at that stage where your body kind of like is used to the weed so it’s kind of like feels a bit weird and stuff.’

Participant_11

These symptoms represent a substantial challenge for people, even if they know cannabis is problematic for them and they are strongly motivated to quit, a key reason why participants do not succeed is that they experience withdrawal symptoms or urges. These
withdrawal symptoms include sleeplessness for many participants, but for others included anxiety and paranoia:

‘Sleeplessness came when I tried to stop. Because when I stopped, you know, you get sweats at night, your dreams start coming back again, you know. They’d become more visual, they’d become more intense.’

Participant_05

Coping with these symptoms was a significant challenge for the participants who experienced them. Some spoke about needing to slowly reduce their cannabis use, others described trying to stay motivated by focusing on their reasons for wanting to quit, and some said that they engaged with other activities to distract themselves, amongst other strategies:

‘Wasn’t easy, it was mostly withdrawal and change of mood and stuff. I said to myself, you know what, these people are trying to help you and stuff.

(interviewer) Which [withdrawal symptoms] do you think you felt?
Just a lot of mucous and stuff ... Anxiety, paranoia. I asked myself is it really worth it, and all those things... I did it a bit abruptly, some people take time and I just tried to do all at once.’

Participant_06

9.3.2.3 – Like using cannabis or find it helpful

While no participants had entirely positive views of cannabis, a few participants said they enjoyed being intoxicated too much to quit substance use or said that cannabis use otherwise benefited them in a sense. This divided into people who had taken the decision to self-medicate with cannabis, and those who used because they enjoyed it.

Only one participant reported self-medicating with cannabis, which they said was because it helps them manage their emotions. Although they found quitting quite easy, they had decided to use for this reason. However, they also reported not enjoying it particularly:

‘I got engaged on April 5th, and I had been clean for three weeks at that point... And I was quite stable, but I noticed that if I experienced high levels of stress, I’d be absolutely ballistic... So yes, I ended up getting back on the weed, which was weird.'
First time in my life I’ve actually had to force myself to go and get a bag of weed to calm down... [to] stabilise my emotions a little bit. I mean, I don’t get happy from it, really.’

Participant 14

Amongst those who reported enjoying being intoxicated too much to quit substances, one said that they had only managed to quit cannabis by substituting it with other substances:

‘I’ve cut down on the cannabis and I have cut down on the drink. But cutting down still ain’t really doing anything. I am leaning to cocaine now. I am leaning to other drugs now. You know what I mean? I am going from one drug to another.’

Participant 13

Another said that although they wanted to quit, they found it too difficult. They said that they thought this made them an addict:

‘I just don’t like being sober... I’m a drug addict. I love taking drugs. So, I think, yes, I am an addict.’

Participant 15

Overall, only a small number of participants expressed positive use expectations with cannabis or said that they self-medicated with it. However, it may be that other participants, and particularly those who still use, do so because they enjoy or benefit from the effects of cannabis, even though they did not mention it in the interviews. In this sense, as exemplified by these participants, the pleasurable aspects or beneficial aspects of cannabis intoxication present a barrier to quitting. These positive aspects of use, along with the negative experiences of withdrawal symptoms and urges, were the main drivers that participants described for their continued use.

9.3.3 – Theme 3: support and strategies for quitting

Most participants reported receiving support for quitting cannabis, which is discussed here in two sub-themes: 1) Formal support received, typically received through the Mental
Health services. 2) Informal support, typically from friends and family. A third sub-theme explores the strategies participants adopted for changing their cannabis use.

Overall, support from people with lived experience of quitting substances (especially cannabis) themselves was generally the most valued form of formal support (peer-support). Such support was typically received through group sessions arranged by Drug and Alcohol Services or Dual Diagnosis teams, and it was evident from participants’ reports that some of the group sessions they had been offered were not particularly relevant to them, either because others were using ‘harder’ substances or because the groups did not focus enough on substance use. Both those who reported finding formal peer support helpful received the treatment via Narcotics Anonymous. Narcotics Anonymous offers self-help treatment groups, in which peers provide support to each other. Peer support was viewed positively because participants felt that peers with similar lived experience could empathise with their own difficulties in quitting cannabis better than clinicians or peers with experience of quitting other substances. Secondly, peers could discuss the strategies for quitting that they had themselves found helpful or unhelpful, and how they implemented them in practice. In this sense, participants said that they thought that peers with similar lived experiences had a better understanding of quitting cannabis and could provide better support both emotionally and practically than other groups.

9.3.3.1 – Formal support

This sub-theme covers support received via the Mental Health services for cannabis use. As the CIRCLE trial is discussed in chapter 7, this sub-theme only considers formal support other than the CIRCLE trial.

The most common kind of formal support participants reported receiving or being offered was from the Mental Health services. This was typically support from dual diagnosis
workers based in the EIP team, or Dual Diagnosis services. Fairly often, treatment involved
group sessions with peers.

Around a third of participants said that the support they had helped them or would help
them quit. Most of these participants said that they found talking to other cannabis using
peers to be particularly helpful. Most participants said that they had only received peer-
support through group therapy sessions organised through a drug or alcohol service, but
one participant had also received one-to-one peer-support through Narcotics Anonymous
services. Participants reported that peer-support was particularly helpful because it helped
to speak to someone who could empathise their own experiences and give them advice
from personal experience of what is useful for quitting. Having the opportunity to speak to
a peer at points when remaining quit was particularly difficult, such as when experiencing
low moods or anxiety, was especially important:

‘In the six years that I've been using cannabis the only time that I have actually
felt prompted to not do it anymore was when I was at the Narcotics Anonymous
meeting. And I was around people who were like me, who could relate to me and
understand what I'm going through from a personal way. Not just because they
read it in a text book or because they studied it at university. It's because they've
lived through those experiences. And that to me is the most important thing
being able to relate to someone on a personal level... I actually thought I would be
laughed at if I turned up there and said I had an addiction to cannabis and
someone there who has been addicted to heroin or something would look down
at me or something. But I did not feel that in the slightest.’

Participant_17

One participant spoke at some length about the benefits of support from people with lived
experience of quitting cannabis benefits. They said that without lived experience,
therapists do not really understand what it is like to quit cannabis and cannot really
empathise with patients or give advice. Instead, clinicians without lived experience can
sound patronising:
'As an addict, I would never ever take advice in regard to drugs from someone who has never taken them. That’s just my rule, I would never give someone advice who has been beaten up for being black, because I’ve never had that. I would give them as much help and love as I can, but I would never give them advice because I myself have never been through that. And I just found it a little bit, want of a better word, patronising for the people [delivering CIRCLE] to be drilling this information into me about how drugs are bad, when they themselves have never experienced what that is like and how that can affect your life... I think that enlisting the help of people who do smoke and people who have smoked in the past or people who have had personal experiences with these drugs, I think it [would be beneficial].’

Participant_17

However, participants’ experiences of support were very variable. Around a quarter of participants had only received support from their EIP or Community Mental Health Team (CMHT) clinicians, which was often minimal, or nothing at all:

[About the CIRCLE trial] ‘I thought it was a great idea to first just approach the idea, instead of ignoring it, like it feels the CMHT does. Yes, I felt good about it.’

Participant_14

Moreover, amongst those who had received more substantial treatment, many found it unhelpful. Some had been offered psychotherapy sessions with a dual diagnosis worker or psychologist, but none reported finding this particularly useful. This was often because it was not particularly well tailored to cannabis use and was instead more suited to heroin or cocaine. In other cases, it was because people felt that the clinician did not really understand what the experience of trying to quit substances was like, or that they just did not find it that helpful.

Some other participants, meanwhile, reported not finding group sessions with peers beneficial. This was often because the other patients in the group were using ‘harder drugs’ than cannabis, and so the participant felt that their own experiences had little in common with those of other group members. However, others found that the focus in the group sessions they attended was not really substance misuse or did not do enough to assist them with quitting cannabis. Instead the sessions were more like occupational therapy:
'There was, actually, there was one thing. There’s a thing called New Hope, it’s a drug thing where I live. And I went there, but I didn’t think it was right for me, because it wasn’t just the cannabis, people were on heroin and they’re sitting in front of you and... And I was just like, well, I don’t really want to be here for them to be... Because I’m trying to do one thing and they’re doing something else, and I don’t think it was right for me to be there.’

Participant_18

‘I think it was more so after I started this. I went to... I went over to King George’s and I went to their whole care session, care type of thing. And I just felt like it wasn’t for me, I felt like it was for people that were more in crisis or just coming out of crisis because it was, you know, it was a very nice atmosphere, community aspect, you know, a bit of education. So, they were doing more of a broad spectrum of things rather than for just addiction.’

Participant_10

Overall, many participants found that there was a lack of support from EIP teams for quitting cannabis, and what was offered was often unhelpful. This may reflect both that it is not clear what treatments are effective for cannabis use disorders in cohorts with psychosis, as well as funding pressures and a need to prioritise other types of substance misuse.

9.3.3.2 – Informal support

This sub-theme explores what support participants received from friends and family. Overall, these relationships played a central and critical role in quitting cannabis for almost all participants. As discussed in the previous two themes (chapters 9.3.1.3.3 and 9.3.2.1), participants’ relationships with friends and family are both key reasons for wanting to quit but can also be barriers to quitting. Most participants started using cannabis with other cannabis using friends or family members and see their relationships with cannabis using peers as significant barriers to quitting, even if those peers are supportive of their decision to quit. As discussed in the next sub-theme (chapter 9.3.3.3.1), many expressed a need to change who they spent time with as strategy for quitting cannabis use.

This often took the form of spending less time with cannabis using friends and family, and more time with close friends or family members who supported them in their decision to...
quit cannabis. This was often parents or old friends. Two-thirds of participants reported that their parents do not want them to use cannabis. Amongst those who had quit, almost all described receiving support from their parents, partners, close friends, or other family members. This support was often in the form of just spending more time with them and positive regard, care, and emotional support:

‘She [participant’s mother] was very proud. Yes, very proud to see me actually taking action ... She was happy.’

Participant_06

A few participants said that they were able to confide in friends or family with similar lived experience of quitting cannabis, and this was often viewed particularly positively. Although not everyone had this type of support available to them, those that did often sought it out:

‘Telling a therapist, no, because I have a friend now who's been through a lot of stuff in his life, so, and he's like survived you know what I mean. And he bettered himself and we're kind of close friends. So it's kind of like I'm able to open up with him because he's been through so much in his life. It's easier to open up to him. And he opened up to me as well, so it was kind of like you have that friend, you know what I mean, that can understand.’

Participant_11

Participants spoke about support from people with lived experience of quitting cannabis as being particularly helpful because they felt that they could empathise with the experience and challenges of quitting cannabis better than people without such experiences. They also tended to have a better understanding of strategies for quitting, such as how to cope with the negative aspects of quitting, or how to avoid difficult situations. Participants who had this kind of support when they quit often credited it with being a key element in their ability to quit, and they found it more helpful than any of the treatments that they had received from the Mental Health services.

Meanwhile, other participants said that their family did not seem to care about them using cannabis, that they do not talk about it with their families much. In such cases, this made them feel demotivated to quit. As such, positive regard from parents was an important
motivator to participants to quit and stay quit. Participants found it difficult when their families were ambivalent about their use. Where available, participants spoke particularly highly of support from close friends with lived experience of quitting cannabis and described it as key form of support for them when quitting.

9.3.3.3 – Strategies for changing cannabis use

9.3.3.3.1 – Changing social relationships with family and friends

Changing social networks was one of the most important strategies participants used to quit. While a minority of participants reported that their social networks had changed as a by-product of quitting cannabis, most reported deliberately changing who they spent time with. The main reason for this was that being around cannabis using friends or family members was viewed as high-risk for relapse by participants. Almost all participants reported avoiding such situations as being their primary coping strategy for this type of risk. This meant deliberating spending less time with cannabis using friends and family, at least temporarily after they begin a quit attempt. This was often a difficult process, but one that was viewed as critical to successfully cutting down and abstaining from cannabis use. While almost all participants who had quit spoke about spending less time with cannabis using friends, around a quarter of participants said they also had to spend less time with family members, often siblings, who smoke.

‘There was a lot of people that I had to, kind of, just say, sorry, man can’t be friends with you no more just because... not because I didn’t like them it was very much more so that... not all we used to do together was smoke weed. But we used to smoke weed together a lot I’m trying not to do that, you’re still doing that’

Participant_10

While spending less time with cannabis using friends and family was often difficult for participants, it was especially difficult for those with very limited social networks, for those who had to change their whole social group, or who had made very substantial changes to their lives, such as moving out of their family home. In one instance, a participant reported
that quitting cannabis meant that they no longer spend time with their only friend and that it had negatively impacted his relationship with his brother:

‘I used to have a best friend… [The CIRCLE clinician] made me really question the friendship. Is it a friendship based on friendship alone, or is it a friendship based on… cannabis mostly or the drinking? … So I decided to sever ties because it’s not helping my recovery at all, stuff like that… It wasn’t easy task, but I just, I felt good afterwards… My brother smokes, he took it a bit funnily… Like I didn’t want to hang out with him anymore… He took it a bit personally… And I started to ask, what kind of brother is he really if he’s encouraging you [to smoke cannabis]… He wasn’t too pleased.’

Participant_06

As such, trying to quit cannabis often meant people felt they had to make very substantial changes to their social networks, often resulting in them meeting whole new groups of people, or not spending time with friends at all. Although it was not something that participants discussed in depth, some of those with very minimal social networks spoke briefly of loneliness and low mood as a consequence of this. As such, while spending less time with cannabis using peers was almost universally seen as an important step by participants, in some cases it also had significant, negative consequences.

Similarly, a few participants said that all their family members use cannabis and that moving out of their family home was an important part of quitting cannabis. While some had been able to move out and subsequently quit cannabis, others spoke about not being able to afford to do so, and instead tried to convince their family to support them in quitting:

‘I’ve just cut off all aspects of weed, really… I guess, moving out was one of the ones. It was always in the house, so now I’m away from it. I’m in my own house, well, my own flat… Now I’ve got an environment where it’s weed free, you know… ‘There’re certain friends I’ve not hung out with anymore. I don’t speak to any dealers anymore.’

Participant_05

Typically, changing social networks was strongly tied up with receiving informal support from family and friends. Many participants said that when they decided to spend less time
with friends who used cannabis, it meant spending more time with family or friends who provided them with support, and that was often the most important aspect in helping them quit. As discussed in the previous sub-theme (chapter 9.3.3.2), this was often friends or family with similar lived experiences. But in other cases, it meant people spent more time with their parents. In other instances, participants viewed developing a new social group as helpful for quitting cannabis, even if it did not involve peer support for cannabis. In such cases, participants reported that having new social networks helped them avoid cannabis and focus on other activities:

‘Changing my social circles. I feel that played a role in a way... How to get into something, so if I wanted to get out of the social circle of not even, I don’t call them friends, I call them just people, people, acquaintances that could have been smoking. Getting out of that social circle, but if I’m left alone there’s exposure of going back, so I need to get into the next circle that’s hopefully going to be more productive.’

Participant_20

Only a small minority of participants said that they hoped or expected not to change their social relationships when they quit. However, none of these participants had entirely quit using cannabis and they were typically uncertain about whether they would be able to quit without changing who they spent time with. In most cases, participants reported that their cannabis using friends were not supportive of their decision to quit, which was seen as a barrier to quitting. However, even when cannabis using friends were supportive, participants were sometimes uncertain about whether they could spend time with them. In one instance, a participant lived in a shared house with cannabis using friends. Despite reassurance from their friends that they would not use around them, the participant was nonetheless unsure whether this would mean that they could avoid cannabis and thought that they may need to move out in order to abstain from cannabis use.

‘[Friends] want what’s best for me and they did also suggest that they would not smoke in the house anymore... they’re incredibly supportive... The biggest hurdle that I’m going to have to cross [is smoking in my social group]. Right now, I’m in London at my mum’s house with my sister and my husband and I don’t feel any
pressure to smoke, I don’t feel any temptation. But the house that I live in, in Liverpool with four of my close friends, that is going to be a big difficulty to go back to. To be in the same environment as people smoking... All my friendships have been made because of cannabis, and if I hadn’t smoked cannabis I would not have any friends.’

Participant_17

In another case, the participant lived with their family, who all used cannabis. As they were unable to move out to their own home, they instead tried to encourage their family to quit with them:

‘My problem is, is that the people that I’m around smokers also. So it’s going to be a lot harder. But with my family and that lot, as I said to them already, within these three months, I’m going to cut down, so you lot are going to cut down, too.

(interviewer) Okay, so your family smokes cannabis, as well?
Yes. So I’m kind of around that.’

Participant_01

Overall, while almost all participants viewed changing social networks to avoid spending time with cannabis using friends and family as a key component of quitting cannabis, there was significant diversity around what that meant. For some, it meant spending more time with friends who did not use cannabis and often receiving support from them to help them quit. For others it meant spending more time with family members, and often parents, who also often provided support. But for others, it meant having to make difficult and substantial changes that others found too difficult or prohibitive, or hoped to avoid. In some cases, this meant needing to stop spending time with certain social groups.

9.3.3.2 – Relationships, work, education, and activities

Almost all participants spoke about quitting cannabis because using cannabis was incompatible with other goals that were more important to them, such as having a family, being in work or education, or playing sports. These reasons were discussed in an earlier theme about ‘self-concept’ reasons for quitting (chapter 9.3.1.1). Participants often said that they always knew that they would have to quit ‘one day’, perhaps when they were
ready to have a relationship and start a family, or when they wanted to be more serious about their careers. Amongst those who had quit, several said that they had now achieved those things and that they believe quitting cannabis was pivotal in that. As such, focusing on these goals helped them to keep motivated. Moreover, for these participants, changing their life by engaging in work, education, or starting a family also helped engage them in activities that did not involve cannabis, and so helped distract them from using and helped them move away from social groups of cannabis using friends:

‘This year I’ve done so much with my life. I’m doing a personal training course; my daughter was born two months ago … I’ve been working in a gym. It’s mad.

(interviewer) Do you think that is down to … [quitting] cannabis?

Yes, 100%’

Participant_18

‘I started going to Learn Direct … I did six courses with them. Managed to get a part-time job through them … I started taking care of my fitness, I started doing some good stuff and going to the gym.’

Participant_20

However, amongst those who had not yet quit, many had aspirations for their future life that they thought would help them quit cannabis. As such, as well as being a key reason for wanting to quit cannabis, engaging in relationships, work, and activities also helped participants stay abstinent, or was seen as a good strategy to help in the future when they were ready to quit.

9.3.3.3 – Positive effects of quitting

As discussed above, many of the heavier using participants report withdrawal symptoms when they first quit. Once the withdrawal symptoms subside, participants typically report feeling better. These effects helped to keep participants motivated to remain quit. Some of the most reported benefits were feeling clearer headed, more energetic, and calmer or more relaxed:
'The main thing that I suppose has been affected by my smoking has been my memory which is definitely also affected by my medication, but I noticed that in those three months, just things like being able to remember peoples’ names when I met them and remember things that had happened a few days ago, I was able to do that a lot easier. I suppose my head just felt generally clearer. Once the initial withdrawal had gone I actually found that my sleep was really affected in a good way by not smoking ... I think most people are likely to relapse in those first few weeks. But if they do hold on for just a bit longer they probably would get past the hump.'

Participant_17

‘I feel clear. I’ve got a clear mind, I can do things, I’m not tired all the time. I don’t, I literally just don’t think about weed anymore.’

Participant_18

Several reported having more energy:

‘Sometimes you’ll wake up, you’ll feel lazy, you don’t really want to go out. So, that kind of thing, I just feel more, I don’t know how to put it. Alive, like, you just want to do things, you want to get up, you want to get on with your day, you want to go out.’

Participant_16

‘When I did quit for that month, roughly, like every time I was coming down here to do the tests [CM], I was feeling a little bit more energetic, like my mind wasn’t so paranoid, like, I felt a bit better, you know?’

Participant_01

One participant reported feeling calmer and more relaxed in social situations:

‘I’m able to feel a bit more comfortable around social interactions ... I’m able to focus on the environment, focus on being relaxed in it, not thinking that oh, I need the weed to help me relax and be in this group environment and interact and do what I’ve got to do ... My mind’s more capable of focusing on other things. I can entertain myself.’

Participant_05

Many reported that these feelings were important in helping them stay motivated to abstain. They acted as a form of positive reinforcement of abstinence. As such, focusing on the positive aspects of cannabis was one strategy participants mentioned for keeping themselves motivated.
Several participants spoke about the importance of changing their ‘outlook’ or ‘mindset’ when quitting. Participants used many different terms to express this, however they generally involved the need to change how they viewed cannabis, their attitude to work and friends, and focusing more on their life goals. As discussed in the themes above, these topics arose frequently amongst participants’ reasons for wanting to quit, the barriers to quitting, and the strategies they used to help themselves quit. Central to that was a conscious effort to change how they felt and thought about cannabis and other aspects of their lives, ultimately to stay motivated to abstain from cannabis and achieve their goals.

As described in the reasons for quitting theme (chapter 9.3.1.3), most participants viewed cannabis negatively. However, some participants said that these feelings were the result of a conscious process. Although it did not happen like this in all cases, one participant said that they did this by focusing on the negatives of cannabis, such as that it is harmful to their health and problematic for their family relationships. In this way, they described themselves as ‘reprogramming’ their thoughts:

‘I have a cognitive dissonance between, I shouldn’t do it, but I enjoy it. But I’ve reprogrammed my thoughts and almost for good through conscious effort, maybe affirmations, I like to use that word. When you’re, like, positive affirmations, when people look in the mirror and say I’m beautiful, whatever the hell, but I said that I don’t like cannabis, I hate it, it’s ruined my life, I need to move forward. So, I would program my brain in order towards the more negative attributes to reduce that cognitive dissonance and so the negativity would override the positive idea of engaging in that thing, and nowadays I don’t even contemplate using it.’

Participant_12

Although few participants described a conscious process this complex, most who had quit described needing to pay attention to their thoughts and feelings and focus on the negative consequences of cannabis use as well as the positives of quitting, their life goals, and ignoring thoughts or feelings connected to using cannabis. They also described this process as a way of maintaining motivation to stay quit. Participants described this process in many
ways, but they included the participant saying that they had needed to change themselves, hold themselves to a different standard, or change their thought process:

‘What happened is just my inner self mainly changed. No one else can quit for you.... No one can make you quit. You can only quit yourself. But some people need it all their life. But now I have got to the stage it’s just, it’s nothing. I wish I had never started, mate... My only downfall is that I am not working. I think I need an achievement in my life now. I’ve got to set some goals. I want to make goals and achievements in my life. You’ve got to do it yourself because if you don’t want to do it, it’s not going to get done. You’ve got to get it done for you. You know what I mean? No one can quit for you. You’ve got to do it yourself. If you haven’t got the willpower and the strength, then you are f*cked getting over that.’

Participant_13
9.4 – Discussion

9.4.1 – Main findings

The present study explored participants’ experiences of quitting cannabis, their motivations to quit, and their perspectives on any strategies for quitting they have tried or therapies they have received.

All participants had made attempts to quit in the past. Many had successfully abstained from cannabis for at least six months by the time of the interviews, but others were still trying to reduce or stop using. The most common reason for having quit in the past was that there were times when it was difficult to smoke, such as periods when they lived with their parents, but this was typically not a planned effort to quit. The main reasons for wanting or planning a quit attempt included the negative effects of cannabis use, such as unpleasant experiences when using cannabis or feeling lethargic. Just over half of interviewees said that they no longer enjoyed cannabis or did not find it worthwhile.

Others, meanwhile, found using cannabis made it harder to get other things done, so preferred not to use it. Negative effects also included its impact on mental and physical health, but while most participants thought that cannabis played some role in their psychotic illness, few thought cannabis played a major role. Most attributed their psychotic episodes in the past to a more complex interaction of factors, including low mood, stress, and the use of other drugs like amphetamines or cocaine. However, the possible effects of cannabis on their mental health was a motivating factor for most participants in wanting to quit. For a minority of people, physical health issues, and in particular physical fitness made them want to quit all forms of smoking. Finally, for many participants there were other negative consequences to using. Most reported that the money they spent on cannabis felt like a waste, which could have been used for better things. Meanwhile around a third mentioned that the conflict or tension they experienced with family members because of
their cannabis use, often their parents, was a factor in deciding to quit. Another reason that participants gave for wanting to quit was that cannabis no longer fitted who they wanted to be or the life they wanted to have. In some cases, people felt like they had outgrown cannabis or that it affected them negatively. Some said they felt cannabis use was ethically problematic. Almost all participants had a negative view of cannabis overall. Only one person reported that cannabis had a positive effect for them as it helped them control their mood.

These reasons for wanting to quit were broadly consistent with those reported in previous studies. Those reasons include the negative impact cannabis has on health, finances, ability to achieve desirable goals or engage in hobbies, and family or peer relationships (Lobban et al., 2010; Rebgetz et al., 2016), and there is some evidence of quitting for self-image or to feel more in control (Laudet & White, 2010). Furthermore, while concerns about the impact of cannabis on their mental health tended to be one of participants’ reasons for quitting, it was generally not a primary reason and in some cases participants felt that there was no connection at all. Rather, the most important reasons tended to be cannabis interfering with important relationships with family members or with achieving key life/career goals or engaging with enjoyable hobbies.

While all participants had tried to quit in the past, most found it extremely difficult. One of the main reasons that participants cited were withdrawal symptoms, with urges and cravings being the most common, but sleeplessness and anxiety were also frequently reported. Many participants also reported relapsing because of these symptoms. Another major difficulty was spending time with friends and family members who used cannabis. In many cases, people had to change the amount of time they spent with friends and family to help them quit or avoid relapsing. For some participants, this had been a very difficult process, which involved spending less time with family members or their only friends.
Finally, a few said that, although they wanted to quit, they enjoyed using cannabis too much and so had always relapsed or had never tried. Of these participants, most reported enjoying using substances, or disliking being sober, too much to stop. Amongst those who had quit, most said that it had been part of a wider effort to change several aspects of their lives. For example, some participants were now in education, while others were in work or more focused on their careers. Some had new relationships and one had recently started a family. They often viewed these changes as part of helping them with their mental health and saw them as being incompatible with cannabis use. As such, they also help keep them distracted from using cannabis and help them develop new social relationships that do not involve cannabis. Overall, for many participants, cannabis was or had been central to many facets of their lives. Quitting often required substantial changes to social networks and meant experiencing many unpleasant withdrawal symptoms or coping with urges. Those who had been most successful were often the ones who had been able to make the largest changes, including going back into work or education, and finding new social groups.

Again, these types of support and strategies for quitting are fairly consistent with previously published data. Participants reported changing their social relationships: they spent less time with cannabis using peers, while spending more time with, and in some cases receiving support from, family or friends who did not use cannabis or who had themselves quit cannabis (Lobban et al., 2010; Rebgetz et al., 2016). However, unlike in this study, in some previous literature participants reported engaging in activities to distract themselves from cannabis (Rebgetz et al., 2016). It may be that this reflects a poorer use of coping strategies in this cohort than in other groups that have been more successful in quitting.
Meanwhile, a third topic, which has not been explored in previous literature, is the formal support that participants received from EIP services in the UK. Participants said that they would like more support to help them with abstaining from cannabis. However, while most participants reported receiving either/both formal or/and informal support for quitting cannabis, the majority felt that the formal support that they had received was not particularly helpful or was minimal. Often, if they had received support, participants felt that it was not well tailored to cannabis. This often led most participants to disengaging with treatment. This is broadly consistent with previous literature, which found that services not being supportive enough, perhaps due to understaffing or lack of resources, was a major reason why patients drop out of dual-diagnosis treatment (Sorsa et al., 2017; Priester et al., 2016).

One of the main difficulties with the treatment participants were offered was that it was typically group support for people with any kind of substance misuse, and that ‘harder’ substances, like heroin or cocaine, were more common than cannabis use. Participants found it hard to identify with the experiences of others who were trying to quit these substances as they felt that quitting cannabis was quite different. However, many said that well-tailored support had or would help them quit. Most of these participants said that talking to other people who had quit cannabis themselves was particularly helpful as they understood the experience of trying to quit and could discuss strategies for abstaining. A few participants had received this kind of peer-support. But in most cases, it was group therapy sessions organised by a drug or alcohol service, and one participant had also received one-to-one peer-support through Narcotics Anonymous. Having the opportunity to speak to a peer at points when it was particularly difficult to quit, such as when experiencing low moods or anxiety, was especially helpful. In many cases, participants had only received support from their EIP or CMHT clinicians, which was often minimal, or nothing at all. Meanwhile, others said that while they had been offered psychotherapy
sessions with a dual diagnosis worker or psychologist, they had not found it useful. This lack of benefit from current formal support offered by the Mental Health services may, at least partly, be the result of the lack of evidence for effective treatments for cannabis use in severe mental illness, as well as funding pressures and a need to prioritise treatment for other types of substance misuse. Again, this is broadly consistent with published literature. There is evidence that there can be a mismatch between the priorities or focuses of clinicians compared to patients (Sorsa et al., 2017), and that programs can fail to address the cognitive, social, and behavioural characteristics specific to schizophrenia (such as disorganisation, poorer social networks, lower engagement with work or education) (Sorsa et al., 2017). Such issues have been found to be a deterrent to patients participating in treatment.

