Brazilian Journal of Psychiatry
bjp
Revista Brasileira de Psiquiatria

Braz J Psychiatry. 2023 May-Jun;45(3):280-285
doi:10.47626/1516-4446-2022-2979
Brazilian Psychiatric Association

REVIEW ARTICLE

Efficacy of bupropion and cognitive behavioral therapy in the treatment of methamphetamine use disorder: a systematic review and meta-analysis

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Objectives: We assessed the efficacy of cognitive behavioral therapy and bupropion compared to cognitive behavioral therapy alone for methamphetamine use disorder.
Methods: The selection criteria for this systematic review study with meta-analysis were randomized clinical trials on the efficacy of cognitive behavioral therapy and bupropion in the treatment for methamphetamine use disorder (assessed by urine metabolites). The search was conducted in PubMed, PubMed Central, LILACS, SciELO, Cochrane Library, SCOPUS, Google Scholar, Ovid Medline, Clinicaltrials.gov, and the International Clinical Trials Registry Platform. The primary outcome was relapse. Risk of bias was assessed with the RoB 2 tool. The results of each clinical trial were input into an Excel spreadsheet. We performed a meta-analysis using relative risk and a 95%CI.
Results: Of the 597 initial articles (498 after removing duplicate records), five were included in the meta-analysis, with an aggregate sample of 539 patients. An overall relative risk of 0.91 (95%CI 0.78-1.05) was estimated for relapse.
Conclusion: Our study limitations included publication bias and heterogeneous populations. We found no evidence that cognitive behavioral therapy and bupropion reduced the risk of relapse compared to cognitive behavioral therapy and placebo.

Keywords: Substance-related disorders; antidepressive agents, second-generation; cognitive behavioral therapy; methamphetamine

Introduction

Methamphetamine is a highly stimulating derivative of amphetamine with greater bioavailability in the central nervous system (CNS).[1] It includes the amino group of (S)-amphetamine and bears a methyl substituent. Methamphetamine is stronger than amphetamine because a greater amount reaches the brain at the same dose.[2] Its mechanism of action consists in increasing monoamine levels in the CNS, mainly dopamine, due to monoamine oxidase enzyme inhibition and an additive effect on the tyrosine hydroxylase enzyme. After use, a feeling of euphoria, energy, and alertness is experienced.[3]

A 2020 survey by the U.S. National Institute on Drug Abuse found a methamphetamine use disorder prevalence of 0.6%.[4] According the United Nations Office on Drugs and Crime,[5] the prevalence of amphetamine use disorder was 2.31, 6.10, 5.65, and 2.31% in Australia (2020), Haiti (2018), the United States (2020), and Austria (2020), respectively.

Chronic methamphetamine use is associated with medical problems, such as neuronal damage and cognitive disorder, cardiovascular involvement (especially strokes), dental disease, and infection (HIV, hepatitis B virus, and hepatitis C virus). Methamphetamine use is also linked to increased crime.[6]

The pathology of use disorder is associated with positive reinforcement and stimulation of the reward system, in which dopamine plays an important role during initial drug use. As use becomes more habitual, stimulation of the dorsal striatal regions occurs.[7] The dopaminergic system exhibits modulatory effects on many brain regions related to cognitive functioning, including front striatal and limbic structures. This is associated with complaints of cognitive dysfunction, including memory problems and self-reported deficits in everyday functioning.[8] Moreover, methamphetamine consumption can create a psychological obsession due to drug-induced elation.[9]

The first-line treatment for methamphetamine use disorder is psychotherapy; there is no effective drug for treatment.[1] However, psychotherapy is not always available, which leads to a search for other treatment options. In addition, the efficacy of psychotherapy decreases after discharge.[10]

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Submitted Nov 28 2022, accepted Feb 13 2023.

