A Systematic Review of Psychological Treatment for Methamphetamine Use and Associated Mental Health Symptom Outcomes

Alexandra M. Stuart (BA. Psych Hons)

Empirical thesis submitted in partial fulfillment of the requirements for the degree of

Master of Clinical Psychology

University of Newcastle

December 2017

Declaration

Statement of Originality

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university of other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. I give consent to this copy of my thesis, when deposited in the University Library*, being made available for loan and photocopying subjects to the provisions of the Copyright Act 1968.

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Acknowledgement of Authorship and Collaboration

I hereby certify that the work embodied in this thesis contains a published paper of which I am first author (48). I have included as part of this thesis a statement clearly outlining the extent of collaboration, with whom and under what auspices.

I hereby certify that the work embodied in this thesis has been done in collaboration with other researchers. Alexandra Stuart (AS) is the guarantor of the review. AS, Amanda Baker (AB), Alexandra Denham (AMJD), Kristen McCarter (KM), Jenny Bowman (JB) and Adrian Dunlop (AD) assisted in writing the protocol. AS performed the preliminary searches, and performed data extraction, conducted quality assessments and drafted the systematic review paper. AMJD screened references and cross-checked data extraction and performed independent quality ratings. AS developed the search strategy with the assistance of a research librarian. AB provided expertise on psychological treatment for MA use. Adrian Dunlop (AD) provided expertise on pharmacotherapy. JB provided expertise on the process of systematic reviews. All other authors contributed to the conception and design of this systematic review and assisted AS and AMJD to resolve any discrepancies in relation to data

extraction, study inclusion and quality ratings. Christopher Oldmeadow (CO) and Alix Hall (AH) assisted in conducting the meta-analysis. AS, AB, AD, AMJD, JB, and Nicole Lee (NL) read, provided feedback and approved the protocol manuscript and offered critical revisions for the review manuscript.

_____	30/11/2017
Alexandra M. Stuart	Date
_____	29/11/2017
Professor Amanda Baker	Date
_____	29/11/2017
Professor Jenny Bowman	Date
_____	29/11/2017
Conjoint Professor Adrian Dunlop	Date

Acknowledgements

Thank you to my wonderful family, friends and partner Jamie for their endless support, patience, and love throughout a challenging time. A special thank you to Jamie for being my consistent motivator and biggest support.

Thank you to my supervisors Professor Amanda Baker, Professor Jenny Bowman, and Conjoint Professor Adrian Dunlop. A special thank you to my primary supervisor Amanda. I cannot thank you enough for your incredible support throughout the entirety of my Master's thesis. Your positive reinforcement and encouragement really pushed me to keep going, so thank you! You have been a pillar of strength for me throughout the course and alleviated my stress through your brilliant sense of humour.

Thank you Jenny for your guidance in the rigorous methodology for my thesis and your useful feedback. Thank you Adrian for your wealth of knowledge and expertise and helpful guidance and feedback.

A huge thank you to the other review team members – Professor Nicole Lee, Alexandra Denham and Dr Kristen McCarter. Your assistance and skills were extremely helpful. I could not have done this without you!

A special acknowledgement for Debbie Booth, who assisted me many times with my search strategy and had all the patience in the world! I could not have created such a fine tuned strategy without you. Also, a big thank you to the statisticians Dr Chris Oldmeadow and Dr Alix Hall who assisted me to conduct my meta-analysis. Thank you for answering all my statistical questions!

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Structured Abstract

Scope. Methamphetamine (MA) use is an increasing public health concern. Globally and particularly in Australia there has been a recent shift in the form of MA used to the more potent crystalline form. Methamphetamine use is associated with specific symptoms of mental ill-health, including symptoms of anxiety, depression, hostility and psychosis. Systematic reviews conducted thus far have assessed pharmacological and psychological treatment for MA use, however none have focused specifically on MA use and associated mental health symptom outcomes. Thus, this review addressed a gap in the literature and may assist in tailoring clinical interventions for MA use and co-occurring mental health symptoms.

Purpose. The purpose of this research was to conduct a systematic review on the effectiveness of psychological treatment for MA use and associated mental health symptom outcomes. This review aimed to assess the quality of the literature in order to inform clinical intervention and alleviate the public health burden of MA use.

Methodology. A systematic review was conducted using the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines (Moher, Liberati, Tetzlaff, Altman, & Prisma Group, 2009). Types of studies included reported (1) MA use, (2) mental health symptom outcomes and/or disorders at baseline and post-treatment. Controlled trials were included and cohort studies, cross-sectional studies and one-arm trials were excluded. Participants included in the review were adults (over the age of 18) using MA alone or combined with other substance use. Psychological interventions included were Cognitive Behaviour Therapy (CBT), Contingency Management (CM), Motivational Interviewing (MI), and Acceptance and Commitment Therapy (ACT). Interventions were compared with active-controls and/or inactive controls and could be of any duration, frequency and intensity. The search strategy followed the Cochrane Handbook for Systematic

Reviews of Interventions (Higgins & Green, 2011), and searched MEDLINE, CINAHL, EMBASE, PsychINFO, Scopus and clinical trial registration databases. Titles and abstracts were screened against review inclusion and exclusion criteria and full texts were screened by two reviewers. Data was extracted by two reviewers and risk of bias assessment was conducted using the Cochrane Risk of Bias tool (Higgins et al. 2011). Quality assessment was completed using the GRADE tool (Higgins & Green, 2011). Where possible, meta-analyses were completed for primary outcomes and narrative syntheses were devised for secondary outcomes.

Results. Twelve studies met inclusion criteria. Meta-analyses found no significant differences in change in level of MA use or change in mental health symptom scores when comparing CBT to treatment as usual (TAU). However, when assessed separately by the intensity of the control group, there was a significant difference between CBT and minimal treatment on abstinence rates. Narrative syntheses suggested variable results across seven studies for changes in other drug use. There were high rates of treatment engagement for brief CBT interventions. A small number of studies reported changes in physical health, functioning, and Blood Borne Virus (BBV) risk reduction.

General Conclusions and Implications. The search identified a small number of interventions which assessed MA use and associated mental ill-health. Level of MA use and symptoms of mental ill-health tended to reduce among samples as a whole, regardless of intervention type. However, CBT may offer significant treatment benefits in terms of MA abstinence compared to minimal treatment conditions. Brief CBT interventions were associated with high rates of retention. Contingency Management appears promising and should be tested outside of the United States of America (USA) as findings may not be generalisable to other countries with different welfare options. There was an overall issue of heterogeneity and some risk of bias across studies, therefore an assumption was made about

the methodology of interventions as being consistent across studies. Future research with stronger methodological quality should be conducted with this client population to guide development of psychological interventions.

Keywords: Methamphetamine, Mental Health, Psychological Treatment, Psychological Interventions

Critical Literature Review

Methamphetamine (MA) is a psychostimulant that when used regularly can cause physical and mental health problems (Colfax et al., 2010; Hellem, Lundberg, & Renshaw, 2015). Over recent decades, MA has become an increasing public health concern, due to an increased number of hospital admissions associated with MA use and its potential influence on aggressive and violent behaviour (Degenhardt et al., 2016). People who use MA regularly are at an increased risk of developing psychological problems such as depression, anxiety, psychosis and hostility (Altice, Kamarulzaman, Soriano, Schechter, & Friedland, 2010; Baker et al., 2005; Baker et al., 2004; Kay-Lambkin, Baker, McKetin, & Lee, 2010). Use of MA is also associated with significant socioeconomic, legal and medical consequences (Karila et al., 2010). People who use MA may engage in more frequent sexual and injecting risk-taking behaviours than the general population, meaning that they are at an increased risk for contracting a blood borne virus (BBV) such as human immunodeficiency virus (HIV) or Hepatitis C (Carrico et al., 2015; Colfax et al., 2010). Although randomised controlled trials (RCTs) to date have investigated the efficacy of specific psychological interventions for MA use and associated mental health symptoms, no systematic reviews have investigated the efficacy of the evidence for MA use and mental health symptom outcomes.

Prevalence

Methamphetamine use is increasing in prevalence in Mexico, China, the United States, and parts of South Asia and the Middle East. It is estimated that there are 24 million users worldwide, and that amphetamine-type stimulants are the most prevalent type of psychostimulants used in the world (Chomchai & Chomchai, 2015). However, in Australia, MA use has decreased over the past five years, from 2.1% to 1.4% of the population using MA in the past 12 months (AIHW, 2017). There was a significant decrease in the proportion of the population using one or more forms of MA in a 6-month period between 2014 (47%)

and 2015 in which it fell to 38% (Sindicich & Burns, 2016). Although the rate of MA use has decreased marginally according to household surveys, this has been critiqued by Degenhardt et al. (2016) as being underestimated, as regular MA users are less likely to have completed the surveys. Despite the slight decrease in MA use, as previously mentioned, there has been a change in the form of MA used, which is associated with a range of physical and mental health harms.

Burden of Disease

Substance use contributes to a significant proportion of the global burden of disease and is a growing concern in many countries (Degenhardt & Hall, 2012; Lee & Rawson, 2008). Australians consider MA to be of more concern than any other drug (including alcohol) (Lee & Rawson, 2008). The annual number of overdose, drug and alcohol presentations and mental health presentations at NSW public hospital emergency departments related to MA use increased more than 7-fold between 2009 to 2014, increasing from 394 to 2963 (NSW Health, 2015). Admissions to acute mental health units has increased steadily for amphetamine related admissions per calendar quarter, and for amphetamine-related psychoses since 2009 (NSW Health, 2015). This suggests that MA is a significant public health concern not only in Australia, but also worldwide.

Methamphetamine Related Harms

Despite a decrease in use of MA in many countries, including Australia, harms continue to increase, partly driven by increases in purity and a change in preference from the powdered form to the highest purity crystalline form (Darke, Kaye, McKetin, & Duflou, 2008). The recent change in the form of MA used has been linked with more frequent use and associated MA-related harms, requiring treatment in drug and alcohol services, more hospitalisations, drug related crime and psychoses (Degenhardt et al., 2016). People are more

likely to use the crystal form of MA on a regular basis (32% using at least weekly), than the powder form of MA (5.6% used powder each week) (AIHW, 2017). Use of the powder form of MA has significantly decreased in the past three years, from 29% in 2013 to 20% in 2016 (AIHW, 2017). Use of crystal MA has increased from 22% to 50% in Australia from 2010 to 2013 and now up to 57% in 2016 (AIHW, 2013; Degenhardt, 2017). There has also been an increase in weekly use of crystal MA from 25% to 32% between 2013 and 2016 (AIHW, 2017). This shift in the form of MA used is concerning due to the comorbid mental health problems and public health burden associated with MA.

Methamphetamine-related harms could have increased due to the higher purity associated with crystal MA, resulting in higher doses of the drug and greater influences on behaviour (Lee & Rawson, 2008). Drug-related harms are also increased as people who use MA are more likely to be polysubstance users (AIHW, 2005; Black et al. 2008). Simultaneous use of alcohol and/or cannabis is common among people who use MA, and a selection of people who use MA historically and concurrently use heroin and other psychostimulants (Lee & Rawson, 2008; Pennay & Lee, 2011). In a survey conducted by Hando, Topp, and Hall (1997) of people who used MA, 48% (n=39) reported that they wanted to stop or cut down their MA use due to psychological problems (35%), financial difficulties (45%), physical health problems (35%) and to enhance their quality of life (24%). This indicates that use of MA may result in significant health-related harms.

Substance Use Disorders and the Brain

Substance use disorders, as defined in the DSM-5 (APA, 2013), are characterised by neurobiological changes associated with tolerance, compulsive drug use and loss of control over intake (Koob & Volkow, 2010; Pennay & Lee, 2011; Rajasingham et al., 2012; Rose & Grant, 2008). Substance use disorders are said to be chronically relapsing, and are associated with tolerance and withdrawal (Volkow, Wang, Fowler, & Tomasi, 2012). Withdrawal

symptoms from substances consist of sleep disturbances, fatigue, lethargy, irritability, cravings and depressed mood (Darke et al., 2008). Human and animal studies have revealed discrete circuits that facilitate the addiction cycle, involving the ventral striatum and ventral tegmental area as a central point for the binge/intoxication stage, a substantial role for the extended amygdala in the withdrawal stage and a role in the anticipation stage (Koob & Volkow, 2010).

Methamphetamine withdrawal is associated with indicators of negative affect and dysregulated brain reward systems (Rose & Grant, 2008). Neuroadaptive processes following withdrawal are involved in the development of addiction and vulnerability to relapse (Barr et al. 2006). This can result in depression, anxiety and dysphoria due to an impaired mechanism that facilitates positive reinforcement (Chao & Nestler, 2004). Drug seeking and drug taking behaviour is associated with a decrease in the function of neurotransmitters involved in the positive-reinforcing properties of drugs (Rose & Grant, 2008). The nucleus accumbens and amygdala mediate the acute reinforcing actions of drugs, and involve neurotransmitters like serotonin, gamma-aminobutyric acid (GABA), glutamate and dopamine (DA) (Rose & Grant, 2008; Volkow, Wang, Fowler, & Tomasi, 2012). Dopamine and opioid peptides in the brain mediate the rewarding effects of drugs (Barr et al. 2006). Extensive literature dating back more than 30 years has linked activation of mesocorticolimbic dopaminergic pathways to rewarding events and goal-oriented and incentive-driven behaviours (Chao & Nestler, 2004; Schmidt & Reith, 2005). This means that regular use of MA can result in changes in DA levels and associated depression (Koob & Volkow, 2010).

Methamphetamine induces a rapid inflow of monoamine transmission in the central nervous system following its absorption (Karila et al., 2010). Monoamines such as DA, serotonin and noradrenaline are increased in the cytoplasm (Koob & Volkow, 2010). This occurs by blocking activity of the intracellular vesicular monoamine transporter 2 (VMAT2),

by preventing activity of monoamine oxidase, and by reducing the expression of the dopamine transporter (DAT) (Karila et al., 2010). Brain imaging studies of people who use MA regularly have shown structural abnormalities such as grey-matter deficits in the limbic, hippocampus and cingulate areas of the brain (Karila et al., 2010). The addictive properties of MA are linked to its reinforcing effects, controlled by sustained and rapid increases in monoamine neurotransmission following its ingestion (Chao & Nestler, 2004; Koob & Volkow, 2010).

The longevity and regularity of MA use can result in biochemical alterations in the brain, and degeneration of DA nerve terminals (Darke et al., 2008). This is experienced by the person as depression, lethargy or fatigue (Rose & Grant, 2008). Regular use of MA extending over a long period of time can result in extensive neural damage and cognitive impairment (Rose & Grant, 2008). When people combine MA use with cocaine, alcohol or opiates, its toxicity is increased (Darke et al., 2008). Poly-drug use may also increase neurotoxicity in the brain, and may increase heart rate and blood pressure (Darke et al., 2008). Neurotoxic effects resulting from MA use may lead to the degeneration of serotonin and DA nerve terminals in the frontostriatal region of the brain. This can result in long-lasting depletion of monoamines and changes in the regulation of these systems (Koob & Volkow, 2010). It remains unclear as to whether DA depletion in people who use MA regularly is the result of neurotoxicity or if it is the alteration in regulation of these systems associated with MA (Darke et al., 2008; Nestler & Carlezon, 2006).

Mental Health Symptoms and Cognitive Impairment

Cognitive, psychological and behavioural dysfunction is linked with regular MA use and is associated with the neurotoxic effects of MA (Rose & Grant, 2008). McKetin, McLaren and Kelly (2005) reported that a quarter of people who used MA experienced severe disability in their psychological functioning. Psychological symptomatology from

using MA may include mood and anxiety disorders, suicidal ideation, insomnia, increased rates of psychosis, hostility and violent behaviour (Darke et al., 2008; McKetin et al., 2016; McKetin, Lubman, Lee, Ross, & Slade, 2011). Cognitive deficits may include problems with executive functioning and delayed verbal memory, yet these deficits are not observed consistently (Darke et al., 2008). Cognitive deficits tend to be associated with dysfunction in the frontal, cingulate and striatal regions of the brain.

Methamphetamine and Psychotic Symptoms

In addition to cognitive deficits, psychotic symptoms are also linked with MA use and withdrawal (McKetin et al., 2016; Rose & Grant, 2008). In Australia, hospitalisations due to psychosis tripled in the years between 2009 and 2013, especially in the age groups with the highest rate of MA use (AIHW, 2017). McKetin et al. (2016) suggested that around 30% of people diagnosed with MA-induced psychosis will be re-diagnosed with a schizophrenia spectrum disorder within eight years. The prevalence of psychotic symptoms reportedly increases following onset of MA use, and people who use MA have elevated rates of pre-existing schizophrenia and other psychotic disorders (Darke et al., 2008). Methamphetamine use may increase a number of psychiatric symptoms in susceptible individuals (McKetin et al., 2011). Symptoms such as hallucinations, delusions, poverty of speech, and amotivation induced by MA, make MA-induced psychosis indistinguishable from schizophrenia (Rose & Grant, 2008).

Some affective symptoms such as depressed mood, hostility and mania are linked with MA-induced psychosis, yet it is unclear as to whether these are symptoms of MA-induced psychosis or schizophrenia (Angelo et al., 2013). Longevity and intensity of MA use, a co-existing diagnosis of major depression, antisocial personality disorder and alcohol dependence are linked with the development of psychosis (Rose & Grant, 2008). Psychological symptoms associated with MA use may be due to pre-existing psychological

disorders, yet this remains unresolved (McKetin et al., 2016). It remains unclear as to whether MA acts as a catalyst for an independent neuropathological process, or if it is a trigger for an initial episode of psychosis in vulnerable people (Zarrabi, Khalkhali, Hamidi, Ahmadi, & Zavarmousavi, 2016).

A comorbid mental disorder is seen in almost half of people who regularly use MA, 20% have a primary psychotic disorder and 40% have major depression (Glasner-Edwards et al., 2008; McKetin et al., 2016). Zarrabi et al. (2016) found that out of 152 inpatients in a psychiatric hospital in Iran, the most frequent psychiatric symptoms associated with MA-induced psychosis were ones associated with potential violence, such as delusions of persecution and intimate partner violence. McKetin et al. (2016) reported an increase in violent behaviours among people who use MA compared to when they were not using. The present rates of recorded violent and aggressive behaviour suggest that there are increased rates of violence associated with using MA (Shoptaw, Kao & Ling, 2009; Zarrabi et al., 2016). It remains unclear how to treat MA-induced psychosis and associated violence, and there have not been enough studies conducted to help devise a therapeutic manual for clinicians (Zarrabi et al., 2016).

Depression and Anxiety

People who use MA may experience symptoms of depression or anxiety in association with MA use. The majority of people who use MA report a lifetime prevalence of depression (Hellem et al., 2015). A cross sectional survey in Brisbane and Sydney, Australia, conducted by McKetin et al. (2011) found that out of 400 people entering treatment for MA use, the prevalence of major depression in the year prior to the study was 40%. Almost half (44%) of participants in their study had substance-induced depressive symptoms and four in ten participants met diagnostic criteria for a Major Depressive Disorder (MDD) in the previous year (McKetin et al., 2011). High rates of depression in this population mean that

suicidal ideation and attempted suicide is high (Darke et al., 2008). A quarter of people who use psychostimulants have a lifetime history of attempted suicide. Glasner-Edwards et al. (2010) identified that people who experience depressive symptoms and are using MA, may have a poorer prognosis for both conditions and may experience worse treatment outcomes. Furthermore, Newton, De La Garza, Kalechstein, Tziortzis, and Jacobsen (2009) suggested that depressive symptoms may contribute to negative reinforcement and more frequent use of MA, consequently impacting on treatment outcomes. Rates of anxiety disorders among people who use MA are substantially higher than the general population in Australia. Higher rates of anxiety disorders, depression and suicide are linked with more frequent use of MA and longer use careers (Darke et al., 2008; Hellem, 2016). However, it can be difficult to differentiate between depression and the drug's withdrawal symptoms including increased appetite, anhedonia, depressed mood and hypersomnia (McKetin et al., 2011). It is evident that MA use is associated with an array of psychological difficulties that may affect one's response to treatment (Kay-Lambkin et al., 2010).