In the case of CIRCLE, while most participants viewed the CM and psychoeducation treatments positively, some viewed the psychoeducation in particular negatively and felt that it could have been improved if it was delivered by people with lived experience of quitting cannabis. Overall, given the results presented in this chapter, it may be that the CIRCLE treatments did not provide enough support to help participants in engendering the level of change in the lives that quitting cannabis may require for many people in this cohort. As described above, the most successful participants in this group were often the ones who had made the biggest changes in their lives.

Rather than formal support, most participants reported finding the informal support they had received from friends and family, who often had had similar experiences, more helpful than speaking to a counsellor. Such support often played a critical role in quitting cannabis for participants. But beyond informal support, all participants who had quit reported changing their social circles or reducing how much time they spent with cannabis using
friends or family, either intentionally or as a side effect of quitting cannabis. Doing so was often seen as a difficult but critical step.

9.4.2 – Implications

Much of the data presented in this chapter are consistent with previous literature, and further strengthen the evidence emerging on these topics. Amongst patients’ reasons for wanting to quit cannabis, self-concept, mental health concerns, and its incompatibly with important responsibilities or relationships are amongst the most important. Meanwhile, key strategies for changing their use involve changing their social networks, which often meant spending more time with family, as well as engaging in activities that are incompatible with cannabis use, such as work, education, or hobbies. Meanwhile, most participants found therapy, and especially the therapy they had received through the Mental Health services, to be unhelpful. The participants who had successfully quit were often the ones who had made the biggest changes in their lives. Current therapy seems to be unhelpful to people in supporting them make these changes. Moreover, some participants said that therapy would be more effective if it was delivered by people with lived experience of quitting cannabis. Without this experience, participants sometimes felt that clinicians did not understand what it is like to quit cannabis and could not empathise with the challenges of quitting. This research suggests that a different approach to current therapy may be required. It may be that some of the elements of current treatment can be adopted, such as supporting people in reducing their ambivalence about use, helping them develop strategies for avoiding relapse, and supporting them in coping with withdrawal symptoms. However, more may be required to support people in making wider changes, such as engaging in work or changing social networks.
9.4.3 – Limitations

The main limitation of this study is that all participants had taken part in the CIRCLE trial, and due to time pressures, all were recruited from towards the end of the CIRCLE follow-up phase. Participants were purposively sampled to cover a wide range of demographic and geographic characteristics, and the researchers felt that saturation had been achieved. However, it is possible that a sample that included participants also from earlier on in CIRCLE, or included non-CIRCLE participants as well, would have reported experiences that were not captured here. Secondly, this study explores participants’ views of the cognitive-behavioural change underlying abstaining from cannabis and their views of effective treatment. But participants may lack insight into process or what may be an effective treatment.

9.4.4 – Summary

Overall, almost all participants had or wanted to quit, but most found it extremely difficult. Current treatment offered through the Mental Health services is generally regarded as lacking and ineffective. Several participants said they had not been offered any support, or the only support they had received was from their EIP clinician. Amongst those who had received support, it was often poorly tailored to cannabis use, and was more suited to other substances. Participants instead sought informal support from friends and family, and ideally from someone with experience of quitting cannabis themselves. It may be that an effective formal support for those groups should incorporate elements of peer-support, ideally from peers with experience of quitting cannabis themselves, and should take a wider approach, which looks not just at cannabis use, but that supports people in making broader changes in their life, including to their social circle, getting back into work or education, and helping them change how they use their spare time.
Chapter 10 – Discussion

10.1 – Main findings

The present study was designed and conducted in the context of the CIRCLE trial. Its primary aim was to conduct a process-evaluation of CIRCLE. Secondary aims related to exploring how to improve treatment for cannabis use in people with a history of psychosis and are described below for each chapter. It contained five studies: A systematic review and two quantitative and two qualitative studies. The aims and results of each study are described below:

10.1.1 – Chapter 2

In chapter 2 a systematic review was presented, the aim of which was to evaluate whether combining CM with another formal psychotherapy, such as CBT or MI, has a synergistic effect and is more effective than either stand-alone treatment.

The results of the meta-analyses (n=1,654) found no evidence of a synergistic effect, with PPA being no better in CM plus psychotherapy than CM alone. This was true when CM was compared to all other psychotherapy interventions, or when only CBT or MI were included as adjunct therapies. As such, there is no evidence that combining CM with another intervention improves the short-term or long-term effects of treatment. The conclusions of this review point towards CM perhaps not having a cognitive-behavioural mechanism of action that differs substantially, and is complementary or synergistic with, other structured psychosocial interventions. Thus, it may be that, contrary to the suggestion that CM has a minimal or negative impact on IM to abstain from substance misuse, CM does in fact have a broadly similar effect to other psychotherapies.
10.1.2 – Chapters 3 and 5

The methods of the CIRCLE trial were presented in chapter 3 and its results in chapter 5. The aim of the trial was to test a 12-week CM intervention for cannabis use in EIP service users. 551 EIP service users took part in the trial. However, no effect from the CM intervention was found in the primary outcome (time to admission to an acute mental health service) or secondary outcomes, including clinical and functional factors (such as psychotic symptom severity, engagement with work or education, psychiatric service use, and self-reported and biometrically verified cannabis use). A post hoc analysis found evidence that the CM improved time to acute psychiatric relapse in participants who attended at least 4 out of six psychoeducation sessions, suggesting that the CM may have been effective amongst those who engaged with the intervention. However, overall the results of the trial were mixed and did not provide clear evidence of benefit from the CM.

10.1.3 – Chapters 4 and 6

In chapters 4 and 6, a process evaluation of the CIRCLE trial was presented. The main aim was to test a hypothesised cognitive-behavioural mechanism of action of the CIRCLE CM intervention. As described in chapter 5, the CIRCLE CM intervention had no effect in the intention-to-treat analysis. The results of the cognitive-behaviour evaluation suggest that the CIRCLE CM had no effect on the primary outcome (IM by treatment end) or most secondary outcomes by either 3 month or 18 month follow-up. These results are despite engagement being relatively high (median of 9/12 CM sessions attended), and the analysis adjusting for the number of psychoeducation sessions attended. Therefore, the lack of any effect is unlikely to be the result of poor compliance with the CIRCLE treatments. Rather, it seems that in this cohort, the CIRCLE CM failed to motivate participants to change their use. These results are perhaps surprising given the frequently reported benefits of CM in both populations with severe mental illness and without psychiatric comorbidity.
In chapter 7, a qualitative study was presented that examined participants’ views of the CIRCLE CM intervention. Overall, participants were positive about the CIRCLE trial and the CM intervention. They said that the CM motivated them to engage with treatment, and several said that they would not have accepted therapy for cannabis use without the financial rewards. However, few participants had quit by 18 months. While all participants tried to quit during the intervention, for most it was too difficult. Amongst those who did manage to reduce, their initial motivation to quit had often faded by the end of the treatment phase and they had relapsed. In many cases, this was because the vouchers did not offer enough of a motivation to quit, or they felt that they were not ready to quit at the time. Furthermore, for most the psychoeducation left a bigger impression and greater motivation to abstain by the time of the interviews 18 months post-consent. Participants believed that it was important to combine CM with another therapy, as by itself CM would lack any information about the potential benefits of quitting cannabis.

Overall, there is limited evidence from any of the work in this thesis that CM has a beneficial effect on cannabis use in people with psychosis. Although there was some evidence that the CIRCLE CM improved time to acute psychiatric admission in those compliant with treatment, the process evaluation no evidence of a cognitive-behavioural effect after adjusting for psychoeducation sessions attended. CM is the latest of several psychosocial interventions that has failed to produce a detectable benefit in people with psychosis and comorbid substance misuse. There is a pattern of psychological interventions being effective for substance misuse in the general population, but with mixed or no evidence for substance misuse in populations with severe mental illness (Hunt et al., 2013; Jeffrey et al., 2004; Rygaard Hjorthøj et al., 2014; Bradizza, Stasiewicz, & Dermen, 2014). The question therefore arises, why did it fail to motivate participants? And how do we design an effective treatment for this group? Chapters 8 and 9 explore how to reduce
cannabis use in people with psychosis by considering participants’ reasons for quitting, predictors of cannabis use, and their views of effective strategies for quitting cannabis.

10.1.5 – Chapter 8

In chapter 8, a quantitative study is reported that had two aims: To evaluate service users’ reasons for wanting to quit cannabis use. Secondly, to identify what the predictors of cannabis use at follow-up at treatment end and at 18-months are.

The results found that the key reasons participants gave for wanting to quit included: ‘self-concept’, including to gain more control over their use or to feel better about themselves, to save money, and because of concerns about the impact on their mental health. These results are similar to those of previous studies in this cohort (Laudet & White, 2010; Lobban et al., 2010; Pettersen, 2014; Rebgetz et al., 2016).

Results found good evidence of frequency of urges and overall motivation being associated with cannabis use at 3 months. Meanwhile, there was also weak evidence of an association with physical health concerns and confidence in being able to quit. A model was developed to include the most parsimonious set of predictors of cannabis use. In the final model, the only cognitive-behavioural measure included was frequency of urges. Overall, these results suggest that while there are a few potential therapeutic targets, urges are the most important. Based on this, an effective treatment may need to provide substantial support to participants in overcoming urges and other withdrawal symptoms as one of its central components.

10.1.6 – Chapter 9

A qualitative study was presented in chapter 9 that aimed to explore participants’ reasons for wanting to quit, the barriers to quitting, the strategies that they found effect, and their experiences of treatments. The results found that, in almost all cases, participants reported wanting to quit cannabis and wanting support to help them. Patients’ main reasons for
wanting to quit included its incompatibility with how they saw themselves or who they wanted to be, and the perceived negative effects of using cannabis, such as unpleasant effects of intoxication or its effect on their mental health. Meanwhile, most found quitting extremely difficult. Consistent with the results of chapter 8, the main barriers to quitting included withdrawal symptoms, such as cravings. However, in qualitative interviews, participants also stated that being around cannabis using friends and family members made abstaining more challenging. Both represented significant challenges to treating cannabis misuse in this group.

Secondly, chapter 9 reported that many, but not all, participants had been offered some kind of formal support through the Mental Health services, which was often group session. However, many participants reported that it was typically not very helpful. Group sessions were often better tailored to other substances, such as heroin, and one-to-one therapy sessions generally offered little that helped them quit, often because participants felt that clinicians typically did not understand what abstaining from cannabis was like, and some participants felt that having an opportunity to speak to someone with first-hand experience would be better.

Many participants mentioned formal or informal peer support was the most helpful support that they had received. Informal peer support often took the form of support from family or friends who had similar experiences of quitting cannabis. Formal peer support took the form of group meetings with peers through substance misuse treatment services, Narcotics Anonymous, or an appointed sponsor. Unusually for a formal treatment, participants found it extremely helpful as they benefited from speaking to, and receiving support from, someone who had experience of the challenges of quitting cannabis use, and of effective strategies for maintaining abstinence. However, peer support from people who
were users of other substances, such as cocaine or heroin, was less helpful as the experience of quitting those substances was viewed as very different to cannabis.

**10.1.7 – Implications**

Overall, these data provide mixed and limited evidence of the benefits of CM in this group. While the CIRCLE trial found some benefit to time to acute psychiatric admission amongst those complying with treatment, there was no evidence that during treatment, CM had a cognitive or behavioural impact. Based on feedback from participants in the trial, the CIRCLE CM treatment encouraged participants to engage with treatment and to consider quitting or to make a quit attempt. But most said that their motivation waned or that they found it too difficult to quit. In a sense then, it may be that the biggest impact of the CIRCLE CM treatment was to encourage patients to participate in cannabis misuse treatment who would otherwise be unwilling to engage.

However, participants also thought that CM was not a good standalone treatment, and that it needed to be combined with another form of therapy. But as the systematic review in this thesis demonstrated, there was also no evidence that combining CM with other psychotherapies, such as CBT or MET, improved substance misuse outcomes. Moreover, there is no evidence of such psychotherapies being effective in this cohort (e.g. Barrowclough et al., 2010), and participants interviewed for this thesis reported not finding them helpful. Instead, the data suggest that a more substantial intervention may be required that supports people across multiple domains, such as with changing their social networks and engaging in activities that facilitate them in avoiding cannabis use, like work or education. There is now growing evidence indicating that participants find making such changes to be an effective strategy for quitting, and in this thesis the participants who made the biggest changes to their cannabis use were often also the ones who had made the biggest changes in their lives more widely. Secondly, participants reported that therapy
is most helpful when it is delivered by people with lived-experience of quitting cannabis. In this sense, engaging peer support workers more in the delivery of therapy may help improve engagement and potentially substance use outcomes.

In the following section, current evidence regarding the relevant cognitive-behavioural characteristics of this cohort is summarised and the evidence from this thesis placed in context. Conclusions are drawn regarding why this cohort is relatively unresponsive to substance misuse treatment and potential therapeutic targets are identified. Subsequently, potential future directions for research are discussed based on these conclusions.

10.2 – Understanding abstinence from cannabis in psychosis

As also discussed in chapter 1.6.6, it is plausible that the cognitive, functional, and motivational deficits in psychosis can, at least partially, explain the lack of success of psychotherapies for substance misuse. It may well be that the combination of psychosis and heavy cannabis use results in participants being particularly unresponsive to psychotherapy. Consistent with this, in a recent feasibility study (n=39), Rabin and colleagues. (2018) delivered CM for cannabis to a group with psychosis and to a group without co-morbid psychiatric illness. They found that abstinence rates amongst those with psychosis were lower (42.1%) compared to controls (55%). Although the sample size was very small, the results of the study indicate that motivating behavioural change is more challenging in people with psychosis than non-psychiatric groups.

Witkiewitz and Marlatt’s (2004) cognitive-behavioural model of relapse, described in chapter 1.6, provides a framework for understanding how populations with psychosis may differ from non-psychiatric ones. Published evidence to date suggests that populations with psychosis differ from non-psychiatric ones across several of the domains identified in that model. Compared to non-psychiatric populations, people with psychosis are more likely to experience multiple deficits that are likely to make abstinence from substance use more
challenging. These include greater distal risks, poorer motivation and other cognitive processes associated with use, more problematic affective states, and potentially having poorer coping strategies or finding it more challenging to implement effective ones.

10.2.1 – Motivation

One of the most important factors for understanding why treatments are less effective in this population is motivation. As described in chapter 1.6, in non-psychiatric populations, baseline overall motivation and IM both predict cigarette smoking outcomes (Caponnetto & Polosa, 2008; Buckner, Walukevich, Lemke & Jeffries, 2018; Foster et al., 2015; Pokhrel & Herzog, 2015; Chauchard et al., 2013). However, while in cigarette smoking there is evidence of a moderate association between RFQ measured IM and follow-up outcomes, the association is significantly poorer in cannabis use. This may be attributable to cannabis use, and especially frequent use of high potency cannabis, itself negatively impacting IM. There is good evidence cannabis users tend to have less motivation for behavioural change and demonstrate lower motivation in reward-related tasks than the general population (Lawn et al., 2016). In the context of a CM intervention, it is reasonable then to suspect that the treatment may be less effective in heavy cannabis users than other populations. However, there is currently little direct evidence that compares how CM performs in people with cannabis use disorder with CM for other substances. However, in a systematic review by Davis and colleagues (2016) of CM for alcohol, tobacco, or illicit substance use, evidence for CM for cannabis use was relatively weak compared to that for other substances.

Additionally, as discussed in chapter 1.6.6, motivation, and especially IM, is frequently lower in psychosis (Kremen et al., 2016). This reduction may be a central component of greater apathy in psychosis (Kremen et al., 2016; Luther et al., 2015), and key to understanding why patients in this cohort often have poorer functional outcomes.
(Heinrichs, Hanlon & Carpenter, 1984). This perhaps explains why participants in CIRCLE reported (chapter 7) that the CM was insufficient to motivate them to quit or why their initial motivation quickly waned.

As demonstrated in chapter 8, overall motivation and self-efficacy are important for understanding abstinence in this cohort. Both were found to predict cannabis use status at treatment end (in adjusted analysis presented in chapter 8.3.2), and there was weak evidence of self-efficacy predicting abstinence at 18 months (chapter 8.3.2). Meanwhile, IM remains a central factor in understanding substance use in this cohort. Based on the results of chapter 8, like in non-psychiatric populations, self-concept reasons (e.g. ‘to feel more in control of my use’) were some of most important reasons for quitting in this cohort, as were negative use expectancies. Another concern, more specific to this group, was the potential consequences of use to their mental health. These reasons are all types of IM, and so highlight the importance of this construct for understanding patients’ motivations for quitting. However, consistent with the literature, the role of IM appeared to be diminished as none of these topics predicted cannabis use at treatment end in adjusted analyses (although all predicted cannabis use in unadjusted analyses).

The psychotherapies that have so far been trialled often target motivation, and many specifically IM (e.g. MI or MET). As discussed in chapter 1.5, CM has a substantial evidence base as an effective intervention for motivating behavioural change in relation to substance misuse in non-psychiatric populations. But evidence is more mixed in populations with psychosis, and there was little evidence of the CIRCLE CM intervention having any impact on cannabis use, motivation, self-efficacy, or any other cognitive-behavioural measure.

Similarly, motivation was a central focus of treatment in the MIDAS trial (Barrowclough et al., 2010), which trialled MI and CBT. Despite this, the trial found that this approach was not effective in motivating abstinence from cannabis use in this cohort. As such, this study
demonstrates that even relatively substantial CBT and MI interventions (26 sessions over 1 year) are not effective in this cohort at engendering behavioural change. Between MIDAS and CIRCLE, it appears that while motivation and IM in this cohort to abstain from substance use are low, it also seems that they are also not particularly responsive to psychotherapy explicitly targeting them.

However, there was evidence in both studies of the interventions having some benefit. In MIDAS, the intervention slightly improved readiness-to-change and the amount of cannabis used by treatment end (Barrowclough et al., 2010). While in CIRCLE, there was evidence of a benefit from CM amongst those who complied with treatment, and that CM motivated participants to engage with treatment. In the results reported in chapter 5, compliance with the psychoeducation was slightly higher in the experimental group than controls, meanwhile in chapter 7 participants reported that the CM had motivated them to engage with treatment. This perhaps indicates that these treatments may work, but less so than in other populations. This pattern of results raises the question of how to raise motivation in this cohort sufficiently to engender abstinence.

In the case of CM, one possibility is that more frequent sessions or higher reward values may be needed to see clear benefits to substance use. However, CIRCLE was intended to be a pragmatic trial of an intervention that could be delivered through EIP services. As such, it needed to be convenient and feasible for clinicians to deliver. Based on feedback from clinicians received during the CIRCLE trial, offering multiple CM sessions per week is likely to be viewed as being too laborious by many clinicians, and therefore not particularly practical. Another possibility would be to combine CM treatment with other treatments. However, based on the results of chapter 2, it is unlikely that other motivationally focused psychotherapies would provide additional benefit. Instead more complex interventions may be required.
Overall, there is evidence that this population is less motivated to change behaviour. As such, although targeting amotivation or apathy likely remains critical for successful treatment in this population, there is no clear evidence of any treatment so far trialled being successful in engendering sufficient motivation to abstain in this cohort. Doing so may require taking a broader approach than treatments, such as CM, which focus largely or solely on raising motivation. Instead, motivation needs to be addressed alongside deficits in this population that are likely to mediate or moderate its relationship with abstinence. This includes dependence, distal risks, and affective states, which are covered in the next sections, and may include the cognitive function deficits present in this cohort.

10.2.2 – Dependence

Another concern is that cannabis dependence is especially high in people with psychosis. They are likely to be using cannabis more frequently and using more potent types (Di Forti et al., 2014; 2019), which increases their likelihood of being dependent (Curran et al., 2016). Although in the two trials of CM for cannabis use by Budney and colleagues (2006) and the trial by Bellack and colleagues (2006) all participants were dependent, and so high prevalence of dependence alone is unlikely to explain why the CIRCLE CM intervention failed to provide a benefit. However, as the results of chapter 8 show, urges are perhaps the single most important domain for understanding the likelihood of abstinence in this cohort, which are positively associated with severity of use and dependence (Fidler, Shahab, & West, 2010). Therefore, any treatment needs to consider how to address them. Doing so is likely to be challenging, however pharmaceutic therapies, which are discussed in chapter 1.3, are one possible method for doing this. There is now good evidence that Nicotine Replacement Therapy (NRT) is effective for helping reduce the risk of relapse in tobacco smokers (Stead et al. 2012). Pharmaceutical therapies for cannabis use are intended to offer a similar type of treatment by providing controlled doses of a cannabinoid, which is often THC, as a substitute to using cannabis.
In terms of distal risks, patients with psychosis are often multiply disadvantaged. For example, they are more likely to have experienced emotional abuse, physical abuse, and bullying (Peh, Rapisarda, and Lee, 2019), as well as separation from their parents and other adversity in childhood (Shah et al., 2011). In adulthood they are more likely to experience social isolation and stigma because of their illness (Kinson et al., 2018). Meanwhile, the experience of psychosis itself is often associated with increased stress, and it is estimated that around 40% of people with FEP experience symptoms of post-traumatic stress disorder (PTSD) (Rodrigues & Anderson, 2017). Kolliakou and colleagues (2011) found that people with psychosis reported using cannabis for more dysphoric reasons than non-psychiatric populations, such as anxiety, low mood, or boredom. Tackling substance use in this cohort may require considering carefully how to support patients experiencing dysphoric or negative affective states, which in some cases will be related to experiences of trauma and other significant adversity.

Alongside this, people with psychosis are more likely to have poorer social networks and poorer social support (Gayer-Anderson & Morgan 2013). Treatment may therefore need to consider how to improve social or peer support for patients. Doing so may also help alleviate, or support patients in coping with, negative affective states. As reported in chapter 9, participants frequently reported finding informal support from friends with similar experiences to be very helpful. In most cases, it was preferred to the care they had received from the Mental Health services for substance use, which most did not find helpful. For many, this was because it was necessary to have support from other people with lived-experience, but it was not typically offered. However, the level of support patients received from friends was very variable, with many being very socially isolated and so having very few people they can reach out to for help. Meanwhile, the only two qualitative interviewees who had received suitable formal peer support had done so
through Narcotics Anonymous, and both found it very helpful. Others had received peer support through Drug and Alcohol services, but as the other patients in the groups were using other substances, such as cocaine or heroin, they felt that their experiences shared little in common. Meanwhile, participants whose families used cannabis often reported needing to make big changes to their family relationships, such as moving out of the family home, so as to quit. Some of these challenges are typically more present in populations with psychosis than non-psychiatric groups. More may need to be done to help individuals who have poor social networks improve the quality of those networks, including improving their family relationships in some cases, in order to help them quit cannabis.

Finally, as discussed in chapter 1.6.6, cognitive deficits in psychosis may make it harder for people to implement coping strategies for abstaining. DiClemente and colleagues (2008) suggest that the demands of psychotherapy, including decision-making, intentionality, commitment, planning, and self-evaluation (including self-efficacy), may be more difficult to achieve in this population. Bergman and colleagues (2013) meanwhile report that there is evidence that this cohort, compared to non-psychiatric populations, tend to employ less adaptive coping strategies and be less likely to use coping, Relapse Prevention, and harm reduction strategies effectively.

10.2.4 – Summary

Overall, there is growing evidence that the potency of cannabis in the UK is increasing, and that people with psychosis are more likely to be using high potency cannabis and using every day than the general population (Di Forti et al., 2014; 2019). As this is associated with greater dependence (Curran et al., 2016), such use may well be associated with patients finding it much more difficult to quit. On top of this, patients in this cohort are multiply disadvantaged and may have significant difficulties in various cognitive and functional domains, as well as being more likely to have experienced trauma and social adversity.
They may also have greater barriers to abstinence due to more severe dysphoria, poorer social networks, and lower vocational engagement amongst other challenges. These concerns perhaps offer our best insight into why treatments such as CBT or MI, which have a good evidence base in the general population, universally seem to be less effective when delivered to patients with severe mental illness.

10.3 – Directions for future treatment research

Currently there is little reason to believe that any evidence-based psychotherapy is effective in reducing cannabis use amongst people with psychosis. As such, the question of how to tailor interventions to this group arises. Interventions for cannabis misuse in psychosis need to be adapted to the many challenges faced by this population. This may require intensive support to help people with making changes to their social networks, with engaging more in work or education, or supporting people with comorbid psychological symptoms, including anxiety or depressive mood. Thus, a more complex intervention may be needed, which tackles many of functional and clinical deficits in this group, and that tackles cannabis use as one of multiple outcomes. It may be necessary to take a different approach to most current evidence-based therapy. The following sections make suggestions for potential directions for future research and discusses reasons why they may be effective. However, in most cases, there has been little evidence collected evaluating their effectiveness in this cohort.

10.3.1 – Complex interventions delivered through the Mental Health services

Alongside the cognitive, functional, and social difficulties faced by this group, another possible reason for the lack of clear benefit from these interventions is that the context of their delivery may have masked their effects. The CiRCLE trial was conducted in the context of Early Intervention in Psychosis (EIP) services in the UK, and its treatments were intended to be delivered by participants’ care coordinators. However, as discussed in the limitations
section of chapter 4, often the CIRCLE treatments were delivered by other EIP staff, such as support workers or assistant psychologists. As such, the treatments were delivered the CIRCLE treatments were not really integrated into EIP care.

EIP aims to support service users in forming a stable identity, peer network, and engaging in vocational activities (McGorry, Killackey, & Yung, 2013), and there is good evidence that EIP services are effective in achieving these goals (NICE, 2016). It is possible that more could be done within current EIP care to support patients reduce their cannabis use as part of a wider effort to engender change in various domains, consistent with these EIP principles. This is arguably reflected in the qualitative results reported in chapter 9, in which participants said that being in work, education, having families, or other commitments were an important part of them quitting cannabis use.

However, based on the feedback from patients in CIRCLE (chapter 9) that they currently receive little support from their EIP teams, more needs to be done to support people reduce their cannabis use. As was intended in CIRCLE, it is likely to be best if such treatment is integrated into the care delivered by EIP services or similar intensive Mental Health teams. Doing so may be the best way to create an intervention that aims to support patients across a broad range of clinical and functional domains. But it should also be tailored to the specific needs of this group. More work is needed to understand what these characteristics are. However, based on the feedback from patients in this sample, it may be that patients would benefit from treatment being delivered by people with lived-experience of quitting cannabis, and ideally those with comorbid severe mental illness.

10.3.2 – Peer support

In chapter 9, participants reported finding therapy most helpful when they are being supported by other people with similar lived experience. One potentially helpful addition to a future intervention for cannabis use could be to integrate support delivered by clinicians
or support workers with lived-experience. Benefits of peer support can include greater empathy and mutual respect, gained through shared experience. People with lived-experience can bring knowledge to providing support, gained from their own experience, about the challenges of quitting substances and strategies for successfully abstaining. If patients become peer workers, it can also empower them to discover and make use of their own strengths, and to build and strengthen connections to their peers and wider communities (Gillard et al., 2017). Lloyd-Evans and colleagues (2014) conducted a systematic review of peer support for severe mental illness and found some evidence that it benefited patients’ feelings of hope, recovery, and empowerment (although they no evidence of a benefit on hospitalisation rates or overall symptoms). But the quality of the evidence was generally low, suggesting a lack of good quality trials. As such, more work is required to understand the potential benefits of this treatment. As part of this, it is important to consider how the peer support is being delivered. It needs to be designed to make good use of peers’ experiences and knowledge, which is not always the case (Gillard et al., 2017). There was substantial heterogeneity in the results between studies in the review by Lloyd-Evans and colleagues, potentially reflecting significant variation in the way peer support was being delivered. One of the larger and better-quality trials, CORE (Johnson et al., 2018), delivered peer support to people with psychosis (n=441) being seen by a crisis team. It found that peer-delivered self-management reduced readmission to psychiatric acute care by follow-up.

However, to date no peer-support research has been published for this cohort. The two participants in the qualitative study (chapter 9) who reported receiving formal peer support had both received it through Narcotics Anonymous. Narcotics Anonymous is a self-help treatment programme, in which patients are typically asked to conform to 12-steps. These 12-steps set out a set of beliefs that patients are expected to accept about themselves and how to address their use. They conceive of dependence as a condition that the patient is
powerless over, and that spiritual faith may offer a solution. Alcoholics/Narcotics Anonymous has existed for over 80 years, and over that time solid evidence has emerged that it is effective (Kelly, Magill & Stout, 2009; McCrady & Miller, 1993), and as effective as many other psychotherapies including CBT and MET (Mattson et al., 1993). Peer-support in such contexts is typically in the form of self-help groups of people with lived experience of misuse, and often involves patients having a ‘sponsor’ who can provide individual support. However, no trials could be identified that separated out the peer support components from the rest of the treatment program. Participants in the qualitative interviews in chapter 9 did not comment on the other elements of Narcotics Anonymous. It may be that their experience of Narcotics Anonymous did not involve adopting the 12 steps. However, this was unclear from the interviews. However, the two people who reported peer support being helpful had both committed to quitting cannabis. It may be that peer support is most effective amongst those already motivated to change their behaviour.

