Effect of cognitive–behavioural therapy on resilience and relapse in adult patients with substance use disorder: a systematic review protocol

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ABSTRACT

Introduction  Approximately 0.5 million fatalities per year are attributed to substance use disorder (SUD). SUD is refractory to therapy and has a high relapse rate. Cognitive deficits are also common in patients with SUD. Cognitive–behavioural therapy (CBT) is a promising treatment that may build resilience and reduce relapse among people with SUD. Our planned systematic review aims to clarify the effect of CBT on resilience and the relapse rate in adult patients with SUD compared with treatment as usual or no intervention.

Methods and analysis  We will search the Scopus, Web of Science, PubMed, Medline, Cochrane, EBSCO CINAHL, EMBASE and PsycINFO databases from inception to July 2023 for all relevant randomised controlled or quasi-experimental trials published in English. The follow-up period of included studies must be at least 8 weeks. The PICO (Population, intervention, control, and outcome) format was used to develop the search strategy. Search terms will be combined using boolean operators and have been customised for different databases. The Cochrane tool for randomised controlled trials will be used to assess the risk of bias in included studies. Extracted data will include bibliographic data, sample size, intervention method, summary of the findings, follow-up duration and effect sizes with standard errors. A random effects model will be used to combine effect measures. Subgroup analyses will be performed by CBT type, sex and SUD subtype, as applicable. I² statistics will be used to evaluate heterogeneity, and funnel plots will be used to address publication bias. If we detect significant heterogeneity, the findings will be reported as a systematic review without a meta-analysis.

Ethics and dissemination  Ethical approval is not required for this study. The findings will be submitted for publication in a peer-reviewed journal.

PROSPERO registration number  CRD42022344596.

INTRODUCTION

Substance use disorder (SUD) is defined as ‘maladaptive use of a drug, resulting in impairment of functioning or distress, as manifested by: a failure to perform adequately at home, school or work; repeated drug use in dangerous circumstances, such as when driving or operating machinery’. The United Nations Office on Drugs and Crime reported that the number of individuals using illegal drugs had increased by 2% between 2010 and 2019, partly attributed to global population growth. The WHO estimated that 35 million people worldwide are affected by drug use disorders. Based on demographic changes, current projections suggest an 11% increase in drug users worldwide by 2030.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This systematic review will include all types of substance use disorder except for tobacco use.
⇒ The review will be restricted to studies published in the English language.
⇒ The review may be limited by publication bias.

after being discharged. Numerous factors can contribute to relapse, making SUD a complex health concern. Cognitive deficits in memory, attention, executive function and decision-making along with deficits in reward expectancy, valuation and learning are common in patients with SUD; these factors can be significant predictors of relapse. In addition, the presence of multiple aetiological factors is associated with an increased risk for relapse in patients with SUD.  

The main goal of SUD treatment is to reduce the relapse rate and maintain abstinence. Several interventions have been introduced to reduce relapse. For example, physical activity may contribute to reducing relapse through improving neuroplasticity and cognitive functioning, reducing impulsivity and urgency, improving emotional regulation, and reducing cravings.  

A combination of methadone maintenance therapy and cognitive–behavioural therapy (CBT) has been found to improve emotional regulation in patients with opioid use disorder. Mindfulness-based relapse prevention integrates evidence-based practices to decrease relapse probability and severity for patients with SUD.  

Resilience is defined as ‘a process whereby people bounce back from adversity through the protective factors that serve to moderate the effects of adversity’ or ‘successful stress-coping ability’. In the context of SUD, components of resilience include self-efficacy, emotional strength and coping as protective factors, and craving and stress as adverse factors. However, resilience is modifiable. A previous review found that enhancing protective factors that counter balanced the effects of adversity resulted in improved resilience. Previous studies showed that resilience among university students could be improved through willpower strengthening exercises, which involved correcting posture, relaxation exercises and acknowledging thoughts and emotions. A meta-analysis of 25 randomised controlled trials (RCTs) that used various formats and theoretical approaches to enhance resilience in diverse adult populations showed small-to-moderate effects in improving resilience. However, another systematic review revealed disagreement in terms of whether resilience persisted over time or not, as some of the included studies showed patients lost resilience over time, whereas others maintained favourable adaptation characteristics.  

Applying resilience to SUD requires investigating adversities that contribute to the development of SUD and factors that protect against SUD. For example, religion and prayer served as significant protective factors against substance use among adolescents. Risk and protective factors for substance use are present at individual, family and community levels. A systematic review published in 2014 that assessed various interventions to improve resilience concluded that although the interventions varied in format and theoretical approaches, they were mainly built on resiliency-specific interventions (eg, the 5 Cs model, Lazarus’ stress model and the resilience model). That review also noted these interventions were operationalised in diverse ways and lacked common theoretical or scientific specificity. However, few studies were designed based on generalised stress-directed programmes or CBT.  

