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SUMMARY WITH CRITICAL APPRAISAL

Residential Treatment for Substance Use Disorder: A Review of Clinical Effectiveness

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Abbreviations

ABM	Attentional bias modification
AMSTAR 2	Assessing the Methodological Quality of Systematic Reviews
ASI	Addiction Severity Index
AUD	Alcohol use disorder
DSM-5	Diagnostic and Statistics Manual of Mental Disorders 5th edition
EPI	echoplanar imaging
fMRI	Functional magnetic resonance imaging
FOV	Field of view
NR	Not reported
NRS	Non-randomized study
OH	Oxford House
M	mean
MA	Methamphetamine
Mo.	months
MPRAGE	Magnetization-prepared rapid-acquisition gradient echo
N/A	Not applicable
NR	Not reported
PFC	Prefrontal cortex
PICO	Population, Intervention, Comparator, Outcome
RCT	Randomized controlled trial
RoB 2	Revised Cochrane Risk of Bias tool for randomized trials
SADQ	Severity of Alcohol Dependence Questionnaire
SD	Standard deviation
Sig.	Significance
TC	Therapeutic Community
TE	Echo time
TR	repetition
UA	Usual aftercare

Context and Policy Issues

The Public Health Agency of Canada reported that an average of 10 people per day in Canada died due to an illicit drug overdose between January 2016 and March 2018.[1] In addition, there were 16 hospitalizations per day on average due to opioid poisoning in 2016 to 2017.[2] Furthermore, at least 3.1 million Canadians consumed enough alcohol to be at risk for immediate injury and harm in 2013, and 4.4 million were at risk for chronic health effects.[3]

Indigenous populations are among those particularly vulnerable to substance use disorder in Canada. Several factors, such as history of colonization and poverty, are among the factors that increase the risk of substance use problems among First Nations, Inuit, and Metis Canadians.[4] In a national survey conducted by Health Canada between 2008 and 2010, 82.6% of respondents who identified as being from First Nations communities reported alcohol and substance abuse as the single greatest challenge for on-reserve community wellness.[4]

The Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) recognizes substance-related disorders resulting from the use of ten separate classes of drugs: alcohol, caffeine, cannabis, hallucinogens, inhalants, opioids, sedatives, hypnotics, anxiolytics, stimulants and tobacco, and other or unknown substances.[5] Substance use disorder is defined within the DSM-5 as patterns of symptoms that result from the use one or more of these substances that a person continues to use, despite experiencing problems as a result.[5] Eleven problems or symptoms of substance use disorder are identified, and

the severity of the disorder is diagnosed based on the number of symptoms.[5] Symptom severity ranges from mild to severe, with more symptoms reflecting greater severity.[5]

Options for the clinical treatment of substance use disorders may vary according to the needs of the individual and the intensity of the disorder. For example, the American Society of Addiction Medicine defines five levels of care for treating alcohol and drug use disorders: Level 0.5 (early intervention services), Level I (outpatient services), Level II (intensive outpatient services), Level III (residential and in-patient services), and Level IV (medically managed intensive in-patient services).[6] Residential treatment aims to help people with substance use disorders and a high level of psychosocial needs become stable in their recovery before engagement in outpatient settings and before return to an unsupervised environment, which may otherwise be detrimental to their recovery process.[7]

The objective of this report is to summarize the evidence regarding the clinical effectiveness of residential treatment for substance use disorders.

Research Question

What is the clinical effectiveness of residential treatment for individuals with substance use disorders?

Key Findings

Two systematic reviews and one randomized controlled trial were identified describing the clinical effectiveness of residential treatment for individuals with substance use disorders. In addition, three randomized controlled trials describing ineligible comparisons, but reporting eligible before-after data (and therefore assessed as non-randomized studies) were included in the report. No eligible studies examined the clinical effectiveness of residential treatment in Indigenous populations. Evidence of limited quality from the included studies suggested that residential treatment may improve substance use, severity of substance misuse, and associated cravings. Furthermore, residential treatment was equally or more effective than other less intensive treatment modalities.

Methods

Literature Search Methods

A limited literature search was conducted on key resources including Medline and PsycInfo, the Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit the retrieval to health technology assessments, systematic reviews, and meta-analyses, randomized controlled trials, and non-randomized studies. Where possible, retrieval was limited to the human population. The search was also limited to English-language documents published between January 1, 2008 and November 28, 2018.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for eligibility. The final selection of full-text articles was based on the selection criteria presented in Table 1.

Table 1: Selection Criteria

Population	Individuals of any age with substance use disorders
Intervention	Residential/in-patient treatment centre or program
Comparator	Outpatient treatment or program, wait list, before-and-after, no treatment
Outcomes	Clinical effectiveness (e.g., symptom reduction, substance abstinence/relapse)
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, were duplicate publications, or were published prior to 2014. Eligible articles published earlier than 2014 and after 2008 are included in Appendix 6.

Critical Appraisal of Individual Studies

The included systematic reviews were critically appraised by one reviewer using the revised Assessing the Methodological Quality of Systematic Reviews (AMSTAR 2) tool.[8] Randomized studies were critically appraised using the Revised Cochrane risk-of-bias tool for randomized trials.[9] Non-randomized studies were critically appraised using the Downs and Black Checklist.[10] Summary scores were not calculated; rather, the strengths and limitations for each included study were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 517 citations were identified in the literature search. Following screening of titles and abstracts, 484 citations were excluded and 33 potentially relevant articles from the electronic search were retrieved for full-text review. One potentially relevant article was retrieved from the grey literature search for full text review. Full text articles were screened in reverse chronological order. Of these potentially relevant articles, 28 were excluded for various reasons, including those published after 2014, whereas 6 articles met the inclusion criteria and were therefore eligible for inclusion in this report. These comprised two systematic reviews, one randomized controlled trial (RCT), and three non-randomized studies. Appendix 1 presents the PRISMA[11] flowchart of the study selection.

Articles published between 2008 and 2013 and additional references of potential interest are provided in Appendix 6.

Summary of Study Characteristics

Additional details regarding the characteristics of included studies are provided in Appendix 2.