People with lived-experience are likely to understand better what it is like to quit cannabis and may be better able to aid people in developing effective strategies for abstaining. Moreover, if people feel a greater empathy and understanding during treatment, it may improve satisfaction with treatment. Satisfaction has been associated with greater adherence (Holding, Gregg, & Haddock, 2016). As such, it may well be that this approach could help engage people in the intervention and potentially improve the benefits people receive from treatment.

10.3.3 – Family intervention

As discussed before, one important domain to address is social support. While peer support may help with this, another potentially promising area is family intervention. Family interventions aim to work with family members alongside patients to improve knowledge, support, and coping skills (Drake, O’Neal, & Wallach, 2008). To date, it has only
been trialled in a relatively small randomised controlled trial, also by Barrowclough and colleagues (2001). It delivered family therapy alongside CBT and MI for comorbid substance use in severe mental illness, with cannabis being the most used drug (61%). They found that the intervention was significantly more effective than routine care at reducing substance use as well as positive symptoms of psychosis and improving general functioning. However, only 36 pairs of a patient and a family member or carer took part. Reasons for the small number are unclear, but recruiting carers was challenging during the CIRCLE trial. During the qualitative data collective from the pilot phase of CIRCLE, which is described in chapter 7, three groups were interviewed: participants, clinicians, and carers of participants. As described in appendix 7.2, only one carer interview was performed, which was due to difficulties in recruiting carers. The primary reason for this was that patients were reluctant to allow researchers to contact their family members to discuss cannabis or their participation in the trial. It may be therefore that family interventions would suffer from poor uptake by participants, potentially making such an intervention extremely difficult to practically implement in Mental Health services. However, they offer the potential to improve the quality of support patients receive from their families, which may be an important facet of improving substance misuse outcomes.

10.3.4 – Tackling withdrawal symptoms

Based on the results of chapter 8, cravings are perhaps the single most important therapeutic target, and any treatment needs to consider how to address them. In chapter 6, there was some, albeit weak, evidence of an effect of the CM on frequency, but not strength, of urges. It may be that a more substantial CM intervention, if it helped people reduce their use, would also help reduce urges in this group. However, presumably the mechanism here, as discussed in chapter 1.7, is that CM helps motivate people to quit despite withdrawal symptoms making doing so unpleasant or difficult. One option for how to alleviate withdrawal symptoms is pharmaceutic treatment. Such treatment would be
comparable to Nicotine Replacement Therapy (NRT), such as nicotine gum or patches.

However, the best evidence of effective pharmaceutical treatments for cannabis use in non-psychiatric populations is for substitutes that contain THC (chapter 1.3). As such, they do not eliminate the dangers of cannabis use in cohorts with psychosis. But they may help mitigate it under certain circumstances. It may be that such drugs can be used to taper or minimise THC intake over time as a short-term strategy to assist with withdrawal symptoms, with the aim of eventually achieving abstinence. Doing so may be more effective than requiring patients to manage their own use. However, it would also carry the risk of patients combining cannabis substitutes with illicitly bought cannabis, and so patients may need to be monitored carefully. More research is required to understand potentially effective treatments and the best guidelines for its use in this cohort. Ideally, they would either not contain THC or would contain a high ratio of CBD to THC, which may ameliorate the negative consequences of THC exposure in this cohort.

10.3.5 – Cognitive Enhancement Therapy.

DiClemente and colleagues (2008) and other authors have suggested that the significant cognitive and functional deficits present in this cohort are why otherwise effective psychotherapies for cannabis use are unsuccessful in this population.

Cognitive Enhancement Therapy (CET) is a form of cognitive remediation for people with psychosis focused on improving cognitive deficits, such as memory, attention, language, and executive function problems (Galletly & Rigby, 2013). Cognitive remediation delivered to people with psychosis has been found to have positive effects on some dimensions of cognitive and functional deficit. In a meta-analysis by Wykes and colleagues (2011), the authors identified 40 studies (n=2,104) in schizophrenia. They found evidence of improvement in global cognition and functioning, and a small effect on symptoms that disappeared by follow-up. The benefits of remediation therapy were improved when
patients were stable and provided with other forms of psychiatric rehabilitation. Other reviews have found similar benefits to cognitive and functional deficits (Revell et al., 2015).

However, to date there have only been a small number of studies of CET for substance use in psychosis. In a fairly recent study, Eack and colleagues (2014) delivered 18 months of CET to 31 outpatients with schizophrenia who met addiction criteria for alcohol and/or cannabis. In this intention-to-treat analyses, the authors found substantial improvements to neurocognition (such as memory, attention, and reasoning) (d=0.86), social cognition (d=1.13), and social adjustment (d=0.92). CET also led to patients reducing alcohol use (67% amongst those receiving CET compared to 25% in usual care). However, no similar benefit was found for cannabis use. The authors conclude that amongst those patients who are stabilised in treatment, CET is an effective approach for tackling cognitive and functional deficits and potentially for reducing substance misuse. However, like CIRCLE, there were high levels of attrition over 18 months (50%). It may be that CET would be a useful facet of a wider treatment programme for cannabis use in this population, particularly in improving global functioning and facilitating people in developing and implementing effective coping strategies.

10.3.6 – Summary

Substance use is often the result of a complex set of processes and interactions between many facets of patients’ cognitive, behavioural, and social functioning. Future treatments need to take an individually tailored approach to supporting patients in changing what is driving their substance use. This may include supporting them in getting back into work or education if they are currently unemployed; developing better social support if they use is associated with alleviating dysphoria caused by social isolation; or changing social networks if they often use cannabis with friends. However, in qualitative data reported in this thesis (chapter 9), participants reported receiving little support from the Mental Health services
that they found helpful. Mental health care delivered by EIP services already aims to provide individually tailored support to patients across multiple domains, and it is effective in helping to improve long-term clinical and functional outcomes for psychotic illness. As such, more could be done to integrate substance use treatment into already established and effective health care.

However, the current lack of evidence supporting any particular psychotherapy is a barrier to implementing substance misuse treatment. Evidence from this thesis and previous literature suggest that future interventions need to incorporate a more complex approach, which addresses multiple challenges faced by this group simultaneously. For example, it may be that CM would be more effective if delivered as part of a program of treatment tackling multiple cognitive and functional domains, such as improving social networks or vocational engagement. Such an approach would need to support participants individually in addressing the challenges they face in changing their behaviour. Further, it needs to address high attrition in this cohort, by tackling amotivation and consider how to provide support that is engaging to patients. One approach would be to incorporate several elements of current forms of tested treatment into a single intervention.

However, how to develop effective complex interventions in this cohort is currently unclear. More needs to be done to examine potentially beneficial treatments, which may involve incorporating elements from different formal psychotherapies. But, as seen in chapter 2, theoretically complementary treatments do not always result in better results when combined. Trials of complex interventions featuring well thought through study designs that allow researchers to identify the contribution of individual components and patient groups best targeted by them would help address this problem.

Overall, complex, individually tailored, and intensive interventions may be required in this population. This is because patients with psychosis appear to require more intensive
support and broader interventions than non-psychiatric populations. Poor levels of motivation and significant cognitive and functional deficits, as well as social difficulties (such as greater isolation and poorer support from family and friends) make treatment substantially more challenging. This is reflected by the lack of effectiveness of psychotherapy in this population. Some suggestions of potentially beneficial components of such therapy include cognitive remediation, CM, and peer-support, alongside more functionally targeted interventions, aimed at improving vocational and social outcomes. However, in many cases evidence is currently lacking regarding their individual benefits for treatment. Furthermore, it is unclear which combinations, if any, are likely to be effective. More work is needed to explore these topics.

10.4 – Limitations

While limitations were included for each of the studies throughout this thesis, there are some overall limitations. Firstly, the research contained in this thesis was designed during the recruitment phase of the CIRCLE trial and data collection was completed at the same time as the trial. As such, the results of the trial were not known when the process evaluation study was designed. Given the lack of effectiveness of the CIRCLE CM, it may have been preferable to change the focus of some of the work contained in this thesis. One possibility would have been to focus more on exploring what treatments may work in this population. While this question was addressed to a degree in chapters 8 and 9, further work is required.

Secondly, the research in this thesis relies heavily on the self-report of participants. As there is little published self-reported (particularly quantitative) data on this topic and especially in relation to IM, this is one way that it contributes to the literature. However, there are potential limitations with self-reported data as participants’ reports may lack validity due to several factors. These include the acquiescence response bias, which is the
tendency for participants to give affirmative responses to statements regardless of their content (Krosnik, 1991); social desirability, or the tendency for participants to give responses they think will be viewed more favourably by others (Ben-Porath & Waller, 1992); and respondent knowledge or insight into their own cognition, such as degree of motivation. As such, these data may contain biases that limit their validity.

10.5 – Conclusion

In conclusion, there was no clear evidence in the CIRCLE trial that CM helped people with psychosis and comorbid problematic cannabis use reduce their cannabis use. There was some evidence that amongst those who engaged with treatment, people who received CM had a longer time to relapse on average. However, there was no clear evidence of any cognitive-behavioural impact from the CM treatment. Participants reported that the CM treatment motivated them to engage in treatment, but not enough to quit, which was extremely difficult to achieve for many.

CIRCLE is the latest trial to find no clear effect from psychotherapy for cannabis use in this cohort. Currently finding effective ways to support people quit using cannabis in this cohort appears to be an intractable problem. This is perhaps due to the many disadvantages faced by people in this cohort. People with psychosis have greater cognitive and functional deficits. They often have poorer social networks, and some report having few or no friendships or family relationships that do not involve cannabis. They are often less likely to be in work or education, and more likely to have comorbid psychological conditions (e.g. anxiety or depression) or have experienced adversity. It is also possible that they may find it harder to implement coping or Relapse Prevention strategies due to having more chaotic lives, poorer cognitive functioning or being more cognitively disorganised, and other difficulties. However, one thing to clearly emerge from the qualitative data was that patients wanted support for helping them quit cannabis, but they felt that the support that
they have received from the Mental Health services had been largely unhelpful. As such, there is a demand for effective treatments in this group. But it is currently unclear what such treatments would be.

Many participants spoke of seeing CM primarily as a way to help them engage with treatment and in some cases made them feel that their time was valued. However, only a minority saw the vouchers by themselves as a good motivation to quit and very few participants felt that it was appropriate to deliver CM as a standalone intervention. Instead, it may be that a more complex intervention, which addresses a broad range of domains, is required. Moreover, it may be preferable to deliver treatments that are individually tailored and provide intensive support to patients to help them address the specific barriers they face in quitting. Such an intervention may need to integrate elements of various therapies targeting different domains associated with substance use, such as suitable forms of counselling, cognitive enhancement therapy, or peer support. Having a motivational component, such as CM, may be valuable for encouraging engagement and behavioural change. It may also be desirable to integrate any such treatment into appropriate forms of already established mental health care (such as EIP). However, currently more work is needed to understand what combination of treatments would be effective.
References

A


problematic cannabis use following a first episode of psychosis: a randomized controlled trial. *Psychological Medicine*, 44(13), 2749-2761. doi: 10.1017/s0033291714000208


British Medical Journal (BMJ) Converting an odds ratio to a range of plausible relative risks for better communication of research findings. (2014). *BMJ*, 348(mar17 11), g2124-g2124. doi: 10.1136/bmj.g2124


C


Cannabis use and psychosis: re-visiting the role of childhood trauma, *Psychological Medicine*, 41(11), 2339-2348. doi: 10.1017/s0033291711000559


Carroll, K., Nich, C., LaPaglia, D., Peters, E., Easton, C. and Petry, N. (2012). Combining cognitive behavioral therapy and contingency management to enhance their...
effects in treating cannabis dependence: less can be more, more or less. *Addiction*, 107(9), pp.1650-1659.


D


Houston, J., Murphy, J., Shevlin, M., & Adamson, G et al. (2011) Cannabis use and psychosis: re-visiting the role of childhood trauma. Psychological Medicine, 41(11), 2339-2348. doi: 10.1017/s0033291711000559


Kesby, J., Eyles, D., McGrath, J., & Scott, J. (2018). Dopamine, psychosis and schizophrenia: the widening gap between basic and clinical neuroscience. *Translational Psychiatry, 8*(1). doi: 10.1038/s41398-017-0071-9


Microsoft (2016) Microsoft Word for Office 365; Microsoft Corporation


Moadel, A., Bernstein, S., Mermelstein, R., Arnsten, J., Dolce, E. and Shuter, J. (2012). A Randomized Controlled Trial of a Tailored Group Smoking Cessation Intervention


schizophrenia associated with increased use of cannabis. Molecular Psychiatry, 19(11), pp.1201-1204.


StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: StataCorp LP


Watson, J. B. (1913). Psychology as the behaviorist views it. (Psychological Review, 20, 158-178.)


Zvolensky, M., Vujanovic, A., Miller, M., Bernstein, A., Yartz, A., Gregor, K., McLeish, A., Marshall, E. and Gibson, L. (2007). Incremental validity of anxiety sensitivity in terms of motivation to quit, reasons for quitting, and barriers to quitting among...
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Appendix 2.1 – Prospero protocol

PROSPERO
International prospective register of systematic reviews

A systematic review of the addictive effect of combining contingency management with other psychosocial interventions

Luke Sheridan Rains, Sonia Johnson, Oliver Mason

Citation

Review question
Is there an addictive effect of combining financial incentives/contingency management interventions with other psychosocial interventions, such as CBT or motivational interviewing?
Are the long term outcomes of contingency management interventions improved if the treatment is combined with another psychosocial intervention?

Searches
A literature search will be performed using the following electronic bibliographic databases: MEDLINE, PsyIntINFO, EMBASE, Scopus (Elsevier), Web of Science (WoS), and Cumulative Index to Nursing and Allied Health Literature (CINAHL). Databases of clinical trials will also be searched for completed and ongoing trials, including: Cochrane Central Register of Controlled Trials (CENTRAL), International Standard Randomised Controlled Trial Number Register (ISRCTN registry), ClinicalTrials.gov (US National Institutes of Health), the NIH UK Clinical Trials Gateway, and the WHO’s International Clinical Trials Registry Platform (ICTRP). Grey literature will be searched through the British Library’s e-thesis online service (ETHOS) and the APA’s PsycEXTRA database. In addition, reference lists for related systematic reviews and included publications will be hand searched.

The search strategy will initially identify trials of contingency management for substance use. Publications meeting the inclusion criteria will be identified from the search results. Only studies focusing on substance use, including illicit drugs, alcohol, and tobacco, will be included. The following terms will be used in both keyword and subject heading searches:
Contingency management search terms: contingency management, prize*, behavior* contract*, token econom*, (finance* or voucher* or mone*) [proximity operator] (reward* or incentive* or reinforcement* or pay*)
AND
Substance use search terms: substance*, drug* [proximity operator] (“use” or “misuse” or “abuse” or “abstinence”); addict*; alcohol*; cannabis*; marijuana; norepinephrine*; cocaine*; crack; opioid*; opiate*; opium; heroin; stimulant*; tobacco; nicotine; snuff*; sedative*; inhalant*; hallucination*; hypnotic*; methylamphetamine; methadone; mdma; amphetamine; crystal meth*; legal high*; khat; methadone; ketamine; codeine; PCP; Phencyclidine; Psilocybin; mescaline; LSD; Lysergic acid diethylamide; Peyote.

Types of study to be included
Only randomised controlled trials will be included. Studies will feature at least 2 groups: one receiving the contingency management in combination with another psychosocial intervention, and a group receiving the CM intervention only. Studies featuring more than these 2 groups will also be included if the main comparison (CM plus Ps compared to CM only) can be extracted from the data.

Condition or domain being studied
Participants will be either receiving combined contingency management (CM) and cognitive behavioural therapy (CBT)/motivational interviewing, or CM alone. Participants in this group are often being treated for substance misuse disorders.

Participants/population
Participants will be enrolled in experimental trials receiving either a combination of CM and another psychosocial intervention, or CM only. Only studies focusing on substance use, including illicit drugs, alcohol, and tobacco, will be included.
Intervention(s), exposure(s)
Contingency management is a psychosocial intervention that uses financial incentives to reinforce/encourage target behaviours. The present study will examine the additive effect of such interventions when combined with psychosocial interventions, including motivational interviewing or cognitive behavioural therapy (CBT). The intervention is contingency management delivered in combination with another structured evidence based psychosocial intervention (Ps). A list of suitable interventions has been taken from the World Health Organisation’s Commission on Narcotic Drugs (2016). These are: cognitive behavioural therapy (CBT), couples therapy, psychodynamic therapy, behavioural therapies, social network therapy, and motivational interventions including motivational interviewing and motivational enhancement therapy, and twelve-step facilitation for alcohol dependence.

Comparator(s)/control
The comparison group will be receiving CM only.

Context
Any treatment or work setting will be included. There are no restrictions on study publication data. Articles will be excluded if they cannot be translated into English.

Main outcome(s)
Point prevalence abstinence (PPA) at treatment end.

Timing and effect measures
PPA will be measured using biometrics, typically involving urinalysis, breath, or saliva analysis.

Additional outcome(s)
Secondary outcomes will include; PPA at follow up at least 3 months following treatment cessation; self-reported substance use at treatment end and follow up.

Timing and effect measures
PPA at treatment end will be measured using biometrics.

Data extraction (selection and coding)
Studies will be included that meet the above criteria (RCTs of interventions for substance misuse, must include CM plus Ps and CM only groups, population is adults 18-65). Data to be extracted include: cohort size and description; comorbid illnesses, inclusion criteria, setting, gender, ethnicity, age. Stratification and randomisation procedures, as applicable. Intervention groups and description of the Psychosocial and CM interventions as well as descriptions of the outcome measures. Outcome data, PPA and self-reported substance use at treatment end and follow up.

Risk of bias (quality) assessment
Studies will be evaluated for bias using the Cochrane bias risk tool

Strategy for data synthesis
Data will be extracted and synthesised using meta-analysis if feasible. However, it may be that the characteristics of the Ps and CM interventions are too diverse for a meta-analysis to be appropriate. In this case, a narrative synthesis of included studies will be performed.

Analysis of subgroups or subsets
None planned.

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Type and method of review
Intervention

Anticipated or actual start date
01 September 2015

Anticipated completion date
01 May 2016

Funding sources/sponsors
None

Conflicts of interest
None known

Language
English

Country
England

Published protocol
https://www.crd.york.ac.uk/PROSPEROFILES/25525_PROTOCOL_20171216.pdf

Stage of review
Review Ongoing

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Behavior Therapy; Behavior; Addictive; Humans

Date of registration in PROSPERO
18 December 2017

Date of publication of this version
18 December 2017

Details of any existing review of the same topic by the same authors

Stage of review at time of this submission
### PROSPERO

**International prospective register of systematic reviews**

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**Versions**

18 December 2017

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PROSPERO

This information has been provided by the named contact for this review. CRD has accepted this information in good faith and registered the review in PROSPERO. The registrant confirms that the information supplied for this submission is accurate and complete. CRD bears no responsibility or liability for the content of this registration record, any associated files or external websites.
Appendix 2.2 – Search strategy for Medline (OVID)

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7. prize.mp. [mp=title, abstract, full text, caption text]

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9. substance*.mp. [mp=title, abstract, full text, caption text]

10. exp drug abuse/

11. drug abuse/ or drug usage/

12. exp alcoholism/

13. exp drug addiction/

14. exp drug addiction/

15. exp drug abstinence/

16. drug abuse/ or codependency/ or drug abuse prevention/ or intravenous drug usage/ or "substance use disorder"/

17. exp alcohol abuse/

18. exp cannabis/

19. exp cannabinoids/
20. cannabis/ or tetrahydrocannabinol/

21. exp narcotic drugs/

22. exp hypnotic drugs/

23. exp hallucinogenic drugs/

24. exp opiates/

25. exp cocaine/

26. tobacco smoking/ or nicotine/ or smoking cessation/

27. exp sedatives/

28. exp ampa/ or amphetamine/

29. dual diagnosis/

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52. study.mp. [mp=title, abstract, full text, caption text]

53. 49 or 50 or 51 or 52

54. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8

55. 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48

56. 53 and 54 and 55
Appendix 2.3 – Funnel plot of studies included in the meta-analysis (primary outcome)

Figure Appendix 1 - Funnel plot of comparison: 1 PPA, outcome: 1.1 PPA at treatment end.
Appendices for chapter 3 (appendix 3)

Appendix 3.1 – CIRCLE protocol paper

A randomised controlled trial of the clinical and cost-effectiveness of a contingency management intervention compared to treatment as usual for reduction of cannabis use and of relapse in early psychosis (CIRCLE): a study protocol for a randomised controlled trial

Sonia Johnson, Luke Sheridan Rains, Steven Manvaha, John Strang, Thomas Craig, Tim Weaver, Paul McCrean, Michael King, David Fowler, Stephen Pilling, Louise Marston, Rumana Z. Omar, Meghan Craig, and Mark Hinton

Abstract

Background: Around 35–45% of people in contact with services for a first episode of psychosis are using cannabis. Cannabis use is associated with delays in remission, poorer clinical outcomes, significant increases in the risk of relapse, and lower engagement in work or education. While there is a clear need for effective interventions, so far only very limited benefits have been achieved from psychological interventions. Contingency management (CM) is a behavioural intervention in which specified desired behavioural change is reinforced through financial rewards. CM is now recognised to have a substantial evidence base in some contexts and its adoption in the UK is advocated by the National Institute for Health and Care Excellence (NICE) guidance as a treatment for substance or alcohol misuse. However, there is currently little published data testing its effectiveness for reducing cannabis use in early psychosis.

Methods: CIRCLE is a two-arm, rater-blinded randomised controlled trial (RCT) investigating the clinical and cost-effectiveness of a CM intervention for reducing cannabis use among young people receiving treatment from UK Early Intervention in Psychosis (EIP) services. EIP service users (n = 544) with a recent history of cannabis use will be recruited. The experimental group will receive 12 once-weekly CM sessions, and a voucher reward if it analysis shows that they have not used cannabis in the previous week. Both the experimental and the control groups will be offered an Optimised Treatment as Usual (OTAU) psychoeducational package targeting cannabis use. Assessment interviews will be performed at consent, at 3 months, and at 18 months. The primary outcome is time to relapse, defined as admission to an acute mental health service. Secondary outcomes include proportion of cannabis-free urine samples during the intervention period, severity of positive psychotic symptoms, quality-adjusted life years, and engagement in work or education.

(Continued on next page)
Background
Cannabis is the most commonly used drug among people with psychosis, with rates of current use around the time of the onset of psychosis regularly recorded as between 35 and 45 %, well above use patterns in same-age, non-psychotic populations [1, 2]. Continued use following the onset of psychosis is associated with poorer individual outcomes and greater societal burdens. Hazards include delays in remission, suicidal behaviour, violence and homelessness [1, 3, 4]. In prospective investigations in first-episode psychosis, cannabis use is associated with markedly higher relapse rates: an Australian study reported a 51 % relapse rate over 15-month follow-up among substance users (mostly cannabis) compared with 17 % among nonusers [5], accompanied by a threefold difference in inpatient admission rates. Similarly, a Dutch study reported a 42 % relapse rate among persistent cannabis users compared with 17 % among those who never used or stopped round the time of first onset [3]. A dose-response relationship between severity of cannabis misuse and time to relapse was also reported in this study. Studies of comorbid substance misuse among people with established psychosis indicate that people who persist in problematic drug use are heavy users of acute mental health services, are more likely than others with psychotic illnesses to engage in acts of violence, and are less likely to work; sometimes using disability benefits to sustain drug use [6–8]. Thus, if a reduction in cannabis use can be achieved very early in the course of a psychotic illness, this has potential to improve the life experiences and social recovery of young people who develop psychosis, and to reduce the burden on carers, on mental health, criminal justice and welfare services and on the wider society over many years. This is the overall aim of the current study.

Systematic reviews find that the evidence on effective interventions for comorbid substance misuse in established psychosis is very limited [9, 10]. Despite a promising pilot study [11], a large MRC-funded trial, the MIDAS study, has shown no effect on primary or secondary outcomes from a relatively lengthy intervention (29 sessions over 9 months) consisting of motivational interviewing (MI) and cognitive behavioural therapy (CBT). The difficulties in intervening effectively in established psychosis suggest that it may be fruitful to target an earlier stage of illness, when several recent studies indicate that patterns of use are in a state of substantial flux [12, 13]. Many people are ambivalent about persisting with use and have substantial motivation for change, though some who initially abtain soon return to use [14]. This contrasts with the very limited motivation for change found in established psychosis [15], so that early psychosis may well be a stage at which achieving change with a relatively brief intervention is more feasible. However, in a similar study [16] to the MIDAS trial, a MI and CBT intervention was trialled for cannabis in Early Intervention In Psychosis (EIP) service users, also over 9 months (24 sessions), and again found no benefit for the intervention compared to treatment as usual.

The very limited benefits achieved from psychological interventions, such as MI and CBT in comorbid substance misuse in psychosis, have made us look elsewhere for a potentially effective intervention. Contingency management (CM) is an approach that involves offering rewards contingent on engagement in substance use treatment and on evidence of abstinence. CM is now recognised to have a strong evidence base supporting the efficacy of the intervention in a range of contexts, such as smoking cessation [17] and substance misuse disorders [18], and its adoption in the UK is advocated in guidance issued by the National Institute for Health and Care Excellence (NICE) [19]. However, with the exception of a small number of recently evaluative studies in Europe [20], the evidence base is drawn almost entirely from the US. There is relatively little UK experience of using CM, with only a few evaluations of CM reported. Recent examples include the CONMAN trial, which provided an evidence base for CM in the uptake of hepatitis B vaccines among opiate users [21], and FIAT, which found incentives to be effective for reinforcing adherence to antipsychotic medication [22]. The NICE review of psychosocial interventions [19] identified 14 trials of CM, all from the US, that met criteria for inclusion, of which three involved cannabis use. A consistent finding of a benefit for CM was reported, with most studies using abstinence at 12 weeks as their outcome measure.

Just one North American CM study has so far been reported among people with comorbid substance misuse and psychosis; the substances included were cocaine, heroin, and cannabis. This was unusual among treatment studies in this population in finding a positive effect. Bellack et al. [23] reported that CM, combined with a psychological intervention, resulted in more drug-free
urine samples than an enhanced treatment as usual intervention (Supportive Treatment for Addiction Recovery), and in reduced hospitalisation, and a better quality of life. However, only a small proportion of participants abused cannabis (7%) with 93% abusing cocaine or heroin. Simion et al. [24, 25] performed two small feasibility studies using a within-subjects reversal design that also reported a beneficial effect from the intervention. We find no other evidence of CM studies for cannabis use in a population with psychosis.

In the present study, we will investigate the clinical and cost-effectiveness of CM for reducing cannabis use among EIP service users. This will be evaluated in terms of clinical service use, the presence of psychotic symptoms, cannabis use, and health economic measures. The primary outcome will be whether CM improves time to relapse, measured as admission to acute mental health services, compared to recommended standard care.

**Methods/design**

**Design**

CIRCLE is a rater-blind, randomised controlled trial with two arms (Fig. 1). The experimental group will receive a 12-week CM intervention, as well as a manualised psychoeducational intervention delivered by clinical staff, which represents an Optimised version of Treatment as Usual (OTAU) that is offered by EIPs in the management of cannabis misuse. The control group will receive OTAU only. Assessments will be performed at the time of consent, 12 weeks following consent (at the end of the intervention period), and at 18 months following consent. The primary outcome is time to relapse, operationalised as admission to an acute mental health service.

**Recruitment**

Recruitment to the trial will be in EIP services throughout the Midlands and the South East of England. Participants will be on the caseload of an EIP service and aged 18–36. Other inclusion/exclusion criteria are listed below.

**Group allocation**

Following pretrial assessments, consenting clients will be randomised to group, stratified on severity of cannabis use (one to three uses per week, more than three uses per week). A remote, impartial randomisation service will manage the allocation to groups coordinated by the PRIMENT Clinical Trials Unit based at University College London (UCL).

**Trial assessors**

Outcome assessments will be performed by trial research staff. Primary outcome assessors will be blinded.
to randomised allocation. Secondary outcome assessors will be blinded at the 18-month assessment interview. Research staff will be trained in the use of all measures by members of the CIRCLE team. Joint ratings with one another and with senior members of the team supervising them will be used to establish reliability.

Interventions
The OTAU package will provide the context in which we will test the impact of a CM intervention. The CM intervention will involve the offer of voucher rewards for cannabis-free urine samples over a 12-week period to recent cannabis users with first-episode psychosis (defined below). We will first describe OTAU, delivered to both experimental and control groups, and then the CM intervention to be received by the experimental group only.