CBT is a type of psychotherapy that helps people overcome their problems by altering how they think and behave. The Merriam-Webster dictionary defines CBT as ‘psychotherapy that combines cognitive therapy with behaviour therapy by identifying faulty or maladaptive patterns of thinking, emotional response or behaviour and substituting them with desirable patterns of thinking, emotional response or behaviour’. This definition will serve as an operational definition for CBT in our review. CBT is commonly used to improve resilience and substance use outcomes in patients with SUD. For example, a previous study found significant improvement in cognitive behavioural variables between discharge and admission in patients with alcohol use disorder (AUD) admitted to rehabilitation centres. CBT is therefore an essential part of the multifaceted approaches used to address SUD in rehabilitation centres worldwide, and is based on the assumption that SUD is a learnt maladaptive behaviour.  

A previous systematic review on this topic suggested that factors such as self-efficacy and coping skills can be considered intermediary variables in the causal path of addiction treatment using CBT methods. However, a limitation of that study was that it only included RCTs that used path analysis. Therefore, our review will include RCTs that used simple statistical methods to summarise the effect size. We will extract data for different time points and attempt to summarise the effect sizes for each time point in a subgroup meta-analysis to provide insights into how time affects the performance of CBT in improving resilience. To our knowledge, this has not been done since a 2014 study that explored various interventions to enhance resilience in different populations. One of our main interests in conducting this review is to investigate the effect of different CBT subtypes on resilience and relapse to determine if there is a difference between CBT subtypes in SUD treatment. Therefore, we will assess the effect of CBT programmes on improving resilience and relapse in patients with SUD.

**Research questions**  
This review seeks to answer the following three research questions.  
1. What is the effect of CBT on improving resilience and relapse prevention?  
2. Are there any differences in the effect of different CBT methods on resilience and relapse?  
3. Which groups of people benefit most from CBT for SUD?

**METHODS AND ANALYSIS**  
**Study design**  
Work on this systematic review and potential meta-analysis started on 1 April 2022, and the final literature searches are anticipated to be completed by July 2023. The review will be reported following the Preferred Reporting Items
for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The protocol for this systematic review was prepared in accordance with the PRISMA Protocols guidelines.

Based on the following formula and considering an alpha error level of 0.05 and power of 80%, the minimum sample size required to detect a significant relationship was considered to be 20 observations.

\[
n = \frac{2 \times S^2 \times (\bar{x}_1 - \bar{x}_2)^2}{(n_1 - n_2)^2}
\]

where \(n\) = required sample size, \(\bar{x}_1\) and \(\bar{x}_2\) are estimated means of the control and intervention groups and \(S^2\) is the mean estimated variance of the two groups. The \(S^2\) can be obtained via the following formula:

\[
S^2 = \frac{(n_1 - 1) \times S_1^2 + (n_2 - 1) \times S_2^2}{n_1 + n_2 - 2}
\]

where \(S_1^2\) is the variance of the control group, \(S_2^2\) is the variance of the intervention group and \(n_1\) and \(n_2\) are the number of patients allocated to each group. So, the calculation of \(S^2\) is as follows:

\[
S^2 = \frac{39 \times 83.90 + 39 \times 50.52}{78} = 67.21
\]

Therefore, the sample size is calculated as follows:

\[
n = \frac{2 \times 67.21 \times (1.96 + 0.84)^2}{(7.10)^2} \approx 20
\]

The parameters needed to calculate the minimum sample size were obtained from a previous study, which was chosen because a preliminary search of related studies showed it had the closest characteristics to our inclusion criteria.

**Eligibility criteria**

**Types of studies**

Any type of RCT will be eligible for this review, including quasirandomised trials and cluster randomised trials. However, pilot and feasibility studies that do not have good quality and large sample sizes will be excluded. We will also exclude case-control, cohort and other observational studies. Only studies published in the English language will be included but we will not implement restrictions based on the year of publication, country and the study setting. We will conduct this review to investigate the long-term effects of CBT on SUD. Therefore, studies that measured the desired outcomes before and immediately after the intervention or with follow-up periods less than 8 weeks will be excluded.

Pilot and feasibility studies that do not have good quality or a minimum sample size of 20 participants will be excluded.