Study Design

Two systematic reviews of clinical effectiveness outcomes were identified.[7,12] Both reviews were published in 2014 as part of a series of 13 reviews on recovery-focused mental health and substance use services.[7,12] They searched literature published between 1995 and 2012

and identified RCTs, quasi-experimental studies, and review articles.[7,12] In the review by McCarty, naturalistic assessments were also eligible.[12] Nine primary studies appeared in both systematic reviews and are presented in Appendix 5.[7,12]

One multi-centre RCT was identified[13] that examined individuals recovering from alcohol and drug dependence, and had been released from the criminal justice system in the past 24 months.[13] Participants were randomized to usual care or one of two residential treatment facilities (Oxford House or a Therapeutic Community).[13]

Three RCTs (two single-centre and one multi-centre)[14-16] reporting on ineligible comparisons (i.e., both intervention and comparator groups were patients in residential treatment) were included in this review and assessed as uncontrolled, non-randomized studies, due to the fact that before-after data were available describing eligible intervention groups.

Additional details regarding the characteristics of included articles are provided in Appendix 2.

Country of Origin

The body of evidence originated from three countries: four from the US (two systematic reviews,[7,12] one RCT,[13] one RCT assessed as a non-randomized study[14]), one from Australia (1 RCT assessed as a non-randomized study[15]), and one from India (one RCT assessed as a non-randomized study[16]).

Patient Population

All systematic reviews and clinical studies examined adult patients with a substance use disorder.[7] No eligible studies examined Indigenous populations.

Patient characteristics were not explicitly described in the two systematic reviews, but inclusion criteria indicated participants were seeking treatment for alcohol or illicit drug use.[7]

Participants in the clinical studies were undergoing treatment for alcohol dependence,[15] methamphetamine dependence,[14] or any form of drug or alcohol dependence.[13] Residential treatment in the RCT consisted of Therapeutic Communities or Oxford Houses.[13] In the RCTs assessed as a non-randomized studies, residential treatment took place in a community-based residential treatment program,[14] a residential detoxification facility,[15] and an in-patient psychiatry setting in a hospital.[16]

Interventions and Comparators

Two systematic reviews compared in-patient or residential treatment (intervention) to a comparator (any comparator or intensive outpatient therapy).[7,12] One review examined intensive outpatient programs in comparison to in-patient or residential treatment programs.[12] The second review examined residential treatment programs versus any comparator group.[7] Where reported, intervention treatment durations ranged from 14 days to 6 months in one review [12] and were not reported in the other.[7] Where reported, the duration of intensive outpatient therapy ranged from three or more hours per day to eight hours per day; sessions took place three days per week up to seven days per week; and the duration of the treatment program lasted between two weeks and eight months.[12]

Outcomes

Overall, outcomes assessed by included studies can be categorized as substance use, severity of substance misuse, and symptom reduction.

Neither systematic review pre-specified eligible outcomes, except to say they examined service effectiveness.[7,12]

Substance use was assessed in included studies as percentage of days abstinent, number of drinking days,[15] return to significant drinking, and weekly cocaine use. A subscale of the Addiction Severity Index (ASI)[7,12] and the ASI-Lite, and the Form 90 Timeline Follow-back calendar were used to assess alcohol and drug use over the past 30 days and 180 days in the included RCT.[13] Urinalysis was used to confirm self-reported abstinence from illegal drugs and alcohol.[13]

Substance misuse severity describes the extent to which an individual is affected by substance use disorder. Substance misuse severity was assessed in included studies as return to in-patient care for substance use, and also as addiction severity, assessed using composite scores from the ASI[7,12] and the ASI-Lite.[13] Alcohol severity was assessed in two RCTs assessed as non-randomized studies by the Mean Severity of Alcohol Dependence Questionnaire.[15,16] Higher scores indicated greater alcohol dependence.[16]

Regarding symptom reduction, studies that assessed physical symptoms of substance use reported examining cravings. Spontaneous cravings were assessed in one study using the Methamphetamine Craving Scale, as modified from the Brief Cocaine Craving Scale.[14] Cue-induced cravings were assessed in the same study using a computerized cue-induced craving program. During the program, participant responses were measured using functional Magnetic Resonance Imaging, and by self-report describing the extent to which they felt like using methamphetamine in that moment (scores recorded from 1; not at all to 4; very much).[14] Alcohol craving was assessed using the short form of the revised Alcohol Craving Questionnaire.[15]

Authors of the clinical studies reported good psychometric properties for the ASI-lite,[13] the Form 90 Timeline Follow-back,[13] and the Severity of Alcohol Dependence Questionnaire.[16] Properties for other outcome measures were not reported by study authors. No studies included in this report described what constituted a minimal clinically important difference.

Summary of Critical Appraisal

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3.

There were both strengths and limitations demonstrated by the included systematic reviews as assessed by the AMSTAR 2 tool. First, the sponsor of both systematic reviews was transparently reported as the Substance Abuse and Mental Health Services Administration,[7,12] increasing confidence that the study findings were not biased by the interests of the funder. However, it was unclear whether the review authors had competing interests, or whether the individual studies included in the reviews were influenced by funders as this information was not reported by review authors.[7,12] The remaining strengths were primarily related to the planning and conduct of the search strategies; specifically, experts in the field were consulted in the development of the searches, several databases were searched, and key words used in the searches were provided,[7,12] These strengths increase the likelihood that the evidence base was sufficiently captured by the searches.

Several elements were not reported; for example, whether screening was conducted in duplicate. A list of excluded studies was not provided and exclusions were not justified; meaning the appropriateness and impact of their exclusion from the review is unknown. Additionally, interventions and comparators were not described in adequate detail. It is unclear how much of this was due to reporting by included studies and how much was due to poor reporting of the systematic review.

An important potential source of bias is related to critical appraisal of included studies by systematic review authors. Review authors reported that risk of bias in individual studies was not assessed. Rather, risk of bias across studies was considered using a purpose built tool: "We developed an evidence rating scale that builds on the practice and consensus standards outlined in a number of national reports over the past decade or more."[17] The self-developed tool meant that for RCTs, random allocation sequence, allocation concealment, blinding of outcome assessors and/or patients were not assessed. Without a description as to whether the allocation sequence was random and/or concealed, it is difficult to know whether randomization was sufficiently achieved, calling into question the generalizability of the study's findings. Furthermore, unknown blinding status of patients and assessors raises questions about the internal validity of the included studies, as it is unclear whether knowledge of group assignment may have biased the observations. For non-randomized studies, the self-developed tool assessed risk of bias from confounding and attrition, but not selection bias or measurement of exposures and outcomes.[7,12] Therefore, it is unclear whether patients were representative of the populations from which they were drawn, or whether outcomes were appropriately measured.