How to cite this article: Apuy LFM, Barreto MAB, Merino LAH. Efficacy of bupropion and cognitive behavioral therapy in the treatment of methamphetamine use disorder: a systematic review and meta-analysis. Braz J Psychiatry. 2023;45:280-285. http://doi.org/10.47626/1516-4446-2022-2979

Behavioral therapy is an effective way to manage methamphetamine use disorder,[1] but drug abuse is a continuous process, and relapse after a withdrawal period is not uncommon. It has been found that a cognitive mismatch in patients who abuse methamphetamines predisposes them to relapse.[11] Upon drug cessation, many patients experience withdrawal syndrome due to a relative decrease in dopamine and noradrenaline levels. Thus, bupropion therapy could decrease methamphetamine withdrawal symptoms since it increases the concentration of dopamine and noradrenaline in the CNS.[12]

Bupropion is a second-generation antidepressant drug used as an adjunctive treatment for smoking cessation. Bupropion blocks the reuptake of dopamine and norepinephrine and has some effect on nicotinic and serotonergic receptors. Bupropion blocks the dopamine transporter, which could help restore dopaminergic homeostasis by increasing intrasynaptic dopamine. The stimulant-like effects of bupropion might alleviate withdrawal symptoms in methamphetamine use disorder.[13-15]

In an overview and network meta-analysis of bupropion in other substance use disorders, Cahill et al.[16] identified 12 treatment-specific reviews. The analyses covered 267 studies involving 101,804 participants. In both groups, nicotine-replacement therapy and bupropion were superior to placebo.[16] In a Cochrane review of psychostimulant drugs for cocaine use disorder, the proportion of patients achieving sustained cocaine abstinence was higher with bupropion and dexamphetamine than with placebo.[17] In addition, bupropion might help treat patients with gaming disorder and major depressive disorder; according to the Young Internet Addiction Scale, the response rates of groups that used bupropion were higher than placebo.[18]

The main objective of this systematic review and meta-analysis was to evaluate the efficacy of bupropion and cognitive behavioral therapy (CBT) compared with cognitive behavioral alone in the treatment of methamphetamine use disorder according to relapse incidence. The secondary objective was to establish the safety profile of bupropion in patients with methamphetamine use disorder through the incidence of adverse effects and adherence.

Methods

A systematic review with meta-analysis was performed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[19] The protocol was registered in PROSPERO (CRD42021245572) and was approved by the University of Piura research ethics committee (Campus Lima, Peru). Our initial primary outcome was abstinence, but we changed it to relapse due to greater ease of interpretation.

Eligibility criteria

We included randomized controlled clinical trials that studied the following PICOT (population, intervention, comparator, outcome, and time of study or follow-up) parameters: a population consisting of patients diagnosed with methamphetamine use disorder according to the DSM IV, IV-TR, or 5[20]; the intervention group received oral bupropion 150 mg (once or twice daily) and CBT; the control group received an oral placebo and CBT (standard treatment); the outcome was relapse, which was defined as the detection of metabolites in urine in the final weeks of follow-up; the follow-up time was at least 10 weeks; other inclusion criteria were informed consent, approval by an ethics committee, conflict of interest statement, patients aged 18 or older, and clinically stable patients at admission.

The exclusion criteria were other definitions of relapse, patients diagnosed with epilepsy, patients with a medical history of hypersensitivity to bupropion, patients diagnosed with eating disorders, pregnancy/lactation, and CNS alterations (such as tumors, CNS infections, arteriovenous malformations, or history of severe traumatic brain injury). Clinical trials with participants who reported the concomitant use of other substances were also eligible for inclusion.

Data sources

The search began on September 20, 2021. It was updated every month; we modified our search after recommendation from senior researchers. Our final search was performed on January 9, 2023. We placed no restrictions on the date or language of publication. The databases included PubMed Central, LILACS, SciELO, and SCOPUS; the search engines used were PubMed, Cochrane Library, Google Scholar, and Ovid-MEDLINE. The clinical trial records included Clinicaltrials.gov and the International Clinical Trials Registry Platform. The results were transferred to Zotero 6 to eliminate duplicate records.[21]

Search strategy

The search strategy can be seen in Table S1, available as online-only supplementary material.

