Efficacy of Contingency Management or Cognitive-Behavioral Therapy with Pharmacotherapy Versus Placebo in Managing Stimulant Use Disorder: A Systematic Review and Meta-Analysis

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Background

- According to the National Survey on Drug Use and Health in the United States, about 21.5 million (8.4%) of adults experienced both a mental health disorder and a substance use disorder (SUD).[1] Cognitive Behavioral Therapy (CBT) and Contingency Management (CM) have emerged as one of the promising approaches in the treatment of SUD. [2]
- The efficacy of CBT in SUD lies in its ability to address the complex interplay of thoughts, behaviors, and emotions that underlie addictive patterns. While CM operates on the principle of reinforcing desired behaviors, such as abstinence from stimulant use, with tangible rewards or incentives.[3,8]

Objectives

- This study aimed to evaluate the efficacy and tolerability of psychotherapy CBT and contingency management CM augmented with pharmacotherapy, compared to psychotherapy in addition to a placebo, in the management of stimulant use disorders, through a comprehensive systematic review and meta-analysis approach.

Methods

- **Database Search:** Electronic databases were searched from inception through November 2023. Search terms include This study was registered with the International Prospective Register of Systematic Reviews (CRD42023454813).
- **Eligibility criteria**: Population: Participants aged at least 18 years diagnosed with stimulant use disorder as defined through the Diagnostic and Statistical Manual of Mental Disorders (DSM III, IV, or V) Revision or the International Classification of Disease, Ninth or Tenth Revision, Clinical Modification (ICD-9-CM, or ICD-10-CM), or self-report. Intervention: Contingency Management (CM) or cognitive-behavioral therapy (CBT), Comparator: Placebo; Outcomes: Consecutive days of abstinence or treatment retention. Study Designs: Randomized controlled trials (RCTs) and quasi-experimental/randomized studies.
- Non-randomized trials, observational studies, reviews, editorials, letters, comments, conference proceedings, case reports, case series, and abstracts without full texts were excluded from the study.
- **Data Extraction:** Data extraction was performed on eligible studies using study identifiers, including title, country of publication, authors, journals, publication year, study aims, population (age, sex, body mass index, race, disease duration), intervention (dose, duration of use, study duration), and outcomes using Microsoft Excel.
- **Quality Assessment of Studies:** Two reviewers (AO and UE) independently assessed the quality of individual studies using the Cochrane Risk of Bias tool for clinical trials. All articles were categorized into low, unclear, and high risk of bias.
- **Data Analysis:** The analysis was conducted with Review Manager (RevMan) Version 5.4 (The Cochrane Collaboration, 2020). Mean Difference (MD) and its corresponding 95% CI was chosen as the measure of effect to report outcomes on continuous scales. Efficacy was reported as the consecutive days of abstinence and treatment retention, respectively, comparing the group receiving pharmacotherapy to the placebo group. Either fixed or random effect models were fitted based on the heterogeneity of studies included as assessed with I-square (I^2).

Results

Figure 1: PRISMA flowchart for study selection

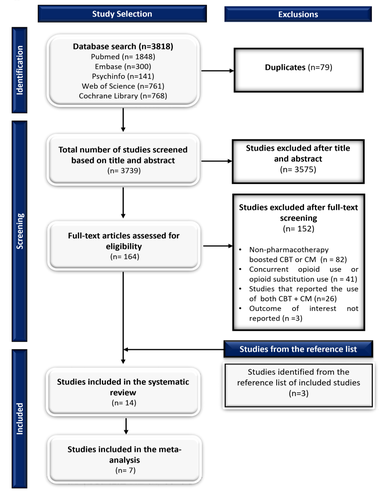

Figure 2: Risk of Bias Assessment

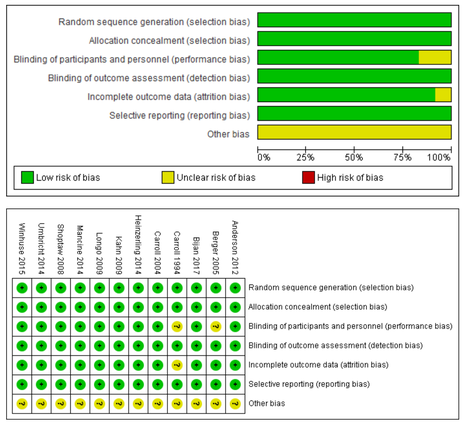

Figure 2: Mean change in consecutive days of abstinence with pharmacotherapy-based CBT

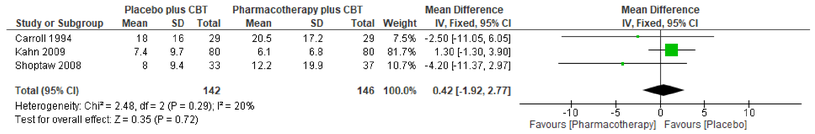

Figure 3: Mean change in treatment retention for CBT (random effect)