The systematic review authors described the level of evidence to be moderate[7] to high;[12] however, as described above, they characterized this using a purpose-built tool across studies as opposed to assessing the risk of bias in individual studies. McCarty noted there was variation in the setting, duration, and intensity of in-patient and outpatient services in included studies, which may limit direct comparisons.[12] Reif noted the included studies lacked rigorous designs that controlled for patient characteristics.[7]

The author of one review reported that RCTs comparing specific treatments were rare, as treatment providers raised concerns about randomly assigning individuals to a less-intensive level of care than was clinically appropriate.[7] Alternatively, some RCTs only accepted patients who were appropriate for outpatient care to avoid undertreating patients. Given that guidelines recommend treatments based on the severity of the symptoms and patient characteristics, patients who would have been best served by more intensive treatments may not have been eligible to participate.

For the included RCT, only bias due to missing data was identified as a limitation.[13] And for the RCTs assessed as non-randomized studies in this report, risk of bias from multiple sources was identified.[14-16]

Additional details regarding the strengths and limitations of included publications are provided in Appendix 3.

Summary of Findings

Appendix 4 contains a table of the main study findings and authors' conclusions.

Clinical Effectiveness of Residential Treatment

Substance Misuse Severity

Based on a narrative synthesis of included studies, the two systematic reviews reported that overall, residential treatment and non-residential treatment comparators tended to lead to improvements in substance misuse severity as measured with the ASI or other undescribed measures. Improvements observed with residential treatment were described as being either greater than those observed with other forms of treatment or did not differ in magnitude (statistics not reported).[7,12]

Substance Use

Narrative syntheses of studies in both systematic reviews showed that overall, residential treatment interventions and non-residential treatment comparators both supported abstinence (abstinence measures were not described). Improvements observed with residential treatment were either greater than those observed with other forms of treatment or did not differ in magnitude (quantitative data not reported).[7,12]

In an RCT, a mixed model examining 270 adults randomized to usual aftercare, Oxford House, or Therapeutic Communities, demonstrated no significant difference between groups in number of days of alcohol or drug use over the past 6 months.[13] At 24-month follow up, there was a statistically significant difference between groups for continuous abstinence from alcohol, with Oxford House being superior to Therapeutic Communities and usual aftercare, and no statistically significant difference between groups for continuous abstinence from drugs.[13]

Two RCTs assessed as NRS within this report examined alcohol consumption.[15,16] One of these (N = 83) investigated a residential alcohol treatment program and reported fewer mean drinking days and fewer mean drinks per day at two-weeks of follow up compared with pre-treatment scores among participants who were no longer abstinent at follow-up.[15] The second (N = 177 men) reported that both residential treatment groups experienced a significant decrease in alcohol consumption at one month and three months of follow up compared with baseline alcohol consumption.[16]

Craving

One NRS showed that spontaneous– and cue-induced methamphetamine craving decreased from baseline to one-month of follow-up in participants in a residential treatment program.[14] Imaging with fMRI showed decreased activation in the ventromedial prefrontal cortex in response to the cue-induced craving paradigm, and no regions showed increased activation over the two-week time frame.[14] Among patients in a residential alcohol detoxification program, alcohol craving scores were significantly lower at two-week follow-up (p=0.04) and immediately following treatment (p<0.002) compared with scores at baseline.[15]

Limitations

There are certain limitations to consider when reviewing the report. Both systematic reviews identified important limitations within their included studies, such as important variability in the interventions investigated, and a lack of methodological rigour. Notable limitations were also identified in the RCTs — including those which were assessed as non-randomized studies. Importantly, incorporation of the RCTs assessed as non-randomized studies into

this report was limited by the fact that the only data eligible was non-comparative; further, critical appraisal of these studies was limited by the discordance between the randomized methods used to generate the data and the assessment of the studies as non-randomized.

An important research gap is that there were no eligible studies identified that examined residential treatment in Indigenous populations. Three literature reviews on cultural interventions and healing communities in indigenous populations were identified; however, they did not use systematic methods and so, are included as additional information in Appendix 6. Further research is needed to establish their clinical effectiveness and consider the quality of the evidence in Indigenous populations.

Conclusions and Implications for Decision or Policy Making

A total of six relevant publications were identified, which comprised two systematic reviews,[7,12] one RCT,[13] and three RCTs assessed as non-randomized studies.[14-16] The methodological quality of the studies was low, largely due to reporting issues. As such, the findings of this report should be interpreted with caution.

Overall the findings tended to show that residential treatment was a favourable treatment option, being at least as effective, if not more effective, than non-residential options for the treatment of substance use disorders. The findings of the current study can be compared with a previous CADTH report (which included one systematic review and three clinical studies), showing better abstinence rates at one- to two-month follow up in outpatient treatment compared with in-patient treatment among adults with alcohol use disorder.[18] Similar to the conclusions of the included systematic reviews, one study showed that in-patients with severe alcohol dependency had an initial benefit in abstinence over outpatient care, however this difference diminished over time.[18]

Reif noted that RCTs comparing specific treatments options were rare because treatment providers had concerns about randomly assigning individuals to a less-intensive level of care than may be clinically appropriate.[7] As a means of addressing this challenge, Reif indicated that some RCTs only accepted patients who were appropriate for outpatient care to avoid undertreating patients. However, this was similarly problematic, as it is likely that different types of patients with different needs require different treatment options. For example, McCarty reported that residential treatment may be the most beneficial treatment option for patients with more severe impairment.[12]

High quality study designs are needed to examine the effectiveness of residential treatment in Indigenous populations, and other groups of increased vulnerability (e.g., ethnic minorities, the homeless). The United Nations Office on Drugs and Crime and the World Health Organization consider Indigenous populations as among the individuals that require differentiated treatment planning tailored to their unique vulnerabilities and needs.[19]