**Types of participants**

The target population will be patients diagnosed with any kind of SUD, except tobacco smoking because these individuals are usually investigated separately to avoid distorting the results; systematic reviews on smokers should therefore be conducted separately. Only studies on patients over 18 years with confirmed diagnosis of SUD will be included. Studies focused on non-human subjects, adolescents, or children will be considered ineligible.

**Types of interventions**

The only interventions considered in this study will be those using CBT methods (eg, acceptance and commitment therapy, cognitive restructuring, mindfulness-based programmes). These interventions can be delivered by any member of healthcare staff (eg, physicians, trained nurses or psychotherapists). Any interventions not classified as CBT will be excluded from the present review. Studies in which the intervention group received another treatment in addition to CBT, such as psychological or drug treatments, will also be excluded because these treatments may interact with CBT and investigating such interaction effects is beyond the scope of this review.

**Comparator conditions**

Acceptable interventions for the comparison groups in the included studies will be treatment as usual or no intervention. In addition, we will include studies that compared participants’ status before and after the intervention. Studies that used any other intervention for the comparison group will be considered ineligible.

**Types of outcomes**

The main outcomes for patients with SUD in the included studies must be resilience and relapse. Therefore, any study that did not measure resilience or relapse as an outcome (eg, those that examined how well resilience training programmes were disseminated and implemented) will not be considered. No other outcomes will be investigated.

**Information sources**

A comprehensive search will be conducted across several databases from inception to July 2023: Scopus, Web of Science, PubMed, Medline, Cochrane, EBSCO CINAHL, EMBASE and PsycINFO. In searching these databases, the output will be filtered using the ‘by author’ filter to identify experts that may be contacted to determine if they are aware of unpublished studies. This method is commonly used by authors of systematic reviews. An initial search using this filter yielded several authors (Dr Steven Southwick, Dr George Bonanno, Dr Rachel Yehuda, Dr Ann Masten, Dr Catherine Panter-Brick, Dr Kathleen Carroll, Dr Charla Nich, Dr Katie Witkiewitz, Dr Edward Nunes and Dr Aimee Campbell).

In addition, authors of the articles identified for inclusion in our systemic review and potential meta-analysis will be contacted regarding details of completed but unpublished research as well as ongoing studies. Finally, prospective clinical trial registries (national and international) will be searched to identify ongoing studies.
Search strategy
The PICOS format was used to develop the search strategy. The most important keywords for each PICOS component are as follows.

Population

Intervention
Cognitive behavioural therapies, cognitive therapies, cognitive psychotherapy, cognition therapies, CBT, acceptance and commitment therapy, cognitive restructuring, cognitive reframing, mindfulness, relapse prevention, ‘Marlatt’s model,’ relapse management.

Comparison
No keywords will be used here to avoid missing any related articles.

Outcome
Resilience, flexibility, post-traumatic growth, psychological adaptation, adjustment, coping behaviour, coping skills, coping strategy, adaptive behaviour, cope, emotional adjustment, stress-related growth, psychological hardiness, bounce back, abstain, abstinence and relapse.

Study design
Randomised controlled trial, controlled clinical trial, randomised clinical trial, clinical trial and controlled trial
Both controlled vocabulary (eg, MeSH term and emtree) and title/abstract fields will be searched to ensure we do not miss any important results. The keywords in each concept will be combined using the ‘OR’ logical operator. The ‘AND’ operator will be used to combine all concepts and ensure the results address all of the desired aspects. The final search strategy is shown in online supplemental appendix 1.

Study procedures
Data management
Endnote software will be used to manage the identified references and merge duplicates.

Selection process
In the first phase of the screening process, two authors will separately read the title and abstract of each identified article to determine whether the article should be excluded or if full-text review is needed to make a decision. Disagreements will be resolved through discussion between these two authors and a third author. Next, two authors will read the full texts of the remaining articles to make the final decision regarding article inclusion. Discrepancies in the second phase will be resolved by consulting a third author. In the full-text screening, the reason for excluding each article will be recorded. The reviewing authors will not be blinded to information about the articles (eg, authors, institutions, and journals). The number of studies at each stage of the selection process and the reason for exclusion in full-text screening will be documented in a PRISMA flowchart.

Data collection
Data extraction will be performed by two authors that will first receive training to ensure that the data are extracted appropriately. The Cochrane data extraction form will be used for extracting the data; however, before starting the formal data extraction phase, a pilot data extraction will be conducted to customise the form if needed. An MS Excel spreadsheet will be used for data recording.