Risk-Taking Behaviour

People who use MA are at an increased risk of contracting Human Immunodeficiency Virus (HIV), due to unsafe injecting practices and unprotected sex whilst under the influence of MA (Baker et al., 2004; Reback, Peck, Fletcher, Nuno, & Dierst-Davies, 2012; Roll et al., 2006). Menza et al. (2010) found that men who use MA and who report having sex with men, have higher rates of psychiatric disorders and are 1.5 to 2.9 times more likely to contract HIV. Use of MA by homosexual men has increased from 11% in 2011 to 14% in 2014 in Australia (Hopwood, Cama, Treloar, 2016). In the United States in 2006, around 53% of new HIV infections occurred among men who have sex with men (MSM) (Darke et al., 2008). This population of HIV-infected men who use MA can experience a range of harmful outcomes including increased sexual risk behaviour, reduced access to medical care, and

failure to adhere to medications (Rajasingham et al., 2012). Greater understanding is required for the psychological, social, developmental and environmental factors contributing to MA use and associated harms (Colfax et al., 2010).

Despite the apparent increased risk-taking behaviour present in people who use MA, the methodological quality of cross-sectional and longitudinal studies must be considered (Roll et al. 2006). The majority of research has focused on MSM in developed countries, and little is known about sexual risk-taking in other populations (Colfax et al., 2010). Many behavioural trials were not exclusively conducted with an HIV-infected MSM population, and they may not have the same relationships with medical providers regarding healthy behaviours compared to an HIV-uninfected population (Rajasingham et al., 2012). This means that their response to psychological treatment might be different to those that are uninfected. Numerous studies that have researched risk behaviour and adherence were retrospective or cross-sectional, suggesting a gap in the methodological quality of the research on these populations (Colfax et al., 2010). Additionally, sexual behaviour, substance use and medication adherence was measured using self-report and not objective means such as a Sexually Transmitted Infection (STI) test or toxicology screen (Rajasingham et al., 2012). Treatment studies have failed to show a continued impact in reducing MA use (Rajasingham et al., 2012). Treatment for this population may need to address poly-drug use to reduce risk of drug-related harm and HIV infection (Colfax et al., 2010).

Treatment

Treatment for people who use MA may be implemented in an inpatient or outpatient setting. Outpatient treatment for people using MA is usually aimed at reducing drug use or adopts a harm minimisation approach (Ciketic, Hayatbakhsh, Doran, Najman, & McKetin, 2011). Treatment for people who regularly use MA can pose many challenges, and may involve high rates of relapse, poor treatment retention, and reduced treatment engagement

(Rose & Grant, 2008). Despite widespread use of MA across the globe including Australia, treatments with known effectiveness are not widely available (Lee & Rawson, 2008).

Pharmacological Treatment

Improvement in the understanding of the fundamental neurobiology of MA use has led to research on pharmacological treatments (Karila et al., 2010). However, pharmacological treatments do not have a solid evidence base and have not produced long-lasting changes in people using MA (Ciketic et al., 2011; Karila et al., 2010). Antidepressant medication has been used to treat regular use of MA. Galloway, Newmeyer, Knapp, Stalcup, and Smith (1996) conducted an RCT on the efficacy of Imipramine (a tricyclic antidepressant) for 32 people using crystal MA and found that this medication was unsuccessful in reducing MA use between the control group (10mg/day) and the intervention group (150mg/day).

The effectiveness of pharmacological treatment for MA use has produced conflicting results. Selective serotonin reuptake inhibitors (SSRIs); bupropion and sertraline, were compared by Shoptaw and colleagues (2006) and neither medication was found to be more efficacious than placebo (Rajasingham et al., 2012). However, bupropion may be effective in reducing MA use among less regular users (Karila et al., 2010). Other double-blind placebo-controlled trials found that bupropion, modafinil and naltrexone were somewhat efficacious for treating MA use (Karila et al., 2010). McElhiney, Rabkin, Rabkin, and Nunes (2009) found that modafinil, a dopamine agonist, was useful in situations when people started to decrease their use, whereas baclofen and bupropion were effective in managing abstinence. Authors concluded that bupropion reduced craving in this population. Pharmacological treatments such as creatinin and risperidone have been associated with a reduction in positive urine drug screens and may improve anxiety symptoms (Hellem, 2016). Overall, there is no strong evidence for efficacious pharmacological treatments for MA use. Further investigation

on pharmacotherapies for people using MA should be conducted with larger sample sizes (Hellem, 2016; Karila et al., 2010).

Psychological Treatment

Psychological treatments are suggested as being the most efficacious treatments available for people using MA, and have been associated with reduced MA use in numerous studies (Lee & Rawson, 2008; Rose & Grant, 2008). Psychological treatment may also reduce symptoms of mental ill-health. Predominant evidence based therapeutic approaches include: Cognitive Behaviour Therapy (CBT), Acceptance and Commitment Therapy (ACT), Contingency Management (CM), the Matrix Model, 12-Step Facilitation (Roll, 2007), and Motivational Interviewing (MI).

Motivational Interviewing is a therapeutic approach that has been suggested as efficacious for people with substance use issues. An RCT conducted by Baker et al. (2005) found a larger reduction in MA use among regular users of MA at 12-month follow up for those who had received a 10-session CBT intervention incorporating MI. Therapeutic techniques such as MI have been suggested as efficacious in engaging people in drug and alcohol treatment (Barrowclough et al., 2009). Studies have suggested that MI increases self-efficacy for maintaining abstinence, and thus may be effective for people who use MA (Lee & Rawson, 2008).

Acceptance and Commitment Therapy

Third wave psychological therapies such as ACT significantly reduced MA use and MA-related negative consequences in an RCT conducted by Smout et al. (2010). Acceptance and Commitment Therapy and CBT were found to have similar positive outcomes on MA use and mental health outcomes. Notably, on average, only four sessions were attended across the sample, suggesting potential efficacy of brief interventions (Smout et al., 2010).

An RCT conducted by Luoma, Kohlenberg, Hayes and Fletcher (2012) found that an ACT group intervention targeted at shame for people with substance use disorders resulted in large substance use reductions at 4-months in days of substance use and higher retention rates than control participants (Luoma, Kohlenberg, Hayes & Fletcher, 2012). Bahrami and Asghari (2017) conducted an RCT comparing a 12 session ACT group with a waitlist control and found that ACT significantly reduced addiction severity for people using MA, in social domains as well as psychological and other health domains. Despite these positive results, very few studies have researched the effectiveness of ACT for MA use. Further, higher powered studies are warranted, incorporating both statistical significance and magnitude of effect using Cohen's d.

Contingency Management

Reward based psychological treatments such as contingency management (CM) have resulted in healthier behaviours and reduced crystal MA use (Colfax et al., 2010; Rajasingham et al., 2012; Roll, 2007). However, at times they have failed to create relapse prevention plans and address participants' mental health needs (Rajasingham et al., 2012). Contingency management involves rewarding clients with a voucher for goods or cash rewards when they produce a MA-free urine sample (Lee & Rawson, 2008; Rajasingham et al., 2012). Drugs of abuse function as positive reinforcers, and an approach like CM adopts this philosophy, by decreasing MA's reinforcing efficacy and limiting the control the drug may have over one's behaviour (Roll, 2007). Meta-analyses have reported the efficacy of CM for treating substance use disorders, and found that participants were more likely to remain abstinent if receiving CM than control (Lussier, Heil, Mongeon, Badger, & Higgins, 2006; Prendergast, Podus, Finney, Greenwell, & Roll, 2006). However, small effect sizes (0.15 on average) were found (Roll, 2007). This approach can be combined with other psychological

and pharmacological treatment approaches, and incorporating a strategy such as this may enhance abstinence (Rajasingham et al., 2012; Roll, 2007).

Cognitive Behaviour Therapy

Cognitive behaviour therapy (CBT) is based on principles of learning and conditioning to encourage, teach and support individuals about reducing their harmful drug use (Lee & Rawson, 2008). Cognitive Behaviour Therapy can assist in teaching people skills to reduce or abstain from drug use, and assist in relapse prevention (Lee & Rawson, 2008). Randomised controlled trials conducted by Baker et al. (2001; 2002; 2005; 2006) found reductions in MA use following CBT compared to control or treatment as usual (TAU). Individuals who engaged in treatment incorporating a CBT framework for MA use have reported enhanced quality of life outcomes, and in particular mental health outcomes, compared to those not engaged in treatment (Gonzales, Ang, Marinelli-Casey, Glik, Iguchi, & Rawson, 2009). Brief CBT-based psychological interventions have been suggested to reduce MA use, alleviate MA-related harms and increase abstinence rates (Lee & Rawson, 2008). A four-week 1-hour session of CBT has been found to improve levels of depression, anxiety, social dysfunction and overall health (Feeney, Connor, Young, Tucker, & McPherson, 2006).

Interventions incorporating CBT and CM have been moderately effective in reducing MA use (Rajasingham et al., 2012). A study conducted by Roll et al. (2006) randomised 113 participants, and utilised 12 weeks of treatment incorporating CM and CBT combined treatment. Participants in the combined group were abstinent for longer and had more drug free urine samples ($p < .01$). Rawson et al. (2006) compared CM+CBT vs CM vs CBT in an RCT for stimulant users of MA and cocaine. This 16-week trial involved thrice weekly group sessions and they found a reduction in stimulant use for all groups. However, CM produced reduced stimulant use during the treatment period and greater retention (Lee & Rawson,

2008). Shoptaw et al. (2005) found that interventions that incorporated CM demonstrated the most MA-free urine samples, improved treatment retention and increased treatment effectiveness scores. Treatment retention, higher rates of abstinence and stimulant free urine samples were found in a CM treatment study by Petry et al. (2005) of 415 participants who used MA (Lee & Rawson, 2008). A series of papers utilising a common dataset adopted gay-specific CBT interventions for men using MA, demonstrated that self-reported MA use decreased for up to one-year post-treatment (Jaffe, Shoptaw, Stein, Reback, & Rotheram-Fuller, 2007; Peck, Reback, Yang, Rotheram-Fuller, & Shoptaw, 2005; Shoptaw et al., 2005). Peck et al. (2005) found that participants allocated to the CBT intervention showed higher levels of depression at one-year post-treatment, yet depression improved post-treatment across the groups. There was no greater effect of gay-specific CBT than other conditions (Lee & Rawson, 2008).

Overall, CBT combined with CM may not enhance treatment outcomes over the CM only condition (Lee & Rawson, 2008). However, using CM as an adjunct to treatment strategies can assist in increasing abstinence for people who use MA (Roll, 2007). It is unclear as to whether CM would be as efficacious in Australia (compared to the USA) due to Australia's better welfare system. This is worth further exploration, and future research could evaluate the effectiveness of CM in Australia and other countries. Most studies on these interventions have focused on abstinence based outcomes, however reductions in harms associated with MA use are also imperative (McKetin, McLaren & Kelly, 2005).

Matrix Model

The Matrix Model was developed at the Matrix Institute on Addictions in the USA (Rawson et al. 1995). It is a day patient program that incorporates social support groups, intensive CBT including CM, family education and individual counselling (Roll et al., 2006). An RCT of 978 people using crystal MA tested the efficacy of this model compared to TAU

over a period of 16 weeks, and found that at post-treatment the group that received the Matrix Model attended more sessions, had higher rates of retention, produced more drug-free urine samples, and had longer periods of abstinence; however these differences between intervention and TAU were lost at follow-up (Lee & Rawson, 2008; Rajasingham et al., 2012; Rawson et al., 2004). Gonzales, Ang, Marinelli-Casey, Glik, Iguchi, and Rawson (2009) used a Matrix Model intervention for MA use and found that participants in the Matrix Model condition had better mental health outcomes than those who did not complete treatment. The Matrix Model may offer substantial benefits for abstinence, mental health symptoms and increased treatment engagement, yet the longevity of these outcomes is uncertain (Gonzales et al., 2009).

Existing Reviews and This Review

Systematic reviews include studies by Hellem et al. (2015), Colfax et al. (2010), Minozzi, Saulle, De Crescenzo, and Amato (2016), Shoptaw, Kao, Heinzerling, and Ling (2009), Shoptaw, Kao, and Ling (2009), Karila et al. (2010), Knapp, Soares, Farrel, and Lima, (2007), Lee and Rawson (2008), and Rajasingham et al. (2012). These have researched psychological interventions for a wide range of psychostimulants, including amphetamine-type stimulants, cocaine and MDMA (Minozzi, Saulle, De Crescenzo, & Amato, 2016). Existing systematic reviews have not evaluated psychological interventions for MA use and a range of mental health outcomes. Cochrane reviews by Shoptaw and colleagues have focused on psychological and pharmacological treatment for the MA withdrawal syndrome and for MA use and psychosis, and found no efficacious medication approaches (Shoptaw, Kao, & Ling, 2008; Shoptaw et al., 2009). Other reviews have focused on MA use and mental health symptoms such as depression. Hellem et al. (2015) studied MA use and co-occurring depressive symptoms or diagnoses, and found no benefit of one single treatment approach over others. Another review conducted on psychological interventions; pharmacological

only; and psychological combined with pharmacological interventions, for MA use and co-existing depressive symptoms found no research supporting one treatment approach over others (Rose & Grant, 2008).

Further clarity regarding evidence for the efficacy of psychological treatment for MA use and co-occurring mental health symptoms or conditions is required. The present review will highlight any existing gaps in the efficacy of interventions for MA use and mental health symptoms, potentially resulting in suggestions for tailoring interventions. Longevity of the effectiveness of treatment for mental health symptom outcomes and MA abstinence should be considered (Lee & Rawson, 2008; Tait et al., 2015). Treatment retention is also important for people who use MA, and this difficulty may be increased by symptoms of mental ill-health. Existing Cochrane reviews by Minozzi et al. (2016), Shoptaw, Kao, and Ling (2009), Shoptaw, Kao, Heinzerling, and Ling (2009), and Knapp, Soares, Farrel, and Lima, (2007), have not focused on the outcomes of mental health symptoms and MA use. A review of this kind will allow for investigation into what psychological interventions are most efficacious for MA use and mental health symptomatology (Sullivan & McDonough, 2015).

Summary

In conclusion, MA use is associated with significant psychological symptomatology. Evaluating evidence based psychological interventions for MA use is vitally important for informing clinical utility. Psychological interventions appear to have the most solid evidence base for reducing MA and increasing abstinence. Thus far, there has not been a systematic review that has focused on the efficacy of psychological treatment for MA use and mental health symptoms. This systematic review represents an important step in analysing the available evidence for psychological treatment for MA use and co-existing mental health symptoms, and will allow for identification of future research areas.

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Manuscript for Submission to 'Addiction'

A Systematic Review of Psychological Treatment for Methamphetamine Use and Associated Mental Health Symptom Outcomes

Miss Alexandra M. Stuart, The University of Newcastle

Professor Amanda Baker, The University of Newcastle

Professor Nicole Lee, Curtin University

Conjoint Professor Adrian Dunlop, The University of Newcastle

Professor Jenny Bowman, The University of Newcastle

Alexandra Denham, The University of Newcastle

Dr Alix Hall, HMRI, The University of Newcastle

Dr Chris Oldmeadow, HMRI, The University of Newcastle

Dr Kristen McCarter, The University of Newcastle

Corresponding Author: Professor Amanda Baker

School of Medicine and Public Health, University of Newcastle

University Drive, Callaghan NSW 2308

Australia

Email: Amanda.baker@newcastle.edu.au

Phone: +612 40335690

Fax: +612 40335692

Abstract

Aims. People who use methamphetamine (MA) regularly experience symptoms of mental ill-health associated with MA use. These include symptoms of psychosis, depression and anxiety. Accordingly, research examining psychological treatments often measure MA use and related mental health problems. Although there has been a substantial body of research reporting on the effectiveness of psychological treatments for reducing MA use, there is a paucity of research addressing the effectiveness of these treatments for co-occurring symptoms of mental ill-health. We addressed this gap by providing a systematic review of the evidence for psychological treatments for co-occurring MA use and symptoms of mental ill-health in experimental/controlled clinical studies. **Design and method.** A meta-analysis and a narrative synthesis of studies was conducted following the Cochrane Handbook for Systematic Reviews of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement to inform methodology. Eight electronic peer-reviewed databases were searched. Twelve eligible articles were assessed. **Findings.** Most studies found an overall reduction in level of MA use and mental health symptoms among samples as a whole. There was significant heterogeneity across studies, therefore generalisability of results was limited. There was some evidence to suggest that Cognitive Behaviour Therapy (CBT) was more effective than other psychological treatments and treatment as usual for reducing levels of MA use. Cognitive Behaviour Therapy was significantly more effective than minimal treatment and was associated with significantly higher abstinence rates compared to minimal control conditions. **Conclusions.** Contingency Management and CBT interventions may enhance abstinence from MA. Future clinical research should consider how psychological treatment may play a role in reducing MA use and associated mental health symptoms.

A Systematic Review of Psychological Treatment for Methamphetamine Use and Associated Mental Health Symptom Outcomes

Methamphetamine (MA) is a psychostimulant that when used regularly is associated with a range of physical and mental health harms (1-7). Despite a decrease in use of MA in many countries, including Australia, harms continue to increase, partly driven by increases in purity and a change in preference from the powdered form to the highest purity crystalline form (8, 9). In Australia, frequency of use has increased significantly (8), as has the rate of dependence (7). Hospitalisations, ambulance calls out, overdose and death related to MA have all increased in Australia (8).

Substance use accounts for an increasing proportion of the global burden of disease (10, 11). Amphetamine-type stimulants have become the most prevalent type of psychostimulants in the world, and it is estimated that there are 24 million users worldwide (12). In South Asia and the Middle East, MA is becoming increasingly popular, with the current market in the United States, China, Mexico and Thailand (12, 13). Due to the drug's psychosocial and medical impact, the detrimental effects can be seen in entire communities, whole populations as well as in individual users (12).

Rates of illicit drug use in Australia are similar to those in other high-income countries (13). In Australia in 2016, MA was used by approximately 1.4% of adults in the previous 12 months (8). From 2009 to 2014 the annual total number of mental health presentations, overdose and drug and alcohol presentations at NSW public hospital emergency departments related to MA use increased more than 7-fold, from 394 to 2963 (14, 15). These statistics suggest that MA use is a growing public health problem in Australia.

Psychostimulants are a unique group of substances that are more likely to induce psychosis than other illicit drugs (16, 17). Although vulnerability to psychotic symptoms differs among people who use MA, these symptoms are more apparent in people who use

MA on a regular basis (16). In Australia, hospitalisations due to psychosis tripled in the years between 2009 and 2013, especially in the age groups with the highest rate of MA use (8). Depression, anxiety, suicidal ideation and dysphoria have been commonly reported to co-occur in people using MA (1, 18, 19). Methamphetamine use is associated with an array of psychological difficulties that may affect one's response to treatment (20-23). People who experience depressive symptoms and are using MA have a poorer prognosis for both conditions and depressive symptoms may contribute to more frequent use of MA through negative reinforcement, consequently impacting on treatment outcomes (20, 21).