Selection process

The studies were selected by all three researchers independently and blindly. Eligibility criteria were applied using Rayyan Intelligent Systematic Review.[22] In case of conflict, consensus was reached by discussion. The researchers first read the title and abstract and, if these were insufficient, they read the full text.

Data collection

Two researchers (LFMA and MABB) extracted the results of each clinical trial independently and input them into an Excel 2016 spreadsheet. This information was verified by the third researcher (LAHM). The following information was collected: authors, year of publication, design characteristics, sample size, distribution of the groups, intervention, comparator, definition of outcomes, and results (Table S2, available as online-only supplementary material). The data were transferred to the Review Manager 5.4.1 for meta-analysis.[23]

The main outcome was efficacy, determined through relapse incidence (methamphetamine use), which was defined as the detection of methamphetamine metabolites

in urine during the final weeks of follow-up. There is currently no exact data on the sensitivity or specificity of the immunoassay or similar tests. Still, every clinical trial included in our meta-analysis used a confirmatory test after a positive urine test, as recommended.[24]

The secondary outcome was the safety profile of bupropion (compared to control), defined according to the incidence of adverse effects (adverse effects in general, not a specific one) and adherence, defined as the percentage of pills consumed compared to the number that should have been taken.

To decide which clinical trials were eligible for each synthesis (primary and secondary outcome), we made sure they reported results as percentages or frequencies. Almost all results were compatible with each outcome domain, although it was necessary to calculate the frequency of the main outcome in three studies[14,25,26] and that of the secondary outcome (adherence) in one study.[14]

Furthermore, no meta-analysis was performed for adverse effect outcomes, since only two articles provided information about adverse effects in general.[14,27]

Risk of bias assessment

Risk of bias was assessed according to Cochrane recommendations with the RoB 2 tool; the risk of bias graph was made using Robvis.[28,29] The following domains were used: risks of bias arising from the randomization process, bias due to deviations from the intended intervention, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the reported result.[28] Clinical trials with a high risk of bias in at least one domain or at least three domains with some concerns were excluded.[28] The risk of bias was assessed independently for each trial and the trials were reviewed.

Statistical analysis

The meta-analysis was performed in Review Manager 5.4.1,[23] using relative risk (RR) and a 95%CI for each result. The heterogeneity of values between studies was evaluated with chi-square. The degree of heterogeneity (I^2) was determined according to reference values: unimportant or low (0-40%), moderate (30-60%), substantial (50-90%), or considerable (75-100%).[30] The forest and funnel plots were produced in Graph Pad Prism 9 and Jamovi 2.2.5, respectively.[31,32] Publication bias was assessed using Egger and Begg tests in Epidat 3.1.[33] A sensitivity analysis (Epidat 3.1) was applied to determine variation in the overall results after excluding a given study. We used random effects for the primary outcome due to its moderate heterogeneity, and fixed effects for the secondary outcome (adherence) due to its low heterogeneity.

Certainty of evidence assessment

The certainty of the evidence was assessed using the GRADEpro GDT platform.[34] This estimate was made through researcher consensus.

Results

Study selection

A total of 597 articles were found in the initial search, from 99 duplicates were eliminated. Thus, 498 articles were screened, and no additional articles were identified. Another 483 articles were eliminated in preliminary screening, leaving 10 for full-text review. Incompatible population (252 articles) was the most frequent reason for exclusion (Figure S1, available as online-only supplementary material). Five articles were used to analyze the primary outcome and three were used for the secondary outcome (adherence). The overall sample for the primary outcome was 539 patients. No meta-analysis was performed for adverse effects (secondary outcome) since only two articles provided information about adverse effects in general.

Risk of bias assessment

Risk of bias was assessed in five studies (Figure S2, available as online-only supplementary material).[14,25-27,35] The only domain that had a risk of bias of some concern was the randomization process. Regarding global risk of bias, two studies had a low risk[27,35] and three were classified as being of some concern.[14,25,26] No study had a high global risk of bias. The five articles were included in the qualitative and quantitative synthesis of the information.[14,25-27,35]

Results of individual studies

The five included articles were randomized, controlled, double-blind clinical trials. All of the trials evaluated subjects in an outpatient setting.[14,25-27,35] Every patient received standard treatment (CBT) regardless of allocation to the intervention or control group. Control group patients received a matching placebo.