Optimised Treatment as Usual (Psychoeducational package)
To be confident that we are measuring the effects of CM, a psychoeducational intervention will be delivered to both experimental and control groups. Guidelines on EIP care recommend that psychoeducational interventions for cannabis should be an important component of routine care, but consultations with EIP managers and staff suggest that the extent to which this is realised in practice is very variable between services and individual clinical staff. Our aim is thus to create a standardised version to be delivered by staff working in EIPs recruiting to the trial. A training manual for delivering the package, and supporting materials will be provided by trial staff to clinicians delivering OTAU. The intervention is designed to be sufficiently highly structured for staff without high-level clinical qualifications, such as support workers or assistant psychologists, to be able to deliver it competently following brief training.

OTAU has been designed to be an individually tailored psychoeducational approach to cannabis use for generic EIP clinicians, which applies general psychoeducational approaches used in first-episode psychosis [26]. It draws on the psychoeducational package offered in the control arm of a previous Melbourne pilot study of psychological intervention for cannabis use, the Cannabis and Psychosis (CAP) trial [27]. The package is comprised of six modules to be delivered via a standard PC. Full delivery of all six modules is typically achieved over approximately 3 h, normally offered over six regularly programmed sessions of 30 min duration. The package includes a pdf, video material, short quizzes, audio files, and further information and written records of the modules for the service user to keep. The material will remain focused on providing information in accordance with psychoeducational procedures, and will not act as a psychological intervention. The clinician's main aim is harm minimisation, with an acknowledgement that in a young person with psychosis, cannabis abstinence may be required to ensure that no harm is done. The content is based on MI principles, relapse prevention, and harm-reduction strategies.

Psychoeducational materials including video, written, and web-based materials will present current information on the potential advantages and disadvantages of cannabis use and of cannabis abstinence. To help the participant to make an informed decision about continued use, the EIP staff will discuss the positives and negatives of cannabis use by exploring its impact on seven areas: family, finance, activity/engagement in work or education, mental health, physical health, legality, and social groups/friendships. Finally, staff will discuss setting goals regarding the young person's future use of cannabis in the context of harm minimisation, as well as strategies for achieving their goals and avoiding relapse into patterns of cannabis use that compromise those goals.

Contingency management
The CM intervention offers financial incentives contingent on urinalysis results indicating cannabis abstinence. The intervention voucher schedule and rules are adapted from Budney et al. [28, 29], which offered a voucher-based CM intervention for treatment of cannabis dependence in the general population. The intervention comprises 12 once-weekly urinalysis sessions and will be delivered by EIP clinicians. At each session, the participant will be required to provide a urine sample. A temperature strip on the side of the specimen cup will allow the EIP staff to check whether the sample has been tampered with. In week 1 of the intervention, details of the intervention will be explained to the participant, and they will be asked to sign an 'abstinence contract' indicating that they understand and accept its rules, and agree to abide by the test results. In the first week, participants will receive a £5 voucher for attending and providing a urine specimen independent of the drug test results, which provides a 'baseline' result. From week 2 to week 12, participants will receive vouchers, increasing by £5 every 2 weeks, contingent upon producing negative specimens. Vouchers will be for a local supermarket. Participants who abstain from cannabis use for the full duration of the intervention will earn £240.

Urinalysis will be performed using a small benchtop analyser capable of providing rapid test results of drug misuse urinary concentration (Kauido CHR-110). To perform the analysis, the EIP staff member pipettes a fixed amount of urine into a buffer solution tube to give a 7:1 serial dilution. This allows a standard 50-ng/ml marijuana test cassette placed in the analyser to provide a urinary cannabis concentration reading between 0 and 350 ng/ml. Guidelines will be provided to the EIP staff to allow interpretation of the test results, whereby a sufficient drop in urinary tetrahydrocannabinol (THC) concentration will be taken as indicative of abstinence since the previous urinalysis session.
These guidelines are based on published data regarding the urinary half-life of cannabis [30].

Participants are able to prearrange missing scheduled sessions ('holiday week') and still receive the reward for that week if they have a valid commitment that prevents them from attending. They can do this on a maximum of two occasions for 1 week only each time. They will still be expected to show evidence of abstinence at the following session to receive a reward for the holiday week. If the participant misses the following week or provides a positive sample, no financial incentive will be received for the holiday week. Holiday weeks need to be arranged with the staff member performing the intervention no later than at the time of the previous scheduled appointment. The intervention will be suspended for a maximum of 1 month if a participant relapses or otherwise loses mental capacity. If capacity is not regained in 1 month, the intervention will not continue. If a participant fails to attend on multiple consecutive weeks, or if contact is lost with the participant entirely, each missed week will be counted as a failure to attend.

Failure to attend intervention sessions, specimens suggesting cannabis use, or failure to submit a scheduled specimen will reset the value of vouchers back to the initial £5.00. If the participant attends the next week and provides a negative sample, they will be rewarded with £10. In the subsequent week, if the participant provides a second negative sample voucher values will continue from the highest previous level of reward.

Selection and training of staff
Staff in the EIP services will deliver the CM and OTAU interventions. Training will be delivered to all staff delivering the interventions by members of the research team over a period of half a day on average.

Inclusion/exclusion criteria
Inclusion criteria
The cohort will be EIP service users who have recently abused cannabis. Recent cannabis use is operationalised as having used cannabis at least once during 12 of the previous 24 weeks. Additional eligibility criteria include (1) being aged 18–36, (2) having stable accommodation (i.e. not street homeless or roofless), (3) speaking enough English to be able to understand fully and answer the assessment instruments, and (4) being able to give informed consent. EIP teams have been set up across England following the 2000 NHS Plan [31]. Standard criteria for EIP include developing symptoms of psychotic illness for the first time, with positive psychotic symptoms persisting for at least a week and accompanied by evidence of significant risk and/or functional decline. Service users are typically discharged after 3 years on the caseload of an EIP team.

Exclusion criteria
Exclusion criteria include (1) those who fail EIP service inclusion criteria, (2) those currently engaged in treatment for cannabis use with another agency, (3) those currently compulsorily detained in hospital or prison, or (4) those on probation or Community Treatment Order requiring drug testing for cannabis.

Obtaining informed consent
In the first instance, a member of the EIP staff will obtain agreement from potential participants to be contacted by a member of the CIRCLE research team. The researcher will then meet with the service user to provide a participant information sheet, written in plain English, which will explain all aspects of the study. They will also explain all benefits of the study and known risks. The service user will be given at least 48 h to consider participation prior to consent being taken.

Ethical approval
Ethical approval for the trial was received on 16 March 2012 from the London – South East NRES Committee (REC reference 11/LO/1939). Written informed consent will be obtained from all participants in the trial. The original consent forms will be stored at the author's institutions (UCL, KCL, University of Sussex, and Warwick University), and a copy will be kept in the patients’ clinical notes.

Assessment interviews
Participants will be given three assessment interviews: at the time of consent, at 12 weeks following consent, and at 18 months following consent, a time at which a significant proportion of young persons with psychosis will relapse if they are going to do so [32, 33]. All participants will be given a £20 voucher for their time, and at the follow-up assessment all participants will be given an extra £10 for the provision of a urine sample. At 18 months, the primary outcome and some secondary outcome data will also be collected from electronic patient records.

Outcome measures
At all assessment interviews the following measures will be performed in addition to the collection of standard demographic information (Fig. 2):

- Cannabis use
  - The Time Line Follow Back (TLFB) [34] will be used to record self-reported cannabis use over the last 6 months. The TLFB is a retrospective calendar-based measure of daily substance use, with good test-retest reliability demonstrated for cannabis [35]. This will be used to establish
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<td>Acute admissions data recorded from patient notes</td>
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**Fig. 2 Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) figure. Overview of the schedule of events**

- Eligibility in terms of cannabis use and extent of recent use
  - Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, version 4 (DSM-IV) (SCID) part E will be used to assess history of alcohol and substance misuse disorders
  - Specimens for urinalysis will be obtained with the threshold set at a level for detecting cannabis use in the previous 28 days (i.e. 50 ng/ml cannabis metabolites)
- Psychotic symptoms
  - The positive and negative subscales of the Positive and Negative Syndrome Scale (PANSS) [36]. The PANSS is a well-established measure of psychotic symptoms, with strong psychometric properties in terms of validity, reliability, and sensitivity [37]
- Service use and health economic analysis
  - Client Service Receipt Inventory (CSRI), developed originally by Beecham and Knapp [38] will be used to record clinical service use, medication use, receipt of state welfare, and use of other state-funded services including criminal justice services
  - The 12-Item Short Form Survey (SF-12) [39] and the EuroQoL, 5 dimensions (EQ-5D) questionnaire [40] are widely used measures of health status with good psychometric properties [41, 42], which will be used to derive quality-adjusted life years' (QALYs) data

**Primary outcome**
The primary outcome will be time to relapse. Admission to a psychiatric hospital, crisis resolution team or crisis house, or other acute mental health service will be used as a
marker of relapse. The primary outcome will be assessed at 18-month follow-up based on electronic patient records. Dates of admission will be recorded and participants will be followed until they have relapsed, are lost to follow-up, or until the end of the 18-month study period.

Secondary outcomes
Secondary outcomes will be collected mainly through assessment interview, and will include:

- Cannabis use, including self-reported use and urinalysis results at follow-up
- Positive symptom severity (Positive and Negative Syndrome Scale [36])
- Social functioning, based on self-reports of engagement in work or study
- Number of days cannabis use in the previous 12 weeks (for 12-week follow-up) or 6 months (for 18-month follow-up)
- Number of admissions over 18 months' follow-up
- QALYs (SF-12 and EQ-5D) [43] and service use (CSRI) will be used in the cost-effectiveness analyses, as described in the analysis section below. Service utilisation data will be augmented where possible from participants' medical records at 18 months

Proposed sample size
Our sample size for the main trial is based on data suggesting a usual relapse rate of around 50% over the study timeframe in cannabis users [3, 5]. A 15% decrease in this relapse rate due to the intervention is clinically beneficial. Using a power of 90% and a significance level of 5%, a total sample size of 460 subjects will be required. This sample size is based on an analysis of time to relapse and will allow us to detect a 37% decrease in the hazard of relapse (hazard ratio of 0.63) in the intervention group using a Cox proportional hazards model. This sample size has been calculated using Stata version 11 [44]. The sample size is inflated by a factor of 1.06; assuming that each person delivering the intervention sees an average of four service user participants in the trial, and an intraclass correlation coefficient of 0.02 for clinician clustering, this gives a total sample size of 488. Finally, the sample size is inflated by 10% to account for attrition for the primary outcome, giving a total sample size of 544.

Statistical analysis
A detailed analysis plan will be written and signed off by the Data Monitoring and Ethics Committee for the trial before the analysis commences. Initial analyses will look at summary statistics for all variables, both overall and by randomised group. Summary statistics for continuous variables will be mean, median, standard deviation (SD), lower quartile, upper quartile, and minimum and maximum and will be reported appropriately according to distribution. Summary statistics for categorical variables will be frequency and percentage within each category.

Summary statistics of baseline variables by whether a participant has dropped out of the study will also be examined to determine whether the dropouts had similar characteristics to those who remained in the study at baseline.

After checking the assumptions of proportional hazards, Cox proportional hazards modelling to compare the intervention and control groups, adjusting for severity of cannabis use at baseline (dichotomous – one to three times a week versus four or more times a week), will be carried out for the primary outcome. Robust standard errors will be used to account for clustering by care coordinator. If the assumption of proportional hazards is not fulfilled, alternative modelling strategies will be employed. The secondary outcomes will be analysed using appropriate regression models, separately for data collected at 12 weeks and 18 months. Estimates and 95% confidence intervals will be presented for the secondary outcomes. In a supportive analysis, all analyses will be adjusted for an indicator as to whether or not the participant was in the pilot trial and for potential baseline predictors of missingness related to outcome. All analyses will be carried out on an intention-to-treat basis using all available data.

Missing data
It is expected that there will be few missing data for the primary outcome as data for this will be extracted from the participants' medical records. There is likely to be more missing data for the secondary outcomes as the majority require the participant to be interviewed to complete the measures. For both the primary and secondary outcomes we will check the extent and patterns of missing data and identify predictors of missingness. Multiple imputation or adjustment for potential predictors of missingness related to the outcome will be performed if appropriate.

Economic evaluation
For the health economic analysis, intervention costs will be calculated using available data on staff costs, incentives, on-costs, other overheads, and activity levels. These will be added to the costs of other health and social care services derived from the Client Service Receipt Inventory and records combined with nationally applicable unit costs (e.g. Curtis [45]). Cost comparisons at 3 and 18 months will be made using regression models, with bootstrap methods used to generate confidence intervals around the cost differences. Cost-effectiveness from an NHS perspective at 3 and 18 months will use three outcome measures: number of cannabis-negative urine samples, days of reported cannabis abstinence and
QALYs (derived from the EQ-5D with SF-12 QALYs used in secondary analyses). If, for any of these the intervention has higher costs and better outcomes than usual treatment, then cost-effectiveness will be expressed in the form of incremental cost-effectiveness ratios, estimated by dividing the incremental costs by the incremental benefits of the intervention. Uncertainty around cost-effectiveness estimates will be explored using cost-effectiveness planes (through generating a large number of cost-outcome combinations using bootstrap methods) and cost-effectiveness acceptability curves (showing the probability of the intervention being cost-effective at various levels of willingness to pay for health benefits). The range of values for QALYs will be £0 to £100,000 so as to include the threshold used by NICE. The values for the other measures will be chosen so that the points at which one arm has 50 %, 60 %, 70 %, 80 %, and 90 % of being the most cost-effective can be observed. It will then be a value judgement as to whether these values are acceptable. Cost-effectiveness will be investigated regardless of clinical outcome.

Discussion
The present study is a rater-blinded RCT investigating the clinical and cost-effectiveness of CM for reducing cannabis use in EIP patients with a history of recent cannabis use. Cannabis is a significant issue in this population. Rates of cannabis use among people with first-episode psychosis are high, resulting in poorer clinical, social, and functional outcomes, and greater clinical service use. However, there is little evidence for any effective interventions for comorbid substance misuse in established psychosis. If CM is found to be clinically and economically beneficial, it will offer strong support for using such interventions to reduce cannabis use among EIP service users.

Strengths and limitations
With a recruitment target of 544 participants, CIRCLE is one of the largest trials of CM worldwide. To the best of our knowledge it is also the first RCT of CM specifically for cannabis use in psychosis, although there are a number of related studies. Bellack et al. [23] trialled CM for substance use in psychosis, including cannabis, cocaine, or heroin, which required participants to test negative from the first session. Sigmon et al. [24, 25] performed two small feasibility studies of CM for cannabis use in psychosis, but used within-subject designs rather than a CM design. Participants are followed over a relatively long period of 18 months in accordance with NICE recommendations for future research for psychosocial interventions for substance misuse in psychosis [46]. The rationale for targeting EIP patients in particular is that there is also good reason to believe that motivation to change patterns of cannabis and other substance use is high in this cohort [15]. Secondly, EIP is a form of secondary preventative care [47], with the aim of preventing or attenuating the risk of relapse to improve long-term prognosis. Given the substantial evidence base linking cannabis use to higher rates of relapse, reducing cannabis use in EIP services is consistent with EIP aims.

One potential concern regarding the use of CM interventions in publicly funded health services is its acceptability to the public, clinicians, and service users. A mixed-method substudy to the main trial to explore this topic is planned. However, there is already some evidence that public opinion is in favour of CM for treatment adherence in severe mental illness [48]. Potential concerns about the use of financial incentives were also carefully considered in the design of the CIRCLE intervention. The design is based on Budney et al. [28, 29] and feedback on it was sought from service users, pilot study participants, carers, and clinical teams before and after the pilot study through focus groups and one-to-one interviews.

One technical issue for CM for cannabis use is the relatively long effective half-life of cannabis. Conventional marijuana urinalysis tests could not be used for the CM, as a positive urine result may be related to cannabis use that had taken place more than 1 week previously. Use of such tests would delay the initiation of treatment by up to 4 weeks to allow a participant's urinary THC level to fall below 50 ng/ml. To address this, CIRCLE uses desktop analysers capable of providing a urinary THC concentration reading. As discussed, a reduction in urinary THC in line with trial guidelines will be taken as evidence of abstinence. However, it is possible that a reduction in urinary THC over a 1-week period could occur due to a reduction in cannabis use rather than abstinence. As such, it is possible that participants can receive the voucher reward while still using in the short term. However, medium and long-term trends, detectable over two or three sessions, will clearly indicate abstinence rather than reduction of cannabis use as urinary THC will not continue to decline or fall to below 50 ng/ml. Participants will be informed that they will need to abstain fully throughout the intervention period to receive all the voucher rewards.

Trial status
The pilot phase of CIRCLE began on 1 January 2012 and ended on 28 February 2013. Approval to proceed to the full trial was received in April 2013 and recruitment to the main trial is currently ongoing. The end date for CIRCLE is 31 October 2017.
Funding
CIRCLe is funded by the National Institute for Health Research Health Technology Assessment Programme (11/14/53). The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the NHS, NIHR, NHS or the Department of Health.

Availability of data and materials
Not applicable.

Authors’ contributions
The trial was developed on the basis of ideas from NIH and SJ, SJ, SL, TW, Z, DF, TC, SM, MK, PM, LM, RO, LSR, MC, and SP developed the trial design. SJ is the chief investigator, based at University College London. SM (University of Warwick), DF (University of Sussex), and TC (King’s College London) are local collaborators. JS and TW provided expertise with regard to performing CM intervention trials in severe mental illness. MK provided oversight as the director of PIRMEN. The Clinical Trials Unit for CIRCLe was jointly led by SJ and RC. The trial statisticians, PM is responsible for the health economics analysis. MC and LSR contributed as trial managers. All authors contributed to writing the trial protocol manuscript. All authors read and approved the final manuscript prior to submission.

Competing interests
The authors declare that they have no competing interests.

Consent for publication
Not applicable.

Ethics approval and consent to participate
The trial received a favourable opinion from the South East London NRES Committee on 16 March 2012. REC reference 11/L3/139/93. The following sites have approved the trial: Coventry and Warwickshire Partnership NHS Trust, East London NHS Foundation Trust, Camden and Islington NHS Foundation Trust, Barnet, Enfield, and Haringey Mental Health NHS Trust, Central and North West London NHS Foundation Trust; Birmingham Children’s Hospital NHS Foundation Trust; Forward Thinking Birmingham; Black Country Partnership NHS Foundation Trust; Surrey and Borders Partnership NHS Foundation Trust; Sussex Partnership NHS Foundation Trust; North East London NHS Foundation Trust; Oxleas NHS Foundation Trust; South West London and St. George’s Mental Health NHS Trust, South London and Maudsley NHS Foundation Trust; Leicester Partnership NHS Trust; Kent and Medway NHS and Social Care Partnership Trust; South Essex Partnership University NHS Foundation Trust; Northamptonshire Healthcare NHS Foundation Trust; Dudley and Walsall Mental Health Partnership NHS Trust; Nottinghamshire Healthcare NHS Trust; West London Mental Health NHS Trust; Berkshire Healthcare NHS Foundation Trust; Oxford Health NHS Foundation Trust; Cambridge and Peterborough NHS Foundation Trust.

Written informed consent will be obtained from all participants in the trial. The Consent Forms will be held by the authors’ institutions and a copy kept in the patients’ clinical notes, and are available for review by the Editor-in-Chief.

Author declarations
JS has contributed to UK guidelines which include consideration of the potential role of contingency management in the management of opiate addiction (NICE, 2007, chaired by SJ, and JS also chaired the broader-scope pan-UK working group preparing the 2007 Orange Guidelines for the UK Departments of Health, providing guidance on management and treatment of drug dependence and misuse, including guidance on possible inclusion of contingency management and is also currently chairing the new expert group updating these Guidelines for the UK Departments of Health. JS and his institution have received support and funding from the Department of Health (England) and National Treatment Agency (England), and JS and his 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 nor the analyses in this paper. JS’s employer (King’s College London) has registered intellectual property on a novel buccal naltrexone preparation with which JS is involved, and JS has been named in a patent registration by a pharmaceutical company as the 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 on his personal web-page of the Addictions Department at http://id.ic.ac.uk/opcrp/.

dept/addictions/people/frad.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.

Author details

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References
Clinical and cost-effectiveness of contingency management for cannabis use in early psychosis: the CIRCLE randomised clinical trial

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Abstract

Background: Cannabis is the most commonly used illicit substance amongst people with psychosis. Continued cannabis use following the onset of psychosis is associated with poorer functional and clinical outcomes. However, finding effective ways of intervening has been very challenging. We examined the clinical and cost-effectiveness of addictive contingency management (CM), which involves incentives for abstinence from cannabis use, in people with a recent diagnosis of psychosis.

Methods: CIRCLE was a pragmatic multi-centre randomised controlled trial. Participants were recruited via Early Intervention in Psychosis (EIP) services across the Midlands and South East of England. They had had at least one episode of clinically diagnosed psychosis (affective or non-affective); were aged 18 to 36; reported cannabis use in at least 12 out of the previous 24 weeks; and were not currently receiving treatment for cannabis misuse, or subject to a legal requirement for cannabis testing. Participants were randomised via a secure web-based service 1:1 to either an experimental arm, involving 12 weeks of CM plus a six-session psychoeducation package, or a control arm receiving the psychoeducation package only. The total potential voucher reward in the CM intervention was £240. The primary outcome was time to acute psychiatric care, operationalised as admission to an acute mental health service (including community alternatives to admission). Primary outcome data were collected from patient records at 18 months post-consent by assessors masked to allocation. The trial was registered with the ISRCTN registry, number ISRCTN:93576915.

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Results: Five hundred fifty-one participants were recruited between June 2012 and April 2016. Primary outcome data were obtained for 272 (96%) in the CM (experimental) group and 259 (95%) in the control group. There was no statistically significant difference in time to acute psychiatric care (the primary outcome) (HR 1.01, 95% CI 0.67, 1.40) between groups. By 18 months, 90 (33%) of participants in the CM group and 85 (30%) of the control groups had been admitted at least once to an acute psychiatric service. Amongst those who had experienced an acute psychiatric admission, the median time to admission was 196 days (IQR 82, 354) in the CM group and 245 days (IQR 99, 362) in the control group. Cost-effectiveness analyses suggest that there is an 81% likelihood that the intervention was cost-effective, mainly resulting from higher mean inpatient costs for the control group compared with the CM group; however, the cost difference between groups was not statistically significant. There were 58 adverse events, 27 in the CM group and 31 in the control group.

Conclusions: Overall, these results suggest that CM is not an effective intervention for improving the time to acute psychiatric admission or reducing cannabis use in psychosis, at least at the level of voucher reward offered.

Keywords: Financial Incentives, Contingency management, Cannabis, Psychosis, Early intervention, Substance misuse

Background
Cannabis is the most commonly used illicit substance amongst people with psychosis [1]. In longitudinal studies, cannabis use in first episode psychosis is associated with substantially higher acute psychiatric admission rates [2]: an Australian study reported a 53% admission rate over 15 months follow-up amongst substance users (mostly cannabis) compared with 17% amongst non-users [3], accompanied by a threefold difference in inpatient admission rates. Similarly, a Dutch study reported a 42% admission rate amongst persistent cannabis users compared with 17% amongst those who never used or stopped round the time of first onset [4]. A dose-response relationship between severity of cannabis misuse and time to admission was also reported in this study. Problematic cannabis use in psychosis is also associated with marked delays in remission [5], and lower engagement in work or education, as well as poorer outcomes in other clinical and social domains [3, 6, 7]. Despite the clear need for effective treatments in this group, so far none have been identified. A Cochrane review [8] of psychosocial interventions for substance misuse in severe mental illness identified 32 randomised controlled trials but found little evidence that any type of therapy was more effective than treatment as usual, including Cognitive Behavioural Therapy and Motivational Interviewing.

Contingency management (CM) is an operant conditioning-based intervention for substance misuse that typically uses financial rewards to reinforce target behaviours, such as abstinence from substance use or treatment adherence. CM has an increasingly substantial evidence base in a variety of contexts, including cannabis misuse [9–11], smoking cessation [12], heavy drinking [13], and other illicit drug misuse [14, 15]. The National Institute for Health and Care Excellence (NICE) advocates its adoption in England in the management of substance use [16]. In a review conducted by NICE as part of its guidance of psychosocial interventions for substance misuse, 14 trials of CM were identified, all from the USA, of which three involved cannabis use. A consistent finding of a benefit for CM was reported, with most studies using abstinence at 12 weeks as their outcome measure. In the context of severe mental illness, a number of trials have found CM to be effective in reducing use in patients with severe mental illness for alcohol [17], stimulant use [18], and cigarette smoking [19]. This includes a fairly recent trial of a 12-week CM intervention for stimulant misuse that found the treatment to be clinical and cost-effective [20].

However, to date there is little research on CM for cannabis use in severe mental illness, with only one randomised controlled trial [21] reported. The trial found that CM, combined with an enhanced treatment as usual psychosocial intervention (Supportive Treatment for Addiction Recovery), resulted in more drug-free urines, reduced hospitalisation, and better quality of life than treatment as usual alone. However, only a small proportion of participants abused cannabis (7%), with 93% abusing cocaine or heroin. Beyond this, there have also been three small feasibility studies [22–24], which taken together also provide some evidence that CM may be feasible, acceptable, and efficacious in this cohort. Furthermore, with the exception of a small number of recent evaluative studies in Europe [25], the evidence base for CM is drawn almost entirely from the USA. There is relatively little experience of using CM in the UK, with only a few studies reported in any clinical group. Some recent examples include the CONMAN trial, which provided an evidence base for CM in uptake of hepatitis B vaccines amongst opiate users [26], and FIAT, which found incentives to be effective for reinforcing adherence to antipsychotic medication [27].

The present study investigated the clinical and cost-effectiveness of CM for reducing cannabis use and thus
time to acute psychiatric admission amongst Early Intervention in Psychosis (EIP) service users. The objectives were (1) to conduct a pilot study of a CM intervention for cannabis use in early psychosis; (2) if the pilot was successful, to proceed with a full multi-centre pragmatic randomised controlled trial; (3) to test whether the intervention results in an increase in the time to acute psychiatric admission (the primary outcome); (4) to test whether the intervention results in a decrease in cannabis use, reduced positive psychotic symptoms, and an increase in participation in work or education (secondary outcomes); (5) to assess the cost-effectiveness of the intervention from an NHS perspective.

Methods

Trial design and participants

CIRCLE was a rater-blind, multi-centre randomised controlled trial with two arms. The experimental (CM) group received a 12-week CM intervention together with a Treatment-As-Usual (TAU) package targeting cannabis use, which was a standardised and optimised psychosocial package of the type of psychosocial intervention recommended in EIP practice [28]. The control group received the optimised TAU psychosocial intervention only. Assessments were performed at the time of consent, at 3 months (treatment end) and at 18 months following trial inclusion. The primary outcome was time to acute psychiatric admission, operationalised as admission to an acute mental health service. Ethical approval for the trial was received on 16 March 2012 from the London – South East National Research Ethics Service committee (REC reference 11/LO/1939). The trial was conducted according to the trial protocol published by Johnson et al. [29], and trial procedures are described here only in brief. Oversight was provided by an external Trial Steering Group that was appointed as agreed by the funding body.

Participants were recruited via EIP services throughout the Midlands and South East of England. Sites were added to the trial until the recruitment target was achieved. EIP services accept individuals who have developed psychotic illness for the first time and aim to treat the initial episode early and effectively, minimising acute psychiatric admissions and optimising clinical and social recovery. They are now standard provision in English mental health Trusts following policy mandates, and typically work with service users for 3 years prior to discharge to primary care or to other mental health teams for continuing care [16]. Inclusion criteria were (1) on an EIP service caseload, (2) having used cannabis at least once in the previous 24 weeks, (3) age 18–36, (4) living in stable accommodation, (5) sufficient English to understand fully and answer the assessment instruments, (6) able to give informed consent to participate, (7) not subject to a compulsory community treatment or court order requiring urine testing for cannabis, (8) not in receipt of treatment for cannabis use from another agency, and (9) not compulsorily detained in hospital, or in prison.

Randomisation and masking

Following the baseline assessment interview, participants were randomised with a 1:1 ratio, stratified on severity of cannabis use (1–3 uses per week, >3 uses per week). An independent randomisation service was used, coordinated by Priment Clinical Trials Unit based at University College London. Primary outcome assessors were masked to allocation throughout the trial. Secondary outcome assessors were masked to allocation at follow-up assessments in the main trial. However, masking was not feasible at the 3-month assessment interview in the pilot as sufficient researchers were not available for different staff to conduct initial and follow-up assessments. The statistical and health economic analysis plans were finalised before database lock and statisticians and health economists undertaking the analysis were masked to trial arm allocation.