Pharmacotherapies have been used in conjunction with the aim of improving treatment engagement and retention, however no pharmacotherapy has been approved for the treatment of MA-related problems. There is no evidence to suggest that agonist drug treatments can reduce psychological distress or symptomatology associated with MA use (23-30). The current evidence suggests treating mental health symptoms in line with current guidelines for those disorders (4, 22). For example, a review of the limited research into the pharmacological treatment of amphetamine-related psychosis reported that antipsychotic medications reduced symptoms of amphetamine psychosis (31, 32).

In the absence of effective pharmacotherapy, psychological therapy for MA dependence, such as psychotherapy, psychoeducation and relapse prevention continues to be the first line treatment option (1, 2, 4) and is effective (28, 29, 33). Psychological treatments for reducing MA use show high rates of treatment success (24, 34-38). However, less is known about mental health outcomes from these treatments or which psychological interventions offer the most solid evidence base for reducing MA use and mental health symptoms (33-35). Cognitive and behavioural therapies (CBT) (including the Matrix Model), Contingency Management (CM) and approaches such as Motivational Interviewing (MI), have been effective in reducing depression, increasing wellbeing and reducing MA-related

risk behaviour in people who use MA (5, 33, 34, 39-42). A number of reviews have been conducted but fail to provide clarity on this topic (26).

Knapp, et al. (31) primarily reviewed outcomes for regular users of cocaine and not MA. Minozzi, et al. (43) did not focus on MA use and mental health outcomes, and only included two studies measuring depression and MA use. Other reviews by Shoptaw, et al. (44) focused on treatment for amphetamine withdrawal, incorporating psychological and pharmacological treatment and primarily focusing on the withdrawal syndrome when using amphetamine and found no effective medication approaches (23, 26, 44).

Hellem, et al. (4) conducted a review of MA and co-occurring symptoms of depression, reviewing nine studies incorporating psychological intervention only; psychological combined with pharmacological interventions; and pharmacological only, and found no research supporting one single treatment approach over others on either MA or depression outcomes. Psychological therapies remain the most effective treatment option and pharmacotherapies may be used as an adjunct (23, 24, 27). As it is difficult to maintain enduring behaviour changes in people who experience problems with drug use (34, 36), the longevity of treatment effects relating to long-term abstinence and psychological wellbeing should be further assessed (31, 44, 45).

An enhanced understanding of the current psychological treatment available will allow for analysis of the most efficacious treatment for people who use MA, may permit for improvements in current therapy, and will highlight existing gaps in treatment (43). Systematic reviews conducted thus far have not focused on psychological treatment for MA and a range of co-occurring mental health symptoms (31, 32, 46). This review aimed to: i) examine the effectiveness of psychological treatments in reducing MA use and/or increasing abstinence rates among people who use MA; ii) examine the effectiveness of psychological treatments for MA use or co-occurring mental health symptoms; iii) examine secondary

outcomes (e.g., other drug use) following psychological treatment; and iv) identify future research directions.

Methods and Analysis

A systematic review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (47). The paper by Stuart, et al. (48) describes the methodology in detail. The quality of the evidence of included studies was assessed using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach (49).

A systematic search using PsycINFO, Medline, EMBASE, CINAHL and Scopus was conducted for eligible studies up until August 2017. Registration databases were also searched, including the Cochrane Central Register of Clinical Trials, US Government Website of Clinical Trials and WHO International Clinical Trials Registry. Search terms were developed from existing reviews of psychological (2, 4, 25, 29) interventions (see Appendix A). Search terms were grouped into three central categories so that results were based on at least one keyword from each group (Appendix A). Publications were limited to human studies, were available in English, and no limits were placed on publication year. If studies met inclusion criteria, they were downloaded as full text. Reference lists of included articles and systematic reviews were also searched manually to find further papers.

Study Selection

Inclusion/Exclusion Criteria

Studies were included if they tested a psychological intervention and measured the following outcomes: i) MA use and (ii) mental health symptoms and/or disorders at baseline and post-treatment. Participants included were adults (over 18), using MA alone or in combination with other substances (poly-drug use). Interventions could be delivered in any setting including in inpatient units (drug and alcohol rehabilitation or hospital setting),

community or prison settings. Psychological interventions included one or more psychological strategies designed to modify MA use. Controlled trials such as RCTs, cluster and parallel designs were eligible. Interventions were compared with active controls (e.g. psychosocial interventions, 12 step programs), TAU and/or inactive controls (e.g. wait-list control or standard care). Interventions were of any duration, delivery, frequency and intensity. Primary outcomes were: i) any outcome measure reporting change (reduction/increase) or abstinence in MA use following psychological treatment for MA use; and ii) any outcome measure reporting change (reduction/increase) in mental health symptoms or diagnoses following psychological treatment for MA use. Secondary outcomes included: i) change in other drug use; ii) treatment engagement; iii) BBV risk reduction; iv) change in physical health; v) change in quality of life; and vi) difference in functioning. Outcomes reflected any time frame (e.g. short-term, long-term) and were rated by clients or clinicians, in the form of an assessment by objective or subjective measures.

Studies were excluded if they met any of the following criteria: a) were not peer reviewed journal articles; b) did not use a controlled design; c) did not include a psychological intervention; d) did not include relevant behaviour change outcome measures associated with MA use and mental health outcomes, or e) were case control, cross-over trials, one-arm trials, non-randomised trials, cross sectional studies or cohort studies.

Data Analysis

The Cochrane Handbook for Systematic Reviews (49) was used to guide data extraction. A data extraction form was developed to organise information. Extraction forms were pre-tested in 10% of the identified articles to ensure functionality. Data extracted included participant information, methods of each study, type of intervention, primary and secondary outcomes and results of studies.

The 'Cochrane Collaboration's Risk of Bias' tool was used to measure risk of bias (49) with items judged as 'low', 'high' or 'unclear' risk. Allocation concealment and selection bias was deemed as a 'high' or 'unclear' risk of bias, as these factors have been suggested to be sources of bias (50). The overall quality of evidence of outcomes was assessed using the GRADE (49) approach. The overall quality of evidence was rated at four levels: 'very low', 'low', 'moderate' and 'high'. This involved contemplation of directness of evidence, risk of bias, heterogeneity and risk of publication bias.

Measures of Treatment Effect

A narrative synthesis of the findings was undertaken. Characteristics and outcomes of included studies, context of treatment (e.g. psychological vs active control) and the type of outcomes were described. Tables 7 and 8 (Appendix E) provide key information regarding evidence quality, a summary of available data on outcome variables, and the degree of effect of the interventions.

Meta-analyses

A quantitative synthesis of the outcomes from eligible included studies was reported using a meta-analysis to assess the effect of psychological interventions on MA use and mental health outcomes (see Appendix C for further methodology). Data were cleaned and cross-checked in Microsoft Excel before being uploaded using the Data Analysis and Statistical Software STATA v13.0 (StataCorp Ltd, College Station, TX). To allow for comparisons to be made between CBT and other treatment types, CBT was classified as the intervention in all studies included in the meta-analyses, regardless of whether CBT was the intervention in the original study.

The aim of the meta-analysis was to examine whether CBT was significantly more effective than other treatment types in reducing MA or mental health outcomes. Separate

meta-analyses were conducted using the mean follow-up value and mean change from baseline value as the estimated mean difference for each of the following continuous outcomes: i) MA use; ii) scores on the psychiatric component of the Addiction Severity Index (ASI) (51) and Brief Symptom Inventory (BSI) (52); and iii) scores on the Beck Depression Inventory (BDI) (53). Characteristics of the included studies varied substantially, with differences observed in methodology, control conditions, outcomes and measures used. To account for the between-study variability the Dersimonian and Laird random effects method of meta-analyses was used to estimate the pooled mean difference. For each of these analyses Hedges g was used to estimate a standardised pooled mean estimate, as there was variation across studies with regards to how each outcome was defined and/or measured. For the outcome of abstinence from MA the log odds and standard error were calculated using the number of participants reported as abstinent from MA and the number reported as not abstinent from MA. This data was used in the analysis, as were odds ratios and 95% confidence intervals.

A forest plot was created for all meta-analyses conducted and inspected for between group heterogeneity. Significant between group heterogeneity was determined by a significant Q test and an I^2 value above 50%. To account for the wide variation in control conditions, the pooled estimates are presented overall for all control groups combined, as well as aggregated by the intensity of the control condition (i.e. minimal care vs. active treatment). Active treatment was classified as a control group that received any treatment above usual care or receipt of information. Contour enhanced funnel plots were created for all models to allow for the assessment of potential publication bias (Appendix B).

Results

The database search returned 1689 results, providing 1143 unique citations after duplicates were removed. A further 1074 studies were excluded at the title-abstract stage. For

the remaining 69, the full paper was screened. Of these, 12 met full eligibility criteria and were included in the review (22, 34, 39, 54-62). We found 12 papers reporting on 11 studies. Searching the reference lists of these papers did not identify any additional eligible studies. The full study selection process is shown in Figure 1.

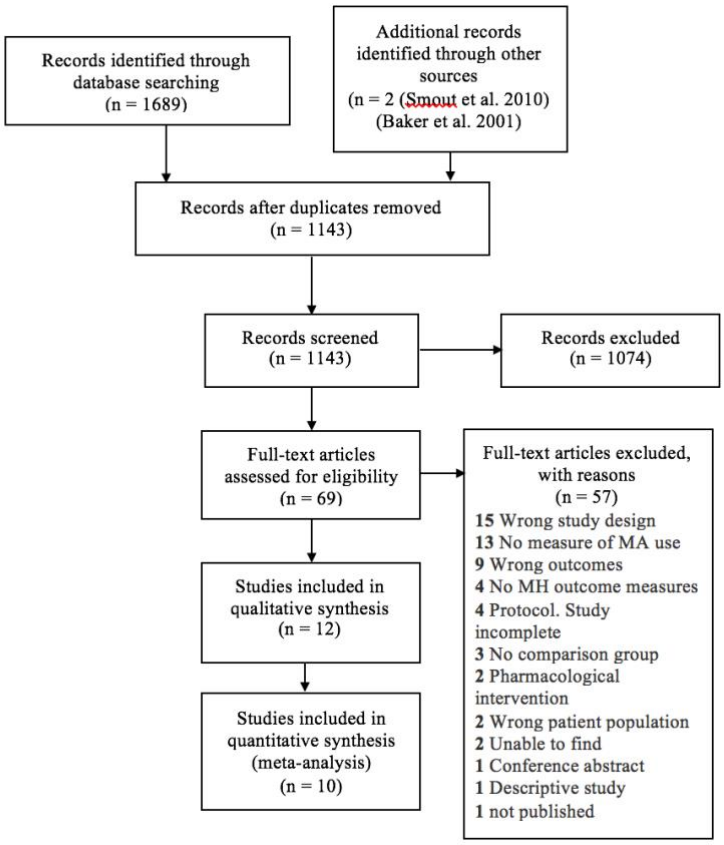

Figure 1. PRISMA chart for study selection process.

Study Characteristics

A description of the trial characteristics of included studies is provided in Appendix E. Included RCTs were published between 2001 and 2014. All participants used MA, were predominantly male (67.38%), and the mean age was 33.5 years. All trials compared interventions with another type of treatment (considered to be a lesser form of CBT, CM, MI or non-contingent control), TAU or a minimal treatment control group consisting of self-help material. Overall, studies aimed to identify whether a psychological intervention was

effective in increasing abstinence from MA or reducing level of MA use and changing mental health outcomes.

The average length of intervention ranged between 1 to 12 sessions (over 4 months). Studies were single and/or multicentre and participants were recruited from inpatient and outpatient drug and alcohol services and community mental health centres. Interventions incorporated assessment at pre-treatment and post-treatment. The follow-up periods varied from 1 to 12-months post-intervention. Psychological interventions were delivered by therapists, psychologists and social workers. Interventions consisted of CBT, CM, ACT, CM+CBT, CBT+MI, Matrix Model or MI. Two studies (60, 62) reported changes in mental disorders pre and post-treatment (Table 7 and 8, Appendix E). Using the Cochrane Risk of Bias tool (50), we assessed individual risk of bias as low or unclear for many domains, and assessed some studies as high risk for incomplete outcome data or allocation concealment.

Meta-analyses

Methamphetamine Use

A total of eight studies assessed MA use as a continuous outcome in the same direction (i.e. higher values represented greater use), and were thus included in the meta-analyses (Table 1). See Appendix D for the contour enhanced funnel plots and further meta-analyses results and Appendix F for secondary outcomes.

Table 1. *Studies assessing the effect of CBT on reducing MA use*

Study	Intervention	Control/TAU
Baker, et al. (2001)	MI & CBT	Booklet
Baker, et al. (2002)	MI	Booklet
Baker, et al. (2005)	CBT	Booklet
Baker, et al. (2006)	MI & CBT	Usual care
McDonnell, et al. (2013)	CM	Usual
Polcin, et al. (2014)	Intensive MI	Standard MI
Rawson, et al. (2004)	Matrix MA	Usual care
Smout, et al. (2010)	CBT	ACT

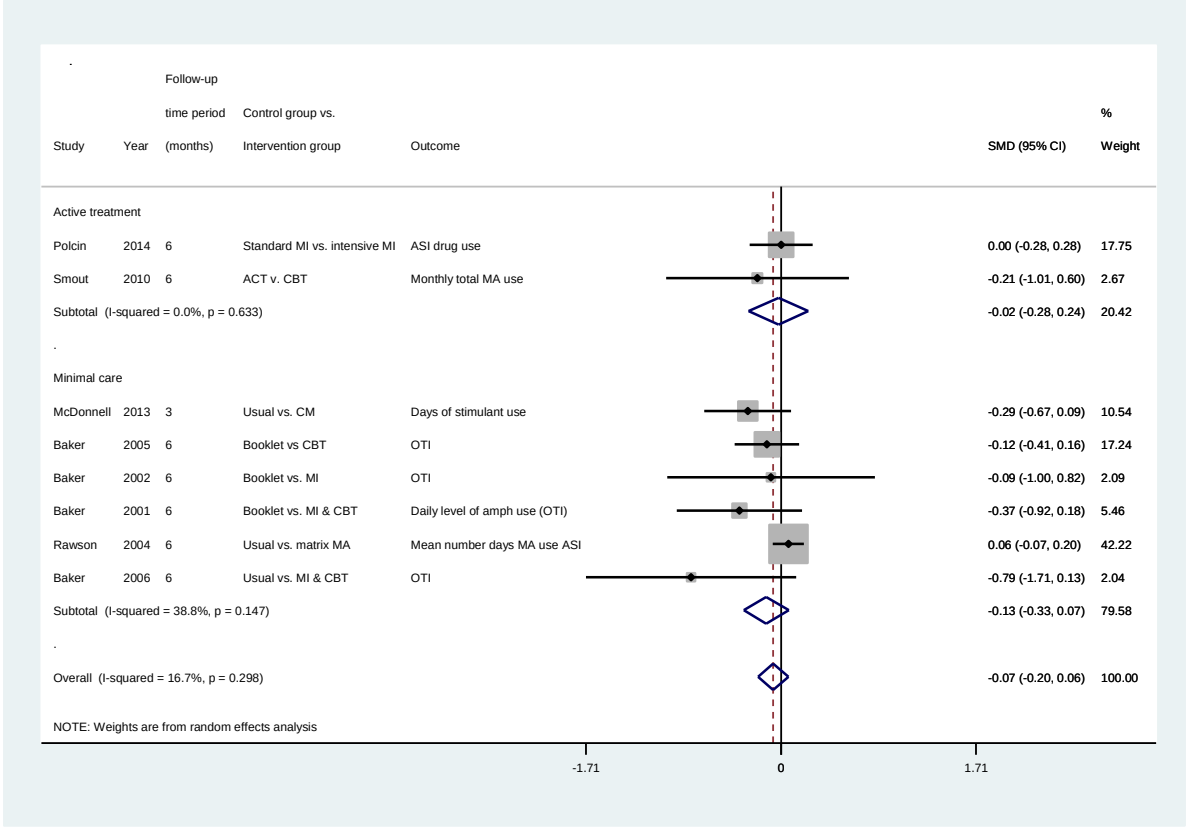

Figure 2. Forest plot for MA use using mean follow-up scores as the mean difference.

Figure 2 illustrates the forest plot for the outcome of level of MA use when mean follow-up score was used as the estimated mean difference. As shown in Figure 2, there was no significant difference in MA use at follow-up between those receiving CBT and those receiving other treatment types (SMD = - 0.07, 95% CI = - 0.20, 0.06, p = .314). Even when separated by the intensity of the control group there was no significant difference between

CBT and minimal treatment on MA use at follow-up (SMD = - 0.13, 95% CI = - 0.33, 0.07, p = .198).

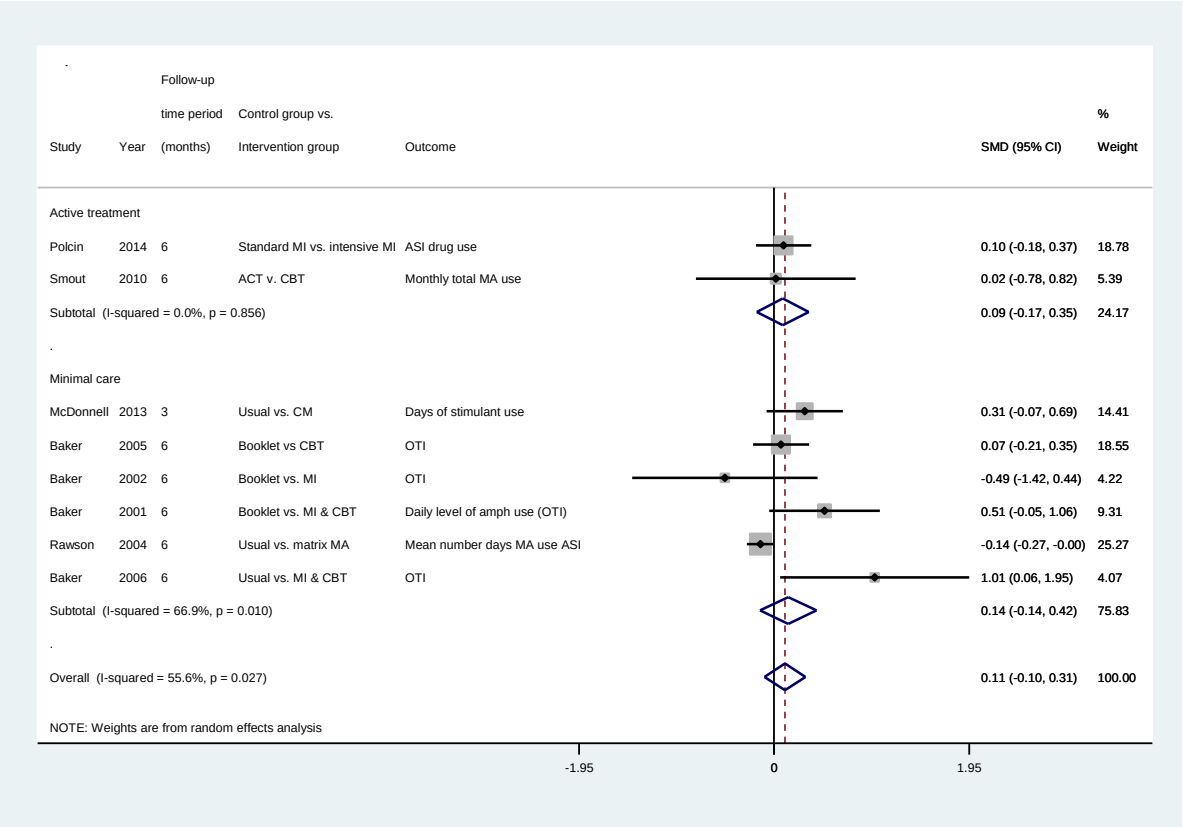

Figure 3. Forest plot for MA use using mean change from baseline scores as the mean difference.