Table S2, available as online-only supplementary material, shows the general characteristics of each study, as well as the primary outcomes. None of the trials reported a significant difference in relapse between the intervention and control groups. Although neither RR was significant, four clinical trials favored the intervention group[14,25-27] and one favored the control group.[35]

Overall outcomes

A random-effects model was applied for the primary outcome (relapse) and a non-significant overall RR of 0.91 (95%CI 0.78-1.05, p = 0.21) was found between the intervention and control groups (Figure S3, available as online-only supplementary material). Heterogeneity was moderate and non-significant (I^2 = 46%, p = 0.11). The sensitivity analysis showed a change in the overall RR after excluding Anderson et al.,[35] with an RR of 0.84 (95% CI 0.73-0.97).

Concerning the secondary outcomes (adverse effects and adherence), no meta-analysis was performed for adverse effects since only two articles provided information

about them. Three clinical trials included information about adherence[14,25,26] and a fixed effects model was applied for the adherence outcome in the meta-analysis. A non-significant overall RR of 0.96 (95%CI 0.89-1.04, p = 0.28) was found between the intervention and control groups (Figure S3). The heterogeneity was low and non-significant (I^2 = 0%, p = 0.52). The sensitivity analysis showed no significant change.

Publication bias assessment

Regarding the primary outcome (relapse), publication bias (Figure S4, available as online-only supplementary material) was assessed through a funnel plot, which was asymmetrical and, thus, suggestive of publication bias. The result of the Begg test was a Z-statistic of 0.74 and a non-significant p-value (0.46), while that of the Egger test was a t-statistic of -3.87 with a significant p-value (0.03), indicating publication bias.

For the secondary outcome (adherence), publication bias was assessed through a funnel plot, which was symmetrical. There result of the Begg test was a Z-statistic of 0.00 and a non-significant p-value (1.00), while that of the Egger test was a t-statistic of -0.21 and a non-significant p-value (0.87), indicating no publication bias.

Certainty of evidence assessment

A low level of evidence was estimated for the primary outcome (relapse), a moderate level of evidence was obtained for adverse effects, and a low level of evidence was obtained for adherence.

Discussion

This meta-analysis found no evidence that an association of CBT and bupropion reduced the risk of methamphetamine relapse compared to CBT and placebo. In fact, none of the included trials found a reduced risk of relapse in patients who received CBT and bupropion compared to CBT and placebo. However, the sensitivity analysis showed that, after excluding Anderson et al.,[35] there was a significant protective effect against relapse in the CBT and bupropion group compared to the CBT and placebo group. This change in the overall effect estimate was probably because this clinical trial obtained a non-significant association that favored the control group and had the highest weight in the meta-analysis. However, there was no reason to exclude this study from the meta-analysis since it fulfilled all the eligibility criteria and had a low risk of overall bias.[35]

Although bupropion was not effective for treating methamphetamine use disorder in clinical trials, on a preclinical level the results indicated a potential clinical benefit. Muley et al.[36] found that bupropion blocked (dose-dependently) methamphetamine-induced stereotypy in mice when methamphetamine use followed bupropion. A neurochemical study by Marek et al.[37] found that dopamine-uptake inhibitors like bupropion had neuroprotective effects against methamphetamine-induced neurotoxicity due to their capacity to block neostriatal dopamine absorption sites. Schindler et al.[38] observed that bupropion significantly reduced methamphetamine response compared to pre-treatment, without affecting food response in adult male rhesus monkeys. They concluded that drugs that activate the dopamine system could decrease methamphetamine self-administration.