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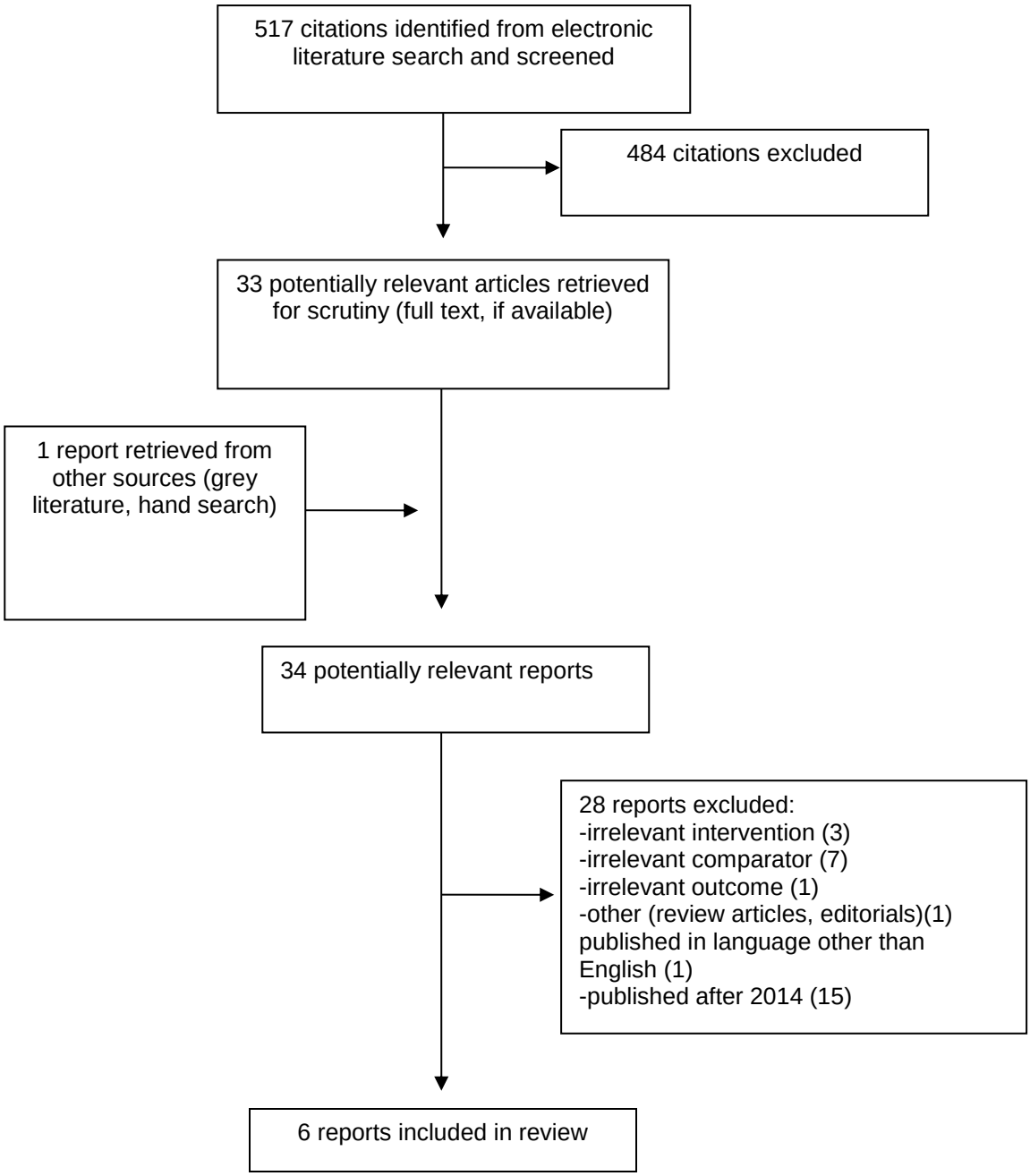
Appendix 1: Selection of Included Studies



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Systematic Reviews and Meta-Analyses

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
McCarty, 2014 USA	Search dates between 1995 and 2012 Inclusion criteria: English language studies; Study designs were RCTs, quasi-experimental studies, naturalistic assessments, and qualitative reviews; Patients were adults seeking treatment for alcohol or illicit drug use. Exclusion criteria: Residential treatment only; Ambulatory treatment only; Aftercare only; treatment for mental disorders only; Developmental disability programs; hospital based in-patient treatment programs without comparisons to less intensive services; treatment services for adolescents. 6 RCTs (including 2 RCTs with patients who refused randomization), 6 natural cohort studies, and 1 qualitative study were included in the review.	Adults with substance use disorders (alcohol and or drug diagnoses) Participant characteristics and number of participants included were not reported.	Intervention (In-patient or residential care): Durations ranged from 14 days to 6 months of active treatment. Duration not specified in 6 studies. Studies also included orientation and transition periods to aftercare, halfway house, or mental health provider Comparator: Intensive outpatient treatment Durations ranged from ≥ 3 hours/day to 8 hours/day; at least 3 days/week to 7 days/week; 2 weeks to 6–8 months. Where weekly aftercare was specified, duration ranged from 3 to 6 months. Duration not specified in 7 studies Note. No included studies examined pharmacotherapy as part of treatment	Addiction severity assessed with ASI Substance Use assessed as percentage of days abstinent, number of drinking days, return to significant drinking, return to in-patient care, weekly cocaine use 1 year after discharge (measures not described) Follow-up ranged between 3 and 18 months after baseline assessment
Reif, 2014 USA	Search limited to 1995 to 2012 Inclusion criteria: RCTs, quasi-experimental studies,	Adults with substance use disorders or co-occurring mental health and substance use disorders were eligible.	Intervention: Substance use treatment that occurs in non-hospitals, freestanding residential facilities, therapeutic	**Substance Misuse Severity** Drinking, substance use, problem severity, ASI composite scores,

Table 2: Characteristics of Included Systematic Reviews and Meta-Analyses

First Author, Publication Year, Country	Study Designs and Numbers of Primary Studies Included	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
	review articles (e.g., meta-analyses and systematic reviews) Exclusion criteria: Solely adolescent populations; residential treatment in criminal justice settings; cost-effectiveness studies; studies with no comparator group; measured only effects that occurred during treatment; use pre-post analysis without controlling for baseline differences Eight reviews (unclear if systematic reviews) and 21 individual studies not included in the reviews (7 RCTs and 13 quasi-experimental studies had outcomes eligible for this report; 1 did not report an eligible outcome) were included in the review.	Participant characteristics and number of participants included were not provided.	communities Comparator: Studies that did not have a comparison group were excluded. Eligible comparators not specified. Comparators in included studies were described as day treatment, outpatient, non-residential, other residential or other in-patient treatments.	abstinence, in-patient re-admission, drinking status, drug use, ASI drug severity score, ASI alcohol, methamphetamine use, substance misuse severity (measurement tools not reported)