Figure 3 shows results for MA use when mean change from baseline was used as the estimated mean difference. As shown in Figure 3 there was no significant difference in the change in MA use from baseline to follow-up for the CBT group compared to controls (SMD = 0.11, 95% CI = - 0.10, 0.31, p = .303). This result was maintained even when CBT was compared to minimal treatment (SMD = 0.14, 95% CI = - 0.14, 0.42, p = .322).

Heterogeneity between effect sizes when mean follow-up score of MA use was used as the outcome was not significant, with p-values >0.05 and I^2 values <50% (I^2 = 16.7%, p = .298). This indicates that less than 50% of the variation in point estimates was explained by heterogeneity for this outcome. However, heterogeneity was indicated when significant mean

change from baseline was used as the estimated mean difference, with approximately 56% of the variation in point estimates being explained by heterogeneity (I^2 = 55.6%, p = .027).

Abstinence

Four studies assessed the percentage of participants abstinent at six-month follow-up, and were included in the meta-analyses (Table 2).

Table 2. S*tudies assessing the effect of CBT on increasing the number of participants exhibiting abstinence*

Study	Intervention	Control/TAU
Baker, et al. (2001)	MI & CBT	Booklet
Baker, et al. (2005)	CBT	Booklet
Baker, et al. (2006)	CBT & MI	Usual care
Rawson, et al. (2006)	CBT & CM	CM

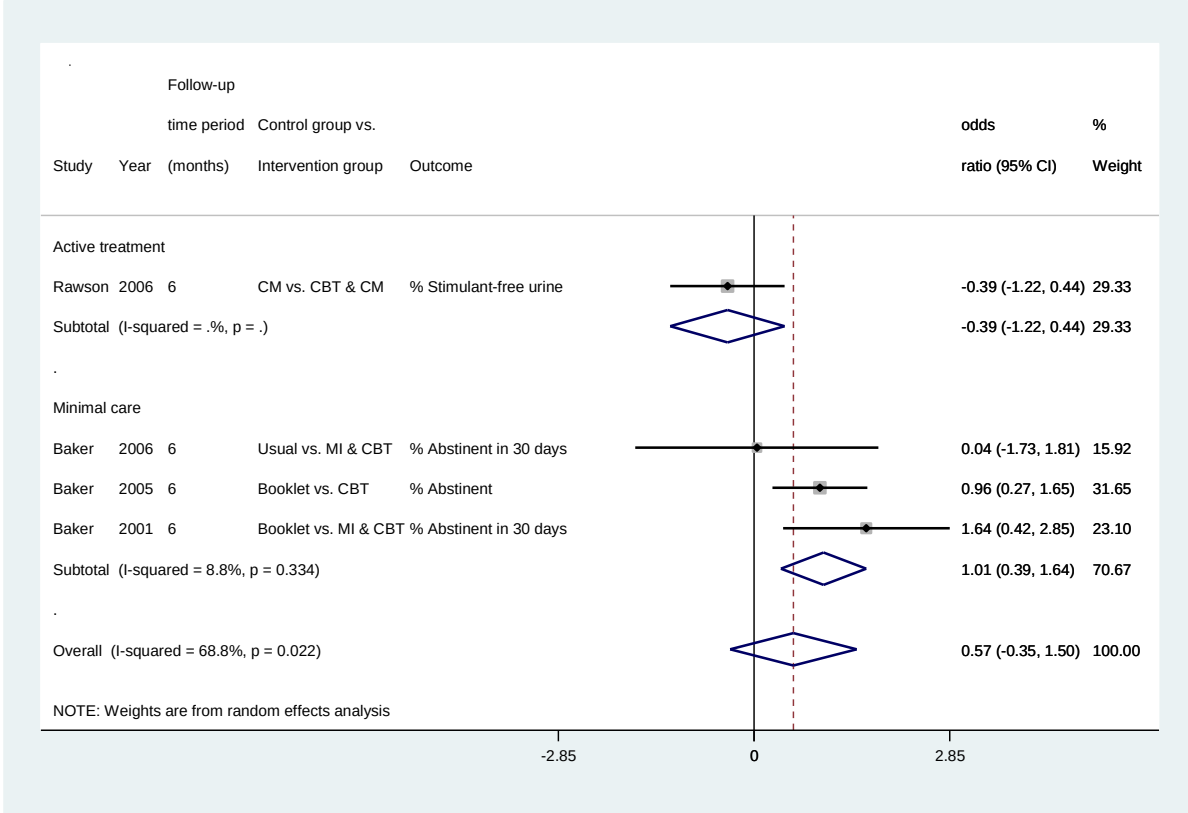

Figure 4. Forest plot for participants abstinent vs. not abstinent at six-months follow-up.

Figure 4 shows the results for the outcome assessing the number of participants abstinent from MA at six-month follow-up. Overall there was no significant difference

between abstinence rates for those who received CBT compared to those who received other treatments (RR = 0.57, 95% CI = - 0.35, 1.50, p = .223). However, when assessed separately by the intensity of the control group there was a significant difference between CBT and minimal treatment (TAU or self-help booklet) on abstinence rates, with CBT illustrating significantly higher log odds than the control condition (RR = 1.01, 95% CI = - 0.39, 1.64, p = .001).

Heterogeneity between effect sizes was significant with almost 69% (I^2 = 68.8%, p = .022) of the variation in point estimates explained by heterogeneity (Figure 4). Figure 14 (Appendix D) presents the contour enhanced funnel plot for this outcome. As shown by this figure there was limited evidence to suggest publication bias, with a mix of significant and non-significant findings published. However, due to the small number of studies included in the meta-analysis the results from such plots should be interpreted with caution.

Mental Health Outcomes

Addiction Severity Index and Brief Symptom Inventory

Five studies assessed scores on the psychiatric component of the ASI (51) and on the BSI (52), and were thus included in the meta-analyses (Table 3).

Table 3. *Studies assessing the effect of CBT on ASI and BSI scores*

Study	Intervention	Control/TAU
Baker, et al. (2002)	MI	Booklet
Baker, et al. (2005)	CBT	Booklet
Baker, et al. (2006)	MI & CBT	Usual care
McDonnell, et al. (2013)	CM	Usual care
Polcin, et al. (2014)	Intensive MI	Standard MI

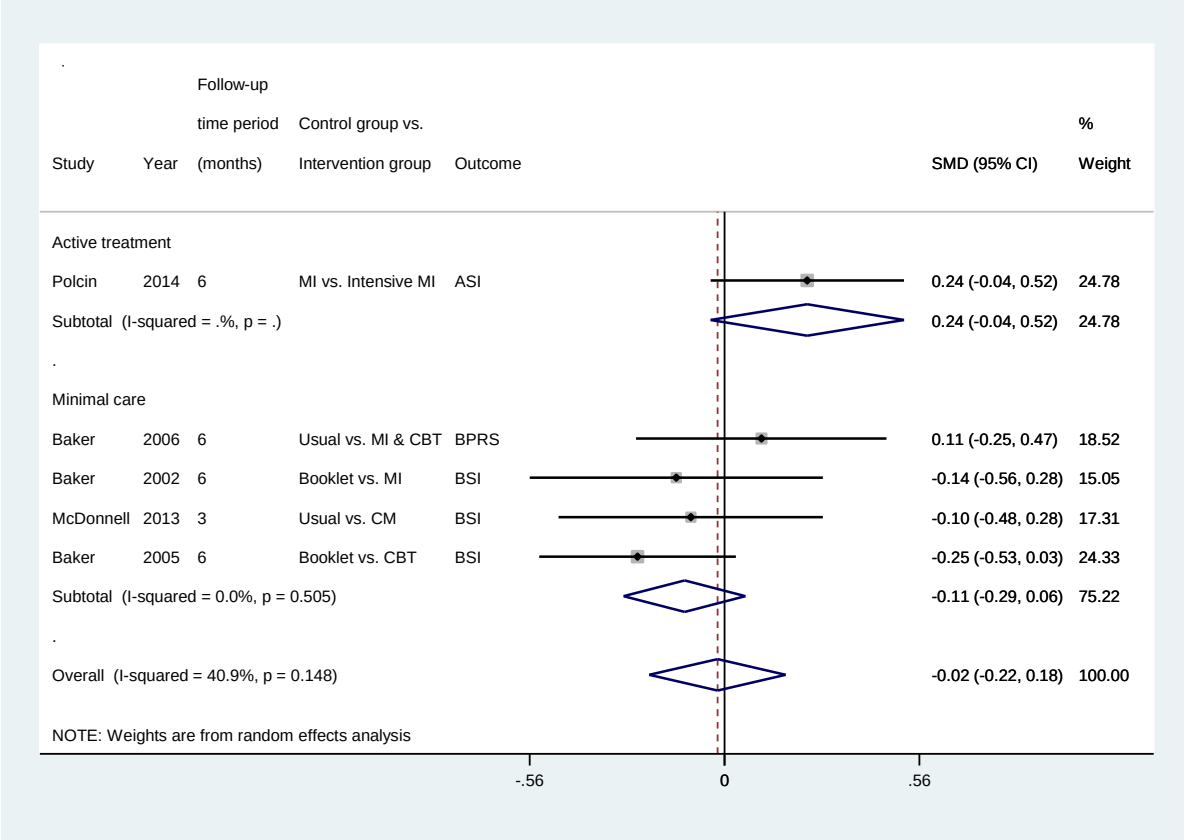

Figure 5. *Forest plot for ASI and BSI using mean follow-up scores.*

Figure 5 shows the forest plot for ASI (51) and BSI (52) scores when mean follow-up score was used as the estimated mean difference. There was no significant difference in follow-up ASI/BSI (51, 52) scores between those receiving CBT and those receiving other treatment types (SMD = - 0.02, 95% CI = - 0.22, 0.18, p = .842).

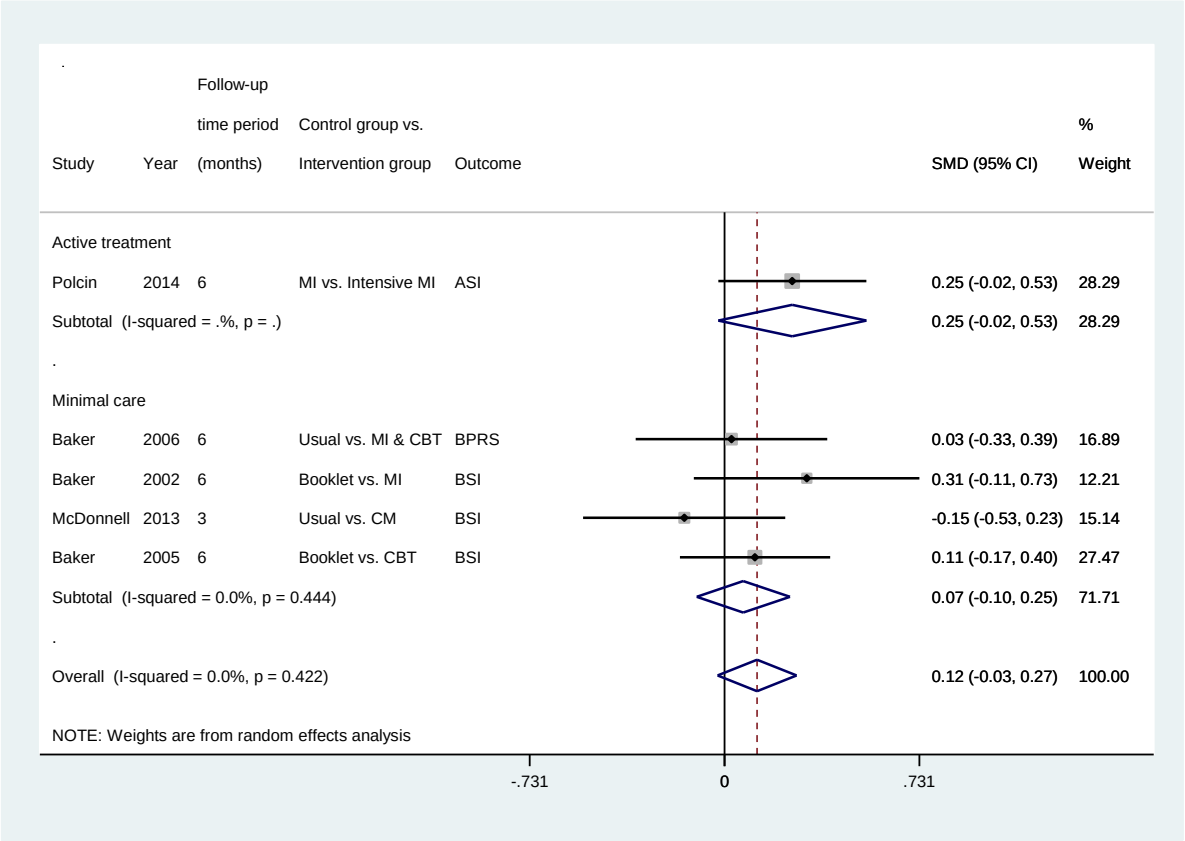

Figure 6. *Forest plot for ASI/BSI using mean change from baseline as the mean difference*.

Figure 6 illustrates the results for ASI/BSI (51, 52) scores when mean change from baseline was used as the estimated mean difference. There was no significant difference in the change in ASI/BSI (51, 52) scores from baseline to follow-up for the CBT group compared to control (SMD = 0.12, 95% CI = - 0.03, 0.27, p = .104).

Heterogeneity between effect sizes for both outcomes of ASI/BSI (51, 52) was not significant, with p-values >0.05 and I^2 values <50% (Figure 5 and 6). Less than 50% of the variation in point estimates was explained by heterogeneity for both outcomes.

Beck Depression Inventory

Four studies assessed scores on the BDI (53), and were included in the meta-analyses (Table 4).

Table 4. *Studies assessing the effect of CBT on BDI scores*

Study	Intervention	Control/comparison
Baker, et al. (2005)	CBT	Booklet
Baker, et al. (2006)	CBT & MI	Usual care
Peck, et al. (2005)	CBT	CM
Smout, et al. (2010)	CBT	ACT

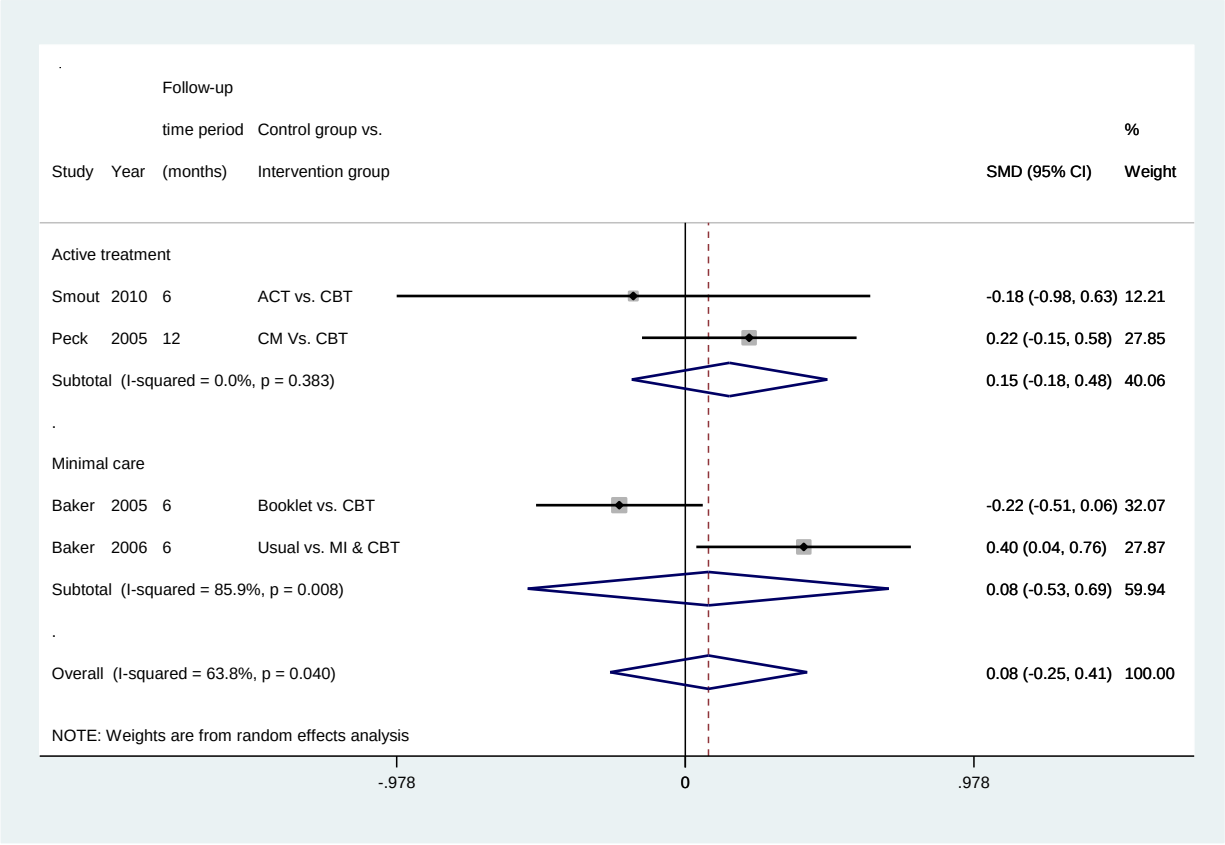

Figure 7. Forest plot for BDI using mean follow-up scores as the mean difference.

Figure 7 illustrates the forest plot for the outcome BDI (53) scores when the mean follow-up score was used as the estimated mean difference. There was no significant difference in follow-up BDI (53) scores between those receiving CBT and those receiving other treatment types (SMD = 0.08, 95% CI = - 0.25, 0.41, p = .642). This non-significant result was maintained when the control group was evaluated separately by treatment intensity

(comparing CBT to TAU or a booklet), with no significant difference found between CBT compared to minimal treatment (SMD = 0.08, 95% CI = - 0.53, 0.69, p = .803).