Associating bupropion with other medications might lead to an effective treatment for methamphetamine use disorder. A clinical trial by Trivedi et al.[39] found that bupropion and naltrexone significantly decreased relapse compared to placebo. We decided to exclude this clinical trial from our meta-analysis because the objective was to assess the efficacy of bupropion alone. However, the bupropion dose used in Trivedi et al.[39] (450 mg daily) differed from the clinical trials in our meta-analysis (150 mg twice daily), which may have been insufficient.[39] However, another possibility is that naltrexone is responsible for the significant results in Trivedi et al.[39] A clinical trial by Tiihonen et al.[40] investigated the efficacy of naltrexone as a treatment for heroin and amphetamine use disorder, finding significant differences in favor of the naltrexone group regarding abstinence (defined by urine detection and patient retention). Thus, if naltrexone was effective for heroin and amphetamine use disorder, it might also be effective for methamphetamine use disorder.[40]

Perhaps different methods of analysis should be used to determine a drug's efficacy in the treatment of substance use disorders. According to some researchers, using analyses that compare the rate of patients in each treatment group who achieve the desired response is too ambitious.[41] For example, reanalysis of a multisite trial by McCann et al.[42] showed that bupropion helped achieve abstinence in patients with methamphetamine use disorder. Using data from Elkashef et al.[14] (a clinical trial included in our meta-analysis), they measured the effectiveness of bupropion according to the number of beyond-threshold weeks of success.[42]

Although bupropion showed no efficacy for reducing relapse in our study, it may help reduce discomfort from withdrawal syndrome. Newton et al.[43] found that bupropion treatment significantly reduced reported drug cravings. This would indicate that bupropion could relieve cravings without, however, reducing the risk of relapse. Nevertheless, Elkashef et al.[14] found no significant differences in craving or self-reported methamphetamine use between CBT and bupropion vs. CBT and placebo groups. However, in a subgroup analysis they found that bupropion increased the number of weeks of abstinence in men with low-to-moderate methamphetamine use, despite comorbidities.[14]

We could find no systematic reviews that only investigated the efficacy of bupropion in the treatment of methamphetamine use disorder. Investigating treatment for opioid and stimulant use disorder, Chan et al.[44] conducted a search until April 2019. They found a moderate level of evidence against the use of antidepressants (bupropion) for cocaine use disorder, i.e., more adverse effects than placebo and no positive effects. In addition, antidepressants increased damage and led to significantly lower treatment adherence. Nevertheless, their review only included two clinical trials that used

bupropion as an intervention. They concluded that there is no evidence that any drug is effective in the treatment of psychostimulant use disorders and that further studies are needed.

In a systematic review of treatment for methamphetamine use disorder, Siefried et al.[45] included only randomized clinical trials (published in English) in which patients were treated with pharmacotherapy and CBT, conducting their search until July 2019 using the same keywords in all databases. Although they performed no meta-analysis, they found some positive results for topiramate, naltrexone, methylphenidate, and dexamphetamine, but not for bupropion and mirtazapine. Finding no convincing results for any medication, they concluded that antidepressants in general were ineffective, but due to the insufficient evidence further studies are necessary.[45] Thus, our results were consistent with these two systematic reviews.

In our meta-analysis, the intervention group's adherence was similar to that of the control group. Although we could find no systematic reviews on bupropion adherence, Hermanstyne et al.[46] used two clinical trials on antidepressants (one on bupropion and another on mirtazapine) in the treatment of methamphetamine use disorder, finding a significant negative association between relapse and adherence to pharmacotherapy. Our results differed from Hermanstyne et al.[46] because they used clinical trials with two different drugs, finding lower adherence for mirtazapine than bupropion. In addition, their clinical trial on bupropion found similar adherence between intervention and placebo. Thus, their overall low adherence may have been due to mirtazapine.

Regarding adverse effects (secondary outcome), Heinzerling et al.[27] reported a higher but non-significant incidence of at least one adverse effect per patient in the intervention group compared to placebo (70.73 vs. 51.2%, respectively). However, Elkashef et al.[14] found that the incidence of adverse effects was similar in both groups (30 vs. 31%).