ASI = Addiction Severity Index; RCT = Randomized Controlled Trial

Table 3: Characteristics of Included Primary Clinical Studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Jason, 2015 USA	Multi-centre RCT Individuals released from the criminal justice system were randomized to a residential treatment facility (OH or TC) or UA	N = 270 (224 men, 46 women) UA, 38.83 years; OH 39.19 years; TC 43.28 years (sig. different across conditions, *P* < 0.01, TC higher than UA and OH) Inclusion criteria: aged > 18 years; recovering from alcohol and drug dependence; and had been released from prison or jail within the past 24 months. Exclusion criteria: conviction of violent crimes or sex offenses. Recruited between March 2008 and May 2011 from in-patient substance abuse treatment facilities where they were receiving in-patient services (n = 251), where they were not receiving in-patient services (n = 13), or on referral from reentry/case management programs (n = 6) Substance of choice: Heroin, 43.2%; Crack/cocaine, 28.9%; Alcohol, 14.7%; Marijuana, 7.1%; Polysubstance use, 5.6%; Amphetamine/crystal methamphetamine, 0.4%	Comparator: UA What naturally occurred after discharge from treatment at time of recruitment Intervention 1: OH Self-run abstinent setting with no professional staff for individuals dealing with substance abuse problems. Requirements of staying in OH: pay own rent (~$100/week), abstain from alcohol and drugs, comply with assigned weekly chores. Intervention 2: TC Licensed, private, structured sober living residential program. Residents follow a regimented recovery program supervised by trained staff and site managers. Requirements of staying in TC: in First few months must undergo random urine testing for substance abuse, attendance at 5 self-help meetings per week, make ≥4 recovery-related phone calls per week, and obtain employment. During later months, residents attend 4 12-step meetings / week, continue making 4 phone calls to sponsors, and move toward financial	**ASI-Lite** Assessed alcohol and drug use over past 30 days Authors reported good validity and reliability (citation provided).[13] **Form 90 Timeline Followback** (modified from 90 to 180 days) 180-day recall of important days and events recorded by patient on a calendar (e.g., employment, health care utilization, incarceration, drug use). Authors reported excellent test-retest reliability for core substance abuse variables (citation not provided). **Urinalysis** Used to confirm/refute self-reported abstinence from illegal drugs and alcohol during wave 5. Urinalysis was accepted over self-report. Measurement properties not reported. Follow up at 6- 12- 18- and 24-months from baseline interview.

Table 3: Characteristics of Included Primary Clinical Studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
		,	stability. Option to move to independent living arrangements owned by the TC after 12 months, with continued drug screening tests and following regimented recovery plan.	
RCTs assessed as Non-Randomized Studies				
Dean, 2018 US	Single-centre, single-blind (patients) NRS: Patients were recruited from a community-based residential treatment program for drug use. Participants were randomized to receive residential treatment plus (a) ABM or (b) attentional control condition. Both groups were residential and therefore only combined changes from baseline to follow-up are presented in this report.	Diagnosis with current Methamphetamine Dependence (DSM-5 critieria), currently testing negative for drugs on urinalysis N = 42 (27 men, 15 women) Aged: ABM, 35.7 years; Control, 34.9 years Comorbid diagnoses: -Substance abuse/ dependence: Alcohol, 21 Marijuana, 20 Cocaine, 8 Opiate, 11 Other, 16 -Affective disorder, 18 Inclusion criteria: Exclusion criteria: (1) neurological disorders; (2) head injury with loss of consciousness > 30 min; (3) untreated or unstable medical illness; (4) schizophrenia, psychotic disorder, or bipolar I disorder; (5) any illness, condition,	Intervention: Residential program consisted of a combination of cognitive behavioral therapy, 12-Step facilitation, motivational interviewing, and group counseling. Patients in residential treatment were assigned to a 4-week, 12 session attentional bias modification or contact control. Only overall findings reported in this report.	**Methamphetamine Craving Scale** (modified from Brief Cocaine Craving Scale) Assessed self-reported spontaneous Methamphetamine craving. 10 items on a Likert-scale (number of points on scale not provided). Assessed prior to each training session and at 1 month follow-up. Measurement properties not reported. **Cue-induced craving paradigm** Participants were shown a series of images presented on MRI compatible goggles. **(1) Self-report** Following ~3 seconds participants were asked to rate, “How much do you feel like using meth right now?” Participants had 3 seconds to rate responses on a

Table 3: Characteristics of Included Primary Clinical Studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
		or use of medication that PI and study physician determined would preclude safe participation Recruitment period NR		Likert-type scale ranging from 1 (not at all) to 4 (very much). **(2) fMRI** "Imaging was performed using a 3-T Siemens AG (Erlangen, Germany) Prisma MRI scanner with a 32-channel head coil." (p.4) Functional T2*-weighted images acquired with Multiband EPI (multiband acceleration factor, 8; slice thickness, 2 mm; 72 slices; TR , 0.8 s; TE, 37 ms; flip angle, 52°; FOV, 208 mm). "A T2-weighted matched bandwidth high-resolution anatomical scan (same slice prescription as EPI with TR, 5000 ms; TE, 60 ms) and a T1 MPRAGE high-resolution scan (slice thickness, 0.8 mm; 208 slices per slab; TR, 2400 s; TE, 2.24 ms; flip angle, 8°; matrix, 256 × 256; FOV, 256 mm; sagittal orientation) were acquired for each participant. The orientation for matched bandwidth and EPI scans was oblique axial in order to maximize full brain coverage and to

Table 3: Characteristics of Included Primary Clinical Studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
				optimize signal from ventral prefrontal regions." (p.4) Measurement properties not reported.
Manning, 2016 Australia	Multi-centre (i.e., 2) NRS In-patients in one of two residential detoxification facilities in a 7-day withdrawal management program were assigned to CBM or sham treatment. Both groups were residential and therefore only combined changes from baseline to follow-up are reported in this review.	Alcohol-dependent in-patients (N = 83) 50.6% male; 49.4% female; Mean age = 40.4 years Comorbid psychiatric disorder , 91.6%; Mean severity of alcohol dependence = severely dependent (score = 32.5 on SADQ); Mean drinking in 2 weeks prior to admission: 12.2 days per week, 20 standard drinks per day Inclusion criteria: Aged 18-60 years; English speaking; At least weekly alcohol use in past month; DSM-5 criteria for AUD Exclusion criteria: History of neurological illness or TBI involving loss of consciousness > 30 minutes Recruited between July 2014 and December 2015	7-day withdrawal management program in residential facility. Residential treatment patients were assigned to CBM or sham training delivered over 4 consecutive days of their in-patient withdrawal treatment. Only overall findings reported in this report.	**Alcohol Craving Questionnaire Short-Form – Revised** Assessed alcohol cravings. Interpretation of scores not provided. **Mean Severity of Alcohol Dependence Questionnaire (SADQ)** Assessed alcohol severity. Interpretation of scores not provided.
Satyanarayana, 2016 India	Single centre NRS Psychiatry in-patients were recruited from	N = 177 male alcohol dependent in-patients Mean age = ICBI, 37.50 years; TAU,	All patients were treated with pharmacotherapy and one session of	**Severity of Alcohol Dependence Questionnaire** Assessed severity of