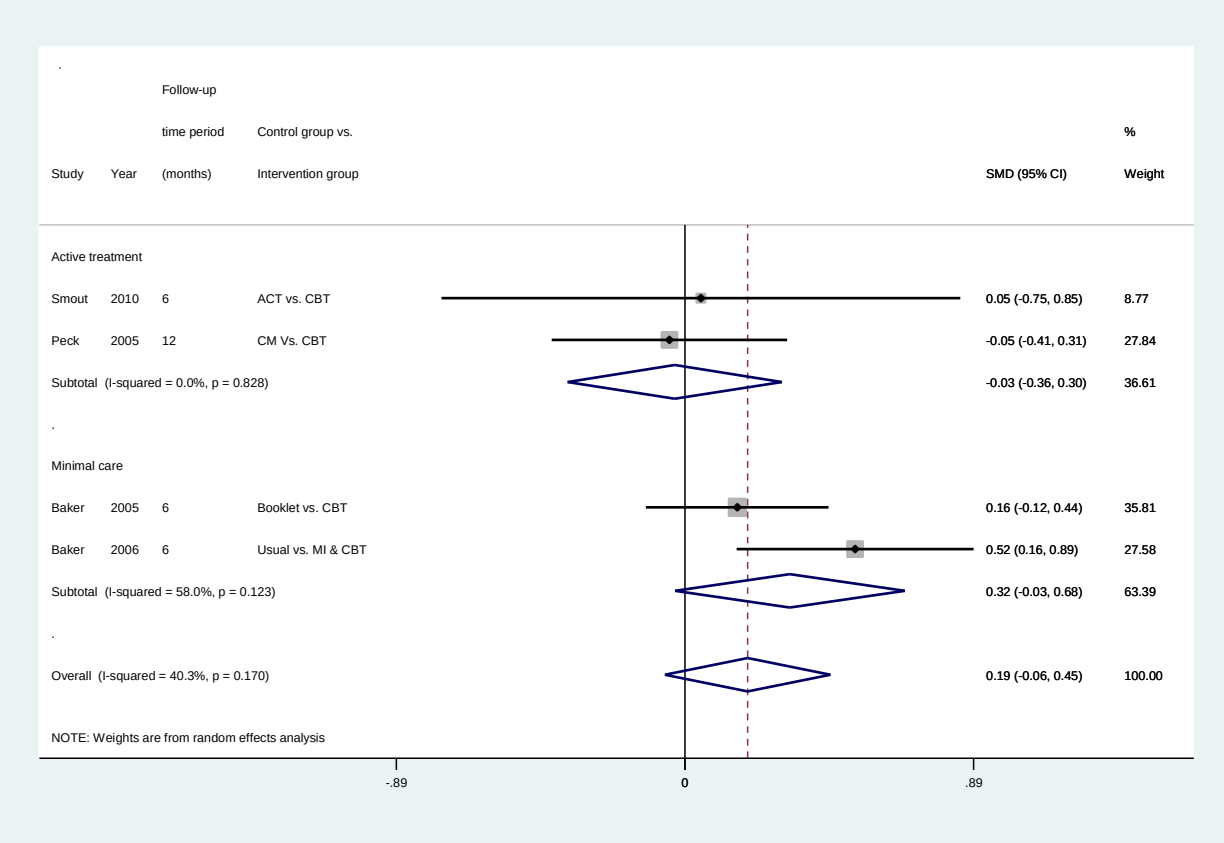

Figure 8. Forest plot for BDI using mean change from baseline scores as the mean difference.

Figure 8 illustrates the results for BDI (53) scores when mean change from baseline was used as the estimated mean difference. There was no significant difference in the change in BDI (53) scores from baseline to follow-up for the CBT group compared to control (SMD = 0.19, 95% CI = - 0.06, 0.45, p = .138).

Heterogeneity between effect sizes was significant when mean follow-up score was used as the estimated mean difference (Figure 7). For this outcome almost 65% (I^2 = 63.8%, p = .04) of the variation in point estimates was explained by heterogeneity for both outcomes. Comparatively, when mean change from baseline was used as the estimated mean difference heterogeneity was not significant (I^2 = 40.3%, p = .170) (Figure 8).

Methodological Quality Assessment

The details of the risk of bias assessment are shown in Appendix G. Overall, six studies were judged to have a high risk of bias (high risk of bias for one or more domains: (22, 54, 62)) and 11 studies to have an unclear risk of bias (unclear risk of bias for one or more domains: (22, 54-61)).

Discussion

This systematic review aimed to capture all relevant controlled studies of psychological interventions for MA use also reporting on co-occurring symptoms of mental ill-health. A total of 12 papers reporting on 11 trials were reviewed in full, primary outcomes were assessed via meta-analyses and secondary outcomes were synthesised narratively.

Meta-analyses

Results from meta-analyses provided limited evidence to suggest that CBT was more effective than other treatments in: i) reducing MA use; ii) reducing scores on the psychiatric component of the ASI (51) and on the BSI (52); iii) reducing scores on the BDI (53) (22, 59, 60); and iv) increasing abstinence rates. Furthermore, when assessed separately by the intensity of the control group there was a significant difference between CBT and minimal treatment (such as TAU involving a self-help book) on abstinence rates, with CBT showing a positive effect. This was consistent with previous research conducted by Roll (42) and Manning, et al. (38) who found in a multi-site treatment outcome study of Australian alcohol and other drug services, that higher rates of abstinence were seen when there was consistent rather than fragmented care provision. This suggests that more frequent and consistent interventions incorporating CBT, may offer an advantage for abstinence over TAU or fragmented care. The meta-analysis found little overall difference between intervention and comparison conditions (Appendix E). However, our meta-analysis suggested that CBT was associated with increased abstinence from MA. This is consistent with studies conducted by

Dutra (63) and Prendergast (64), in which they found that CBT combined with CM for psychostimulant use was effective when compared to low-intensity controls. However, our findings deviate from existing meta-analyses, which have studied all amphetamine-type stimulants (including MA, amphetamine, ecstasy and analogues) and not solely MA (31, 43, 63, 64).

Three additional studies that reported on abstinence could not be included in the meta-analyses. McDonell, et al. (56) reported the percent of participants with stimulant-negative urine samples, only for time-points during treatment but not follow-up. This data would have exaggerated any treatment effects observed. Polcin et al. (60) and Rawson et al. (34) reported continuous data relating to participant abstinence (i.e. mean percent days abstinent and mean number of MA-free urine samples, respectively) and thus could not be combined with the binary outcomes of the other studies. Further studies should use a common measure such as bio-verification of MA use and the Opiate Treatment Index (OTI) (65) for abstinence to enhance comparability of outcomes.

Brief interventions produced higher rates of retention and similar outcomes to longer interventions, implying that these may be more feasible and effective (39, 57, 61). This is in line with previous research, suggesting that brief interventions are efficacious for reducing substance use (42, 61, 63, 66). Consistent with previous research conducted by Knapp (31), it was evident from our narratively synthesised results (Appendix F) that if people are retained in treatment, combined interventions such as CBT + MI or CBT + CM, may be most effective.

Participants were recruited from inpatient services as well as drug and alcohol outpatient services in Australia and North America. There were differences between studies in the types of interventions received (Appendix E). Overall, studies indicated a significant reduction in poly-drug use and MA use for both intervention and TAU/control groups,

however there were no differences between groups, suggesting that intervention is not superior to control in reducing MA or poly-drug use (22, 39, 56-58, 61, 62). An improvement in social and global functioning was found for samples as a whole, however only two studies assessed these outcomes suggesting limited generalisability of results (39, 62). Three studies found a reduction in BBV risk-taking behaviour for the sample as a whole, indicating no differences between CBT interventions and TAU (56, 58, 62). Included studies utilising CBT or MI interventions exhibited significant decreases in ASI (51) psychiatric severity in both groups (54-56, 60-62). However, a few studies adopting CM or MI interventions found a significant improvement in ASI (51) scores when compared to TAU (54, 56, 60) (Appendix E). Most study results suggested that as MA use reduced for samples as a whole, symptoms of mental ill-health and depression reduced also (22, 34, 39, 55, 58-62).

Interventions such as CBT, CM and the Matrix Model exhibited a significant increase in abstinence from MA (34, 39, 54, 56-61). Contingency Management may be considered a behavioural counterpart of a CBT-based intervention, and may be worth further research in contexts outside of the USA. Considering the effectiveness of CBT for abstinence from MA, the CBT based mutual aid groups, SMART Recovery, or other mutual aid programs that incorporate elements of CBT and MI are worthy of further research (66).

Quality of the Evidence

The quality of the evidence was formally assessed using the GRADE (49) approach by two individual raters and then a decision was made via consensus (see Appendix H). Using GRADE (49), we formally assessed the overall certainty of the evidence, and rated it as moderate or low for evidence for which data were available. From this review it is evident that the quality of the primary research evidence on which the review is based is relatively low in terms of homogeneity (with evidence of substantial heterogeneity, inconsistent comparison groups and outcomes). The level of evidence for primary outcomes was as

follows: moderate for MA use, low for abstinence, and for mental health measures it was moderate for ASI (51) and BSI (52), and low for BDI (53). From this review it is evident that the quality of the primary research evidence is relatively moderate in terms of conduct and reporting. There was sparse data for several secondary outcomes indicating that further trials are needed. Some studies presented a gender bias as participants were mostly male and women were under represented (22, 34, 39, 54-62). Furthermore, studies were based on high income countries such as Australia and the USA, and numerous studies excluded participants with a psychiatric diagnosis. However, it has been widely researched that people who use MA have co-existing mental health problems (1, 16, 20).

Limitations

There was a relatively small number of RCTs examining MA and mental health outcomes. Thus, we created broad intervention categories in order to make meaningful comparisons. Within each category, there was substantial heterogeneity, which may influence estimates of effectiveness. The sample size for the meta-analysis was small. Only a few studies were homogenous enough to meet eligibility for meta-analyses. Several studies did not report the appropriate means or standard deviations, in which measures were taken to estimate the values needed, including imputation of values and data mining (67) (Appendix C). There was substantial variability between all studies in terms of the experimental and control conditions used, duration of treatment received, outcomes assessed, measures used and other characteristics of the studies included. Such between study variability may have impacted on the ability to observe treatment effects. A meta-regression could explore the possible impact that treatment engagement (i.e. treatment quantity, frequency and duration) has on the effectiveness of CBT on the outcomes assessed; however, the limited number of studies reporting consistently on these outcomes prevented such an analysis.

Studies reported outcome data differently and had different follow up periods, which caused difficulty in determining treatment engagement. Hence, a similar measure of engagement at similar time points could be considered. It is challenging for this client population to remain in treatment and this is evident across studies (Appendix F) (44). Severity of mental health conditions may influence outcomes in terms of reducing mental health symptoms and/or MA use (38, 43, 45). Our review was unable to address these issues.

There were no studies examining anxiety or quality of life outcomes. Given that the comorbidity of anxiety disorders and MA use can influence treatment outcomes (68), studies investigating treatment options for this comorbidity are warranted. Finally, future well-designed studies would benefit from larger sample sizes to increase generalisability. There were no eligible studies for Dialectical Behaviour Therapy (DBT), Schema Therapy (ST) or Mindfulness-Based Cognitive Behaviour Therapy (MBCBT), representing a gap in the literature.

Conclusion

The results of the meta-analysis showed no difference between control and intervention groups for reducing MA and co-occurring mental health symptoms. This systematic review provided limited evidence to support interventions like CBT and CM in reducing MA use and co-occurring mental health symptoms compared to control conditions. However, compared to minimal control conditions, brief CBT interventions may enhance abstinence from MA, suggesting possible clinical utility of brief CBT interventions. Overall results suggested a reduction in MA use and mental health symptoms among samples as a whole with only few studies showing a difference between conditions. There is much scope for developing the evidence base in this area. As MA use is a global public health burden, it is imperative that further studies with strong methodological quality are conducted in this population to guide future development of psychological interventions.

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Appendices

Appendix A

Table 5. *Medline Search Strategy*

#	Searches
1	methamphetamine.tw. or Methamphetamine/
2	Amphetamine-Related Disorders/ or Amphetamine/ or amphetamine.tw.
3	1 or 2
4	Psychotherapy/ or psychotherapy.tw.
5	((psychosocial or psycho social) adj5 (treatment* or therap*)).mp.
6	cognitive therapy/ or "acceptance and commitment therapy"/ or mindfulness/ or (cognitive adj5 (therap* or treatment*)).tw.
7	Behavior Therapy/ or contingency management.mp.
8	Motivational Interviewing/
9	brief intervention*.mp.
10	(cognitive behavio?r* adj5 (treatment* or therap*)).mp.
11	(abstinence adj5 (treatment* or therap*)).mp.
12	4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13	Mental Disorders/
14	Mental Health/
15	Anxiety/
16	Depression/
17	Psychotic Disorders/
18	(mental health or mental disorder* or mental illness* or anxiety or depression or psychosis or hostil*).tw.
19	13 or 14 or 15 or 16 or 17 or 18
20	3 and 12 and 19
21	animal/ not (human/ and animal/)
22	20 not 21
23	limit 22 to english language

Appendix B

Table 6. *Secondary Outcomes*

Outcome	Studies
Change in other drug use	Baker, et al. (2001), Baker, et al. (2002), Baker, et al. (2005), Baker, et al. (2006), Kay-Lambkin, et al. (2011), McDonell, et al. (2013), Smout, et al. (2010)
Treatment engagement	all
BBV risk reduction	Baker, et al. (2001), Baker, et al. (2005), McDonell, et al. (2013), Peck, et al. (2005)
Change in physical health	Smout, et al. (2010)
Change in quality of life	Nil reported
Difference in functioning pre/post (GAF)	Baker, et al. (2002), Baker, et al. (2006)

Appendix C

Meta-analysis Methodology

Introduction and Study Aims

The aim of this meta-analysis was to examine whether Cognitive Behaviour Therapy (CBT) was significantly more effective than other treatment types in improving the following outcomes in methamphetamine users:

(i) Reducing methamphetamine use;

(ii) Reducing scores on the psychiatric component of the Addiction Severity index (ASI) (51) and Brief Symptom Inventory (BSI) (52);

(iii) Reducing scores on the Beck Depression Inventory (BDI) (53); and

(iv) Increasing rates of abstinence.

General Statistical Methodology

Data Preparation

The data was cleaned and cross-checked in Microsoft Excel before being uploaded into STATA. To allow for comparisons to be made between CBT treatment and other treatment types, CBT was classified as the intervention in all studies included in the review, regardless of whether CBT was the intervention in the original study.

For this review separate analyses were conducted for each of the four outcomes. Three of the outcomes were continuous, and included: (i) methamphetamine use; (ii) ASI/BSI (51, 52) scores; and (iii) BDI (53) scores. While the fourth outcome was binary: number abstinent vs. number not abstinent at six-months follow-up.

Preparation of Continuous Outcomes

To conduct a meta-analysis on a continuous outcome the following variables are required for both the intervention and control group: sample size, mean difference and

standard deviation (SD). For several studies these values were not reported. In such instances measures were taken to estimate the values needed; such measures included: using recommended formula to convert the statistics reported in the publications into the required values;[1] imputation of values; and data mining. A summary of the specific measures and conversions used for this review are provided below:

- When the standard error was reported rather than the standard deviation, the standard deviation was calculated as: $SD = SE\sqrt{n}$[1]
- When the interquartile range (IQR) was reported rather than the SD, the SD was calculated as: $IQR/1.35.$[1]
- When the median was reported rather than the mean, the median was used as a direct substitution for the mean.
- For the studies by Baker et al. (57) Baker et al. (61) and Peck et al. (59) there were more than one CBT (i.e. intervention) group. As we were only interested in comparing the effect of CBT to other treatments a pooled mean estimate and SE for the CBT groups were calculated using the *metan* package in STATA. An SD was then calculated by converting the pooled SE using recommended formula.[1]
- For the study by Peck et al. (59) only means and SDs were reported for the outcome BDI scores individually for each experimental group for the 12-month follow-up; no estimates were provided for baseline. However, mean baseline scores were reported graphically. The software '*webplotdigitiser*' was used to extract estimated mean baseline scores from the graph. However, baseline SDs were not reported in the graph, consequently SDs that were reported for the 12-month follow-up were imputed and used as the estimated SDs for baseline.
- For Rawson et al. (34), no SD or measure of variance was provided for the individual experimental groups; thus, SDs could not be calculated directly for this study. Rather

an estimated SD was imputed for this study, which was calculated by averaging the weighted standardised SEs from all other studies using the change from baseline measure of mean difference (see below). An SD was then calculated using recommended formula[1] and weighted by the sample size of this study.

- For Rawson et al. (34) and Peck et al. (59), individual sample sizes were not available for each experimental group; rather only a total sample size was provided for all groups combined. An estimated sample size for the individual groups was obtained by dividing the total sample size by the number of experimental groups and distributing as evenly as possible between the number of experimental groups.
- For studies that imputed missing data the statistics from the imputed dataset were used in the meta-analysis.

There are several different values that can be used as an estimated mean difference. Two common values include: (i) the mean follow-up value; and (ii) mean change from baseline. Both of these values have been used in this study. Six-month follow-up scores were used for studies where they were reported; otherwise the closet follow-up period to six months was used. To calculate mean change from baseline, six-month follow-up scores (or follow-up scores closest to six months) were subtracted from the baseline scores. For this particular estimate of mean difference, a change from baseline SD is also required. For this study the following recommended formula[1] was used to calculate SDs for change scores:

$$SD_{change} = \sqrt{SD_{baseline}^2 + SD_{follow-up}^2 - 2 * r * SD_{baseline} * SD_{follow-up}}$$

In this equation the value of r is equal to the correlation between baseline and follow-up scores. As r was not available for any of the studies included in this meta-analysis, a value of 0.5 was used. This is a conservative estimate, which is recommended to be used when no value for the correlation is available (66).

Preparation of Binary Outcome

To conduct a meta-analysis on binary data you require the number of events and the number of non-events that occurred. In this case the number of events (i.e. abstinence) and number of non-events were calculated using the percentage of abstinent participants and sample size reported for each group. For Rawson et al. (54), the percentage of stimulant free urine samples were only presented graphically; thus the software '*webplotdigitiser*' was used to extract an estimation of these values. These percentages were then used along with the total number of participants reported to have completed a follow-up at 26 weeks, to calculate the estimated number of people who were abstinent vs. non-abstinent at approximately 6-months follow-up.

Analysis

Statistical analyses were programmed using Stata v13.0 (StataCorp Ltd, College Station, TX). The characteristics of the included studies varied substantially, with differences observed in the methodologies, control conditions, outcomes and measures used. To account for the between-study variability the Dersimonian and Laird random effects method of meta-analyses was used to estimate the pooled mean difference in all meta-analyses.

Meta-analyses of Continuous Outcomes

A separate meta-analysis was conducted using the mean follow-up value and mean change from baseline value as the estimated mean difference for each of the following continuous outcomes: (i) Methamphetamine use (MA use); (ii) scores on the psychiatric component of the Addiction Severity index (ASI) (51) and Brief Symptom Inventory (BSI) (52); and (iii) scores on the Becks Depression Index (BDI) (53). For each of these analyses Hedges g was used to estimate a standardised pooled mean estimate, as there was variation across studies with regards to how each outcome was defined and/or measured.

Meta-analyses of Binary Outcome

For the outcome abstinence the log odds and standard error were calculated using the number of participant reported as abstinent and the number reported as not abstinent. This data was used in the analysis and the odds ratios and 95% confidence intervals are reported.

A forest plot was created for all meta-analyses conducted and inspected for possible between group heterogeneity. Significant between group heterogeneity was determined by a significant Q test and an I^2 value above 50%. Furthermore, to account for the wide variation in control conditions the pooled estimates are presented overall for all control groups combined, as well as aggregated by the intensity of the control condition (i.e. minimal care vs. active treatment). Active treatment was classified as a control group that received any treatment above usual care or receipt of information. This was done to provide an indication of the impact CBT has on the outcomes compared to minimal care. Contour enhanced funnel plots were created for all models to allow for the assessment of potential publication bias.

Appendix D

Results

Methamphetamine Use

Figures 9 and 10 illustrate the contour enhanced funnel plot for the two outcomes of MA use. As shown by these figures the funnel plots are not symmetrical with larger gaps on the lower right hand-side for Figure 9 and middle left-hand side for Figure 10. This may suggest some publication bias, particularly for Figure 9 with smaller studies seeming to report data that is more in favor of CBT having an effect. However, the majority of these studies are not significant, which may actually suggest limited evidence of publication bias. Rather the asymmetrical shape may be caused by other factors rather than publication bias, such as heterogeneity between studies.