Procedures

The intervention under evaluation was 12 weeks of CM delivered by clinical staff who included graduates without mental health professional qualifications, such as assistant psychologists. Participants attended weekly CM sessions at which they were immediately rewarded with vouchers if urinalysis indicated cannabis abstinence since the previous session. Urinalysis was performed using a small bench-top analyser capable of providing rapid test results of drug of misuse urine concentration (Kiedwood CHEM-110). To perform the analysis, the clinician pipetted a fixed amount of urine into a buffer solution tube to give a 7:1 serial dilution. This allowed a standard 50 ng/ml marijuana test cassette placed in the analyser to provide a urine cannabis concentration reading between 0 and 350 ng/mL. Guidelines were provided to all staff delivering the intervention to allow interpretation of the test results. The guidelines set out upper and lower thresholds for urinary tetrahydrocannabinol (THC) based on recommendations from the suppliers of the urinalysis equipment, SureScreen Diagnostics. Results greater than the lower threshold (350 ng/mL) clearly indicated use within the last week, so were not rewarded. Results below the lower threshold indicated urinary THC concentration below 50 ng/mL, the accepted standard for detecting urinary THC, so were rewarded. Within these thresholds, urinary THC was expected to fall each week until it reached the lower THC threshold, which should be reached within 1 month. A drop in urinary THC would receive the reward. A
similar result to or higher than, the previous week would fail. A temperature strip on the side of the specimen cup allowed staff to check whether the sample had been tampered with.

The CM schedule and rules were adapted from Rudney et al. [30, 31], which both investigated CM for cannabis misuse. It used a variable reward schedule that began at £5 for providing a baseline sample in the first week. In the pilot, voucher values rose by £2 each week, with a £10 bonus voucher every other session. Based on feedback from clinicians and service users, the schedule was simplified in the main trial. The voucher value rose by £2 every two clean samples and the bonuses were removed. In total, participants could receive £240 (US$307, €267 equivalent (11 Jan. 2019)) in vouchers in both versions of the reward schedule. If a participant submitted a urine specimen indicating cannabis use in the previous week, they would receive a £5 voucher. Patients who failed to attend intervention sessions or submit a scheduled specimen did not receive a voucher. If the participant attended the next week and provided a negative sample, they were rewarded with £10. In the subsequent week, if the participant provided a second consecutive negative sample, the voucher values returned from the highest previous level of reward. Participants could arrange in advance to miss scheduled sessions and still receive the reward for that week if they had a valid commitment that prevented them from attending and they subsequently demonstrated that they had not used since the previous sessions. They could do this on a maximum of two occasions for 1 week only each time. Vouchers were for major supermarkets.

The TAU was a standardised version of a good quality psychoeducation, which was delivered by EIP staff in a digital format. It was designed to be sufficiently highly structured for staff without high-level clinical qualifications, such as support workers or assistant psychologies, to be able to deliver it competently following brief training. The package was comprised of six modules that were delivered via a standard PC or laptop. Full delivery of all six modules was intended to take approximately 3 h, normally offered over six regularly programmed sessions of 30 min duration. It included a PDF package for clinicians to work through with their clients, which presents information regarding the effects of cannabis, motivational materials, and strategies for coping, minimising potential harms, and abstaining from cannabis. It also included video materials, short quizzes, audio files, and further information and written records of the modules for the service user to keep. The primary aim was to deliver information to meet psychoeducation goals that were tailored to the individual needs of the participant, but not to act as a psychological intervention. It adopted a harm minimisation approach, with an acknowledgement that in a young person with psychiatric cannabis abstinence may be required to ensure that no harm is done. The content was based on motivational interviewing principles, relapse prevention, and harm reduction strategies [link to psychoeducation package - https://www.ucl.ac.uk/psychiatry/research/epidemiology-and-applied-clinical-research-deps/projects/circle-trial/trial-materials].

A full day’s training to provide CM and the TAU psychoeducational package was delivered to EIP clinical staff by members of the CIRCLE research team. Training was tailored to the knowledge and experience of clinicians, some of whom were assistant psychologists with psychology degrees, but not mental health professional training. Clinicians were provided with written documentation on delivering the CM and the psychoeducation and supported by the CIRCLE team throughout the trial. Records of urinalysis results and voucher rewards received for each participant were checked by the CIRCLE research team to ensure fidelity to the intervention protocol.

Outcomes
The primary outcome was time to admission to an acute psychiatric service, including psychiatric hospital, crisis resolution team or crisis house, or other acute mental health service intended as an equivalent to hospital. The primary outcome was assessed over an 18-month period using electronic patient records.

Secondary outcomes were between-group differences at follow-up for the following:
1. Severity of positive symptoms of psychosis.
2. Social functioning based on self-reports of engagement in work or study.
3. Self-reported number of days’ cannabis use in the previous 3 months at 3-month follow-up, or the previous 6 months at 18 months.
4. Proportion of cannabis-free urines at assessment.
5. Number of admissions over 18 months follow-up.
6. Quality-adjusted life years (QALYs) (SF-12 and EQ-5D) and service use (CSRI) were used in the cost-effectiveness analyses. Baseline and secondary outcome data were collected primarily during assessment interviews. Some secondary outcome data were checked or collected using electronic patient records at each assessment. The following measures were performed at all assessment interviews:

- Demographics, most recent diagnosis and social information. Where feasible, data were checked using patient records.
- Cannabis use
  - The timeline followback (TLFB) [30] was used to record self-reported substance use, including cannabis, other illicit substances, and alcohol, over the previous 6 months at baseline and 18 months,
and over the previous 3 months at the 3-month follow-up assessment interview.
- Structured Clinical Interview for DSM-IV (SCID) part E was used to assess history of alcohol and substance misuse disorders.
- Urinalysis for cannabis, performed using a commercially available immunoassay test for metabolites of the cannabinoids tetrahydrocannabinol (THC) using the standard cut-off of 50 ng/ml [31].

- Psychotic symptoms
  - The positive and negative symptom subscales of the Positive and Negative Syndrome Scale (PANSS) [32].

- Service use and health economic analysis:
  - The Client Service Receipt Inventory (CSRI) [33] was used to record clinical service use, medication use, receipt of state welfare benefits, and use of other state-funded services including the criminal justice system. Data were collected for the previous 6 months at baseline and 18 months, and for the preceding 3 months at 3-month assessment. Data were collected at assessment interview and checked using patient records. To minimise attrition, at 18 months, data were collected from patient records for a subset of the resources deemed most likely to contribute to higher costs and that feasible could be collected. Patient record data were collected for all patients still in the trial, unless they had withdrawn or their patient records could not be identified.
  - 12-Item Short Form Survey (SF-12) [34] and the EQ-5D [35] were used to derive quality-adjusted life years (QALYs).
  - Details of the participant's referral to the EIP service, history of admission to acute mental health services, and time spent on a Community Treatment Order (CTO) in the last 6 months at baseline. At 3 months and 18 months, history of admission to acute mental health services and time spent on CTO were recorded since study inclusion. Data were obtained from patient records.

### Statistical methods

The sample size for the trial was 544. This was based on data suggesting a usual acute psychiatric admission rate of around 50% over the study timeframe in cannabis users [3, 4]. A 15% decrease in this rate due to the intervention was considered to be clinically beneficial. Using a power of 90% and a significance level of 5%, a total sample size of 460 subjects was determined to be required. This sample size was based on an analysis of time to acute psychiatric admission and allowed a 37% decrease in the hazard of admission (hazard ratio of 0.63) in the intervention group to be detected using a Cox proportional hazards model. The sample size was inflated by a factor of 1.06, which assumed that each clinician delivering the intervention would see an average of four trial participants, and an intraclass correlation coefficient of 0.02 for clinician clustering, which gave a total sample size of 488. Finally, the sample size was inflated by 10% to account for attrition for the primary outcome, giving a total sample size of 544. This calculation was performed using Stata version 11 [36].

All analyses were carried out comparing the CM and control groups as randomised using all available data. The continuous variables were summarised using mean (standard deviation (SD)) or median (interquartile range (IQR)) as appropriate. Categorical variables were presented as frequencies and percentages. Logistic regression was used to determine baseline predictors of missingness. Kaplan-Meier survival curves by randomised groups were used to examine the primary outcome (time to acute psychiatric admission) descriptively. A Cox proportional hazards model was used to compare the primary outcome in the intervention and control groups, adjusting for severity of cannabis use (the stratification variable at 1 to 3 times a week versus 4 or more times a week) at baseline and whether the participant was part of the pilot trial. The assumption of proportional hazards was checked using Schoenfeld residuals [37]. The supportive analyses for the primary outcome were as follows:

- Adjusting for significant baseline predictors of missingness.
- Excluding those participants who had no secondary outcome data (for 12 weeks and 18 months separately).
- Including those in the main trial only as some minor changes were made to the protocol at the end of the pilot before the main trial commenced.
- Adjusting additionally for the number of psychoeducation sessions attended (which was offered in both arms of the trial).
- Adjusting additionally for the number of admissions in the 6 months prior to baseline.
- Adjusting for the same factors at the primary analysis but using centre as the clustering variable instead of clinician.

Secondary outcomes were analysed separately at 3 and 18 months. Models were adjusted for severity of cannabis use at baseline and whether the participant was part of the pilot trial. For the dichotomous outcomes (cannabis-positive urine, engaged in work or study), logistic regression was used. The residuals for the positive and
negative symptoms from PANSS outcomes were not normally distributed and were therefore log transformed and analysed using linear regression models. Zero-inflated Poisson regression was used for count outcomes including number of cannabis days and number of admissions over follow-up, as there were excess zeroes in these outcomes. The number of cannabis days at 3 months was analysed using Poisson regression. All secondary outcomes were also analysed after adjusting for predictors of missingness. An additional supportive analysis for number of admissions was to include all those who were discharged from psychiatric services within 18 months and assuming they did not have any admissions over 18 months. Robust standard errors were used in all regression models to account for clustering by a clinician delivering the CM in the analyses [38]. Results from all supportive and secondary analyses are presented as estimates and 95% confidence intervals (CI) as specified in the statistical analysis plan. All analyses were carried out using Stata version 14 [39].

Health economic analyses
The cost-effectiveness analysis was conducted from an NHS/social care perspective over 18 months. Costs of the CM intervention and psychoeducation were calculated using the salaries of staff delivering the CM and psychoeducation, supervision time, and overheads. Other service use was measured with the CSRI and from data collected from patient records. Costs were calculated using existing resource use with 2015/2016 unit costs. Average costs were used to cover the gap between 3 and 12 months. This did not apply to inpatient costs which were available throughout the follow-up period. Imputation for missing non-inpatient costs was carried out with predictors being community costs for available periods and inpatient costs. (This was done so that analyses could be conducted on the sample with complete inpatient data.) Costs were compared between arms at 18-month follow-up using a regression model, controlling for baseline, and with bootstrapped confidence intervals based on the percentile method and 10,000 resamples.

Quality-adjusted life years (QALYs) were derived from the EQ-5D-3L and SF-12 (for secondary analyses) using area under the curve methods incorporating scores at baseline and 3- and 18-month follow-ups. Missing utility scores were imputed from all available scores. QALY comparisons were made after adjusting for baseline scores. Costs and QALY differences were obtained from 10,000 bootstrapped resamples. Cost-effectiveness planes and cost-effectiveness acceptability curves (CEACs) were generated.

Results
Recruitment and follow-up
Recruitment to the pilot phase occurred between June 2012 and March 2013. The pilot study successfully achieved its aims by recruiting within 10% of its target (n = 68), demonstrating the feasibility of recruiting, delivering the interventions, and retaining at least 60% of participants at 3 months. Subsequently, a full RCT was performed. Recruitment to the main trial occurred between October 2013 and March 2016. Follow-up data collection was completed by October 2017. Figure 1 shows the flow of service users through the trial. Seventy EIP teams took part in the trial from 23 NHS trusts. Two thousand four hundred two service users were initially approached by EIP clinicians. Of these, 551 service users gave consent and were randomised into the trial. Primary outcome data were obtained for 530 participants (92%). Assessment interviews were performed with 371 participants at 3-month follow-up (67%) and 278 participants at 18-months (50%).

Baseline characteristics
Most baseline characteristics were similar between the two groups. In both groups, over 83% of participants were male, with a mean age of around 25 (SD 4). 72% were using cannabis more than three times a week and reported using on 111 days on average in the previous 6 months. Around a third of participants were diagnosed with schizophrenia or schizoaffective disorder and half had diagnoses of other types of psychosis, perhaps in part because EIP services tend to be reticent about making a diagnosis of such as schizophrenia because of concerns regarding stigma and diagnostic instability. A quarter of participants were currently engaged in some form of work or education, but a large majority (over 80%) had held open market employment at some point. Median PANSS positive symptom score was 12 (IQR 9, 17) in the control group and 13 (IQR 9, 16) in the CM group. Lifetime rates of cannabis dependence were very high (87% of control and 85% of intervention group members), and around three quarters in both groups were dependent at baseline. Lifetime rates of alcohol misuse or dependence, and of reports of using substances other than cannabis, were also fairly high (e.g. 47% of control and 52% of intervention group members reported using cocaine; 36% of control and 32% of intervention group members met the criteria for alcohol dependence) (Table 1). In the 6 months prior to baseline, median days of substance use other than cannabis were low (0) in the CM group (IQR 0, 4) and in the control group (0; IQR 0, 1). Median alcohol using days was 6 in both the CM (IQR 0, 26) and control groups (IQR 0, 26).
Participation in CM and psychoeducation
Participants in the CM group obtained a mean of 564 (out of a maximum of 720) in vouchering rewards and attended a median number of 9 (IQR 3–12) (maximum of 12) CM sessions. Forty-six participants declined the CM intervention or did not attend any sessions. Participants attended a median of 6 and 4 (maximum of 6) psychoeducation sessions in the CM and control groups respectively. However, 86 participants in the control group and 65 in the CM group declined the psychoeducation or did not attend any sessions.

Primary outcome
For the primary outcome, there was no statistically significant difference in time to admission to an acute mental health service between the randomised groups (hazard ratio (HR) 1.03, 95% CI 0.76, 1.40) (Fig. 2 and Tables 2, 3, and 4).

Supportive analyses
Results from the supportive analyses were similar. The odds of at least one admission over 18 months of follow-up were similar across randomised groups (OR 1.03,
Table 1 Baseline demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Control Mean (SD)</th>
<th>Control Median or utility score</th>
<th>Control IQR or CI</th>
<th>CM Mean (SD)</th>
<th>CM Median or utility score</th>
<th>CM IQR or CI</th>
</tr>
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<tr>
<td>Male</td>
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<td></td>
<td>236/278</td>
<td>64</td>
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<td>144/178</td>
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<td></td>
<td>65/77</td>
<td>23</td>
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<td></td>
<td>20/27</td>
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<tr>
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<td></td>
<td>56/77</td>
<td>13</td>
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<td></td>
<td>254/378</td>
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<td></td>
<td>17/27</td>
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<tr>
<td>Other</td>
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<td>52/58</td>
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<tr>
<td>Educational attainment</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No qualifications</td>
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<td>18</td>
<td></td>
<td>48/97</td>
<td>16</td>
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<td>GCSE or equivalent</td>
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<td></td>
<td>85/106</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>A level or equivalent</td>
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<td></td>
<td>63/98</td>
<td>21</td>
<td></td>
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<tr>
<td>Post 16 education (including HNC, trade degree)</td>
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<td></td>
<td>46/97</td>
<td>18</td>
<td></td>
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<tr>
<td>Ever had open market employment</td>
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<td>12</td>
<td></td>
<td>24/28</td>
<td>18</td>
<td></td>
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<td>Any current work or study</td>
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<td></td>
<td>20/27</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>Schizophrenia or schiz-affective disorder</td>
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<td>31</td>
<td></td>
<td>80/956</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Bipolar affective disorder</td>
<td>76/956</td>
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<td></td>
<td>19/206</td>
<td>7</td>
<td></td>
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<tr>
<td>Depression with psychotic symptoms</td>
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<td></td>
<td>8/93</td>
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<tr>
<td>Other psychoses</td>
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<td></td>
<td>15/255</td>
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<td></td>
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<tr>
<td>1–3 times a week</td>
<td>71/72</td>
<td>28</td>
<td></td>
<td>72/72</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>More than 3 times a week</td>
<td>194/273</td>
<td>72</td>
<td></td>
<td>194/273</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>Any work or study</td>
<td>50/956</td>
<td>52</td>
<td></td>
<td>50/956</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>Cannabis-positive urine</td>
<td>23/262</td>
<td>20</td>
<td></td>
<td>21/262</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Number of days using cannabis*</td>
<td>108</td>
<td>(97, 156)</td>
<td></td>
<td>114/165</td>
<td>(10, 162)</td>
<td></td>
</tr>
<tr>
<td>History of cannabis dependence</td>
<td>21/273</td>
<td>87</td>
<td></td>
<td>21/273</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>Current cannabis dependence</td>
<td>18/256</td>
<td>77</td>
<td></td>
<td>18/256</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>PANSS: positive symptoms median (IQR)</td>
<td>12</td>
<td>(9, 17)</td>
<td></td>
<td>13/16</td>
<td>(9, 16)</td>
<td></td>
</tr>
<tr>
<td>PANSS: negative symptoms median (IQR)</td>
<td>14</td>
<td>(11, 24)</td>
<td></td>
<td>14/16</td>
<td>(10, 14)</td>
<td></td>
</tr>
<tr>
<td>EQ5D-3L utility score</td>
<td>0.761</td>
<td></td>
<td></td>
<td>0.702</td>
<td></td>
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<tr>
<td>EQ5D utility score</td>
<td>0.692</td>
<td></td>
<td></td>
<td>0.683</td>
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<td></td>
</tr>
</tbody>
</table>

95% CI 0.70, 1.48. Approximately, a third of participants experienced at least one acute admission to a mental health service, including hospital alternatives such as crisis teams and crisis houses, by 18 months in both the CM (90/272) and control groups (85/259). Amongst those who experienced an acute psychiatric admission, the median number of days until admission was 245 (IQR 99, 362) in the control group and 196 (IQR 82, 364) in the CM group.

Secondary outcomes

For participants who had a full 18 months' follow-up, those in the CM group had a slightly higher rate ratio for number of admissions than those in the control group (incidence rate ratio (IRR) 1.08, 95% CI 0.75, 1.54); this changed little when assuming those who were discharged from services had no admissions during follow-up or when including predictors of missingness. Those in the CM group had lower odds of paid work or
study at both 3 and 18 months (OR 0.95, 95% CI 0.62, 1.46 OR 0.82, 95% CI 0.50, 1.35 respectively). However, those in the CM group also had slightly lower odds of cannabis-positive urine at 3 and 18 months (OR 0.86, 95% CI 0.56, 1.34; OR 0.84, 95% CI 0.59, 1.21 respectively). None of these results approached statistical significance at the 5% level. Illicit substance use other than cannabis was very low in both follow-ups (3-month median days of use: 0; IQR 0, 1 in both groups; 18-month: 0 in both groups, IQR 0, 0 in control; IQR 0, 1 in CM). The median number of alcohol-years was 4 (control IQR 0, 12; CM IQR 0, 15) in both groups at 3 months and 6 (IQR 0, 24) in both groups in 18 months. For the log-transformed PANSS positive outcome at 3 months, the CM group score was on average 7% lower (better) than the control group (95% CI -14%, -4%). There were 50 reported serious adverse events (SAE). In the CM group, these were 21 psychiatric hospital admissions and 3 deaths. In the control group, there were 28 psychiatric hospital episodes, 2 deaths, and 1 arrest.1

CM in the context of psychoeducation

A post-hoc analysis was performed to help understand the results in the context of whether people had received psychoeducation as planned. Attending at least four of the six psychoeducation sessions planned was selected as the measure of compliance (137/263 [52%] in the control group and 168/273 [62%] in the CM group). There were no marked differences in demographic, social, or clinical baseline characteristics between compliers and non-compliers between randomised groups. A dichotomous variable indicating compliance was created. A Cox model with robust standard errors was conducted. The primary outcome of the trial (time to acute psychiatric admission) was used as the dependent variable in the analysis. Randomisation group, compliance, severity of cannabis use at baseline, and whether the participant was part of the pilot trial were included as covariates, and an interaction term between compliance and randomisation groups was used. The interaction term was statistically significant (p-value for interaction 0.016), which suggests that CM might be effective in participants who receive sufficient psychoeducation. This may be due to the psychoeducation being effective amongst those who engaged with treatment, and engagement was higher in the CM group.

Health economics

Intervention costs were on average £298 for the CM group and £140 for controls. Inpatient use (based on 531 participants) over the follow-up period was virtually the same between trial arms, with around one quarter receiving this and for about 3 months across the period (Table 4). Other service use (based on the smaller sample of 231 who were followed up with the CSRU) was relatively similar between the arms over the follow-up period. Costs for drug and alcohol services were however greater for the CM group. After imputation, the mean (SD) health and social care costs over the 18-month period were £15,614 (£29,360) for the CM group and £16,620 (£33,283) for controls. After adjusting for baseline costs, the CM group had costs that were on average £1625 lower than for controls (bootstrapped 95% CI, £535 to £5069).

EQ-5D-3L and SF-6D utility scores increased gradually over time for both groups (Table 2). The total mean QALYs over the follow-up period were 1.2218 for the CM group and 1.1855 for controls. Adjusting for baseline utility, CM reached 0.034 more QALYs than controls. QALYs based on the SF-6D scores were 1.0682 for CM and 1.0585 for controls. With adjustment, CM resulted in 0.0063 more QALYs than controls. Therefore, CM had lower costs and produced more QALYs and so dominated the control. There is uncertainty around the results shown by the cost-effectiveness planes. With the EQ-5D-3L (Fig. 3), the most likely result is that CM has lower costs and better outcomes (72% of replications), followed by higher costs and better outcomes (26%), lower costs and worse outcomes (2%), and higher costs and worse outcomes (1%). With the SF-6D, there is more uncertainty (Fig. 4), but the most likely outcome is still CM having lower costs and better outcomes (52%), followed by lower costs and
Table 2 Outcomes at 3 months (treatment end) and 18 months.

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th></th>
<th>CM</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>mean or median (%)</td>
<td>n (%)</td>
<td>mean or median (%)</td>
</tr>
<tr>
<td>Admitted to an acute mental health service</td>
<td>18 months</td>
<td>85/149 (8.8)</td>
<td>90/77 (7.0)</td>
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<tr>
<td>Number of admissions</td>
<td>18 months</td>
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<td>0 (0.1)</td>
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</tr>
<tr>
<td>Any work or study</td>
<td>3 months</td>
<td>59/133 (32)</td>
<td>36/109 (31)</td>
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</tr>
<tr>
<td></td>
<td>18 months</td>
<td>45/15 (53)</td>
<td>42/14 (28)</td>
<td></td>
</tr>
<tr>
<td>Cannabinoid-positive urine</td>
<td>3 months</td>
<td>12/170 (7.2)</td>
<td>128/144 (70)</td>
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</tr>
<tr>
<td></td>
<td>18 months</td>
<td>76/144 (57)</td>
<td>77/166 (47)</td>
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<tr>
<td>Number of days using cannabis (median)</td>
<td>3 months</td>
<td>33 (3.84)</td>
<td>36 (1.63)</td>
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<tr>
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<td>18 months</td>
<td>26 (1.43)</td>
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<td>PANSS positive symptoms (median)</td>
<td>3 months</td>
<td>11 (0.16)</td>
<td>10 (0.14)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18 months</td>
<td>10 (0.15)</td>
<td>11 (0.18)</td>
<td></td>
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<tr>
<td>PANSS negative symptoms (median)</td>
<td>3 months</td>
<td>14 (0.18)</td>
<td>12 (0.13)</td>
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<tr>
<td></td>
<td>18 months</td>
<td>12 (0.17)</td>
<td>12 (0.17)</td>
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<tr>
<td>Number of days of using illicit substances other than cannabis (median)</td>
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<td>0 (0.1)</td>
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<tr>
<td></td>
<td>18 months</td>
<td>0 (0.2)</td>
<td>0 (0.1)</td>
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<tr>
<td>Number of days using alcohol (median)</td>
<td>3 months</td>
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<td>4 (0.13)</td>
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<td>18 months</td>
<td>6 (0.24)</td>
<td>6 (0.24)</td>
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<tr>
<td>EQ-5D-3L utility score (mean)</td>
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<td>0.720</td>
<td>0.715</td>
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<td>18 months</td>
<td>0.802</td>
<td>0.736</td>
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<tr>
<td>SF-6D utility score (mean)</td>
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<td>0.214</td>
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<td>18 months</td>
<td>0.210</td>
<td>0.220</td>
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<tr>
<td>Number of psychoeducation sessions attended (median)</td>
<td>3 months</td>
<td>4 (0.6)</td>
<td>6 (1.6)</td>
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<tr>
<td></td>
<td>18 months</td>
<td>9 (1.2)</td>
<td>9 (1.2)</td>
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<tr>
<td>Number of contingency management sessions attended (median)</td>
<td>137/381</td>
<td>32 (160/273)</td>
<td>67</td>
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</tr>
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</table>

*At 3 months, this was for the previous 12 weeks/84 days. At 18 months, this was for the previous 188 days.

worse outcomes (22%), higher costs and better outcomes (18%), and higher costs and worse outcomes (8%). The CEACs (Fig 5) show that even with a zero value attached to a QALY there is still a high probability of CM being the most cost-effective option. At a threshold value of £20,000, the probabilities are 0.81 for the EQ-5D-3L and 0.75 for the SF-6D.

Discussion
The results of this trial indicate that CM confers no clinical advantage over TAU for patients with psychosis who use cannabis. Neither was any effect seen in our secondary outcomes, including cannabis use, engagement in work or education, and positive psychotic symptoms. However, a post hoc analysis found that compliance with psychoeducation in the CM arm resulted in a statistically significant improvement in time to acute psychiatric admission, while the same was not true for the control group. This suggests that CM had a clinical benefit amongst those who also engaged with psychoeducation.