Table 3: Characteristics of Included Primary Clinical Studies

First Author, Publication Year, Country	Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
	a teaching hospital	38.63 Inclusion criteria: Aged ≥ 21 years; currently married; had at least one child <16 years; screened positive for perpetration of any intimate partner violence (physical, sexual, psychological) in the past 6 months; wife was primary care giver Exclusion: Other axis I major mental illnesses and axis II disorders Recruited between August 2012 and March 2014; consecutively screened admissions to psychiatry department	psychoeducation for Alcohol Dependence Syndrome delivered in a residential psychiatric services setting. Patients were randomized to (1) treatment as usual or (2) integrated cognitive behavioural intervention: 8 sessions, 45 to 60 minutes each of cognitive–behavioral intervention sessions addressing alcohol dependence and intimate partner violence, and teaching relaxation, anger management, assertiveness training and cognitive restructuring Duration of in-patient treatment not reported	alcohol dependence by asking participants to rate 20 statements on a 4-point Likert scale; higher scores indicated greater alcohol dependence. Authors reported high reliability and validity.

ABM = attention bias modification; AUD = alcohol use disorder; AG = publicly listed company CBM = cognitive bias modification; DSM-5 = Diagnostic and Statistical Manual of Mental Disorders - fifth edition; EPI = echoplanar imaging; fMRI = functional Magnetic Resonance Imaging; FOV = field of view; ICBI = integrated cognitive behavioural intervention ; mm = millimetre; MPRAGE = magnetization-prepared rapid-acquisition gradient echo; MRI = magnetic resonance imaging ; ms = acronym not elaborated in the article; N = sample size ; NR = not reported; NRS = non-randomized study; OH = Oxford House; PI = principal investigator ; RCT = randomized controlled trial; sig. = significantly; SADQ = Severity of Alcohol Dependence Questionnaire; T1 = time one; T2 = time two; TAU = treatment as usual; TBI = traumatic brain injury; TC = Therapeutic Community; TE = echo time; TR = repetition time; UA = usual aftercare;

Appendix 3: Critical Appraisal of Included Publications

Table 4: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR 2[8]

Strengths	Limitations
McCarty, 2014[12]	
• Research question and inclusion criteria for the review included the PICO elements. • Several databases searched, key words provided for the literature search, and bibliographies of major reviews and meta-analyses searched. • No significant heterogeneity reported. • Study sponsor was reported transparently as the Substance Abuse and Mental Health Services Administration	• No explicit statement that the review methods were established prior to the conduct of the review • Explanation of selection of study designs for inclusion in the review not provided • Unable to determine if the search was conducted within 24 months of completion of the review. • Unable to determine if study selection or data extraction performed in duplicate • List of excluded studies not provided and exclusions not justified • Interventions and comparators not described in adequate detail. It is unclear how much of this was due to reporting by included studies and how much due to poor reporting of this review • Risk of bias in individual studies was not assessed. Risk of bias across studies was considered using a purpose built tool: "We developed an evidence rating scale that builds on the practice and consensus standards outlined in a number of national reports over the past decade or more."[17] (p. 12). For RCTs, random allocation sequence, allocation concealment, blinding of outcome assessors or patients were not assessed. For non-randomized studies, risk of bias from confounding and attrition, but not selection bias or measurement of exposures and outcomes were not assessed • Unable to determine if authors looked for information on the sources of funding for the studies included in the review. None were reported • No mention of competing interests or potential conflicts by authors of the review
Reif, 2014[7]	
• Several databases searched and key words provided for the literature search; experts in the field were consulted • Study sponsor was reported transparently as the Substance Abuse and Mental Health Services Administration	• Research question and inclusion criteria for the review clearly described population and intervention. However, comparator and outcomes were not defined • No explicit statement that the review methods were established prior to the conduct of the review • Explanation of selection of study designs for inclusion in the review not provided • Unable to determine if the search was conducted within 24 months of completion of the review, or if reference lists of included studies, trial/study registries, or grey literature were searched • Unable to determine if study selection or data extraction performed in duplicate

Table 4: Strengths and Limitations of Systematic Reviews and Meta-Analyses using AMSTAR 2[8]

Strengths	Limitations
	• List of excluded studies not provided and exclusions not justified • Risk of bias in individual studies was not assessed. Risk of bias across studies was considered using a purpose built tool: "We developed an evidence rating scale that builds on the practice and consensus standards outlined in a number of national reports over the past decade or more."[17] (p.12). For RCTs, allocation concealment, random allocation sequence, blinding of outcome assessors or patients were not assessed. For Non-randomized studies, risk of bias from confounding and attrition, but not selection bias or measurement of exposures and outcomes were not assessed • No mention of competing interests or potential conflicts by authors of the review

Table 5: Strengths and Limitations of RCT using Cochrane RoB 2[9]

Strengths	Limitations
Jason, 2015[13]	
Bias due to confounding Low risk of bias. Authors tested for potential confounders at baseline (age was statistically sig. different between groups). Age and other potential confounders (i.e., treatment dose, measurement time point) were accounted for in the mixed model analysis **Bias in selection of participants into the study** Low risk of bias. Selection of participants was not based on characteristics observed after the start of intervention. Start of follow-up and start of intervention coincided for all patients. Intervention started immediately following baseline testing. Follow up occurred at 6 month intervals following baseline testing. **Bias in classification of interventions** Low risk of bias. Intervention groups were clearly defined / recorded at the start of the intervention. A random sequence was generated via random number generator and group assignment was concealed in sealed opaque envelopes, opened when the baseline interviewer first met each participant at baseline. **Bias due to deviations from intended interventions** Low risk of bias. No deviations from intended interventions were reported. Intervention (OH, TC) patients were permitted to stay in residential treatment as long as they chose to and followed the rules of the facility. Duration of stay varied across treatments and was accounted for in mixed model analyses. **Bias in measurement of outcomes** Low risk of bias. Although outcome assessors were not reported to be blinded, urine analysis was used to confirm self-reported abstinence. **Bias in the selection of the reported result** Low risk of bias. Results reported as in methods. **Overall bias** N/A	**Bias due to missing data** Moderate risk of bias. Authors reported using intention-to-treat analysis for one outcome (not eligible for this report) but not others. Two participants died during the follow up period for unreported reasons. Similar number of patients in each group were reached for at least one follow up interview (OH = 82%, TC = 81%, UA = 78%) Amount of missingness at each time point was not clearly reported.