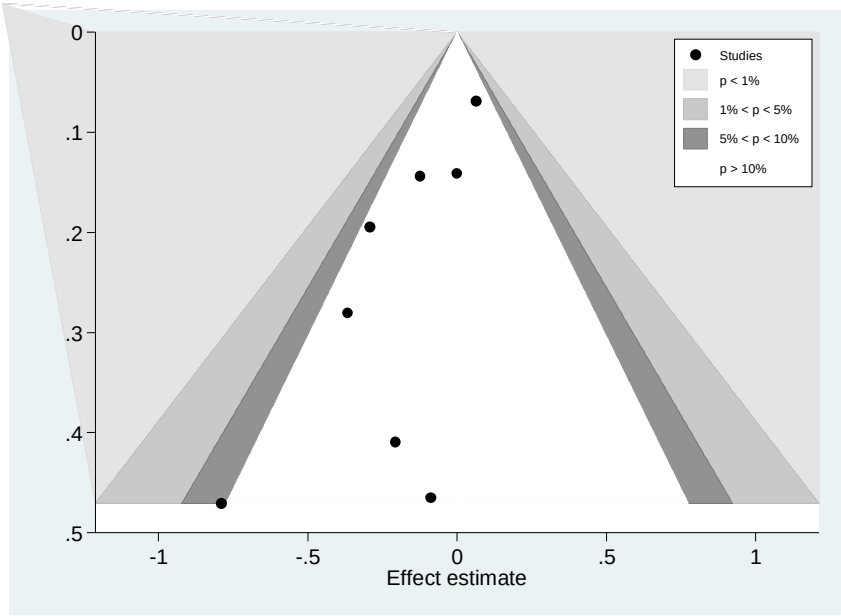


Figure 9. *Contour enhanced funnel plot for MA use using mean follow-up scores as the mean difference*.

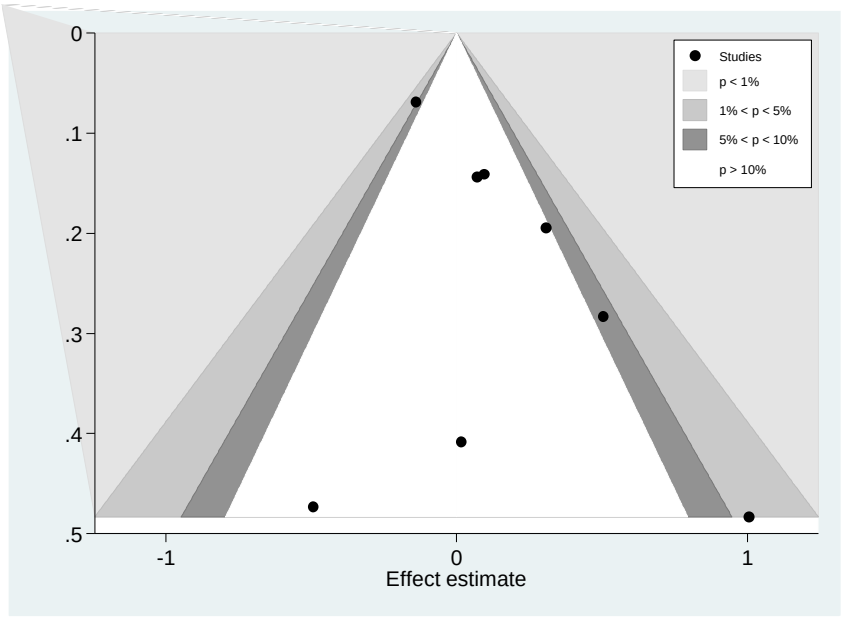


Figure 10. *Contour enhanced funnel plot for MA use using mean change from baseline as the mean difference*.

Addiction Severity Index (ASI) and Brief Symptom Inventory (BSI)

Figures 11 and 12 illustrate the contour enhanced funnel plot for the two outcomes of ASI/BSI scores. As shown by these figures there was limited evidence to suggest publication bias for any of the outcomes, with only not significant findings having been published. There is also a relatively even spread of positive and negative results across studies.

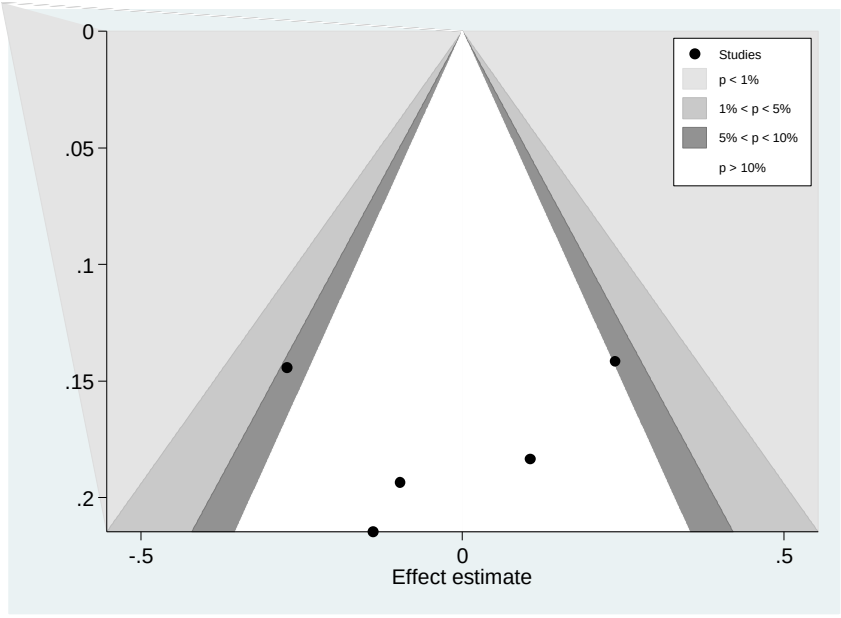


Figure 11. *Contour enhanced funnel plot for ASI/BSI using mean follow-up scores as the mean difference.*

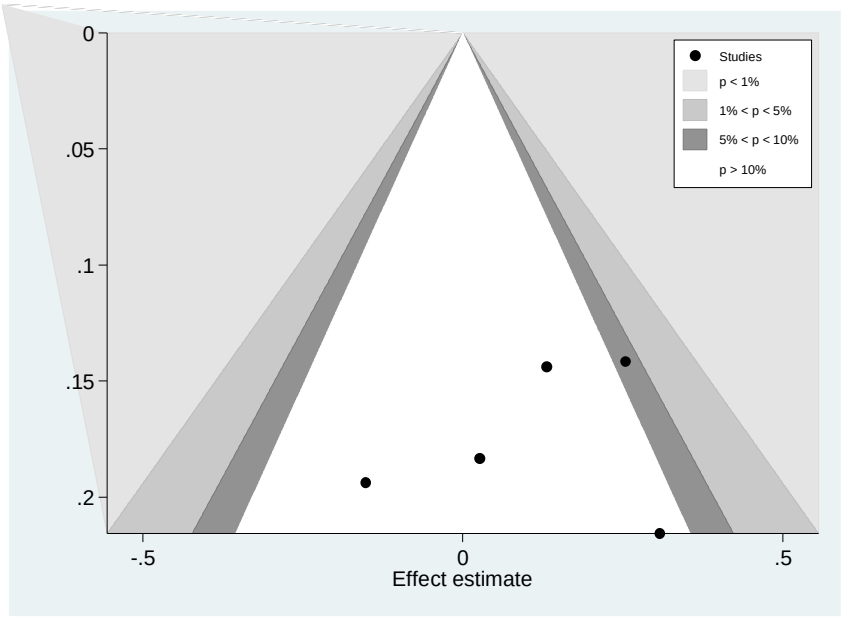


Figure 12. Contour enhanced funnel plot for ASI/BSI using mean change from baseline as the mean difference.

Beck Depression Inventory (BDI)

Figures 13 and 14 present the contour enhanced funnel plots for the two outcomes of BDI scores. As shown by these figures there was limited evidence to suggest publication bias for any of the outcomes, with mostly not significant findings having been published. However, due to the small number of studies included in this meta-analysis the results from such plots are difficult to interpret and thus must be interpreted with caution.

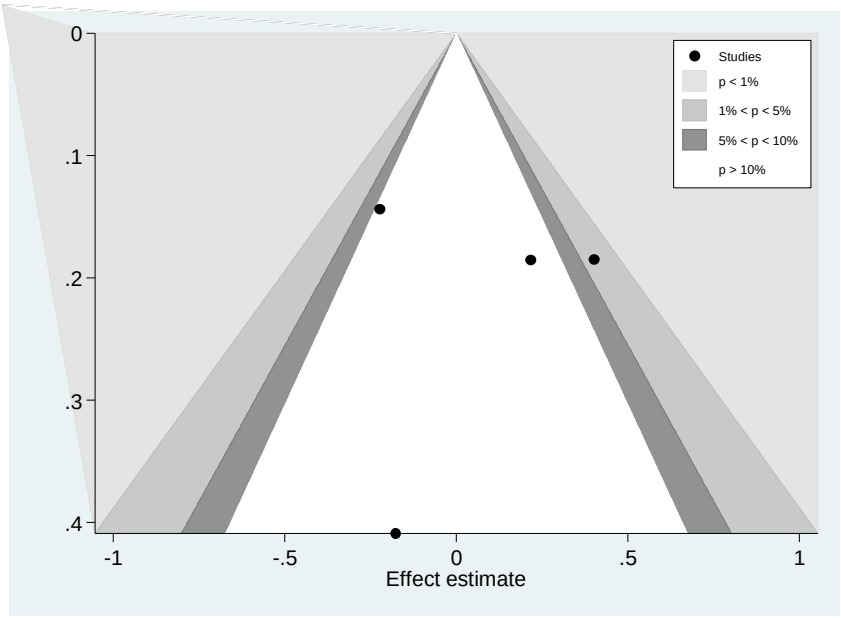


Figure 13. *Contour enhanced funnel plot for BDI using mean follow-up scores as the mean difference.*

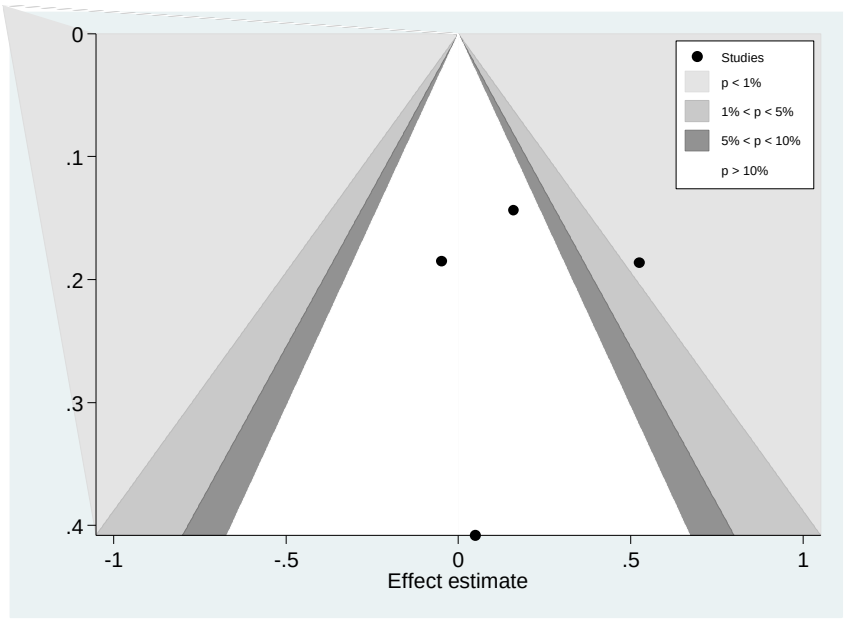


Figure 14. *Contour enhanced funnel plot for BDI using mean change from baseline as the mean difference.*

Abstinence rates

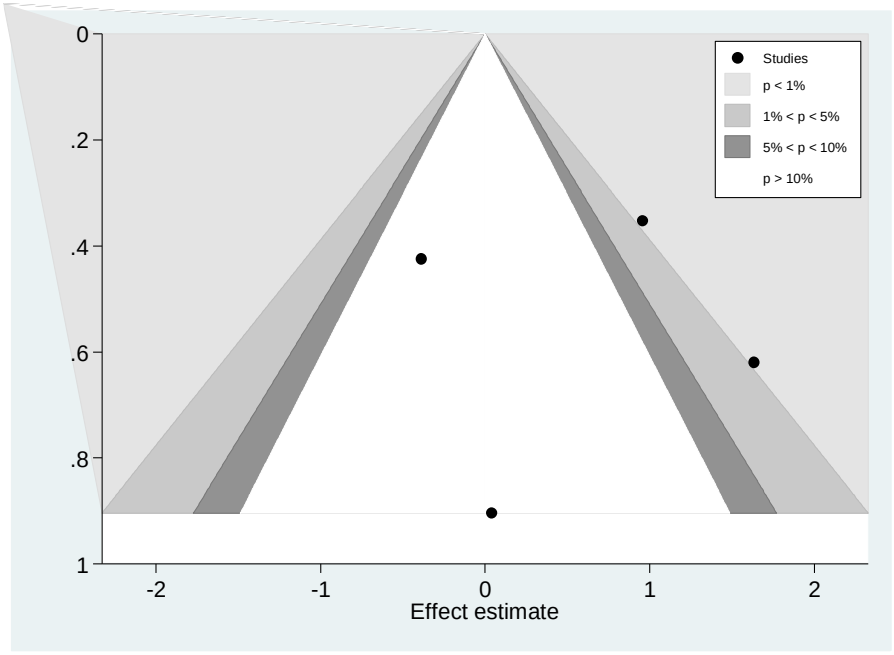


Figure 15. *Contour enhanced funnel plot for number of participants abstinent vs. not abstinent at six-month follow-up.*

Figure 15 presents the contour enhanced funnel plot for this outcome. As shown by these figures there was limited evidence to suggest publication bias, with a mix of significant and not significant findings having been published. However, due to the small number of studies included in this meta-analysis the results from such plots are difficult to interpret and thus must be interpreted with caution.

Appendix E

Table 7. *Intervention details and feasibility*

Study, Design, Recruitment Period, Location	Aims	Participant inclusion/exclusion criteria Number of participants (N)	Participants details	Healthcare Providers	Intervention	Control/comparison	Time points MH measure/tool	MA use measure/tool
Baker, Boggs & Lewin, (2001) RCT Newcastle, New South Wales Recruited between July and December 1998	The aim of the study was to: (1) identify whether brief CBT interventions were feasible among regular MA users; (2) assess the effectiveness of the intervention overall; and (3) to pilot two- and four-session interventions.	*Inclusion:* Regular use of amphetamine, poly-drug users and people enrolled in MMT were not excluded from the study provided they reported regular MA use. N =64	**Employment rates not reported.** Mean years of education 10.58**.** **Mean age (SD)** 31.68 (SD not reported) **Gender – Male % (n)** 61.5% (32)	Two research assistants with four years training in psychology	Four or two 30-60 min sessions of CBT. Each session focused on the acquisition of cognitive behavioural coping strategies to assist in reducing MA use. Participants were provided with a self-help booklet on reducing MA use and related harms. n = 32	Self-help booklet on reducing MA use and related harms. n = 32	Pre-treatment, 6-month follow-up SDS; Contemplation Ladder GHQ-28	OTI
Baker, et al. (2002) RCT Participants were recruited from September 1996 and July 1998.	Examine the effectiveness of MI among hospitalized psychiatric patients with comorbid substance use	*Inclusion:* Must be a patient at the psychiatric hospital; capable of interview; likely to be a local resident over the next 12 months; levels of alcohol and other drug use during months before admission warrant intervention N = 160	**Employment/education not reported** **Mean age (SD)** 30.88 (SD not reported) **Male % (n)** 75% (120)	Four psychologists with an honours degree in psychology	One MI session, 30 - 45 minutes long. n = 79	Brief advice on alcohol and other drug use, and a self-help booklet on alcohol and other drug services. n = 81	Pre-treatment and at 6- and 12-month follow-ups SCID, BSI	OTI
Baker, et al. (2005), & Kay-Lambkin, et al. (2011) RCT Oct 2001 – Sep 2005. 6-month duration from recruitment to follow up Multicentre – Newcastle and Brisbane, Australia	To repeat and extend on a smaller pilot study of a CBT intervention to reduce MA related harms in a sample of regular MA users.	*Inclusion:* At least weekly use of MA *Exclusion:* suicidality or acute psychosis, acquired cognitive impairment, current enrolment in treatment for MA use N = 214	74.8% unemployed 49.1% post school qualifications Mean age leaving school 16.14 **Mean age (SD)** 30.22 (7.84) **Gender – Male % (n)** 62.6% (134)	3 psychologists and one social worker	Counselling sessions of 45-60 minutes, weekly basis depending on location CBT 2 sessions (n) = 74 CBT 4 sessions (n) = 66	Self-help booklet n (control) = 74	Pre-treatment, post-treatment, 6-month follow-up BSI, GSI, BDI-II Pre-treatment only SCID-I/NP	OTI