The following data will be extracted from the included articles: author, year of publication, setting, methods, total sample size, sample characteristics, intervention description, comparator, intervention period, follow-up period, theoretical basis, measured outcomes, measurement instruments and methods, a summary of the findings and follow-up, odds or relative risk ratio, and the SE and SD of each effect size. The sample size, mean and SD for both the intervention and control groups will be extracted to calculate the mean difference and SE.

Risk of bias in individual studies
Each included study will be evaluated using the Cochrane Collaboration tool for assessing the risk of bias in RCTs. This tool is structured using a fixed set of bias domains that cover different aspects of trial design, conduct and reporting. Risk-of-bias assessment will be performed independently by two authors.

The risk of bias for random sequence generation, allocation concealment, blinding of participants and research personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other biases will be assessed and reported. Any disagreements in the risk-of-bias assessment will be resolved through discussion between the two evaluating authors and a third author. The reports for risk of bias in the studies will be entered into an algorithm to calculate a risk-of-bias score, and the articles will be categorised as having a low, medium or high risk of bias using this score. We will also perform sensitivity analyses by excluding high-risk studies to check the robustness of our analyses.

Data synthesis
To examine resilience, the mean difference in resilience scores before and after delivering CBT will be standardised with consideration of the different questionnaires available for measuring resilience. To assess relapse, we expect to encounter different measures of association, including ORs, relative risk ratios, HRs, mean difference and percentage of relapse in the CBT and control groups. If considered appropriate and if the included articles report the necessary information about these measures, we will transform the measures to mean differences, which will be standardised. The mean rate
of relapse in the intervention and control groups will be required to calculate the standardised mean difference, but this mean may be reported in different ways (eg, the mean score for different questionnaires or a mean number of days with substance use during the last month, and average number of drinks per day). These averages are generally divided into two categories: (1) averages that use a continuous scale (eg, the average number of days with substance use during the past 90 days) and (2) averages that use a ratio scale (eg, the average percentage of substance use during the past 90 days).

The mean and SD in ratio scales will be converted to a continuous scale using mathematical rules for multiplication, division, addition and subtraction of mean and SD. For example, if the mean percentage of days with substance use during the last 90 days was 50%, the mean number of days with substance use would be 45 days. If possible, abstinence measures will also be converted into relapse measures. For example, if the mean number of drug-free days in the previous 90 days was 30 days, the mean number of drug-using days would be 60 days, but in this case, the SD would be the same. After transforming ratio outcomes into continuous outcomes, all standardised mean differences will be pooled. This is a preplanned strategy to examine the effect size, and the selection of the final effect measures for analysis may alter depending on how the effect sizes are reported in the included studies. After transforming the effect measures, we will try to minimise heterogeneity between studies by conducting subgroup analyses based on the following variables.

1. Type of participants: participants will be divided into two groups: AUD and other kinds of SUD (considered as ‘drug use disorder’). We will also perform a subgroup analysis to investigate the effect of CBT on participants by sex.

2. Types of CBT: the results will be categorised as ‘acceptance and commitment therapy,’ ‘cognitive restructuring’ or ‘mindfulness’ to reduce both methodological and statistical heterogeneity and explore the potential differences between different CBT methods.

To address any remaining heterogeneity, we will calculate the $I^2$ statistic, which describes the percentage of variation across studies that is due to heterogeneity rather than chance. If we do not encounter substantial heterogeneity ($I^2 < 50\%$), a random effects model will be used to combine the effect sizes and publication bias will be evaluated via funnel plots and the Egger test. If a meta-analysis is not appropriate, we will narratively interpret the results. Tables will be used to summarise the most important data such as the author, year, CBT subtype, SUD subtype and a summary of the findings.

If a measure is needed and that measure is not mentioned in the original article, the following approaches will be adopted. (1) If measures of occurrence have been mentioned in the original article, we will calculate the measure of association (OR or relative risk) from those data. (2) The corresponding author of that article will be contacted to obtain the needed measures. (3) If neither of the above approaches are applicable, we will omit that article from the meta-analysis for that measure of effect.

**Patient and public involvement**

None.

**Ethics and dissemination**

As no individual data will be collected, ethical approval is not necessary for this systematic review. At the time of submitting the revised version of this protocol, preliminary searches have been completed and full-text screening has begun. The findings of this review will be submitted for publication in peer-reviewed journals. This systematic review has been registered with PROSPERO (CRD42022344596).

**Contributors** AM-J designed the template. IM, HY and MRT wrote the initial manuscript. SSHN is responsible for data synthesis strategy and writing that part of the report. NA-Y, AMAM and SAR provided critical insights. All authors approved the final version of the manuscript.

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