N/A = not applicable; RoB 2 = Revised Cochrane risk-of-bias tool for randomized trials

Table 6: Strengths and Limitations of NRS using Downs and Black Checklist[10]

Strengths	Limitations
Dean, 2018[14]	
• Objective of the study, main outcomes, patient characteristics, interventions, and main findings were clearly described. • Participants received care in the usual location, provided by the usual staff of the facility. The additional components were performed by research staff. • Participants were blinded to intervention received (although data were pooled, so not likely relevant). • Statistical tests were appropriate. • Compliance with the interventions was reliable	• Unable to determine if there was a comprehensive attempt to measure adverse events. • Characteristics of patients lost to follow up were not described. • Actual probability values were not reported. • Unable to determine if patients asked to participate or patients who were prepared to participate in the study were representative of the entire population of the treatment centre from which they were recruited. • Outcome assessors were not blinded to main outcomes. Since study hypotheses were not supported, this is not expected to have introduced bias. • Outcome measures were clearly described, however measurement properties of outcome measures were not reported. • Unable to determine the period of time of participant recruitment • 14% (6/42) of participants were lost to follow up. 29% (5/17) of patients were lost to follow-up in the cued-craving sub-analyses. Reasons for missingness were drop out (n = 4, reasons not reported) and did not complete MRI scanning (n = 1). • Participants in residential treatment were randomized to an attentional bias modification treatment or contact control. For the present purposes, only combined data were considered. Thus, randomization did not occur and there was no non-residential treatment control condition. • Effect of residential treatment on methamphetamine use could not be measured as residential treatment continued after this study concluded. • Analysis of fMRI data were not as planned at outset. Data were combined across intervention groups in response to finding no significant differences between groups.
Manning, 2016[15]	
• The study was registered with clinicaltrials.gov prior to the end of data collection. • The objectives, hypotheses, main outcomes, patient characteristics, interventions of interest, and main findings were clearly described. • Estimates of random variability were provided for main study outcomes. • The study was conducted in the treatment facilities where patients were already being treated. • Outcome assessors were blinded to treatment. • Actual probability values were reported for the main outcomes.	• Unable to determine if there was a comprehensive attempt to measure adverse events. • Characteristics of the 12 patients lost to follow-up were not described. • Unable to determine if patients asked to participate or patients prepared to participate in the study were representative of the entire population of the treatment centres from which they were recruited. • Outcome measures were clearly described, but measurement properties of outcome measures were not reported. Abstinence was determined by self-report over telephone interview rather than objective measures • 15% of participants withdrew from the study, and the reasons were not provided.

Table 6: Strengths and Limitations of NRS using Downs and Black Checklist[10]

Strengths	Limitations
	• Unable to determine the timeframe for participant recruitment.
Satyanarayana, 2016[16]	
• The objective, main outcomes, patient characteristics, and main study findings of the study was clearly described. • Principal confounders were addressed through exclusion criteria. I.e., patients with other axis I or II diagnoses were excluded as authors indicated these disorders are known to confound study variables. • Standard deviations are provided. • Staff, places, and facilities were representative of the treatment the majority of patients receive. • All analyses appear to have been planned at the outset of the study. • Participants were followed up for the same duration of time.	• Unable to determine if there was a comprehensive attempt to measure adverse events. • Characteristics of patients lost to follow-up not described • Actual probability values for change scores not provided. • Consecutive patients were screened for study eligibility. Unable to determine if invited patients or included patients were representative of the entire population from which they were recruited. • 7.9 and 11.9% of participants had missing data at 1-month and 3-month follow-up, respectively. Reasons for missingness were not reported and missing data were not considered in analyses.

ABM = attentional bias modification; fMRI = magnetic resonance imaging; NRS = non-randomized studies

Appendix 4: Main Study Findings and Authors' Conclusions

Table 7: Summary of Findings of Included Systematic Reviews

Main Study Findings	Authors' Conclusion
McCarty, 2014[12]	
"*The randomized trials and quasi-experimental studies consistently reported significant reductions in problem severity and increases in days abstinent at follow-up interviews (between 3 and 18 months after baseline assessment) for study participants receiving intensive outpatient or day treatment services and for individuals in inpatient or residential care*." (p.6) "*…all randomized trials reported similar reductions in Addiction Severity Index measures when inpatient and intensive outpatient settings were compared. Lastly, the studies that included participants who were randomized and those who self-selected levels of care reported a similar lack of overall differences in study outcomes when levels of care were compared*." (p.6) Only two of six naturalistic analyses reported main effects for treatment setting. Both favoured in-patient over intensive outpatient for improvement in symptoms. The other four studies did not show differential effects between in-patient and outpatient settings.	*"Although there is still some debate about the equivalence of inpatient and intensive outpatient care for patients with the most severe levels of dependence, there appears to be general consensus that for most patients the levels of care are equivalent."(p.7)*
Reif, 2014[7]	
For the eight review studies, residential treatment was either better than comparators or equally as effective/ineffective for substance use outcomes Overall, there was no difference between any form of residential treatment and non-residential treatment among the seven RCTs. One study reported those with higher alcohol involvement and poorer cognitive functioning at baseline had greater improvements in residential versus non-residential treatment. Another study showed more favourable relapse rates at 6 months but groups did not differ at 12 or 18 months The 13 quasi-experimental studies showed residential treatment was more effective than non-residential treatment for some substance use outcomes for nine studies. The remaining four studies reported no difference between residential and comparator groups.	*Regarding drug and alcohol use, "this review found a moderate level of evidence for the effectiveness of residential treatment. Despite the prevalence of methodological concerns–primarily the appropriateness of the samples and equivalence of comparison groups–some evidence indicates that residential treatment is effective for some types of patients. Further, much of the literature suggests that residential treatment is equally as effective as comparison modalities and a few studies suggest that it is more effective. However, research with more rigorous methods is conducted, these conclusions remain tentative" (p.310)*