The economic analyses show that the costs associated with CM were less than for the TAU, although the difference was not statistically significant and this analysis
Table 3. Analysis of primary and secondary outcomes in terms of contingency management

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Estimate</th>
<th>95% CI</th>
<th>N</th>
<th>Estimate</th>
<th>95% CI</th>
<th>N</th>
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</thead>
<tbody>
<tr>
<td>Time to acute psychiatric admission (hrs)</td>
<td>1.03</td>
<td>(1.00, 1.06)</td>
<td>531</td>
<td>1.02</td>
<td>(1.00, 1.04)</td>
<td>531</td>
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<tr>
<td>Cannabis-positive urine sample 3 months (OR)</td>
<td>0.36</td>
<td>(0.26, 0.49)</td>
<td>354</td>
<td>0.69</td>
<td>(0.55, 0.87)</td>
<td>352</td>
</tr>
<tr>
<td>Cannabis-positive urine sample 18 months (OR)</td>
<td>0.24</td>
<td>(0.17, 0.36)</td>
<td>290</td>
<td>0.25</td>
<td>(0.17, 0.37)</td>
<td>260</td>
</tr>
<tr>
<td>log PANSS positive symptoms 3 months</td>
<td>−0.027</td>
<td>(−0.04, −0.01)</td>
<td>366</td>
<td>−0.07</td>
<td>(−0.07, −0.06)</td>
<td>364</td>
</tr>
<tr>
<td>log PANSS positive symptoms 18 months</td>
<td>−0.04</td>
<td>(−0.07, −0.01)</td>
<td>376</td>
<td>−0.03</td>
<td>(−0.05, −0.00)</td>
<td>376</td>
</tr>
<tr>
<td>log PANSS negative symptoms 3 months</td>
<td>−0.08</td>
<td>(−0.11, −0.05)</td>
<td>360</td>
<td>−0.08</td>
<td>(−0.12, −0.04)</td>
<td>360</td>
</tr>
<tr>
<td>log PANSS negative symptoms 18 months</td>
<td>−0.05</td>
<td>(−0.06, −0.03)</td>
<td>376</td>
<td>−0.06</td>
<td>(−0.08, −0.03)</td>
<td>376</td>
</tr>
<tr>
<td>Paid work or study at 3 months (OR)</td>
<td>0.98</td>
<td>(0.92, 1.04)</td>
<td>372</td>
<td>0.99</td>
<td>(0.96, 1.03)</td>
<td>370</td>
</tr>
<tr>
<td>Paid work or study at 18 months (OR)</td>
<td>0.99</td>
<td>(0.93, 1.06)</td>
<td>280</td>
<td>0.99</td>
<td>(0.93, 1.06)</td>
<td>280</td>
</tr>
<tr>
<td>Number of days cannabis used in the previous 12 weeks (3 months follow-up) (SD)</td>
<td>0.86</td>
<td>(0.76, 0.98)</td>
<td>376</td>
<td>0.88</td>
<td>(0.78, 0.98)</td>
<td>360</td>
</tr>
<tr>
<td>Number of days cannabis used in the previous 6 months (18 months follow-up) (SD)</td>
<td>1.15</td>
<td>(1.03, 1.29)</td>
<td>274</td>
<td>1.15</td>
<td>(1.03, 1.28)</td>
<td>274</td>
</tr>
<tr>
<td>Number of admissions over 18 months follow-up</td>
<td>1.08</td>
<td>(0.95, 1.25)</td>
<td>374</td>
<td>1.08</td>
<td>(0.95, 1.25)</td>
<td>374</td>
</tr>
<tr>
<td>At least one admission over 18 months follow-up (OR)</td>
<td>1.02</td>
<td>(0.70, 1.48)</td>
<td>381</td>
<td>1.01</td>
<td>(0.70, 1.48)</td>
<td>381</td>
</tr>
</tbody>
</table>

Q: confidence interval; OR: odds ratio; SD: standard deviation
*
Adjusting for level of cannabis use at baseline and whether in the pilot study
Additional adjustment for baseline predictors of missingness. These are:
Time to admission, number of admissions, at least one admission in any week or study
Hours positive 3 months, PANSS positive 3 months, PANSS negative 3 months, any work or study 3 months, number of days cannabis used 3 months: exempt from work due to disability
Unemployment 18 months: any work or study
PANSS positive 18 months, PANSS negative 18 months, any work or study 18 months, number of days cannabis used 18 months: voluntary work

Table 4. Service use for the health economies

<table>
<thead>
<tr>
<th>Service</th>
<th>Control</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient stays</td>
<td>23.3</td>
<td>45.9</td>
<td>11,921</td>
<td>24.0</td>
<td>48.4</td>
</tr>
<tr>
<td>Early intervention team</td>
<td>60.9</td>
<td>11.1</td>
<td>30.2</td>
<td>68.7</td>
<td>11.7</td>
</tr>
<tr>
<td>GP</td>
<td>44.7</td>
<td>2.9</td>
<td>13.1</td>
<td>51.1</td>
<td>3.1</td>
</tr>
<tr>
<td>Psychiatrist</td>
<td>53.1</td>
<td>3.7</td>
<td>4.7</td>
<td>54.3</td>
<td>3.2</td>
</tr>
<tr>
<td>Psychologist</td>
<td>20.9</td>
<td>5.6</td>
<td>4.4</td>
<td>22.7</td>
<td>5.0</td>
</tr>
<tr>
<td>Home treatment/crisis team</td>
<td>10.3</td>
<td>13.8</td>
<td>3.1</td>
<td>9.0</td>
<td>13.7</td>
</tr>
<tr>
<td>Mental health nurse</td>
<td>13.9</td>
<td>7.0</td>
<td>1.9</td>
<td>15.1</td>
<td>7.1</td>
</tr>
<tr>
<td>Adult education class</td>
<td>5.7</td>
<td>5.0</td>
<td>1.8</td>
<td>2.5</td>
<td>5.4</td>
</tr>
<tr>
<td>Assertive outreach team</td>
<td>1.1</td>
<td>6.0</td>
<td>0.5</td>
<td>1.8</td>
<td>6.4</td>
</tr>
<tr>
<td>Class/group at a leisure centre</td>
<td>4.4</td>
<td>25.2</td>
<td>3.3</td>
<td>4.0</td>
<td>14.6</td>
</tr>
<tr>
<td>Community mental health centre</td>
<td>11.6</td>
<td>7.6</td>
<td>4.0</td>
<td>11.7</td>
<td>7.8</td>
</tr>
<tr>
<td>Day care centre/day hospital</td>
<td>0.7</td>
<td>23.0</td>
<td>0.3</td>
<td>1.4</td>
<td>5.2</td>
</tr>
<tr>
<td>Drug in centre</td>
<td>4.8</td>
<td>103.8</td>
<td>3.3</td>
<td>1.4</td>
<td>16.5</td>
</tr>
<tr>
<td>Drug and alcohol service</td>
<td>48.6</td>
<td>6.1</td>
<td>23.4</td>
<td>40.7</td>
<td>6.4</td>
</tr>
<tr>
<td>Drug and alcohol advisor</td>
<td>10.6</td>
<td>7.9</td>
<td>1.1</td>
<td>9.4</td>
<td>7.5</td>
</tr>
<tr>
<td>Occupational therapist</td>
<td>0.7</td>
<td>3.7</td>
<td>0.3</td>
<td>0.6</td>
<td>3.1</td>
</tr>
<tr>
<td>Other controlled therapy</td>
<td>5.1</td>
<td>7.1</td>
<td>1.0</td>
<td>4.0</td>
<td>7.5</td>
</tr>
<tr>
<td>Other doctor</td>
<td>8.1</td>
<td>3.7</td>
<td>7.3</td>
<td>7.6</td>
<td>2.1</td>
</tr>
<tr>
<td>Self-help/support group</td>
<td>5.1</td>
<td>6.5</td>
<td>9.1</td>
<td>7.2</td>
<td>6.8</td>
</tr>
<tr>
<td>Social worker</td>
<td>10.3</td>
<td>7.3</td>
<td>5.8</td>
<td>7.9</td>
<td>10.4</td>
</tr>
<tr>
<td>Medication</td>
<td>2.88</td>
<td>3.08</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

347
was carried out after imputation for a large proportion of cases, while we had primary outcome data for most who entered the trial. QALY differences based on the EQ-5D-3L were relatively large compared to other studies, but less so with the SF-6D. The lower costs and greater number of QALYs mean that CM is more cost-effective than TAU even though the differences for both costs and QALYs were not statistically significant. While interpretation of this is complex as there was little difference between CM groups in the intention-to-treat analyses one possible explanation is that time to acute psychiatric admission was better amongst those who complied with psychosocial intervention in the CM group, but not the control group. The admission rate was lower than anticipated in the trial as a whole. Only around a third in each group required admission to acute care, while it was expected [3, 4] for the purposes of our sample size calculation and based on previous literature that half would experience an acute psychiatric admission. This suggests that a comparatively stable group of
patients was recruited to trial and/or that the psychoeducation and/or the extra attention of being in a research study had a beneficial impact. Although the majority still had cannabis-positive urine, the number of reported cannabis using days in the previous 6 months fell from over 100 to 26 in each group by 18-month follow-up, indicating that cannabis use declined in both groups over this period. This could be due to the psychoeducation intervention, the normal progression of use in this group, regression to the mean, or a combination of these factors. Low levels of self-reported illicit substance and alcohol use at follow-up indicate that people were not substituting them for cannabis.

Overall, the results of the trial are mixed, and stand in contrast to the frequently positive benefits reported for CM interventions [15, 16], including for substance misuse in psychosis [17–19, 21]. Reasons for this are unclear; however, some possible explanations include the following: Firstly, offering more frequent CM sessions or offering a higher reward might have been more clinically effective. The CM schedule was adapted from two trials by Redmay et al. [10, 11], which both found a positive effect in cannabis misuse. However, the reward sessions in one of those trials occurred once per week, while in the other they occurred twice per week. Bellack et al. [21], which is the only other trial of CM to include cannabis in severe mental illness, also used a twice weekly reward schedule. CIRCLE was intended to be a pragmatic trial of a CM intervention in an EIP context, and based on feedback from EIP clinicians, it was thought that delivering sessions more frequently than once per week would not be feasible, while the reward value was intended to be substantial enough to incentivize abstinence without being viewed as too lavish and thus ethically problematic, and was supported by clinicians, service users involved in the patient and public involvement consultation, and experts in the field. It was also approximately in line with other trials in this field (e.g. [10, 21]). However, it was lower than that offered in some feasibility studies that found a positive effect (e.g. [22, 23]). Further discussions with stakeholders and experts in the field might elucidate this issue.

Secondly, cannabis dependence was high in this sample (around three quarters of participants at baseline), and those with dependence may find it harder to change their behaviour compared to those with less severe problematic cannabis use. However, in the two trials by Redmay et al. [10, 11] and Bellack et al. [21], all participants were dependent, and so it is unlikely that the CM intervention failed to provide a benefit because of high rates of dependence. An alternative explanation is that participants may have been using more highly potent forms of the cannabis and consequently may have found it more difficult to abstain than those using less-potent forms. There is good evidence that this cohort typically uses more potent forms of cannabis than non-psychiatric groups [40] and that high potency cannabis use is relatively prevalent in London, where much of our sample was recruited [41]. It is therefore plausible that use of highly potent types of cannabis may have been relatively widespread in our sample. However, we did not systematically record the type of cannabis participants were using, making further exploration of this possibility difficult.
Thirdly, while engagement was good with people attending a median of 4 psychosocial education sessions in the control group and 6 in the CM group, a substantial proportion of people (around one third of people in the control group and one fifth in the CM group) declined to take part in either the CM and/or the PE or did not attend any sessions. This suggests there may have been a substantial minority who were not particularly motivated to quit cannabis, but perhaps participated due to the enthusiastic approach to recruitment by staff and researchers and/or the small payment received to acknowledge baseline interview assessment participation. Recruitment was slower than anticipated, partly because fewer service users than expected wanted to enter treatment for cannabis use. The post hoc analysis results suggested that people who were motivated to adhere to the psychosocial education had better outcomes. It may be that a more engaged cohort would have benefited more from the CM.

Fourthly, patients in this cohort are often multiply disadvantaged [2, 5, 42], which is likely to make behaviour change much more challenging. This includes being less likely to be in work or education, having poorer social networks, and thereby being more socially isolated but also the nature of psychotic illness itself, which can include greater disorganisation, poorer social skills, and lower motivation [43, 44]. It may be that interventions are needed in this cohort that have a broader focus than just reducing cannabis use. It may be that a better approach would support patients in becoming less socially isolated or spending less time with cannabis-using peers, as well as helping them back into work or engaging in other meaningful activities.

Finally, the trial focused only on cannabis, but baseline data indicated considerable history of alcohol and substance use disorders. It may be that the CM would have been more effective if it had addressed these additional substances as well.

There were several limitations to the study. Firstly, CIRCLE was a pragmatic trial of a CM intervention delivered in EIP services in the UK. The CM and psychosocial education treatments were designed to be feasible for EIP clinicians to deliver in routine practice, which required limiting the additional workload to clinicians. As such, during the intervention period, urinalysis samples were only collected from the CM group and not controls. This makes it more challenging to analyse whether the CM group participants reduced their use more than the controls during the intervention period. However, self-reported days of cannabis use at treatment end did not differ between groups, suggesting no impact from the CM. However, CIRCLE should be viewed as a trial of a pragmatic CM intervention rather than a definitive trial of whether CM reduces cannabis use in psychosis. Studies that more rigorously assess drug use in both treatment groups are needed to investigate whether CM could be effective at reducing use in psychosis.

Secondly, the inclusion of an active control makes it more difficult to interpret results. The fall in cannabis use across the trial population suggests there may have been benefit from the enhanced TAU. While it was intended to be a standardised form of treatment as usual, it became apparent that it was a much better developed and more ambitious psychosocial education than was otherwise available in many of the participating EIP teams.

Thirdly, originally, the CM (and psychosocial education) was originally intended to be delivered by care coordinators (the nurses, occupational therapist or social workers with primary responsibility for keeping in touch with patients and organising their care). However, few care coordinators were prepared to deliver the interventions, largely due to concerns regarding time pressures and potential disruption to therapeutic relationships. Instead, other clinical staff, such as support workers or assistant psychologists, were trained to deliver it. Greater integration into routine care may have improved its effectiveness. However, data on delivery of the CM intervention suggested that those delivering it did adhere well to the intended protocols and it may be that care coordinators would have been less successful in this.

Fourthly, while the follow-up rate for the primary outcome was very high, attrition was greater than anticipated on the interview measures, potentially introducing response bias.

Fifthly, while a standard threshold was used for the urinalysis at assessment interview (50 ng/ml), a lower threshold would have given a slightly more accurate measure of abstinence rates. A lower threshold may have identified a small difference between groups. However, as there was no difference in either the proportion of cannabis-free urine using a threshold of 50 ng/ml or self-reported days of use at either follow-up, it seems unlikely that a clinically significant difference would be identified.

Sixthly, while we approached all EIP patients who were identified to trial researchers as potentially eligible by their clinicians and who agreed to be contacted by a trial researcher, it may be that gate-keeping by EIP clinicians or self-selection by patients could have introduced bias. However, this was a pragmatic RCT and it is likely that the trial sample is a good reflection of the range of characteristics of the EIP service users who would enter treatment if the intervention was offered through EIP or specialist drug treatment services. Similar issues seem likely if the intervention was introduced as part of routine care.

Seventhly, we did not systematically record the type of cannabis participants were using. It may be that those using more potent types of cannabis would respond differently to
the intervention compared to those using milder forms, either by finding it harder to change behaviour or potentially by showing greater benefit from the CM treatment in terms of acute psychiatric service use.

Eighthly, although not a limitation in the analyses, the finding that CM has over 80% likelihood of being cost-effective needs to be treated with caution. In the sample that were followed up at both time points, the costs were lower and QALY outcomes better for the CM group compared to controls, and this led to a favourable cost-effectiveness ratio for CM which applied to most bootstrapped resamples. The cost and QALY differences were thought limited and not statistically significant.

Finally, using acute psychiatric admission as the outcome is a pragmatic choice because it is routinely available data that are relatively accessible via patient records. But it is limited in that some acute psychiatric episodes are likely to be contained without acute service use, for example, it may be handled by the EIP team instead, and also that thresholds for admission to acute care may vary considerably, for example by clinician and by area.

Conclusions

Overall, the lack of effectiveness of CM in these intention-to-treat analyses means that it cannot be recommended as an intervention to reduce cannabis use in patients with recent onset psychosis. However, the adherence and health economic analyses suggest that effectiveness of CM might be better amongst those who engage well with psychoeducation, or if a different reward schedule was offered. Further investigation of stakeholder perspectives would be useful to explore the latter possibility. Overall, this is another trial that demonstrates how challenging it is to address the problem of cannabis use in psychosis. It may be that a substantially different approach is required to address this significant clinical problem. It has been noted that young people who have psychosis and problematic cannabis use are often multiply disadvantaged. Despite this, trials of interventions in this area are often narrowly focused on changing cannabis use. A more inclusive management that takes in patients’ social contexts, including engagement in work or education, might prove more fruitful.

Abbreviations

CIA: Cost-effectiveness; AC: Acceptability; CMI: Contingency management; SST: Smart Stop Treatment; RCT: Randomised controlled trial; HRQoL: Health-related Quality of Life; NICE: National Institute for Health and Care Excellence; PANSS: Positive and Negative Syndrome Scale; QALY: Quality-adjusted life years; SD: Standard deviation; SASS: Short Alcohol Survey; SADS: Structured Clinical Interview for DSM-IV; SSI: Suicide Risk Assessment; SF-12: 12-Item Short Form Survey; TIEA: Timeline Followback

Acknowledgements

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Authors’ contributions

UC was the chief investigator who also managed the primary research centre, UCL, and designed the study with contributions from SM, OP, TC, LM, GM, MI, TM, KA, and JB. UC and GM had a major role in the conception and design of the trial. LM managed the main trial and drafted the final manuscript and TM and GM authored and performed the statistical analyses. UC and GM wrote the protocol and the statistical analyses. UC had a major role in the conception and design of the trial. LM wrote the main proposal and the main trial and drafted the final manuscript. UC and TM and UC and GM and UC and TM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and LM and UC and GM and UC and L

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Appendix 4.1 – Gantt chart showing the schedule of events
Appendix 4.2 – Further methods: protocol as submitted for ethics approval

Below is the protocol for the quantitative studies reported in this thesis. It was originally included in version 6 of the protocol of the CIRCLE trial (dated 12th May 2014).

Cognitive-Behavioural Process Evaluation:

Overview:

A second sub-study will be performed as a process evaluation of the mechanism of cognitive and behavioural change associated with contingency management (CM) interventions. This will constitute part of the required research for a PhD for Luke Sheridan Rains, the CIRCLE Trial Manager.

The primary objective is to investigate the impact of CM on intrinsic motivation to abstain from cannabis use. It is also hypothesised that this relationship will be mediated by treatment engagement (Carroll et al. 2006, Tavares et al. 2009) and perceived competence in being able to abstain (Deci, Koestner, & Ryan 1999). Secondary objectives for the study include investigating the relationship between intrinsic motivation at treatment end and cannabis use in the 6 months following treatment. It is expected that higher self-reported intrinsic motivation at treatment end will be associated with lower rates of cannabis use over the 6 month post-treatment period. The study will also explore whether commonly identified barriers to successful abstinence, including cravings and environmental cannabis use, are also impacted by CM interventions. Finally, it will identify the principle reasons participants have for taking part in the contingency management intervention and consider how they impact cannabis use during and following treatment.

Background:

Budney et al. (2006) describe CM as a ‘method to enhance and maintain initial motivation to abstain from cannabis use by providing a structure (weekly urine testing) and incentive (vouchers) for doing so’. However, some critics (e.g. Deci and Ryan, 1971) of financial rewards for motivating behaviour change argue that if an individual is encouraged to perform a particular behaviour by extrinsic motivational factors, their intrinsic motivation to perform that behaviour will be undermined. In support of this view Deci, Ryan, and Koestner (1999) published a meta-analysis of 128 studies investigating the effect of tangible rewards on participant’s intrinsic motivation to perform a study task. They found that receiving rewards reduced the likelihood that participants would continue performing the task during a ‘free choice’ period following cessation of the rewards. They argue that this results from the rewards making the individual feel like they are being externally controlled, and that their control over their own behaviour has been undermined. Deci and Ryan (2008) argue that contingency management (CM) type interventions are likely to produce only short-lived behavioural change, and that they could undermine any motivation.
the patient had pre-treatment to adopt healthier behaviours. If correct, this would be major problem for the long term efficacy of CM interventions, and may be a significant concern for mental health practitioners considering adopting CM type interventions to reduce substance use.

Contrary to Deci and Ryan it appears that abstinence does not rapidly fall for CM post-treatment in all cases. In a review of CM for substance misuse literature, Prendergast et al. (2006) found that CM was associated with significantly reduced cannabis use at 3 months (d=0.37) and 6 months (d=0.45) post treatment. Several publications since (Kadden et al., 2007; Carroll et al. 2006; Stranger et al. 2009; Litt et al. 2008) have reported that CM compared to a treatment as usual condition had reduced rates of substance use at up to 9 months post-treatment. Possible explanations for the impact of CM post-treatment are varied. Cognitive Evaluation Theory (CET) (Deci & Ryan 1985) suggests that financial rewards can improve the individual’s sense of competency in performing the desired behaviour, and this may lead to improved intrinsic motivation. Alternatively, it may be that CM raises overall motivation to abstain sufficiently during treatment to resist or change certain cognitive-behavioural predictors of relapse. Coffey et al. (2002) found that 75% of people who met the criteria for dependency reported withdrawal symptoms such as cravings, anxiety, or sleeplessness. 38% of those with withdrawal symptoms reported using to avoid those symptoms. CM may benefit such individuals by giving additional motivation to endure withdrawal symptoms while recently abstinent. Given a sufficiently long period of treatment these factors are likely to decline in severity or disappear, thereby aiding long term abstinence without necessarily increasing intrinsic motivation.

While there is evidence of the benefits of CM post-treatment, Kadden et al. (2007) and Litt et al. (2008) found that CM alone failed to produce significant results on reducing cannabis use at 6 and 8 months respectively. Secondly, there is a perception amongst some researchers that CM alone has a relatively short term impact on substance use post-treatment (see Prendergast et al. 2006). It may be that while CM is effective at reducing cannabis use for up to 3-6 months post-treatment, CM alone may not be sufficient to produce longer term abstinence. Kadden et al. (2007), Carroll et al. (2006), and Litt et al. (2008) found that a CM intervention combined with Motivational Enhancement Therapy/Cognitive Behavioural Therapy (MET/CBT) produced longer term effects on cannabis use than CM alone. One explanation for the increased benefit of CM and MET/CBT combined is that each intervention is likely to address different factors influencing relapse. CM is effective at quickly reducing use during treatment compared to MET/CBT alone (Carroll et al. and Litt et al.). Thereby it may also be effective in terms of reducing cravings and other symptoms of withdrawal by treatment end. The aim of MET/CBT interventions meanwhile typically include: 1) to provide educational materials on the likely consequences of continued use; 2) to evoke and strengthen the patient’s own motivation for change; 3) to assist the individual in developing effective coping strategies and harm reduction strategies (Thombs & Osborn 2013). Carroll et al. further found that CM improved engagement with treatment offered alongside CM. A CM plus MET/CBT intervention may therefore improve long term treatment outcomes partially through the benefits of CM and MET/CBT as standalone treatments, but secondly through CM improving engagement with MET/CBT treatments compared to MET/CBT alone.

For CIRCLE, CM is being offered alongside a manualised psycho-education package intended as an Optimised Treatment as Usual (OTAU) intervention. As described in the ‘planned interventions’ section for CIRCLE, it is intended to provide information about the likely consequences of continued cannabis use; to aid the participant in making a decision about their cannabis use; and to help them achieve those goals through strengthening their
motivation and helping them develop effective coping and harm reduction strategies. Based on the above model, one would expect the group receiving CM to show greater engagement in the psycho-education, and to be associated with greater long term abstinence compared to the control group.

Aims:

The overall objective of the present sub-study is to investigate the mechanism of cognitive and behavioural change underlying CM. The aim is to improve our understanding of its efficacy in treating substance use, both during treatment and post-treatment, when used in combination with a psycho-education intervention. The primary objective is to investigate the impact of adding CM for cannabis to routine clinical care on participants’ intrinsic motivation to abstain. The expectation is that participants in the experimental group will show greater intrinsic motivation, and that this relationship will be mediated by engagement in the psycho-education and their perceived competence in abstaining. It is hypothesised that CM will improve intrinsic motivation by treatment end by: 1) encouraging increased engagement in the psycho-education. 2) Improving perceived competence in being able to abstain.

Secondary objectives include: 1) to investigate the impact of adding a CM intervention to routine clinical care on cravings and social networks/environmental cannabis use. 2) To investigate the impact of an added CM intervention at treatment end and 6 months post-treatment on self-reported overall motivation to abstain and cannabis use. 3) To investigate the relationship between self-reported intrinsic motivation at treatment end and post-treatment abstinence. 4) To consider the reasons patients have for taking part in treatment, and explore how they relate to successful long term abstinence. It is predicted that the experimental group (CM plus psycho-education) will display reduced cravings, reduced exposure to environmental cannabis use, and greater motivation at treatment end. Secondly, greater intrinsic motivation will be associated with longer periods of abstinence post-treatment. Thirdly, that health concerns (Coppena et al. 2006) and the prospect of receiving the financial rewards will be the primary reasons participants give for taking part.

Method:

Study Design

The process evaluation will be performed as part of CIRCLE. CIRCLE is a rater-blinded randomised controlled trial of contingency management (CM) offered alongside an optimised treatment as usual intervention. The aim is to investigate how CM offered as an addition to routine clinical care impacts service user motivation to abstain from cannabis use both during the intervention and in the months following treatment cessation. Furthermore, it will explore some of the cognitive and psychosocial processes expected to be underlying this relationship, and consider how this fits with current models of how CM interventions work. Finally, it will investigate the long term benefits of CM interventions compared to treatment as usual type interventions in terms of abstinence from cannabis use and motivation to abstain, and consider how this can inform future applications of CM type interventions for promoting behavioural change.

Once approval has been received, the outcome measures for the process evaluation will be conducted alongside the CIRCLE outcome measures at CIRCLE baseline and 3 month follow up assessment interviews, but not at the 18 month follow up. An additional assessment interview for the process evaluation will be performed at 9 months following.
study induction (6 months following intervention cessation) as a telephone interview. This assessment will be performed for approximately 1/3 of participants recruited after approval has been received. This will happen through 1/3 of study sites conducting the 6 month follow up assessment.

Recruitment:

All participants eligible for CIRCLE will be included in the process evaluation. Participants will be informed of its aims as part of the consent process for CIRCLE. Details of the process evaluation, including objectives and information about the 9 month telephone interview, are included in the participant information sheet. They can opt out of the follow up telephone interview without being excluded from participation in any other part of CIRCLE.

Sample Size:

Outcome data will be collected for the process evaluation for all service users consented into CIRCLE once ethical approval has been received. It is estimated that outcome data will be collected for approximately 400 CIRCLE participants at baseline assessment. Based on the 3 month follow up rate achieved during the pilot phase of 70%, primary outcome data is expected to be collected for approximately 280 participants.

Outcome Measures:

The following measures will be included in the baseline and 3 month follow up assessment interviews for CIRCLE. In total they comprise 32 items, each of which are rated with a Likert type scale. They take around 15-20 minutes to complete in total.

Intrinsic motivation: Reasons for Quitting (RFQ) (McBride et al., 1994). Some changes have been made to the items in the assessment to accommodate better the likely concerns of patients with psychosis and a history of psychosis. Secondly, 4 items have been added explicitly referring to the vouchers participants will receive as part of the intervention.

Motivation and competence: 1) Chung et al. (2011) validated a 3 item measure of motivation to abstain, perceived difficulty of abstaining, and confidence in being able to abstain. The original measure targeted cigarette smoking and has been adapted for the present sub-study by changing references to cigarette smoking to cannabis use. 2) Readiness Ruler (Heather, Smailes, & Cassidy 2008) is a single item measure of readiness to change. The original measure targeted alcohol use, and as above the measure has been adapted for the present sub-study by changing references to alcohol use to cannabis use.

Cravings: Mood and physical symptoms scale (MPSS) (West and Hajek, 2004) craving subscale only (2 items). These items have been adapted to refer to cannabis use instead of cigarette smoking.

Environmental/social cues: The Wisconsin Predicting Patients’ Relapse questionnaire (WIPREPA RE) (Bolt et al. 2009) environmental use subscale only (1 item in total), which has been adapted to refer to cannabis use instead of cigarette smoking.

Engagement with services: Engagement will be judged based on the number of CIRCLE psychoeducation sessions each participant attends. The number of contingency
management sessions attended will not be included, since there isn’t a comparable measure for the control group.

The following will be co-opted for the procedural evaluation study from the current CIRCLE outcome measures. Cannabis use: the Timeline Follow Back (TLFB) will be used for self-reported cannabis use. Cannabis free urines will be used for a biometrically verified measure of cannabis use.

**Data Collection:**

Data for the process evaluation will be collected following ethical approval for the present amendment. The following outcome measures will be collected as part of the CIRCLE baseline and 3 month follow up assessment interviews: RFQ, Chung et al., Readiness Ruler, MPSS, and WI-PREPARE. TLFB and urinalysis outcome data is already collected for CIRCLE and will be co-opted for the present sub-study. Engagement data will be collected as part of the interventions for CIRCLE.

The 9 month follow up will consist of a single telephone interview during which the Timeline Follow Back and the adapted Chung et al. (2011) items will be collected. The telephone interviews are expected to take approximately 15–20 minutes to complete. Only participants who have previously discussed and agreed to being contacted by telephone by a researcher will be contacted. A cluster design will be used, with approximately 1/3 of study sites randomly selected to conduct telephone interviews. All sub-study participants from the selected sites and who have not opted out of the telephone interview will be contacted.

**Statistical Analysis:**

The primary outcome is the impact of treatment on intrinsic motivation at the end of the intervention period. This relationship is hypothesised to be mediated by treatment engagement during the period of the intervention, and by self-reported competence at treatment end. For the analysis, intrinsic motivation will be rated using the RFQ, treatment engagement will be measured as the number of psycho-education sessions attended by the participant, and competence will be assessed using the self-reported confidence measure from Chung et al. The relationship will be tested using linear regression analysis. The regression model will include 3 coefficients: group allocation, competence, and treatment engagement.

The following power calculation was performed to confirm that the predicted sample size should provide sufficient statistical power for the primary outcome: Teynaw et al. (2009) reported an effect size of 0.44 for the effect of CM on intrinsic motivation. Based on a more conservative estimate of 0.3 for the effect size, power of 0.8, and significance level of 0.05, the statistical test for the primary outcome would require a sample size of 82. Following an alternative method, based on Harrell (2001) 15 observations are required for each coefficient for a linear regression analysis. Based on this, a sample size of 45 would be adequate. The expected sample size of 280 should therefore be sufficient for the primary outcome analysis.
Appendix 4.3 – Further methods: cognitive-behavioural questionnaire

This is the cognitive-behavioural questionnaire that was used to collect the quantitative data for chapters 4, 6, and 8.

<table>
<thead>
<tr>
<th>Reasons For Quitting (RFQ) adapted</th>
<th>Strongly Disagree</th>
<th>Strongly Agree</th>
</tr>
</thead>
<tbody>
<tr>
<td>I want to quit using cannabis/stay abstinent at this time:</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>1. To show myself that I can quit if I want to.</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>2. Because I will feel better about myself if I quit.</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>3. So that I can feel in control of my life.</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>4. Because my family or someone else I am close to will stop nagging me about using cannabis if I quit.</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>5. So that I can get praise from people I am close to.</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>6. Because using cannabis does not fit who I want to be.</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>7. Because using cannabis is becoming less socially acceptable.</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>8. Because someone told me I had to 'stop or else' (gave an ultimatum)</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>9. Because I am concerned that I will suffer from a serious illness if I don't quit.</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>10. Because people I am close to will be upset with me if I don't quit.</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>11. Because I have developed lung or chest problems from smoking cannabis.</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>12. Because I want to save the money that I spend on cannabis.</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>13. Because of legal problems related to cannabis.</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>14. Because I know people who have suffered from serious illnesses caused by cannabis.</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>15. To prove to myself that I am not addicted to cannabis.</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>16. To avoid being arrested or receiving a conviction</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>17. Because I want to avoid involvement in anything illegal</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
18. Because there is a drug testing policy where I work.
19. Because I won’t have to leave social functions or other people’s houses.
20. Because I am concerned that smoking cannabis will shorten my life.
21. Because I believe that my mental illness was partly the result of using cannabis
22. Because cannabis makes me feel nauseous or panicky
23. Because I can’t afford to smoke
24. Because using cannabis isn’t enjoyable any more
25. Because I am worried about the impact of cannabis on my mental health
26. Because cannabis prevents me from being able to do other things/think clearly
27. Because of the reward scheme (BASELINE ONLY)

Chung et al.