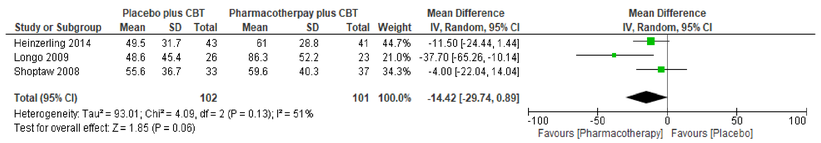

Figure 5: Mean change in consecutive days of abstinence for pharmacotherapy-based CM

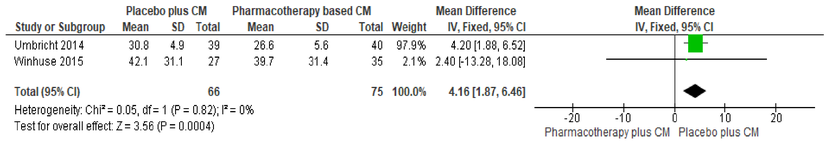

Table 1: Mean change in consecutive days of abstinence for pharmacotherapy-based CM

First Author (Year)	Study design	Study population	Concomitant substance use	Treatment	Treatment duration (weeks)	Number of participants (analyzed)
Kahn et al., 2009	RCT, DB	Cocaine	Alcohol	Baclofen	8	160
Berger et al., 2005	RCT, SB	Cocaine	Alcohol	Reserpine, Gabapentin, lamotrigine	10	60
Heinzerling et al., 2014	RCT, DB	Methamphetamine	Alcohol, marijuana, nicotine	Buproprion	12	84
Bijan P et al., 2017	RCT, DB	Cocaine	NA	Topiramate	12	50
Carroll et al., 1994	RCT, SB	Cocaine	Alcohol	Desipramine	12	58
Winhusen et al., 2015	RCT, DB	Cocaine	NA	Buspirone	16	62
Carroll et al., 2004	RCT, DB	Cocaine	Alcohol, marijuana	Disulfiram	12	60
Longo et al., 2009	RCT, DB	Methamphetamine	NA	Dexamphetamine	12	49
Shoptaw et al., 2008	RCT, DB	Cocaine	Alcohol	Buproprion	16	70
Mancineo et al., 2014	RCT, DB	Cocaine	Alcohol	Sertraline, Gabapentin	12	107
Anderson et al. 2012	RCT, DB	Methamphetamine	Alcohol, marijuana, nicotine	Modafinil	12	210
Kennedy et al, 2012	RCT, DB	Cocaine	Alcohol	D-cycloserine	8	29
Umbridtch et al., 2014	RCT, DB	Cocaine	Alcohol, cannabis, methadone, sedatives, heroin	Topiramate	25	171
McDowell et al., 2004	RCT, DB	Cocaine	Alchohol, cannabis, opiate	Despiramine	12	111

RCT: Randomized control trial; DB: Double-blinded; SB: Single blinded

Results/Discussion

- Our study included fourteen studies in the systematic review of which seven were included in the meta-analysis. The duration of the studies ranged from 8-25 weeks. The average age of study participants ranges from 28.7 to 44.3 years. 12 of 14 included studies focused on cocaine-dependent populations.
- The overall quality assessment of the studies included was low-risk of bias.
- In terms of the consecutive days of abstinence, there was no statistically significant difference between individuals receiving either pharmacotherapy or placebo in addition to CBT [MD = 0.42; 95% CI: -1.92, 2.77; I^2=20%] while in CM-boosted therapy, individuals receiving placebo had statistically significant longer consecutive days of abstinence compared to the placebo [MD= 4.16; 95% CI: 1.87, 6.46; I^2=0%]. The negative sign indicates the study favors the medication relative to the placebo group.
- With regards to treatment retention outcome, participants receiving pharmacotherapy-augmented CBT treatment had greater treatment retention days compared to those receiving placebo-augmented CBT [MD= -14.42; 95% CI: -29.74, 0.89; I^2=51%].
- Our analysis focused on studies where either only cognitive behavioral therapy or contingency management (and not both) were combined with any pharmacotherapy or placebo treatments.
- In relation to safety outcomes, participants treated with Baclofen had minimal serious adverse events, reserpine showed notable blood pressure decreases, bupropion had insomnia and adherence challenges, buspirone had minor adverse effects, disulfiram and dexamphetamine had mild side effects, while modafinil had varied adverse events with moderate retention rates. CBT improved cocaine abstinence and retention rates.

Conclusions

- CM with placebo yielded longer abstinence than CM with pharmcotherapy. No significant differences were observed when comparing placebo plus CBT with pharmacotherapy plus CBT in terms of duration of abstinence and treatment retention.

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