Table 8: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
Jason, 2015[13]	
Days of substance use at each assessment period; M (SD) Not statistically analyzed **Days of alcohol and drug at baseline** OH: alcohol = 16.00 (34.62); drugs = 45.08 (54.30) TC: alcohol = 20.71 (42.23); drugs = 45.12 (59.89) UA: alcohol = 23.53 (45.58); drugs = 44.19(58.90) Days of alcohol and drug use in last 6 mo. at 6 mo. post-baseline OH: alcohol = 7.13 (22.73); drugs = 16.36 (37.63) TC: alcohol = 22.70 (48.25); drugs = 14.75 (39.72) UA: alcohol = 11.47 (34.55) ; drugs = 25.51 (51.32) Days of alcohol and drug use in last 6 mo. at 12 mo. post-baseline OH: alcohol = 13.35 (32.70) ; drugs = 13.24 (33.22) TC: alcohol = 21.17 (45.42) ; drugs = 23.98 (50.21) UA: alcohol = 15.21 (33.50) ; drugs = 28.67 (54.93) Days of alcohol and drug use in last 6 mo. at 18 mo. post-baseline OH: alcohol = 13.35 (32.70) ; drugs = 13.24 (33.22) TC: alcohol = 21.17 (45.42) ; drugs = 23.98 (50.21) UA: alcohol = 15.21 (33.50) ; drugs = 28.67 (54.93) Days of alcohol and drug use in last 6 mo. at 24 mo. post-baseline OH: alcohol = 13.69 (34.79); drugs = 21.39 (47.05) TC: alcohol = 29.27 (49.39); drugs = 26.14 (48.74) UA: alcohol = 25.09 (40.10) ; drugs = 36.07 (57.35) **Mixed model of number of days of alcohol use over past 6 mo. assessed by ASI-Lite** Sig. dose effect for alcohol use over past 6 mo. (i.e., higher number of days in OH or TC led to lower days using alcohol), but no effect for group, measurement time point, group by measurement time point interaction, or age. Time: F = 1.41, *P* = 0.23 Group: F = 0.47, *P* = 0.63 Time x Group: F = 0.66, *P* = 0.52 Age: F = 3.10, *P* = 0.08 Dose: F = 5.15, *P* = 0.02 **Mixed model of number of days of drug use over past 6 mo**. Sig. measurement time point and dose effect for drug use over past 6 mo. (higher number of days in OH or TC led to fewer days using drugs), but no effect for group, group by measurement time point interaction, or age.	*"In conclusion, OHs comprise a large network that provides inexpensive housing and support for abstinence." (p.13)*

Table 8: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
Time: F =9.80, P ≤ 0.01 Group: F = 0.06, *P* = 0.94 Time x Group: F = 1.15, P = 0.32 Age: F = 3.05, *P* = 0.08 Dose: F = 6.26, *P* = 0.01 **Continuous days abstinence from baseline to 24 mo. follow up** • Alcohol Overall comparisons Sig. overall effect: x^2(N = 270) = 12.12, *P* < 0.01 OH vs. TC OH sig. higher continuous days abstinence (66%) than TC (40%); [x^2 (N = 180) = 11.79, *P*<0.01] OH vs. UA OH sig. higher continuous days abstinence (66%) than UA (49%); x^2(N = 180) = 5.01, *P* = 0.02) Drugs Overall comparisons No sig. overall differences between OH (47%), TC (44%), UA (42%); x^2(N = 270) = 0.36, *P* = 0.84	
RCTs assessed as Non-Randomized Studies	
Dean, 2018[14]	
Spontaneous MA craving Sig. main effect of time; craving decreased from baseline to follow-up. F = 33.525, *P* < 0.0001 **Cue-induced MA craving – meth/neutral cue contrast score fMRI** (subsample n = 12) Sig. main effect of time; craving decreased from baseline to follow-up. x^2 = 12.472, *P* < 0.0005	"*Although spontaneous craving and cue-induced craving for MA reduced over time with treatment, ABM training did not facilitate these effects*." (P. 6)
Manning, 2016[15]	
Mixed-effects repeated-measures ANOVA (group x time) **Alcohol Craving (ACQ scores)** Baseline to post-training Sig. main effect of time; craving lower from baseline to post-training (n=64) F(1, 62) = 32.83, *P* < 0.001, η^2 = 0.35 Baseline to 2 week follow up Sig. main effect of time; craving was lower at 2-week follow up than baseline (n=64)	N/A

Table 8: Summary of Findings of Included Primary Clinical Studies

Main Study Findings	Authors' Conclusion
F(1, 62) = 4.53, *P* = 0.04, η2 = 0.07 **Mean drinking days** Baseline to 2-week follow-up Among participants who had relapsed at follow-up, there was a sig. main effect of time. F(1, 28) = 47.96, *P* < 0.001, η2 = 0.63 **Mean drinks per drinking day** Baseline to 2-week follow-up Among participants who had relapsed at follow-up, there was a sig. main effect of time. F(1, 28) = 55.59, p < 0.001, η2 = 0.67	
Satyanarayana, 2016[16]	
Alcohol consumption (SADQ scores) Group 1 (n = 88): Baseline = 28.9 ± 12.8 1-month follow-up = 20.4 ± 8.2; change from baseline *P* < 0.05 3-month follow-up = 18.9 ± 8.4; change from baseline *P* < 0.05 Group 2 (n = 89): Baseline = 27.3 ± 13.1 1-month follow-up = 20.9 ± 9.9; change from baseline P < 0.05 3-month follow-up = 19.7 ± 10.2; change from baseline P < 0.05	N/A

ACQ = Alcohol Craving Questionnaire; ASI-lite = Addiction Severity Index-Lite; df = degrees of freedom; F = F-statistic; fMRI = functional magnetic resonance imaging; M = mean; MA = Methamphetamine; mo. = months; n = number ; N/A = not applicable; OH = Oxford House; PFC = prefrontal cortex; SADQ = Severity of Alcohol Dependence Questionnaire; SD = standard deviation; TC = Therapeutic Community; UA = usual aftercare

Appendix 5: Overlap between Included Systematic Reviews

Primary Study Citation	Systematic Review Citation	
	McCarty, 2014[12]	Reif, 2014[7]
Brunam 1995		X
McKay 1995	X	X
Finney 1996	X	X
Moos 1996		X
Schneider 1996	X	
Guydish 1998	X	X
Hser 1998		X
Guydish 1999	X	X
Harrison 1999	X	X
Pettinatti 1999	X	X
Simpson 1999	X	
Rychtarik 2000	X	X
Schildhaus 2000		X
Greenwoord 2001		X
Weithmann 2005	X	
Witbrodt 2007	X	X
McKay 2002	X	X
Mojtabai 2003		X
Brunette 2004		X
Hser 2004		X
Ilgen 2005		X
Brecht 2006		X
Smith 2006		X
Ilgen 2007		X
Tiet 2007	X	X
De Leon 2008		X
Drake 2008		X
Cleary 2009		X
Finney 2009		X
De Leon 2010		X

Primary Study Citation	Systematic Review Citation	
	McCarty, 2014[12]	Reif, 2014[7]
Morrens 2011		X
Malivert 2012		X

Appendix 6: Additional References of Potential Interest

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