							Pre-treatment, 6-month follow up SDS Post-treatment IPDEQ	
Baker, et al. (2006) RCT Recruited between 2000 and 2002 Single-site – Hunter region, NSW Australia	Compared the effectiveness between MI+CBT compared to usual care at reducing MA-abuse and improving symptomatology and general functioning	*Inclusion:* met alcohol consumption exceeding recommended levels, or at least weekly use of cannabis or amphetamines; ability to speak English; and having a confirmed ICD–10 psychotic disorder *Exclusion:* failure to meet at least one of the specified substance use thresholds; had an organic brain impairment; or intended to move from the geographical area within the subsequent 12 months. N (overall) = 130	65.5% reported receiving post-school qualifications **Mean age (SD)** 28.83 (SD=10.27) **Male % (n)** 78.2% (93)	Three therapists/psychologists	10 weekly, 1-hour sessions of combined CBT + MI counselling/sessions. Self-focus, problem solving strategies and identification of 'unhelpful' patterns of thinking. n = 65	TAU - self-help booklet on substance use. n = 65	Baseline, 15 weeks, 6 months; 12 months ICD-10; SCID I, BDI-II, GAF, BPRS	OTI
Kay-Lambkin, et al. (2010) Adaptive treatment - stepped-care model 20 weeks duration Multicentre – Newcastle and Sydney, Australia	Pilot stepped-care adaptive methods in treatment of MA use and depression.	*Inclusion:* At least weekly MA use for the previous month, and reported moderate levels of depression. *Exclusion:* Did not meet depression criteria N = 18	**Education/employment not reported** **Mean age in years (SD)** 35 (no SD) **Gender – Male % (n)** 56% (10)	Therapists	Adaptive CBT/MI stepped-care intervention involved providing the next level of treatment (step treatment up; step treatment down) based on responses to the previous step. n = 11	Fixed integrated CBT/MI treatment package focusing on depression and MA use. n = 8	Baseline, 5 weeks, 10 weeks, 15 weeks, 20 weeks BDI-II	OTI
McDonnell, et al. (2013) Multisite – multisite RCT Community mental health and addiction agency in Seattle. Recruitment period not reported	Whether the addition of CM for psycho-stimulant drug abstinence would be successful in reducing stimulant use	*Inclusion:* Used stimulants in the last 30 days; meet MINI Criteria for MA, amphetamine or cocaine dependence as well as criteria for schizophrenia, schizoaffective disorder, bipolar I or II disorder, or major recurrent depressive disorder. *Exclusion:* organic brain disorder, dementia, or medical disorders or psychiatric symptoms severe enough to	**Employment rates not reported.** **Education not reported.** **Mean age (SD)** 42.73 (SD = not reported) **Male % (n)** 65.3% (115)	Health care providers were not reported	Both groups received 3 months of TAU, which consistent of mental health, chemical dependency, housing and vocational services. CM – received extra reimbursement based on testing negative for drug use using bioverification. Missing or drug positive samples resulted in no delivery of reinforcement. n (CM + TAU) = 91	Non-CM control – number of opportunities were equalled, however, the ability to gain extra reimbursement was not included. n (non-CM rewards plus TAU) = 85	At weeks 4, 8, 12, 16 and 24 ASI-Lite, BSI, PNSS, HIV risk behaviour scale	Bioverification - Breath and urine samples three times a week

		compromise safe participation in the study. N = 176						
Peck, et al. (2005) RCT Participants recruited from 1996 to 2001. Single-centre – outpatient treatment research clinic in Hollywood, Los Angeles	Aimed to evaluate the severity and prevalence of depressive symptoms at various time points after behavioural interventions among MA-dependent gay and bisexual men	*Inclusion*: seeking treatment for their current MA use problem; diagnosed with MA dependence; self-identified gay or bisexual men; between the ages of 18 and 65; and willing to provide informed consent N = 162	58.6% completed at least high school 25.3% completed a 4-year degree **Mean age (SD)** 36.6 (SD = 6.4) **Male % (n)** 100% (162)	Healthcare providers are not described.	Thrice weekly for 16 weeks. CM group – Monetary reimbursement for urine samples that provided evidence for MA abstinence. n (CM) = 42 CM + CBT group – CBT with the addition of the ability to earn reimbursement for providing urine samples that supported MA abstinence. n (CBT + CM) = 40 GCBT group - a culturally sensitive-version of CBT, plus education, booklets and materials about HIV-related risk behaviours n (G-CBT) = 40	CBT group – met three times a week, focused on teaching participants coping strategies for triggers of MA use. n = 40	<u>Baseline and at 16, 26 and 52 weeks follow-up</u> BDI. SCID	Bioverification, urine sample. 30-day self-report scores of the ASI.
Polcin, et al. (2014) RCT Participant recruitment period is not reported. Single-Centre - outpatient substance abuse treatment facility in Northern California.	To assess MA outcomes of individuals assigned to intensive MI versus a comparison condition at an intensive outpatient treatment program	*Inclusion:* 18 years or older; met DSM-IV criteria for 12-month MA dependence, and comfortable participating in English. N = 217	42.8% had completed high school or less 57.2% had completed some college or more **Mean age (SD)** 38.4 (SD not reported) /note (37.5+39.3/2) **Male % (n)** 50.7% (110)	Three therapists	Intensive MI – weekly therapy sessions for 9 weeks n = 111	Standard MI – single session of standard MI, 8 sessions of nutrition education to match intervention group on time. n = 106	<u>Baseline and 2-, 4-, and 6-month follow-up</u> ASI-lite	Timeline follow-back was used to record MA use (self-report). Administered weekly for the 9 weeks. Administered at 2, 4, and 6-months.

Rawson, et al. (2004) RCT Recruited between 1999 and 2001 16-week intervention Multi-site –8 sites in USA	To compare the Matrix Model with TAU for reducing MA dependence	*Inclusion:* 18 years +; MA-dependent as determined by DSM-IV; willing to complete forms and provide urine samples; can understand scales and instructions; can understand English; and able to participate in all aspects of the treatment condition. *Exclusion:* medical and/or psychiatric condition which precluded safe participation; requiring medical detoxification from opioids/alcohol/other drugs; not having used MA in the last 30 days; having been enrolled in another treatment program in the last 30 days; and having medical, legal, housing and/or transportation precluding consent N = 978	69% employed M = 12.2 years of education **Mean age (SD)** 32.8 years old (SD not reported) **Gender – Male % (n)** 45% (440) Average 7.54 years of lifetime MA use. 11.53 days of MA use in past 30 days.	Clinical staff trained to deliver Matrix Model	4-16 weeks 1-13 hrs per week Matrix model – 16 weeks of CBT (36 sessions), family education groups (12 sessions), social support groups (four sessions) and individual counselling (four sessions) combined with weekly breath and urine testing. n = 489	TAU – varied widely across sites. n = 489	<u>Baseline, six and 12-months post-treatment</u> ASI	Bioverification – urine sample
Rawson, et al. (2006) RCT 2-week screening period. Study period was three years. Single-site – stimulant dependent individuals	To compare the effectiveness of CM and CBT alone and in combination for reducing stimulant use.	*Inclusion:* diagnosed as MA or cocaine dependent based on DSM-IV criteria; evidence of cocaine or MA use during 2-week screening period. *Exclusion:* dependent on alcohol or benzodiazepines. N (overall) = 177	9% unemployed over last 3 years 96% reported having a high school degree or equivalent **Mean age (SD)** 36.2 (SD not reported) **Male % (n)** 76% (135) 160 – cocaine dependent. 17 – MA dependent.	CBT therapist had a master's degree in Marriage and Family Therapy and CM technician had a BA degree	16 weeks CM – Participants required to provide three urine samples and meet with a CM technician. The voucher value was based on an escalating schedule. n (CM) = 60. (7 people using MA) CBT + CM – CM and CBT group interventions simultaneously. n (CM + CBT) = 59. (5 MA)	CBT considered as control/TAU CBT – 48 group sessions of CBT over a 16-week period (three per week). n (CBT) = 58. (5 MA)	<u>Baseline, 17, 26 and 52-weeks follow-up</u> BSI, ASI	Bioverification – urine sample. Abstinence
Smout, et al. (2010) Preliminary RCT Participants recruited from March 2004 - May 2006.	Does ACT increase treatment attendance and reduce MA use and related harms compared to CBT.	*Inclusion:* Between 16 and 65 years of age; met DSM-IV criteria for MA abuse or dependence according to the Mini-International Psychiatric	39% unemployed 39% employed 12% student 17% vocational education 25% 7-10 yrs education	Two therapists, a doctoral-level psychologist and a Masters-level psychologist	12 weekly 60-min individual ACT sessions. Sessions included reviewing drug use from the previous week, learning new skills associated with ACT and	12 weekly 60-minute individual CBT sessions. Sessions included reviewing drug use from the previous week, and	<u>Baseline, 12 and 24-weeks post-entry</u> BDI-II, SF-12	lf-reported A use sessed rough semi-uctured erview

Single-centre – Inpatient, outpatient and phone services of drug and alcohol services, South Australia	Interview (MINI) substance use module; MA was their drug of choice; reported average MA use of at least 2 days per week in the past 3 months; were willing to provide hair samples; and were available to attend appointments. *Exclusion:* Reported commencement or not maintaining antidepressant, antipsychotic or mood stabiliser; had psychiatric or medical condition requiring hospitalisation. N = 104	49% 11-13 yrs education **Mean age (SD)** 30.9 (SD = 6.5) **Gender – Male % (n)** 63 (60%)	mindfulness/acceptance exercises. n = 51	skill instruction/MI depending on progress of the participant. n = 53

Note. RCT = randomised clinical trial, MA = methamphetamine, MH = mental health, N = number of participants for whole sample, n = number of participants in subgroups, MMT = Methadone Maintenance Treatment, SD = standard deviation, CBT = Cognitive Behaviour Therapy, CM = Contingency Management, GCBT = Gay specific Cognitive Behaviour Therapy, ACT = Acceptance and Commitment Therapy, IMI = Intensive motivational interviewing, SMI = standard motivational interviewing, SDS = Severity of Dependence Scale, OTI = Opiate Treatment Index (mean score reflects average number of use occasions per day in the previous month), GHQ = General Health Questionnaire, SCID/ I NP = Structured Clinical Interview for Diagnostic and Statistical Manual (DSM-IV) – research version, BSI = Brief Symptom Inventory, GSI = Global Symptom Index, GAF = Global Assessment of Functioning, ICD-10 = International Classification of Diseases, BPRS = Brief Psychiatric Rating Scale, BDI-II = Beck Depression Inventory, IPDEQ = International Personality Disorder Examination Questionnaire, PNSS = Positive and Negative Symptom Scale, ASI-Lite = Addiction Severity Index Lite version, SF-12 = Short Form Health Survey-12, HIV = Human Immunodeficiency Virus

Table 8. *Outcomes of psychological interventions for MA use*

Study	Attrition (sessions/assessments)	Results at baseline (MA reduction % or abstinence) compared to post intervention (mean, SD)
Baker, Boggs & Lewin, (2001)	65 entered study 52 followed up **Intervention group** Four session CBT initial = 16 Attended all four sessions = 9 (56.3%) Two session (B2) CBT initial = 16 Attended both sessions = 11 (68.8%)	**MA use:** Amphetamine use fell significantly for the sample as a whole. There was a non-significant tendency or fall to be greater among B2 compared to control. Mean daily occasions of amphetamine use fell 0.44 units in control vs 1.02 units in intervention group. % abstinent at follow-up was as follows: (1) control group 21.4% abstinent; (2) two sessions intervention group 33.3% abstinent; (3) overall 58.5% abstinent; (4) all intervention groups 58.3% abstinent; (5) one session intervention group 62.5% abstinent; and (5) three-four session group 85.7% abstinent. Control group had the lowest % abstinent, compared to the three-four session group. **MH:** No significant differences between groups or changes over time in GHQ-28 scores. *Changes in amphetamine related harms:* No differential changes in OTI crime scores across groups. Significant reduction in crime for sample as a whole from mean of 1.87 to 0.79 (p <.01). B2 (2 sessions) had significantly better overall health scores than controls (p<.01). No significant change in levels of injecting risk-taking behaviour, although control group had higher injecting risk-taking scores overall compared to intervention (p<.01). *Other drug use:* No significant change in cannabis or tobacco. Significant overall reduction for total sample in poly-drug use over time (p<.01).
Baker, et al. (2002)	89/160 (55.6%) completed all follow up phases 55 MI and 57 control subjects at 3 month follow up 43 MI and 46 control who completed all assessments	**MA use** (OTI) differed across time points between the control and intervention groups. At pre-treatment, control (0.95, SD = 0.93) had higher scores than the intervention group (0.51, SD = 0.89). At 3-month follow-up, the control group (0.01, SD = 0.03) had lower OTI scores than intervention (0.32, SD = 1.05). At 6-month follow-up, control (0.17, SD = 0.35) had higher scores than intervention (0.14, SD = 0.31). At 12-month follow-up, control (0.03, SD = 0.05) had lower OTI scores than intervention (0.06, SD = 0.17). **MH:** Presence of substance abuse/dependence (SCID scores) differed across time points. At pre-treatment, SCID scores were higher in intervention (1.71, SD = 1.45) than control (1.48, SD = 1.02). At 6-months, SCID scores were higher in intervention (1.19, SD = 1.27) than control (1.16, SD = 1.53). At 12-months, SCID scores higher in control (1.24, SD = 1.29) than intervention (0.821, SD = 1.01). *MH:* Improvement in GSI of BSI (p<.001). Trend for more people in MI group to meet SCID criteria for alcohol abuse or dependence compared with control group. Significant main effect for stage of change on BSI. *Other drug use:* Poly-drug, alcohol and cannabis use fell significantly for the sample as a whole (p<.01). Non-significant reduction in poly-drug use to be greater in MI group compared to control group (P=.04). *Social functioning:* Significant improvement in social functioning over time (p<.01), with improvement between pre-treatment and 6 month follow up (p<.01) and between pre-treatment and 12 month follow up (p <.01).

Baker, et al. (2005)	**2 (CBT) session** – 75.7% **4 (CBT) session** – 62.1% **Completed all treatment sessions** – F (83.3%), M (60.5%) Assessments overall 56.5% All assessments (Newcastle) – 70.4% All assessments (Brisbane) – 44.8%	**MA use:** Pre-treatment (1.41, SD = 1.51) and post-treatment (0.70, SD = 1.01) (p<.001). Between pre-treatment (1.38, SD = 1.47) and 6-month follow-up (0.62, SD = 1.09) (p<.001). No difference between post-treatment (0.58, SD = 0.79) and 6-month follow-up scores (0.53, SD = 0.99). Largest difference between control and 3-4 session group (effect size 0.55 vs 0.75). *At 6 month follow up:* For control group, 17.6% remained abstinent. 2 sessions - 33.8%, 4 sessions - 37.9%. **MH:** Reduction in BSI between pre-treatment (1.43, SD = 0.76) and post-treatment (1.18, SD = 0.77) (P<.001). Reduction in BSI between pre-treatment (1.49, SD = 0.78) and 6-month follow-up (1.08, SD = 0.79) (p<.001). No significant difference between post-treatment (1.19, SD = 0.80) and 6-month follow-up (1.06, SD = 0.79). Significant improvement in depression levels (BDI-II) between pre-treatment (27.19, SD = 13.20) and post-treatment (19.35, SD = 13.09) (p <.001) and between pre-treatment (27.87, SD = 13.09) and 6-month follow-up (17.95, SD = 13.05). No difference between post-treatment (19.22, SD = 13.69) and 6-month follow-up (17.74, SD = 13.42). *Other drug use:* Significant reduction in benzodiazepine use between pre-treatment (3.34, SD = 3.97) and post-treatment (1.03, SD = 2.05) (p <.001). Significant difference between pre-treatment (3.57, SD = 4.40) and 6-month follow-up (0.57, SD = 1.43), no difference between post-treatment (1.18, SD = 2.26) and 6-month follow-up (0.64, SD = 1.55). *Polydrug use*: Reduction from pre-treatment (4.30, SD = 1.47) to post-treatment (3.83, SD = 1.33) (p<.001) and from pre-treatment (4.27, SD = 1.47) to 6-month follow-up (3.44, SD = 1.46) (p<.001). *BBV risk reduction (injecting drugs/sexual risk taking):* Injecting risk-taking score at baseline (OTI, mean), 6.68 (5.49, 0-27). % injected last month – 94.4 (202). Significant decrease in injecting risk-taking behaviour from pre-treatment (7.33, SD = 5.28) to post-treatment (4.53, SD = 4.44) (p<.001) and from pre-treatment (6.71, SD = 5.04) to 6-month follow-up (3.71, SD = 4.35) (p<.001). No significant change between post-treatment (4.58, SD = 4.58) and 6-month follow-up (3.55, SD = 4.12). Sexual risk-taking behavior not reported.
Baker, et al. (2006)	**CBT/MI group** 8 people completed 0 sessions (12.3%); 11 people completed some sessions (16.9%); and 49 people completed all 10 sessions (70.7%). **Follow-up assessments** 15-weeks n = 60 (92.3%) 6-months n = 60 (92.3%) 12-months n = 49 (75.3%) **Control** **Follow-up assessments** 15-weeks n = 61 (93.8%) 6-months n = 63 (96.9%) 12-months n = 55 (84.6%)	**MA use:** Non-significant trend towards differential (baseline v. 6 months) reduction in amphetamine use in treatment compare with control (P = 0.04). Mean daily number of occasions of amphetamine use fell by 1.33 units for treatment compared with -0.40 for control, representing differential change of 1.73 standardised units. **MH:** There was a significant improvement between baseline and the 12-month assessment on the BPRS mania factor, and between baseline and each of the follow up assessments on the BPRS negative symptoms. factor. BDI–II depression scores were also significantly lower at each of the follow up assessments than at baseline, with a marked reduction between baseline and 6-month assessment for intervention than for control (0.78 v. 0.28 standardised units, or a half a standard deviation of differential impact). *Other drug use:* Significant time effects for alcohol, poly-drug use and aggregate hazardous use index, but no group main effects. Alcohol consumption decreased significantly for sample as a whole, with 15 weeks, 6-month, and 12-month follow up. Reduction in alcohol consumption between baseline and 12-month follow up was equivalent to effect size change of 0.80 units. Mean daily cannabis decreased by 0.36 standardised units for treatment compared with -0.02 for control. No main effects in GAF analyses – significant interaction for group x time with deterioration in global functioning between baseline and 12-month assessment for control and small improvement in CBT/MI group.

Kay-Lambkin, et al. (2010)	**Weeks 1 – 4** Intervention (100%) Control (100%) **Weeks 6 – 9** Intervention (54%) Control (71.4%) **Weeks 11 – 14** Intervention (36.6%) Control (57.1%)	**Small sample size, therefore no statistical analyses.** **MA use:** Newcastle participants halved MA use between initial and 20-week post-treatment assessment. Sydney participants reported 80% decrease. **MH:** Depression (based on BDI-II scores) was reported as higher in control group across all time points. Newcastle participants reported an average BDI-II in minimal range at post-treatment and Sydney participants on average still meeting criteria for entry to the study (BDI-II > 17). Reduction in depression in Sydney participants 1 BDI point less than Newcastle.
Kay-Lambkin, et al. (2011)	87% (n=187) of participants completed at least one of the post-treatment assessments. Of these, 155 (72.4%) were assessed at 5 weeks, and 153 (71.5%) were assessed at 6-months follow-up.	**MA use:** MA use (OTI Q score) twice as high in depressed group at baseline compared with non-depressed (P = .002). MA misuse (based on SCID ratings) higher in depressed group (95% v 86%), however this tendency was not significant (P = .078). MA dependence higher in depressed group (91% v 86%), but these ratings were not significant (P = .467). 18% of participants abstinent from MA at 5 weeks, and 41% of participants at 6 months. Abstinence changes relative to baseline not statistically significant at 5 weeks (P = .429) or at 6 months (P = .144). **MH:** Depression associated with significantly greater severity of MA use and related issues (P = .027). Comorbid depression not significant predictor of change in MA use at 6 months (P = .215). Participants with comorbid depression who received 3 or 4 sessions showed significant reduction in depression at 5 weeks (p<.001). No significant reduction in depression at baseline compared to 6-months post-treatment (p >.05). *Other drug use:* Depressed group reported significantly increased use of benzodiazepines (P = .009), tobacco (P = .019), and poly-drug use (P = .006) compared to non-depressed.
McDonnell, et al. (2013)	**During Treatment** CM = 91 Non-CM = 85 **Follow-up** CM = 52 (57.1%) Non-CM = 55 (64.7%) Overall, 60.7% of participants completed follow-up measures.	**Days of stimulant use**: CM (0.91, SD = .40) reported fewer days of stimulant use during treatment compared to Non-CM (4.67, SD = 7.69). At follow-up, CM (1.83, SD = 4.94) continued to report lower scores than Non-CM (3.65, SD = 7.15). ITT revealed participants in CM group 2.4 times (p <.05) as likely as those in non-contingent group to submit stimulant-negative urine sample during treatment period. Participants in CM more likely than those in non-contingent to submit stimulant negative urine test during follow up (46%, 35% respectively). CM reported significantly fewer days of stimulant use during treatment period (p <.05) and follow up (p <.05) compared with non-CM. **MH:** *BSI.* CM (1.04, SD = .79) reported lower scores during treatment than Non-CM (1.24, SD = 0.71). At follow-up, CM (1.17, SD = .85) reported lower scores than Non-CM (1.25, SD = 0.79). *PNSS.* CM group (10.60, SD = 2.58) reported lower scores during treatment than Non-CM (11.69, SD = 3.42). At follow-up, CM (11.17, SD = 3.18) reported lower scores than Non-CM (11.57, SD = 3.01). *Days of alcohol use.* CM (1.84, SD = 4.77) reported less alcohol use during treatment compared to Non-CM (4.32, SD = 8.43). At follow-up, CM (3.60, SD = 7.92) reported lower scores than Non-CM (4.21, SD = 7.86). *HIV risk behaviour:* Injecting drug use. CM (n = 34, 37%) reported lower injecting drug use during treatment compared to non-CM (n = 56, 66%). At follow-up, CM (n = 23, 44%) reported lower injecting drug use than non-CM (n = 31, 56%).