<table>
<thead>
<tr>
<th>“Thinking about the next 30 days...”</th>
<th>not at all</th>
<th>very motivated</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. “How motivated are you to abstain (not use at all) from cannabis,”</td>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
<tr>
<td>2. “How confident are you that you will be able to abstain (not use at all) from cannabis,”</td>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
<tr>
<td>3. “How difficult would or will it be to abstain (not use at all) from cannabis,”</td>
<td>1 2 3 4 5 6 7 8 9 10</td>
<td></td>
</tr>
</tbody>
</table>

Readiness Ruler

4. Which of the following statements best describes how you feel right now? (circle one letter)
   a. Never think about my cannabis use
   b. Sometimes I think about using cannabis less
   c. I have decided to use cannabis less
   d. I am already trying to cut back on my cannabis use
Appendix 4.4 - Further analysis methods: post-hoc diagnostics of model assumptions and outliers for the primary analysis

Model assumptions of linear regression were conducted for all analyses. Here they are described for the primary analysis. Heteroscedasticity was tested for using the Breusch-Pagan test and by plotting residuals against fitted values. To check that parametric assumptions were met, residuals were plotted in qq and pp plots as well of kernel density estimates to test for normality. Collinearity between predictors was tested for using variance inflation factor tests (James et al., 2017). Outliers were identified using scatterplots, as well as Cook’s distance and dfbeta metrics. Data points were identified as potentially influential using standard thresholds (Fox, 1991; Belsley, Kuh, & Welsch, 2013).
Appendices for chapter 6 (appendix 6)

Appendix 6.1 – Cognitive-behavioural measures by CIRCLE trial group at baseline

<table>
<thead>
<tr>
<th>Cognitive-behavioural measures</th>
<th>CM group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Std dev</td>
</tr>
<tr>
<td>Intrinsic Motivation Baseline (max value = 4) (mean)</td>
<td>2.07</td>
<td>0.81</td>
</tr>
<tr>
<td>Extrinsic Motivation Baseline (max value = 4) (mean)</td>
<td>1.82</td>
<td>0.91</td>
</tr>
<tr>
<td>Self-concept (mean)</td>
<td>2.67</td>
<td>1.05</td>
</tr>
<tr>
<td>Legal (mean)</td>
<td>1.75</td>
<td>1.12</td>
</tr>
<tr>
<td>Social (mean)</td>
<td>1.88</td>
<td>0.95</td>
</tr>
<tr>
<td>Health (mean)</td>
<td>1.47</td>
<td>1.04</td>
</tr>
<tr>
<td>Mental health concerns (mean)</td>
<td>2.56</td>
<td>1.25</td>
</tr>
<tr>
<td>Negative use expectancies (mean)</td>
<td>1.95</td>
<td>1.06</td>
</tr>
<tr>
<td>Financial (mean)</td>
<td>2.23</td>
<td>1.33</td>
</tr>
<tr>
<td>Readiness-to-change (max value = 5) (mean)</td>
<td>3.57</td>
<td>1.31</td>
</tr>
<tr>
<td>Overall motivation at baseline (max value = 10) (mean)</td>
<td>6.69</td>
<td>2.52</td>
</tr>
<tr>
<td>Confidence in quitting at baseline (max value = 10) (mean)</td>
<td>6.37</td>
<td>2.53</td>
</tr>
<tr>
<td>Perceived difficulty of quitting at baseline (max value = 10) (mean)</td>
<td>6.50</td>
<td>2.77</td>
</tr>
<tr>
<td>Frequency of urges at baseline (max value = 6) (mean)</td>
<td>3.67</td>
<td>1.44</td>
</tr>
<tr>
<td>Strength of urges at baseline (max value = 6) (mean)</td>
<td>3.56</td>
<td>1.35</td>
</tr>
<tr>
<td>Exposure to peers using cannabis at baseline (max value = 10) (mean)</td>
<td>6.41</td>
<td>3.18</td>
</tr>
</tbody>
</table>

Appendix 6.2 – Confirmatory Factor Analysis

Appendix 6.2.1 – Methods

Below (Figure Appendix 2) is the factor structure tested in the confirmatory factor analysis reported in chapter 6.

Questionnaire items (rectangles) are linked to their hypothesised latent variable (ovals): self-concept, legal, social pressure, and physical health. An error term has been added for each observed item. Covariance terms were included between all latent variables.
Figure Appendix 2: Hypothesised confirmatory factor analysis model with covariance terms between latent variables. $\varepsilon$ = error term

Appendix 6.2.2 – Confirmatory Factor Analysis - Results

Table Appendix 1: Results from confirmatory factor analysis, including unstandardised coefficients
<table>
<thead>
<tr>
<th>Item</th>
<th>Self</th>
<th>Social</th>
<th>Health</th>
<th>Legal</th>
<th>Covariance between factors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Item 15</td>
<td>0.99</td>
<td>0.11</td>
<td>9.00</td>
<td>0.00</td>
<td>0.77</td>
</tr>
<tr>
<td>Social</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Item 4 (constrained)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Item 5</td>
<td>0.92</td>
<td>0.10</td>
<td>9.04</td>
<td>0.00</td>
<td>0.72</td>
</tr>
<tr>
<td>Item 7</td>
<td>0.75</td>
<td>0.10</td>
<td>7.34</td>
<td>0.00</td>
<td>0.55</td>
</tr>
<tr>
<td>Item 8</td>
<td>0.67</td>
<td>0.10</td>
<td>6.80</td>
<td>0.00</td>
<td>0.48</td>
</tr>
<tr>
<td>Item 10</td>
<td>0.98</td>
<td>0.10</td>
<td>9.83</td>
<td>0.00</td>
<td>0.79</td>
</tr>
<tr>
<td>Item 12</td>
<td>0.38</td>
<td>0.09</td>
<td>4.13</td>
<td>0.00</td>
<td>0.20</td>
</tr>
<tr>
<td>Item 19</td>
<td>0.46</td>
<td>0.07</td>
<td>6.73</td>
<td>0.00</td>
<td>0.32</td>
</tr>
<tr>
<td>Health</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Item 9 (constrained)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Item 11</td>
<td>0.65</td>
<td>0.11</td>
<td>5.69</td>
<td>0.00</td>
<td>0.43</td>
</tr>
<tr>
<td>Item 14</td>
<td>0.81</td>
<td>0.14</td>
<td>5.73</td>
<td>0.00</td>
<td>0.53</td>
</tr>
<tr>
<td>Item 20</td>
<td>0.53</td>
<td>0.09</td>
<td>5.86</td>
<td>0.00</td>
<td>0.36</td>
</tr>
<tr>
<td>Legal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Item 13 (constrained)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Item 16</td>
<td>1.30</td>
<td>0.10</td>
<td>12.64</td>
<td>0.00</td>
<td>1.10</td>
</tr>
<tr>
<td>Item 17</td>
<td>1.18</td>
<td>0.10</td>
<td>11.93</td>
<td>0.00</td>
<td>0.99</td>
</tr>
<tr>
<td>Item 18</td>
<td>-0.02</td>
<td>0.01</td>
<td>-1.48</td>
<td>0.14</td>
<td>-0.05</td>
</tr>
<tr>
<td>Covariance between factors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self and social</td>
<td>0.41</td>
<td>0.07</td>
<td>5.59</td>
<td>0.00</td>
<td>0.27</td>
</tr>
<tr>
<td>Self and health</td>
<td>0.40</td>
<td>0.09</td>
<td>4.52</td>
<td>0.00</td>
<td>0.22</td>
</tr>
<tr>
<td>Self and legal</td>
<td>0.40</td>
<td>0.07</td>
<td>5.83</td>
<td>0.00</td>
<td>0.26</td>
</tr>
<tr>
<td>Social and health</td>
<td>0.46</td>
<td>0.09</td>
<td>5.19</td>
<td>0.00</td>
<td>0.29</td>
</tr>
<tr>
<td>Social and legal</td>
<td>0.62</td>
<td>0.09</td>
<td>6.93</td>
<td>0.00</td>
<td>0.44</td>
</tr>
<tr>
<td>Health and legal</td>
<td>0.45</td>
<td>0.09</td>
<td>5.09</td>
<td>0.00</td>
<td>0.28</td>
</tr>
</tbody>
</table>
Appendix 6.3 – Exploratory Factor Analysis

Appendix 6.3.1 – Tests of model assumptions

Prior to conducting the exploratory factor analysis, model assumptions were tested to confirm the viability of the approach for the dataset. Spearman’s rho correlation analyses between questionnaire items indicated that there were many associations over 0.3 (Tabachnick & Fidell, 2007), suggesting that exploratory factor analysis would be suitable in this group. The diagonals of the anti-image correlation matrix were all over 0.5 (Field, 2000). Two measures of sampling adequacy were performed: Bartlett’s test of sphericity ($\chi^2 (190) = 2083.54, p < .01$) and a Kaiser-Meyer-Olkin test (0.85). These indicated an exploratory factor analysis would be appropriate. However, item 18 individually had a MSA score of 0.54, which is below a commonly used threshold for possible exclusion of 0.6 (Cerny & Kaiser, 1977; Kaiser, 1977) or 0.7 (Norman & Streiner, 2001). Item 18 asked participants if they wanted to quit cannabis because of drug testing at work, which had low levels of endorsement (mean = 0.05) and was weakly correlated with the other items. It also had an anti-image correlation diagonal of 0.54, which was significantly lower than the other variables and only just above the threshold of exclusion. However, it was initially left in the analysis.

Table Appendix 2 - Correlations between items (spearman’s rho)

<table>
<thead>
<tr>
<th></th>
<th>item 1</th>
<th>item 2</th>
<th>item 3</th>
<th>item 4</th>
<th>item 5</th>
<th>item 6</th>
<th>item 7</th>
<th>item 8</th>
<th>item 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>item 2</td>
<td></td>
<td>0.51*</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>item 3</td>
<td>0.42*</td>
<td></td>
<td>0.54*</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>item 4</td>
<td>0.23*</td>
<td>0.18*</td>
<td>0.27*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>item 5</td>
<td>0.14*</td>
<td>0.14*</td>
<td>0.18*</td>
<td>0.39*</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>item 6</td>
<td>0.29*</td>
<td>0.40*</td>
<td>0.41*</td>
<td>0.17*</td>
<td>0.23*</td>
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</tr>
<tr>
<td>item 7</td>
<td>0.10</td>
<td>0.02</td>
<td>0.12*</td>
<td>0.25*</td>
<td>0.37*</td>
<td>0.30*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>item 8</td>
<td>0.01</td>
<td>-0.05</td>
<td>0.06</td>
<td>0.25*</td>
<td>0.28*</td>
<td>0.10</td>
<td>0.34*</td>
<td></td>
<td></td>
</tr>
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<td>item 9</td>
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<td>0.33*</td>
<td>0.33*</td>
<td>0.20*</td>
<td>0.12*</td>
<td>0.39*</td>
<td>0.21*</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td></td>
<td>item 10</td>
<td>item 11</td>
<td>item 12</td>
<td>item 13</td>
<td>item 14</td>
<td>item 15</td>
<td>item 16</td>
<td>item 17</td>
<td>item 18</td>
</tr>
<tr>
<td>-----</td>
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<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
</tr>
<tr>
<td>item 10</td>
<td>0.13*</td>
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* p<=0.05s
Appendix 6.3.2 – Exploratory Factor Analysis results

Presented here are the results of the Exploratory Factor Analysis. Initially the unrotated solution is presented (table Appendix 3). The exploratory factor analysis rotation matrix is presented (table Appendix 4). Figure Appendix 3 shows the results of the parallel analysis. The correlation matrix between the final factor solution is shown in figure table Appendix 5. The variance of each factor and proportion of variance explained by each factor in the final factor solution is presented in table Appendix 6.

Table Appendix 3 – Unrotated factor solution

<table>
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<tr>
<th>Item number</th>
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Table Appendix 4 - factor rotation matrix

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<th>Factor3</th>
<th>Factor4</th>
<th>Factor5</th>
</tr>
</thead>
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</tr>
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<td>0.6065</td>
<td>0.0604</td>
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<tr>
<td>Factor5</td>
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<td>0.0501</td>
<td>0.9742</td>
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</table>

Table Appendix 5 - correlation matrix between factors

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<th>Factor3</th>
<th>Factor4</th>
<th>Factor5</th>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Factor3 Social</td>
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<td>0.19</td>
<td></td>
<td></td>
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<tr>
<td>Factor4 Health</td>
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<tr>
<td>Factor5 Drug testing</td>
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<td>-0.13</td>
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</table>

Table Appendix 6 - variance and proportion of variance explained by each factor.

<table>
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<tr>
<th>Factor</th>
<th>Variance</th>
<th>Proportion</th>
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</thead>
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</tr>
<tr>
<td>Factor2 – Self</td>
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</tr>
<tr>
<td>Factor4 – Health</td>
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</tr>
<tr>
<td>Factor5 – Drug testing</td>
<td>1.14345</td>
<td>0.0572</td>
</tr>
</tbody>
</table>
Appendix 6.4 – Results: post-hoc diagnostics for the primary quantitative analysis

Once the primary analysis was performed, post-analysis diagnostic tests were performed to check that the model assumptions of linear regression were met. Described here are the post-hoc diagnostic tests for the adjusted linear regression model for the primary analysis.

Plots of the residuals against fitted values showed no evidence of heteroscedasticity. The Breusch-Pagan / Cook-Weisberg test for heteroscedasticity (p=0.91) and a Cameron & Trivedi’s decomposition of IM-test (p=0.38) indicted that homoscedasticity assumptions were met. Residuals were plotted using normal qq and pp plots and a plot of kernel density estimates, which overall indicate that normality assumptions were met (figures xx4).

Variance inflation factors were calculated and indicated no collinearity between variables (mean vif = 1.02). Model specification was tested using Ramsey’s RESET test (p=0.73) and the link test (p=0.78), which both indicated no potential issues. Outliers were checked for using Cook’s d and dfbeta values. Data points were identified as potentially influential using
standard thresholds (Fox, 1991; Belsley, Kuh, & Welsch, 2013). Although some influential points were identified, added-variable plots and scatter plots of the individual predictor variables against the outcome variable together suggested that removing influential points likely would not improve the model. No data points were removed.
Figure Appendix 4 – pp plot

Figure Appendix 5 – qq plot

Figure Appendix 6 – Kernel density plot of residuals

Kernel density estimate

Density

Residuals

Kernel density estimate
Normal density

kernel = epanechnikov, bandwidth = 0.2457
Appendices for chapter 7 (appendix 7)

Appendix 7.1 – Qualitative study materials

Appendix 7.1.1 – Protocol as submitted for ethics approval

Presented here are the sections of the CIRCLE protocol v.7 (dated 16th August 2016) related to the qualitative study presented in this thesis. It describes data collection from three groups of participants regarding three research topics: CIRCLE experimental participants, CIRCLE control participants, and clinicians involved in CIRCLE. In this thesis, only data collected from CIRCLE experimental participants are presented.

Qualitative data collection

Previous versions of the CIRCLE protocol (v.1-5) included collection of data from all key stakeholders, including participants, clinicians, and carers, in order to investigate the usefulness and acceptability of the contingency management (CM) intervention and to explore its possible mechanism. This qualitative data collection received ethics approval and began alongside the pilot study data collection. A sufficient sample for analysis and publication was not obtained at this stage, but we have reviewed the data obtained and further developed our data collection tools and methods to allow us to realise more fully the qualitative study objectives. We have therefore revised our materials to collect more in-depth data from a larger sample of the participants and clinicians. We will continue to collect qualitative data from participants and clinicians, but not carers. We had limited success during the pilot with collecting data from carers, partly due to few participants consenting to us contacting their family and carers, and secondly because many carers felt they did not know enough about what the study had involved. The qualitative data that we now collect will address the following questions:

1. What is the feasibility of implementing a CM intervention for cannabis use in psychosis in NHS settings? We will investigate views of the procedural aspects of the intervention, its acceptability and the barriers and facilitators to its implementation. Data to address this question will be from Early Intervention in Psychosis (EIP) teams participating in CIRCLE and participants in the experimental arm of CIRCLE.
2. Do CM interventions encourage long-term abstinence? CM is criticised as failing to motivate patients to abstain beyond the period in which incentives are offered. We will explore service user views of the impact of CM on cannabis use since the end of the intervention. Data for this topic will be collected from participants in both the experimental and control arms of CIRCLE.

3. Are psychoeducation (PE) treatments beneficial to service users? Psychosocial interventions, such as PE, are a mainstay for treatment of substance misuse (NICE, 2007). However, there is little qualitative research exploring subjective service user experiences of these interventions. (Childs et al, 2011; Lobban et al 2010). We will explore participants’ views about the strengths and weaknesses of the CIRCLE PE package, including its impact on behaviour and attitudes around cannabis use following completion of the package. Data will be collected from participants in the control arm of CIRCLE.

Methods:

Setting:

Qualitative interviews will take place in EIP services participating in CIRCLE. EIP teams will be selected from across a range of research centres; thereby allowing us to consider how the context and delivery of the intervention may vary between geographical regions and impact trial outcomes, as well as affect implementation of CM interventions in EIP services. We will aim to include teams based in a range of rural and urban areas, with a mix of gender, age, ethnicity, job role and years of experience working in EIP settings.

Sampling:

Qualitative data will be collected through interviews with 3 groups:

• Clinical staff from EIP services that took part in CIRCLE: Data will be collected through focus groups with 6 EIP teams who have delivered or observed the CM intervention, with purposive sampling used to represent a range of professional and demographic characteristics. Each focus group will comprise of approximately 8-10 participants and will be conducted by the researcher within the EIP services. They would be expected to last approximately one hour. Separate one to one interviews will be performed with the team managers or consultants of included EIP teams, with the aim of interviewing 10 participants in one-to-one interviews. These interviews would aim to gauge a more detailed perspective of implementation issues from a service level and an overview of how it was perceived by the teams.

• Experimental arm participants: Views of participants in the CIRCLE experimental group will be explored regarding two topics: the procedural aspects and the acceptability of the CM intervention, which will be used to assess the feasibility of and acceptability implementing CM in NHS settings (question 1). Secondly, the cognitive-behavioural impact of the CM intervention (question 2). Data will be collected from 15-20 participants through one to one, semi-structured interviews, with the possibility of further sampling to achieve saturation. Purposive sampling will be used to include participants with varying degrees of education, work experience, and living circumstances, as well as to include a mix of those who quit cannabis use during the CM period and those who did not. Participants will be
recruited after they have finished the CM intervention and prior to the 18 month follow up. Participants who did not attend any CM sessions will be excluded.

- Control arm participants: As above, data will be collected from 15-20 CIRCLE control group participants through interviews, with the possibility of further sampling if needed. Participants will be invited to participate following the 3 month follow up assessment, and before the 18 month follow up. To explore the views of participants with different experiences of cannabis smoking and abstinence over the study period, a mix of participants based on their smoking status at baseline and 3 month follow-up will be included.

Interviews:

Focus groups and one to one interviews will be conducted by a member of the CIRCLE research team. Interviewers will be guided by semi-structured interview schedules. Memory aids, including a poster of the CIRCLE study design and a copy of the psycho-education handout, will be provided during interviews and focus groups. All interviews and focus groups will be digitally recorded and are expected to last approximately 45-60 minutes. CIRCLE participants will be able to take breaks as required, and informed that the interview can be split over 2 sessions if preferable. Participants will be thanked for their time with a voucher worth £20.

- Focus groups and interviews with EIP staff: Staff attitudes to CM after experiencing it, their experiences of contextual, practical and attitudinal factors which impede or facilitate its implementation, and their views about sustaining the intervention in the long term will be explored. We will also ask about any previous experience of using or delivering a CM intervention, and issue a short questionnaire to obtain demographic details. We will aim for each focus group to have a mixture of job roles and levels of experience of working within the service. Interviews with team managers will explore attitudes and knowledge of the intervention, and ask for an overview of how it was received by the team.

- Interviews with experimental participants: Since experimental participants received both CM and PE, service users’ views will be sought on the benefits and limitations of each, as well as the impact of receiving CM in combination with PE. Subjective experiences of the CM and PE will be explored, including how attitudes towards the treatments changed over time. Perceived changes in cognitive, behavioural, and social factors related to cannabis use will be discussed, including changes to motivation to abstain, social/family support, and cannabis expectancies. Focus will be given to changes both during and since treatment. Experiences of other support offered within mental health services for cannabis use and how this compares will also be examined.

- Interviews with control participants: Interviews will be similar to those for experimental participants. Interviews will focus on the impact of PE on perceived changes in cognitive, behavioural, and social factors related to cannabis use, as well as knowledge regarding cannabis and mental health. Its impact both during and since treatment will be explored.
Analysis

Interviews and focus groups will be digitally recorded and transcribed verbatim. Data will be analysed using thematic analysis, a systematic method for identifying patterns across the data set by organising them into a thematic framework (Braun & Clarke, 2006), which will be performed using the NVivo 11. Thematic analysis will allow exploration of questions relating directly to our research questions and themes arising more inductively from the data. The analysis will be a collaborative process conducted by members of the CIRCLE research team, to enhance the validity of the analysis. Data will contribute both to the study report and to work submitted for PhD or MSc degrees by members of the CIRCLE research team.
Appendix 7.1.2 – Information sheet, consent form, and interview schedule for qualitative studies

Presented here is the information sheet, consent form, and interview schedule used in the qualitative data collection presented in this thesis

Randomised controlled trial of the clinical and cost-effectiveness of a contingency management intervention for reduction of cannabis use and of relapse in early psychosis (THE CIRCLE STUDY)

Service User Information Sheet for Qualitative interview (version 1)

You are being invited to take part in a research interview. Before you decide whether or not to take part it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information.

What is the purpose of the study? For the CIRCLE trial we tested a voucher reward scheme for helping Early Intervention service users to stop using cannabis. We are now interviewing service users and clinicians whom took part in CIRCLE to explore their thoughts and opinions about the trial. We are interested in how beneficial participants found the voucher scheme and psychoeducation package, and what could be improved about it. Our aim is to explore the different experiences of the treatment offered during CIRCLE, to understand better how such programmes could potentially be used to help people quit or reduce using cannabis.

Why have I been chosen? We are asking you to take part in this interview because you took part in the CIRCLE trial, and we would like to hear your thoughts and opinions about the trial.

Do I have to take part? No, it is completely up to you to decide whether or not to take part. If you would like more information, please contact us and we will be happy to provide it and answer any questions you may have. Additionally, you can discuss any issues or concerns you may have with your care coordinator or other members of the Early Intervention Team. If you decide to take part you are still free to withdraw at any time without giving a reason.

What does this study involve? If you would like to take part, a CIRCLE researcher will contact you to arrange the interview. The interview will be between you and the researcher and will take about an hour. The researcher will arrange the location with you, which will normally be in the Early Intervention service you use or other convenient location. At the interview appointment, you will first have an opportunity to ask any questions you may have, and then you will be asked to sign a consent form indicating your agreement to take part. During the interview, the researcher will ask you about your views of the voucher scheme and the psychoeducation package. They will discuss with you how beneficial the scheme was in terms of helping you quit cannabis, as well as your views of cannabis and how they may have changed, and your expectations about using cannabis in the future. The interview will be an opportunity to express your views of the voucher scheme and psychoeducation, and to feedback to the study team what you thought was positive or negative about it.

What are the possible benefits of taking part? The main potential benefit is that you will be contributing to research investigating how helpful voucher schemes are for people wanting
to reduce or stop using cannabis. Your feedback will help inform the development of future similar schemes, and your participation is very valuable to this study. You will also be offered £20 as a gift for taking part.

Will my taking part in this study be kept confidential? Yes, any information you provide will be kept strictly confidential and anonymised. All the data we collect will be stored securely in accordance with the Data Protection Act. The only situation in which we would not be able to maintain confidentiality is if you told a member of the research team something that made us believe that there was a serious risk of your harming yourself or someone else; in this case we would discuss our concerns with staff in the Early Intervention Service, who would decide whether any further action to reduce these risks was required.

Your identity will remain confidential and will not be revealed in any reports or publications arising from the study. You will be provided with a copy of your signed consent form agreeing to take part in the trial. The original will be stored securely and in accordance with the Data Protection Act by research staff at one of the research centres taking part in the trial. A second photocopy will be added to your NHS patient notes.

What will happen to the information collected during the interview? We will record what we discuss during the interview using a voice recorder. Voice recordings will be transcribed verbatim. Similar interviews will be conducted with other CIRCLE participants. The transcripts of those interviews will be analysed together to identify themes and issues experienced by people receiving the CIRCLE intervention. Those findings will be disseminated in a number of ways: presentations at conferences, publications in academic journals and relevant magazines, reports to funding bodies (see below), governments, and will be available on the internet.

Who has reviewed this study? Before any research of this kind can begin it needs to be approved by a research ethics committee. This study has been reviewed by the South East London Ethics Committee.

Who is sponsoring and funding the research study? The study is sponsored by University College London. It is funded by the National Institute of Health Research which is funded by the Department of Health. The study is led by Professor Sonia Johnson and is managed on a day-to-day basis by Luke Sheridan Rains. You can contact us at these addresses:

Prof. Sonia Johnson  
Division of Psychiatry  
University College London  
149 Tottenham Court Road  
London  
W1T 7NF  
s.johnson@ucl.ac.uk

Luke Sheridan Rains  
Division of Psychiatry  
University College London  
149 Tottenham Court Road  
London  
W1T 7NF  
Tel: 02035495973  
l.sheridanrains@ucl.ac.uk

Support provided during the study

If, for any reason, you feel negatively affected or become distressed through participation in the research, you will be offered immediate support from the research team. You can speak to the researcher about any concerns you may have regarding your participation in the study. If you or the researcher feels that additional support is required, the researcher will liaise with the clinical team and senior researcher on your behalf. For independent advice about participating in research or this study, please contact the Mental Health Research Network Patient and Public Involvement (PPI) section. This is a national organisation designed to support the involvement of service users and carers in research.

mhri@kcl.ac.uk  
(T) 020 7848 0644

What if I am unhappy with the way the research is conducted? You are welcome to contact us if you want to discuss any questions about the project. If you have concerns you
would prefer to discuss with an independent person, or wish to make a complaint, you can contact your local Patient Advice and Liaison Service (PALS). PALS will be able to offer help and to advise you if you want to make a complaint. To contact your local PALS please call the number from the list below which covers the drug service you attend:

Camden & Islington: 020 3317 3117
East London: 020 7655 4201
Coventry and Warwickshire: 024 7653 6804

Thank you for taking the time to read this information.
Consent form for CIRCLE participants receiving the qualitative interview

Version 1:

Study Title: Randomised controlled trial of the clinical and cost-effectiveness of a contingency management intervention for reduction of cannabis use and of relapse in early psychosis.

Principal Investigator: Professor Sonia Johnson, UCL

1. I have read and understood the information sheet V1 dated for the qualitative interview for the above study

2. I have had the opportunity to ask questions about the qualitative interview

3. I understand that my participation is voluntary and that I can withdraw from the interview at any time, without giving any reason.

4. I understand that I will be given a £20 gift in the form of a voucher for my participation in the interview.

5. I agree to take part in the qualitative interview.

Name of participant _____________________________________________________________

Date ____________________________

Signature ____________________________

Name of Researcher ____________________________________________________________

Date ____________________________

Signature ____________________________

CIRCLE: Consent form for qualitative study (participants), Version 1. 16th August 2016
INTERVIEW GUIDE – QUALITATIVE INTERVIEWS WITH PATIENTS RECEIVING CIRCLE INTERVENTION
VERSION 1 (16/08/2016)

Before we start, I wanted to let you know that anything you tell me will be kept confidential, so I will not be passing on any of your answers to your care team or family, and your answers will be stored without any identifying information about you.

You took part in a research study investigating a new type of treatment for helping people to quit using cannabis. It involved a combination of voucher rewards for reducing/stopping your cannabis use, and discussion and education about cannabis use. We are trying to find out about how people found participating in this programme, and so would like to ask you about your experience of the scheme.

*(Ask participant if they are happy for us to check their assessment data for demographic information and information about their cannabis use)*

*Briefly outline the CIRCLE study and show the participant the CIRCLE participant poster and psychoeducation material.*

1. I would like to begin by asking you about what you thought of the scheme overall?
   a. What did you think when you first heard about the programme?
   b. Probe for thoughts about the study and how these may have changed during treatment.

2. Why did you want to take part?
   a. Did you want to reduce or quit using cannabis?
   b. Probe for motivations to participating and motivations for behaviour change

3. Had you ever tried to quit cannabis before this study?
   a. Has anyone offered you support or advice about cannabis use in the past?
b. Was that something you were interested in at the time?

c. Discuss previous efforts, if any, to quit/reduce. And if none have been made, what interested them about CIRCLE?