Peck, et al. (2005)	**CBT** – attended 40.8% of 48 sessions. **CM** – attended 32.50% **CBT + CM** – 73.8% of total CBT sessions and earned $662 in vouchers (potential was $1277). **G-CBT** – attended 55.8% of total possible sessions.	**MA use:** Across all treatments, significant reductions in recent self-reported MA use were observed across all time points. Baseline (9.6 days; SD=7.4) to week 16 (M=2.4 days, SD=5.3), week 26 (M=2.2 days, SD=4.8), and week 52 (M=3.6 days, SD=6.4; F3, 505=44.1, p <.0001). **MH:** Depression (BDI) at baseline indicated at mild depressive symptoms for (73.2%) participants. Of 153 baseline BDI scores, 44 (28.5%) were in the moderate to severe range (25.0, SD=5.6); 69 (44.8%) were in the mild to moderate range (13.7, SD=2.3); and 41 (26.6%) in the no depression to minimal depression range (5.5, SD=2.7). No statistically significant differences in severity of reported depressive symptoms between treatment conditions at baseline, 16, or 26 weeks. At 52-week follow-up, CBT condition had higher BDI scores (M=10.3, SD=7.8) than participants in other conditions. All participants reported significant decreases in depressive symptoms from baseline to end of treatment. The criteria for life-time mood disorder (based on SCID scores) was met in more than one-half (52.9%) of participants, with 28.4% of the sample meeting criteria for a lifetime major depressive disorder (MDD). Urine samples indicating recent use of MA predicted future high BDI scores and samples documenting recent prior abstinence of MA predicted future low BDI scores (p<.0001). BDI scores did not predict future MA use.
Polcin, et al. (2014)	**Baseline** 217 completed **2-month follow-up** Intensive MI (IMI)= 91.5% Standard MI (SMI) = 94.5% **4-month follow-up** IMI = 91.5% SMI = 88.2% **6-month follow-up** IMI = 91.5% SMI = 93.6%	**MA use:** Percent of days abstinent increased on both groups across all time points. In the Standard MI group, average baseline scores (0.55, SE = 0.04) increased at two months (0.74, SE = 0.04), at four months (0.76, SE = 0.03) and increased at six months (0.78, SD = 0.03). Similar changes were found in the Intensive MI group at baseline (0.56, SE = 0.04), two months (0.74, SE = 0.03), four months (0.75, SE = 0.03) and six months (0.75, SE = 0.03). **MH**: ASI psychiatric status score. For standard MI, the ASI psychiatric status score decreased across time points. Baseline scores (0.31, SE = 0.02) slightly increased at two months (0.31, SE = 0.02) and decreased at four months (0.29, SE = 0.01) and six months (0.28, SE = 0.01). Intensive MI scores consistently dropped across time points. Baseline scores (0.40, SE = 0.02) decreased at two months (0.37, SE = 0.02) and decreased at 4 months (0.34, SE = 0.02) and six months (0.32, SE = 0.02). *Anxiety status* – No differences between SMI and IMI groups. Significant reduction in depression for IMI. No reduction in depression for SMI. *Number of days had psychiatric problem (ASI)s:* Higher at baseline in IMI than SMI. Scores in the SMI group were relatively consistent at baseline (11.40, SE = 1.11), 2-months (11.76, SE = 1.17), 4-months (11.36, SE = 1.14) and 6-months (11.88, SE = 1.27). Scores in the IMI group consistently dropped across time points. Baseline scores (15.70, SE = 1.08) decreased at 2-months (12.50, SE = 1.18), increased slightly at 4-months (12.72, SE = 1.22) and decreased dramatically at 6-months (10.80, SE = 1.08).
Rawson, et al. (2004)	**During treatment (for total sample):** 798 (81.6%) completed discharge interviews 841 (86%) completed 6-month interviews 12 month interviews ongoing at the time of publication Matrix retained at higher level than TAU – 27% more likely to complete treatment.	**MA urine free samples:** The urine samples were reported for various sites (truncated data). Matrix participants provided an average of 4.3 MA-free urine samples compared to 1.7 for TAU. Matrix participants provided on average, one additional MA free urine sample than TAU. Matrix condition provided a greater number of MA free urine samples than TAU for 8-week and 16-week treatments, however were not statistically significant. Matrix participants provided significantly more MA-free urines in the first 12 weeks of their treatment (4.3 vs 3.3). Matrix participants, compared to TAU, were 31% more likely to have MA-free urine test results (odds ratio = 1.311). The Matrix condition had longer mean periods of abstinence than TAU. At discharge, the Matrix Model had 66% MA-free urine samples, and 69% of urine samples were MA-free in TAU. At 6-month follow-up, both groups had 69% MA-free urine samples. MA use was reduced during treatment over time, yet no significant differences by treatment condition (p <.0001). Self-reported number of days of MA use in the past 30 days was reduced from approximately 11 days at baseline to slightly over 4 days at discharge, and this reduction was maintained at 6-month follow up. In TAU, average MA use for the last 30 days changed from 11.8 days at baseline to 4.0 days at 6-month follow-up. **ASI**. All ASI domains demonstrated significant improvement across treatment. At 6-month follow-up, significant reductions from baseline were seen in the family, drug, psychiatric and alcohol areas. No treatment condition effects.

Rawson, et al. (2006)	**CM** 12.6 weeks retained in treatment (SD = 5.2). 63% completed 16 weeks **CBT** 9.0 weeks retained in treatment (SD = 6.5) 40% completed 16 weeks. Mean number of sessions attended – 19.0, SD = 15.4. **CM + CBT** 12.0 weeks (SD = 5.6) 59% completed 16 weeks. Attended more sessions (26.5, SD = 15.3).	**MA use:** The means for CM and CBT + CM treatment conditions were significantly higher than for CBT-only (p<.0008 and p<.0003, respectively). 3-week criterion revealed significant differences between CBT (34.5%) vs CM (60.0%; p < .0001) and CBT vs CBT + CM conditions (69.5%; p< .0001). All three groups had between 67% and 79% stimulant-free samples across all time-points. Urine samples between groups were statistically significant (p <.0001). The CBT + CM group gave the most stimulant-free samples (M=28.6), followed by CM (M = 27.6). CBT had the lowest stimulant-free samples (M=15.5) across the 16 weeks. **MH – ASI:** Study participants showed statistically significant overall reductions in problems related to employment, alcohol, drugs, family/social, and psychiatric domains. CM participants had significantly lower psychiatric scores at week 17 than those in CM or CBT + CM conditions (p < 0.05).
Smout, et al. (2010)	**CBT** (17/53 = 32%) **ACT** (14/51 = 27.4%) Provided post-intervention data (overall) - 29.8%	**MA use:** Self-reported MA use did not change significantly from baseline (16.1, SD = 6.9) in the intervention (6.0, SD = 7.0) and control (5.7, SD = 9.3) groups over the previous month. Significant within-group reductions in self-reported MA use, MA dependence, and negative consequence scores in both groups from baseline to 12 weeks. Statistical significance for CBT group for MA-free hair samples. **MH:** BDI-II scores were statistically significant across time F (2, 51) = 32.16, p<.01. At baseline, the control group (25.7, SD = 11.2) was lower than the intervention group (27.8, SD = 10.3). At 12-weeks follow-up, the control group was higher (17.7, SD = 12.2) than the intervention group (15.4, SD = 13.6). At 24-weeks follow-up, the control group (14.1, SD = 14.8) reported lower scores than the intervention group (16.9, SD = 16.3). **Physical scale scores** (SF-12 scores) showed a consistent pre-post significant therapy effect which favoured the control group across all time points (F (1,52) = 4.81, P = .03). Not statistically significant, and mental health scores based on the SF-12 were not significant. **MA-related negative consequences** were inconsistent across time points and groups. At baseline, the control group (Median = 9.3, SD = 7.3) had lower MA-related consequences compared to the intervention group (Median = 10.1, SD = 7.5). At 12-weeks follow-up, the control group (Median = 107/0, SD = 17.0) had lowers scores compared to the intervention group (Median = 103.0, SD = 99.0). At 24-weeks follow-up, the control group (Median = 15.0, SD = 30.0) reported higher scores than intervention (Median = 12.0, SD = 29.0). These differences were not statistically significant.

Note: MA = methamphetamine, MH = mental health, SD = standard deviation, SCID = Structured Clinical Interview, GHQ-28 = General Health Questionnaire, GSI = Global Severity Index, BSI = Brief Symptom Inventory, BDI-II = Beck Depression Inventory, MI = Motivational Interviewing, BBV = Blood Borne Virus, OTI = Opiate Treatment Index, BPRS = Brief Psychiatric Rating Scale, GAF = Global Assessment of Functioning, ITT = Intention to Treat Analysis, PNSS = Positive and Negative Symptom Scale, HIV = Human Immunodeficiency Virus, SE = standard error, ASI = Addiction Severity Index, TAU = treatment as usual, IMI = Intensive motivational interviewing, SMI = standard motivational interviewing , CBT = Cognitive Behaviour Therapy, CM = Contingency Management, GCBT = Gay specific Cognitive Behaviour Therapy, ACT = Acceptance and Commitment Therapy.

Appendix F

Secondary Outcomes

Narrative Synthesis

Refer to Appendix B and E for a detailed summary of secondary outcomes for each study.

Change in Other Drug Use

As seen in Table 8 (Appendix B and E), seven studies (39, 55-57, 59, 62) described changes in poly-and/or other drug use. Overall, the majority of studies (39, 55-59, 62) found an overall reduction in poly-drug use for the entire sample over time. Some studies reported significant reductions in alcohol and cannabis use over time (39, 57).

Treatment Engagement

As seen in Table 8 (Appendix B and E), 11 studies (22, 39, 54-62) provided data for treatment engagement and retention in psychological treatment for MA use. Two studies found that a combined intervention such as CBT + CM produced higher rates of retention (60, 61). Overall, participants were more likely to complete a brief intervention and attended 2-4 sessions on average (55, 58, 62). Attendance for fixed stepped care interventions was higher (22). No significant differences were found in attendance for intensive MI interventions compared to TAU (54, 62).

Physical Health

One study by Smout et al. (55) reported changes in physical health using the Physical Health Composite Scale (PCS-12) and found improved physical health in the CBT group, yet not in the ACT group. There was a pre-post significant therapy effect for Short Form (SF-12) physical scale scores, favouring the CBT group at all time points (F (1,52) = 4.81, p = .03).

Difference in Global Functioning Pre/Post

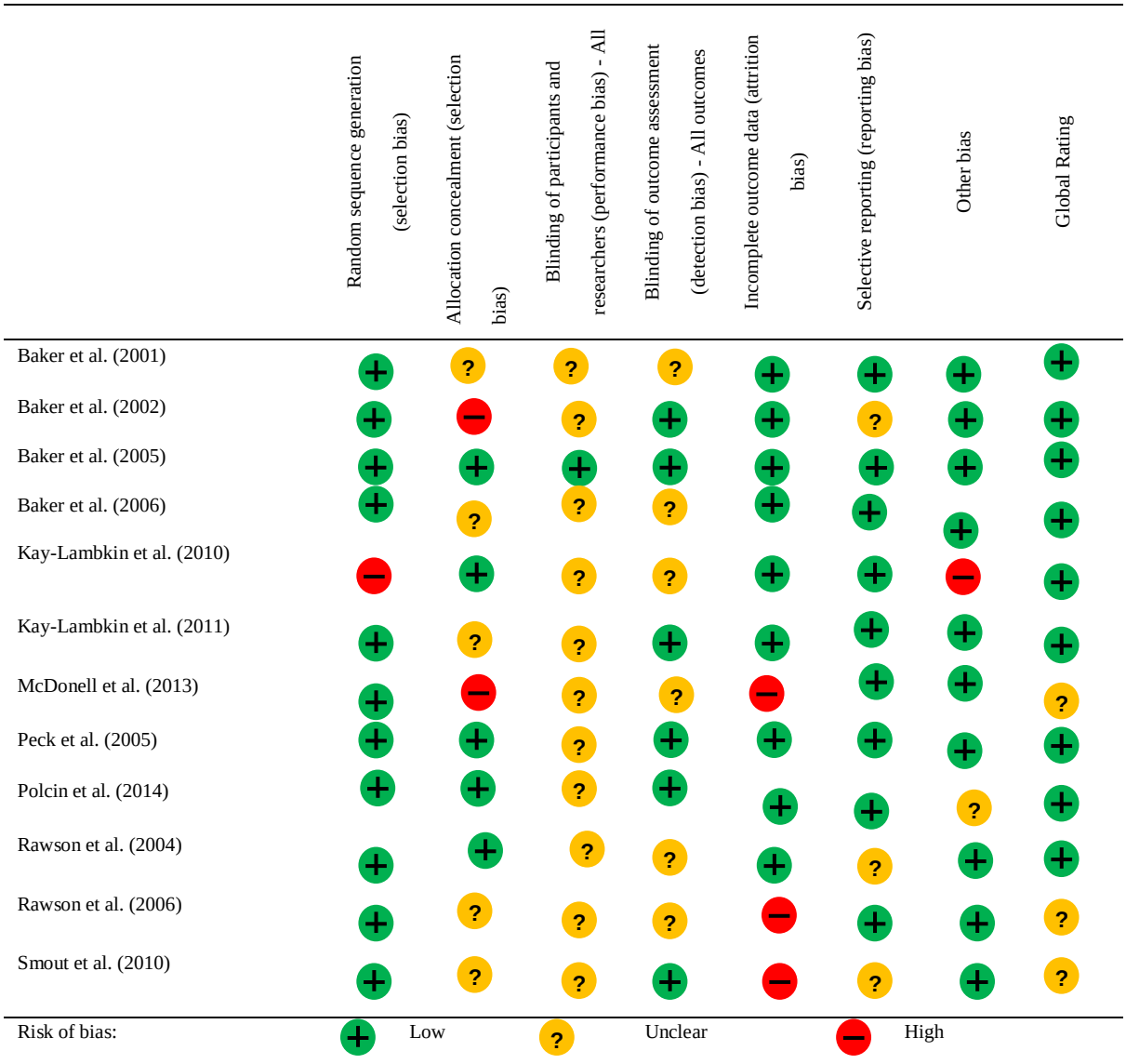
Two studies (39, 62) reported changes in global and social functioning using the Global Assessment of Functioning (GAF) tool. Baker et al. (62) found a small improvement in GAF for the treatment group. An improvement in social functioning for the entire sample was found for Baker et al. (62), with a significant improvement between pre-treatment and 6 month follow up ($p < .01$) and between pre-treatment and 12 month follow up.

BBV Risk Reduction (injecting/sexual risk behaviour)

Three studies (57, 59, 61) reported changes in BBV risk reduction and associated risk behaviour. Overall, some studies found significant reductions for the sample as whole in injecting-risk taking behaviour from pre to post-treatment ($p < .001$) (59, 61). Conversely, Baker et al. (59) found no significant change between CBT intervention conditions in levels of injecting risk-taking behaviour.

Appendix G

Table 9. *Risk of Bias Ratings*



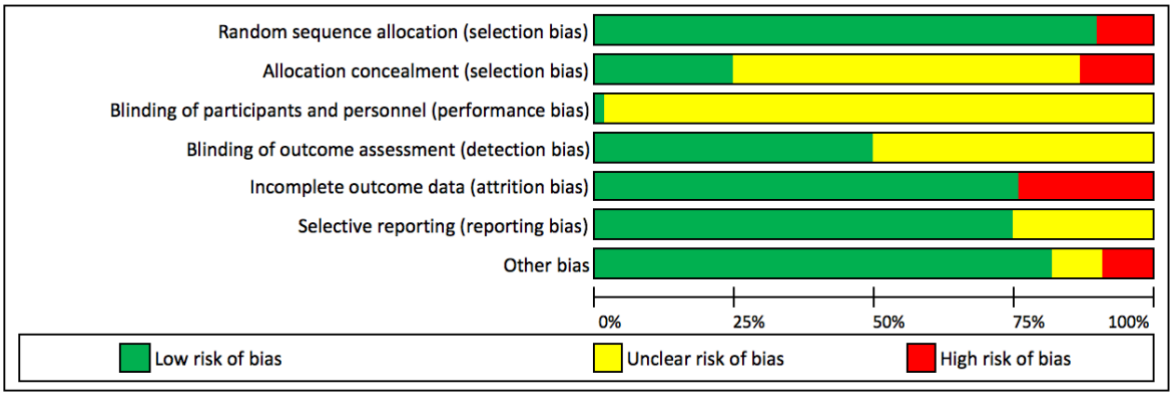


Figure 16. *Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.*

Appendix H

Table 10. *Quality of the Evidence using GRADE*

Outcome (change according to mean follow-up score)	Total number of events	Comparative risks	Relative effect	No. of studies	Quality of the evidence (GRADE)
Primary Outcomes					
Change in MA use	2043	SMD = -0.07, 95% CI = (-0.20, 0.06)	p = .314	8 studies in meta-analysis	⊕⊕⊕⊖ Moderate[1]
Abstinence	585	Risk ratio = 0.57, 95% CI = (-0.35, 1.50)	p = .223	4 studies in meta-analysis	⊕⊕⊖⊖ Low[2]
ASI/BSI	897	SMD = - 0.02, 95% CI = (-0.22, 0.18)	p = .842	5 studies in meta-analysis	⊕⊕⊕⊖ Moderate[3]
BDI	610	SMD = 0.08, 95% CI = (-0.25, 0.41)	p = .642	4 studies in meta-analysis	⊕⊕⊖⊖ Low[4]
Secondary Outcomes					
Other drug use	908		Reduction in poly-drug use for the total sample Lower alcohol use Difference in cannabis/tobacco use	7 studies (1-6)	⊕⊕⊖⊖ Low[5]
Treatment engagement	1962		Little difference between the number of assessment and treatment sessions completed by intervention group compared to controls	12	⊕⊕⊕⊖ Moderate[6]
QOL		N/A	N/A	0	N/A
Difference in functioning			Different constructs measured, therefore GRADE not appropriate	2	N/A

BBV risk reduction	616	Overall no significant change in HIV-risk behaviour between groups, however overall significant reduction over time for entire sample	4	⊕⊕⊖⊖ Low[7]

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

1. Downgraded for indirectness. Based on studies reporting stimulant use and having small number of participants using MA as well as different intervention groups (54, 55)
2. Downgraded 2 levels including indirectness based on high income countries and gender bias, and rated down for substantial heterogeneity indicated by meta-analysis. Wide effect size and wide CI's.
3. Downgraded one level for imprecision based on confidence intervals crossing the line of null effect.
4. Downgraded two levels. Substantial heterogeneity indicated by meta-analysis (I^2 = 63.8%). Downgraded for indirectness based on different comparison groups and high income countries (54, 57). Small number of studies yet not significant enough to downgrade.
5. Downgraded two levels. Downgraded one level for difference between types of interventions and inconsistency in results. Downgraded one level for imprecision for variation in effects among participants in continuous measures (54-58, 61).
6. Downgraded one level due to indirect duration of interventions across studies and different comparison groups.
7. Downgraded one level for inconsistent effects across trials and downgraded one level for indirect population and comparator differed (53).