4. Has your cannabis use changed since you started in the study?

a. (if stopped/reduced) Did you find anything difficult about quitting/reducing your use? Did you experience sleeplessness, anxiety, etc.

b. How about how you feel/think about cannabis? Probe for impact of psychoeducation and CM.

c. How do you feel about cannabis use in the future?

d. Probe for barriers to behavioural change and withdrawal symptoms/undesirable consequences of change, as well as positives.

5. How did you find the voucher reward sessions?

a. What did you like or dislike about them? (Probe for procedural issues, such as providing urine samples, being tested etc.)

b. Overall, did this scheme help you change your cannabis use? Were there any negative consequences? e.g. did you start using other drugs in the place of cannabis?

c. (if they dropped out) Why did you stop going? (probe for feelings of disappointment if they were failing)

d. Probe for positive/negative consequences arising from the scheme. e.g. did anything not so good happen as a result of this programme?

6. How did you feel when you (didn’t) passed?

a. Did you feel encouraged/discouraged?

b. Did you have any unexpected results? (unexpectedly passing/failing) If so, how did they make you feel? (Did they make you feel inclined to give up?)

c. Probe for positive and negative experiences of receiving/not receiving the rewards, and how this impacted motivation.

7. I would like to ask you about the psychoeducation sessions you did alongside the voucher scheme. What did you think of it overall?

a. What did you find helpful/unhelpful in this package?

b. Did you learn anything new about cannabis and mental health? (Probe: did anything surprise you?)

c. Was talking about the impact of cannabis on your life helpful?, for example on your finances or family relationships?
d. Was it helpful to discuss coping strategies? *E.g. alternative activities, mindfulness, refusal strategies, combating cravings.*

8. How did you find doing the psychoeducation sessions alongside the reward sessions?
   a. Would you be more likely to take part in psychoeducation sessions like these if they were offered by themselves?
   b. Do you think you got more out of the CM sessions because you were also receiving the PE sessions?
   c. *Look for evidence of additive effects or engagement with the PE being improved by the CM.*

9. Has how you spend your spare time or your lifestyle changed because of the study?
   a. Are there some friends/family you spend more time or less time with now?
   b. *Probe for evidence of social group/lifestyle changes accompanying cannabis use change – evidence of behavioural change supporting maintenance of reduced/abstinence from cannabis use.*

10. Do your friends or family know about this study, or about you quitting/reducing your cannabis use?
    a. Did they think it was a good idea?
    b. Did your family and friends influence your decision to take part in the study or influence your decisions to attend the weekly sessions?
    c. *Discuss what friends/family thought of the scheme and if they were encouraging/supportive or if they made it more difficult to quit/reduce use. Look for evidence of family/peer support network, and if this has changed since starting the CM.*

11. What did your care coordinator think of you taking part in the study?
    a. *Probe for evidence of encouragement to take part and additional support or better relationship from/with care team as a result of taking part*

12. Would you recommend this type of scheme to a friend?
    a. Can you think of any reasons why people may not want to do it?
    b. Do you think it would be more likely to benefit some people than others? If so, who and why?

13. Is there anything else you would like to feedback to us about the study?
Appendix 7.2 – The CIRCLE pilot qualitative study

Presented here are the results of the qualitative study conducted as part of the CIRCLE pilot phase. These results, along with the study materials, were used when developing the qualitative studies reported in this thesis.

Introduction

The pilot phase of the trial successfully recruited 62 participants and featured 11 EIP teams. Following the pilot study, a qualitative study was performed to explore the usefulness and acceptability of the intervention from the perspective of participants and of clinicians, and of potential mechanisms for change. There were four members of CIRCLE staff involved in the CIRCLE qualitative study: Luke Sheridan Rains, Jo Taylor, Kate Fullarton, Johanna Frerichs.

Methods

Sample:

Qualitative data collection was performed with 3 groups between March and August 2013: one to one interviews with participants in the intervention group, focus groups with clinicians in EIP teams participating in CIRCLE, carers of participants in the intervention group. Interviews were performed by members of the CIRCLE research team (JT and LSR).

Focus groups were performed with 5 EIP teams included in the pilot phase of the trial. Between 2 and 9 clinicians attended each focus group. Service user and carer data collection comprised one to one interviews performed by a member of the CIRCLE research team using a semi-structured interview schedule. Service user qualitative interviews were performed with 11 participants in the intervention group. Due to significant difficulties in recruiting carers, only one interview was performed with a carer of a participant in the intervention group. The main barrier to recruitment was identifying suitable candidates.
For most participants, discussing their cannabis use with family was a sensitive topic, and so few participants felt comfortable with researchers interviewing family about the trial.

**Interview schedules:**

Topic guides were refined in collaboration with the service user and carer steering groups. Focus groups with staff explored clinicians’ experiences of implementing CM schedules and any impediments encountered, the impact of the organisational context and culture on CM delivery, their views regarding the ethical and clinical implications of CM, and their perceptions of service users’ responses to the intervention. Interviews with service users considered their perception of the effects of being offered incentives, their views regarding ethical aspects of this, and suggestions for improvements. The carer interview explored perspectives on the intervention, including their views on use of voucher rewards and how these should be presented.

**Analysis:**

Interviews and focus groups were digitally recorded and transcribed by a professional transcription service (WayWithWords), and imported into the NVivo 9 package for data coding and analysis. A thematic approach was taken to analysing the data for trial participants and clinicians (Braun & Clarke, 2006). As we were only able to conduct one carer interview, their data were not thematically analysed but are summarised in this report. Clinician and trial participant data were analysed and are discussed here separately. The thematic analysis involved the following phases: each transcript was first reviewed by three members of the CIRCLE research team (KF, JF, and LSR) independently to familiarise themselves with the data and make initial notes. The following steps were then performed: 1) KF generated initial codes for all the data were and collated data relevant to each code. JF independently analysed a sub-set of the data (2 focus groups and 3 participant interviews). 2) KF and JF then independently organised the codes into potential themes,
and identified data relevant to those themes. 3) KF, JF, and LSR then reviewed the initial codings and themes each had generated, and whether the identified themes accurately represented the data. Any agreed recoding of data or redefining of themes would then be reviewed further until a consensus between KF and JF had been achieved. While no substantial points of difference were identified, some small changes were made following the initial analyses, and themes again reviewed. 4) Following this, themes were defined and organised by KF into a thematic ‘map’, which sorted themes into ‘main’ and ‘sub’ themes. This map was then reviewed with JF and LSR. 5) KF produced the final report of the results of the analysis.

Relevant conclusions drawn from the qualitative interview informed preparation of materials and changes to the study protocol ahead of the main trial. Topic guides elicited the service user perspective.

Results

Results from the qualitative interviews is presented by group:

EIS clinicians:

Most clinicians did not have a straightforwardly positive or negative view, with some reservations voiced. However, positive comments appeared to predominate, staff reporting that they felt it was acceptable and potentially useful. Staff reported that the scheme was 'taken quite well by clients', and particularly those in the CM group 'did enjoy it'. Two staff members reported that they felt both the Psycho-education and the CM were useful opportunities for their clients, and that 'motivated them' and 'they found helpful'. However, some staff felt there were important limitations to the scheme, particularly with regards to its lasting impact post-treatment. We will discuss in turn the seven main themes emerging from interviews:
1) Opinions of the interventions overall:

Initial impressions: Overall, clinicians were generally positive about both the CM and PE, but some were concerned it would not have a long-term impact.

Positive effects: Staff from the range of focus groups reported positive effects of the scheme for their clients, particularly those assigned to the intervention arm of the study. These positive outcomes included:

- Increased engagement with SU’s. Some clinicians reported that they were seeing their clients more often and found it easier to contact them.
- Encouraging service users to quit smoking cannabis, at least during the period of the scheme. One staff member said: ‘the people who were on the contingency management did remain abstinent you know, during the course of the trial’.
- Even if they didn’t quit, many service users reduced their use. One clinician said ‘[my client’s cannabis use] is not as bad as it was before, [he only] takes a little bit now’.
- Encouraging service users to make positive changes because of reducing cannabis use. One clinicians said of their client: ‘It kind of helped him...he started recognising the changes in himself...he became more kind of alert, concentration wise...and he was doing a bit more...he was much better off, he was eating better’.

Limitations: There were two main limitations discussed by clinicians:

- Difficulty recruiting service users to the trial: Also, some found clients did not engage with the intervention, particularly those in the control group. One clinician said he was not able to ‘engage any of my clients in the CIRCLE trial’ and felt that ‘said a lot as they were kind of young 18 years olds, using quite a lot of cannabis...and there was interest but never able to kind of just follow-up or see it
This staff member said the people he felt would most benefit from the scheme were 'just not interested' and felt that for participants to be interested they required insight into what happened' to them and 'to kind of make the link to cannabis' which he felt 'some people do and some don’t'. Staff felt that it was a difficult area to involve service users in and that service users needed to have their own motivation to be willing and 'ready' to engage.

- Post intervention relapse: A commonly held concern was that the scheme likely would not have a lasting effect on their clients, and that participants may go back to using once the scheme ended. One staff member said the CM was beneficial to her client, but when the trial finished he relapsed. She felt this was because 'he had been using for a long time in his life and any little stresses he gets, he goes back to it'.

*Ethical views:* Views on the ethics of CM were generally positive, with few reservations about whether it is proper to give financial rewards for abstinence. Many staff members saw no ethical problems and felt that if it worked then it should continue. However, a few clinicians did raise questions about whether people should receive rewards for something 'they shouldn't be doing' and asked 'what about the clients who don’t smoke in the first place, that is almost incentivising them to smoke, so they can stop'. However, many of those clinicians also felt that these concerns wouldn't stop them from engaging their clients in the scheme if it would help. Important questions were raised as to whether people will have a problem with public money being given to participants and one staff member felt that people's 'own motivation and moral compass, should be enough, perhaps?'. Another staff member felt that other SU’s could potentially be 'unhappy about cannabis users getting rewards', and queried whether CM should be used for something like cannabis use at all. Another clinician had been concerned that participants may exchange the vouchers for cash, but his clients had actually used the vouchers appropriately.
2) **Voucher scheme:**

Most staff members thought the voucher scheme was beneficial for their clients.

*Motivation:* All staff members reported that the voucher scheme and the monitoring of THC levels motivated their clients to some extent to stop/reduce their cannabis use. One staff member described the scheme as a ‘good incentive’ and reported that his client was ‘looking forward each week...in terms of seeing his...cannabis result’. Even in cases where participants did not stop smoking cannabis, staff felt that it had ‘created some kind of level of motivation...in terms of making decisions... about whether they are ready to stop or not’.

*Pre-existing motivation:* Two staff members reflected that clients who had engaged well with the scheme and had significantly reduced/quit their cannabis use may have quit anyway. One staff member said ‘people have to be really...contemplating giving up smoking to engage in something like that...if they are not interested in giving up then – however much money you throw at them – it’s just not going to make a difference’.

*Not enough incentive:* Staff from two teams felt that even the voucher scheme option was not enough incentive for their clients to stop using cannabis. One staff member said the scheme ‘didn’t seem to be enough of a hook’ and felt this was because ‘they had enough money anyway’.

*Complicated system:* Two staff members reported that a negative aspect of the voucher scheme was the ‘complicated’ reward schedule. One staff member said it was a ‘confusing mechanism that could possibly be simplified’ as he felt it was ‘confusing to try and explain to people’.

*Impact on relationship:* Three staff members raised concerns about the potentially negative impact the CM intervention could have on their relationship with their client, particularly if the client disagreed with the result. But no clinicians reporting any personal experience of
this happening. Most clinicians agreed that this could be resolved by a nominated person in the team delivering the intervention, such as a support worker or assistant psychologist.

One staff member shared that she had a participant who she suspected she had ‘watered down her sample to attempt to cheat’, and that this had led to the participant stopping coming for a while. She reflected that this could have been because the participant may have been ‘ashamed’ to see her. Another staff member said that he always has very good working relationships with his clients, and that delivering the intervention did not impact on those relationships at all.

_Urine testing:_ When staff were asked for their views on delivering the urinalysis aspect of the intervention, generally feedback was positive with no issues raised, staff found it relatively straightforward. One staff member felt that his client was particularly motivated by seeing his result each week.

3) **Psychoeducation**

There were mixed views about the psycho-education package, with some staff reporting that they thought it was less useful than the CM and more difficult to engage their clients with. Staff who were positive about the psycho-education package thought that some aspects of the package were particularly useful, but also reported some improvements that could be made.

**Positive Aspects:**

- Format of material: Staff felt the way in which the psych-education package was presented was very clear and ‘easy to use’. One member of staff commented that they thought it was a ‘good idea’ and felt it was a ‘different format and a way of helping them think about why they are using’.
Knowledge: 4 members of staff felt that the knowledge their clients gained from the psycho-education was useful. Staff felt it was ‘good for reflection’ and clients would be able to ‘look back and have space to think of their own cannabis use’.

Negative Aspects: Staff did have some criticisms of the psycho-education package.

- Repetitive: 4 staff members felt that the content of the psychoeducation was quite repetitive and could be improved in this regard.

Support with delivering intervention

Staff felt that they received a good level of support from the CIRCLE team, felt ‘adequately informed’ and had a good ‘understanding of the programme’ and recruitment process. One member of staff felt they had ‘support and teaching sessions done for the whole team, which was quite beneficial’. Another member of staff said she ‘always found it easy to ask questions’ to members of staff from the research team and felt ‘well supported’.

However, one staff member felt that different CIRCLE team members sometimes gave conflicting answers to the teams’ questions about the urinalysis. The solution he proposed was to have a dedicated member of the team working on the CIRCLE trial.

4) Impact on others

Clinicians delivering intervention: Two staff members highlighted the difficulties of finding time to do the intervention, which they say may impact motivation to engage with the trial. Another staff member said that it would be useful if support workers could help more with delivering the intervention. Some staff from one team spoke of how the perceived lack of support during the pilot meant that staff delivering the intervention felt quite frustrated. Other staff members reported no negative impact.

Families and friends: Two members of staff commented that families were supportive of their relatives taking part in the scheme. One staff member spoke of how one of his clients
was using his vouchers to ‘take his mum to Tesco and buy food’, he reports his client’s mum was ‘pleased’ with him talking part in the intervention and ‘they have seen the changes throughout the trial’.

5) Continuing intervention post-scheme

Staff were generally positive about continuing the CM intervention post-scheme if it was found to be effective. For some though, this view tended to focus on psychoeducation rather than the CM, as many staff members felt the CM intervention was not sustainable in a routine EIP setting. The majority of staff felt that the psycho-education would be a ‘helpful’ and a ‘useful tool’ to continue in clients’ normal sessions. A member of staff suggested that she would be keen to suggest ‘doing some kind of group session’ of psycho-education.

Summary and emerging recommendations for the main trial

Overall, staff impressions of the scheme were positive, believing that the contingency management (CM) and psychoeducation interventions were potentially useful interventions for cannabis use. However, many clinicians expressed mixed opinions about certain aspects of the scheme. Positive views of the CM intervention included that service users liked it and many reported their clients benefiting from it. Also, the scheme helped with engaging service users in both treatment for cannabis and with their EIP care team. The main concerns about the CM intervention was its sustainability past treatment cessation, and the potentially negative effect the intervention could have on their relationship with their client. There were also concerns about the details of the CIRCLE CM intervention specifically, which included that the reward schedule was too complicated and that the urine testing could be incorrect due to adulterated samples. The psychoeducation (PE) intervention was also viewed positively. Some clinicians requested to use the
psychoeducation package once the trial had ended. The main concern raised about the psychoeducation related to some factual inaccuracies.

Wherever feasible, concerns about the psychoeducation and CM interventions were addressed ahead of the main trial. Specifically, the main recommendations to emerge from the focus groups were:

- Make the CM reward scheme simpler.
- Prevent adulterated urine samples.
- Having a dedicated EIP team member to deliver the intervention rather than care coordinators, such as a support worker/ assistant psychologist. That person should ideally be interested in research.
- Consistency of researcher contacting EIP team about CIRCLE and clinician doing the intervention.
- Address inaccuracies in the information given in the PE.

We were able to follow all of these recommendations, but with some limits. The reward schedule was simplified and a temperature strip was added to the sample cups used in the urinalysis to prevent adulteration. Teams could identify a few dedicated members of staff, such as support workers or assistant psychologists, within the team to deliver the intervention if preferred. Materials were developed and provided to clinicians to make it easier for them to explain the trial to their clients when getting consent to being contacted by a researcher. Significant efforts were made by the research team to ensure consistency in the researcher contacting the EIP team, and where needed, supporting clinicians delivering the intervention. Ahead of the main trial, reference manuals and guidelines were developed for the research team, and separate ones for the clinicians delivering the interventions. These aimed to address clinicians’ commonly asked questions, and provide researchers with enough information to support the EIP teams effectively. This way we
improved the support EIP teams received, and ensured that information they were provided by the research team was consistent. Changes were made to the psychoeducation to make it less repetitive.

Service users:

During the analysis, 6 main themes emerged:

1) **Overall impact of the intervention**

All ten participants were generally positive about the scheme, with many saying they thought it was ‘good’ and ‘beneficial’. Sub-themes were:

*Helpful aspects of the intervention*: Participants often felt having their urinary THC level monitored was very helpful and motivating because they could see what was in their body each week, which was information they would not otherwise have access to. Some also felt that the urine testing meant that they could not cheat the process, and found it motivating to know that the clinician would know the result because they did not want to let them down. The scheme also made some participants feel proactive and more in control over their use. Finally, there was common agreement that the combination of learning through the psycho-education sessions and receiving the vouchers was particularly helpful.

*Improvements recommended for the scheme*: Participants often could not think of anything they would have changed to improve the scheme and said they were perfectly happy with the set up. However, some improvements were suggested. One participant felt that there were repeated questions across some of the Psycho-education modules, which he didn’t find useful. Other suggestions included increasing the voucher amount, more opportunity to meet with someone for support/positive conversation, extending the number of weeks the intervention runs for, and one participant suggested encouraging socialising between participants and including group outings.
**Lifestyle changes due to the intervention:** Several participants talked about changes they have made because of the intervention. These include eating more healthily, saving money or adopting a more active lifestyle by attending the gym, and changing the people they spend time with to avoid cannabis users.

**Recommending CIRCLE:** When asked, participants said they would definitely recommend the intervention to friends who would like to give up cannabis.

2) **Psycho-education**

**Helpful:** 7 participants found some or all the psycho-education helpful.

**Unhelpful:** 2 participants did not find the psycho-education helpful at all; one participant said he/she would not have chosen to do this part of the scheme by itself. Another participant said that he/she did not feel he had learnt anything from it.

**Improvements:** One participant suggested that an improvement to the psycho-education modules would be hearing more from people in the videos who had had similar experiences.

**Knowledge:** 7 participants felt that the knowledge they gained by doing the psych-education modules was valuable. The following sub-sub themes emerged:

- Previously unaware of dangers
- Weighing up pros and cons
- Insight into disadvantages/recognising harm
- Weekly reminder of why they are trying to stop

**Experiences of peers:** participants felt that the videos they were shown during the psycho-education were especially helpful. Hearing other people’s stories of having smoked cannabis and experiencing similar symptoms was reported to be very beneficial.
3) **Quitting cannabis**

*Challenges:* Six participants spoke about the challenges of trying to quit cannabis, including: cravings, having to stay strong to say no to friends who smoke, having to alter social networks, and breaking long-term habits. They said the scheme helped with these challenges.

*Changes:* Positive: Six participants explicitly spoke of the positive changes in their lives since reducing/ quitting cannabis, including that their minds felt clearer, they felt healthier, and their family relationships were better. Negative: Only three participants spoke of any negative changes that have occurred since reducing/ quitting cannabis, which focused on withdrawal symptoms and cravings/urges for cannabis.

*Motivation:* Eight participants said they found the scheme motivated them to stop/ cut down their cannabis use. A number of participants felt that their THC levels being monitored weekly was the most motivating aspect and others felt that receiving the vouchers was. Six participants explained that they had already decided to reduce their use/give up cannabis before the scheme commenced, but felt that the scheme made it easier for them to achieve this.

*Quit:* Four participants spoke of managing to cut down and then stop smoking cannabis completely during the scheme.

*Reduced use:* Not all participants quit smoking but all of them felt that they had successfully managed to cut down whilst taking part in the scheme. Four participants said they were managing to continue reducing their usage after the scheme had ended.

4) **Relationships**

When participants were asked if they discussed the scheme with staff from the EIS, care coordinator and or friends or family, the majority of participants had chosen not to talk
about it, but those who had felt it had either made no difference to relationships or had improved them.

_EIS staff_: Three participants felt that taking part in the scheme had a positive effect on their relationships with their care co-ordinators as they provided them with support/encouragement and someone to talk about their progress. Six participants felt it made no difference to their meetings, no positive or negative impact.

_Family and friends_: Six participants said that taking part in the scheme/discussing the scheme with their family had a positive impact on relationships with certain family members and that their family members that they chose to tell were very supportive of them taking part in the scheme. A number of participants didn’t want to discuss the scheme with their family and/or friends.

5) _Testing_

Failed tests: 5 participants shared that they felt disappointment when they failed the test but not about the voucher amount, more about letting themselves down. One participant said that failing the test one week was the motivation they needed to stop completely. One participant felt disappointed that he had failed because he had missed out on the increased voucher amount.

Urine test: Most participants did not have a problem with the experience of giving weekly urine samples and thought the process was fine. One participant mentioned that they found carrying a urine sample in the EIP was awkward.

6) _Vouchers_

Fairness: All participants felt that the voucher system was fair.
Feelings about vouchers: Participants’ feelings about receiving the vouchers were positive with participants saying they appreciated them, were motivated by them or found them really helpful.

Not about the money: Four participants said that the important thing for them was staying focused on the THC levels in their system, and receiving the vouchers was just an added bonus.

Uses for vouchers: Participants gave a range of uses for their vouchers, mainly: buying food, healthy food, presents for their family, enabling them to save money.

Voucher amount: Participants’ views on the voucher amount varied. Two participants felt that the initial voucher amounts and the ‘fail’ £5 voucher amount were too small. One participant linked the motivation with the amount of money and said that if there had been more money they would have been more motivated. 3 participants felt the voucher amount was just right and were satisfied with the process.

Summary and recommendations for the main trial

The CM and psychoeducation interventions were well received. All participants were generally positive about the scheme, describing it as helpful and beneficial, and all participants who were asked said they would recommend it to friends. Specifically, helpful aspects of the intervention included that the intervention gave them motivation to quit and that passing gave them a sense of accomplishment, the urinary THC concentration monitoring provided them with information about how much cannabis was in their system, which many found the most useful aspect of the scheme, and participants said they felt that the process was fair. The scheme also helped people feel more in control of their cannabis use, and some reported feeling good about proving that they had stopped using cannabis. When asked about the combination of CM and PE, all agreed that it was
important that the CM intervention was accompanied by the PE, as otherwise the scheme would provide no rationale for why quitting was worthwhile. Participants could not think of any areas of improvement, except perhaps that the voucher rewards could be higher or that the duration of the scheme could be longer. The issues raised by participants regarding repetitiousness in the psychoeducation and awkwardness associated with giving urine samples were carefully considered ahead of the main trial. Researchers looked for more discrete options for the urinalysis process, and changes were made to the psychoeducation to ensure information was accurate, and not repetitive.

**Carer interviews**

Only one interview was conducted with a carer of a participant in the trial, and so thematic analysis was not used. However, LSR summarised the key aspects to emerge from the interview.

**Overall:**

The carer thought that the scheme was ‘brilliant’ as it helped her son come off cannabis, which she believes is the basis of his mental and physical ‘problems’. She said her son looked forward to the meetings and avoided using cannabis in order to receive the reward.

‘*Being his mother and seeing what he’s been through and the harm that he’s done to himself all because of drugs, you know, it’s been absolutely horrendous and a nightmare... Anything that can help these...young men and women is definitely, yes, I don’t think enough is being done for it.*’

**Positive aspects of the scheme:**

The carer reported that she thought that one of the main benefits of the scheme was that it targeted cannabis, because there is currently very little to help people who use cannabis unlike other substances such as heroin. She said there is a need for cannabis treatment
programs, and that incentives or perhaps cannabis substitutes are ‘very helpful’ and ‘very
useful’. She said that she saw a ‘drastic’ change in her son when he took part in the
scheme.

**Negative aspects of the scheme:**

The carer said she had no concerns about the scheme overall. However, she thought that
her son would benefit from support over a longer period and suggested that perhaps the
scheme should be longer or have ‘follow-up’ sessions.

**Views of the urinalysis sessions:**

She had no concerns about the urinalysis sessions. She said that if her son didn’t pass a
session, he appeared to feel he had let himself down. The more sessions he attended, the
more he got from it, and the more he felt good about himself and what he had achieved.
She knew her son would occasionally smoke a small amount soon after a urinalysis session,
believing that it would not be detectable at the following session. However, she said he
would then feel guilty about trying to deceive her and the clinicians delivering the
intervention.

**Conclusions:**

Overall, the carer had positive views of CIRCLE. In terms of recommendations, they thought
the scheme could be longer or that there should be more support to help people using
cannabis post-treatment.
Appendix 7.3 – Initial conceptual model for the qualitative work in this thesis
Appendix 7.4 – Final conceptual model for the qualitative work in this thesis
Table Appendix 7 – concurrent associations between cognitive-behavioural measures and cannabis use status at baseline

<table>
<thead>
<tr>
<th>Variable at baseline</th>
<th>Logistic Regression results</th>
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</thead>
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<td>Self-concept concern</td>
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<td>Motivation to quit</td>
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<td>Confidence in being able to quit</td>
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<tr>
<td>Readiness-to-change</td>
<td>0.83</td>
</tr>
<tr>
<td>Exposure to cannabis use</td>
<td>1.08</td>
</tr>
<tr>
<td>Frequency of urges</td>
<td>2.11</td>
</tr>
<tr>
<td>Strength of urges</td>
<td>1.77</td>
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</tbody>
</table>

‡ - Odds ratio of testing positive for cannabis at baseline.

Table ... presents the association between cannabis use status at baseline (measured with urinalysis) and the different cognitive-behavioural variables at the same time point.

Amongst reasons for wanting to quit cannabis, mental health concerns (OR=0.75; 95% CI 0.60, 0.93; p=0.01) and negative use expectancies (OR=0.73; 95% CI 0.57, 0.93; p=0.01) were both significantly associated with cannabis use status. There was also very weak evidence of an association between self-concept reasons for wanting to quit and use status. Overall, these point to some dimensions of IM being the most important for understanding use status.
There was also strong evidence of an association with overall motivation (OR=0.73; 95% CI 0.64, 0.83; p<0.01), confidence in being able to quit (self-efficacy) (OR=0.68; 95% CI 0.59, 0.77; p<0.01), perceived difficulty in being able to quit (self-efficacy) (OR=1.12; 95% CI 1.02, 1.23; p=0.02), and urges (frequency OR=2.11; 95% CI 1.68, 2.67; p<0.01; strength: OR=1.77; 95% CI 1.43, 2.20; p<0.01). There was very weak evidence of an association between readiness-to-change and time spent with cannabis use using peers also being associated with cannabis use status.

Appendix 8.2 – Correlations between model candidate variables

Below is a table presenting correlation analysis results between candidate variables for the prediction model of abstinence by treatment end. Correlations were also conducted for the prediction model at 18 months but are not presented here.

Table Appendix 8 - correlations between candidate variables

<table>
<thead>
<tr>
<th></th>
<th>Frequency of urges</th>
<th>Strength of urges</th>
<th>Exposure to cannabis use</th>
<th>Confidence in being able to quit</th>
<th>Overall motivation to quit</th>
<th>Negative cannabis use expectancies</th>
<th>Mental health concerns</th>
<th>Self-concept</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strength of urges</td>
<td>0.70*</td>
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<tr>
<td>Exposure to cannabis use</td>
<td>0.17*</td>
<td>0.15*</td>
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<tr>
<td>Confidence in being</td>
<td>-0.41*</td>
<td>-0.31*</td>
<td>-0.10*</td>
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<tr>
<td></td>
<td>able to quit</td>
<td>Overall motivation to quit</td>
<td>Negative cannabis use expectancies</td>
<td>Mental health concerns</td>
<td>Self-concept concern</td>
<td>Physical health concerns</td>
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<tr>
<td></td>
<td>-0.35*</td>
<td>-0.24*</td>
<td>0.01</td>
<td>0.64*</td>
<td>-0.17*</td>
<td>-0.04</td>
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<td>&lt;0.01</td>
<td>0.21*</td>
<td>0.33*</td>
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<td>0.12*</td>
<td>0.23*</td>
<td>0.55*</td>
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* statistically significant at p=0.05

**Appendix 8.3 – Lowess graph**

Below is the lowess graph, indicating good linearity in the association between the outcome variable (probability of testing positive for cannabis use at 3-month follow-up) and the baseline predictor variables in the final model presented in chapter 8. A lowess
graph was also generated for the model predicting cannabis use at 18 months, which also indicated linearity.

Figure Appendix 7 – lowess graph for the prediction model at 3 months