Concerning CBT efficacy, a systematic review by AshaRani et al.[47] investigated non-pharmacological treatment for methamphetamine use disorder. They concluded that most behavioral therapies were efficacious, finding no significant difference between behavioral interventions such as CBT, motivational interviews, or contingency management, etc.[47] However, along with other researchers, they considered contingency management to be the most effective method, having been studied widely in patients with methamphetamine use disorder. Nevertheless, the duration of the therapy's effect in the post-intervention phase is uncertain.[48]

Research into the efficacy of mindfulness or mindfulness-based interventions in substance use disorder treatment is increasing. A non-concurrent controlled intervention study by Maneesang et al.[49] examined the effectiveness of mindfulness-based therapy and counseling programs. They found significantly less methamphetamine craving and relapse in the experimental group than the control group three months after discharge.[49]

Regarding evidence limitations, we only found five clinical trials, which had a low level of evidence for the primary outcome. In addition, all included trials were conducted in an outpatient setting. As study limitations, statistical and graphical tests indicated publication bias among the included trials. Nevertheless, we performed an exhaustive search of databases and clinical trial registries. We also included articles with heterogeneous populations, given that the sample in Das et al.[25] was of men who have sex with men. In addition, Anderson et al.[35] and Heinzerling et al.[27] included patients with lower daily use of methamphetamine. Furthermore, there was heterogeneity in the pharmacological intervention, since the number of bupropion tablets used per day differed in Shoptaw et al.[26] and Das et al.[25] Likewise, the weighted effect was estimated through RR and not the hazard ratio, since the results were presented as frequency and percentages.[14,25,26]

In conclusion, we found no significant difference in relapse rate between CBT and bupropion vs. CBT and placebo. Due to the low level of evidence (GRADEpro), further studies might be needed to investigate the efficacy of bupropion. Adverse effects and adherence, which are indicators of the safety profile, were similar between the groups.

Acknowledgements

The authors would like to thank Dr. César Gutiérrez for his collaboration and advice throughout the study.

Disclosure

The authors report no conflicts of interest.

References

1 National Institute on Drug Abuse. Methamphetamine research report overview. [Internet]. 2021 [cited 2022 Oct 31]. https://nida.nih.gov/publications/research-reports/methamphetamine/overview
2 National Library of Medicine. National Center for Biotechnology Information. Methamphetamine (compound). [cited 2023 Jan 12]. https://pubchem.ncbi.nlm.nih.gov/compound/10836
3 Yasaei R, Saadabadi A. Methamphetamine [Internet]. In: StatPearls. Treasure Island: StatPearls Publishing; 2023. https://www.ncbi.nlm.nih.gov/books/NBK535356/#_NBK535356_pubdet_
4 Substance Abuse and Mental Health Services Administration. Key substance use and mental health indicators in the United States: results from the 2020 National Survey on Drug Use and Health [Internet]. 2021. https://www.samhsa.gov/data/sites/default/files/reports/rpt35325/NSDUHFFRPDFWHTMLFiles2020/2020NSDUHFFR1PDFW102121.pdf
5 United Nations Office on Drugs and Crime (UNODC). Prevalence of drug use – New psychoactive substances (general population). [cited 2022 Oct 19]. https://dataunodc.un.org/dp-drug-use-prevalence-nps
6 Radfar SR, Rawson RA. Current research on methamphetamine: epidemiology, medical and psychiatric effects, treatment, and harm reduction efforts. Addict Health. 2014;6:146-54.
7 Solinas M, Belujon P, Fernagut PO, Jaber M, Thiriet N. Dopamine and addiction: what have we learned from 40 years of research. J Neural Transm (Vienna). 2019;126:481-516.
8 Rendell PG, Mazur M, Henry JD. Prospective memory impairment in former users of methamphetamine. Psychopharmacology (Berl). 2009;203:609-16.
9 Cadet JL, Bisagno V, Milroy CM. Neuropathology of substance use disorders. Acta Neuropathol. 2014;127:91-107.
10 McKetin R, Najman JM, Baker AL, Lubman DI, Dawe S, Ali R, et al. Evaluating the impact of community-based treatment options on

methamphetamine use: findings from the Methamphetamine Treatment Evaluation Study (MATES). Addiction. 2012;107:1998-2008.
11 Mizoguchi H, Yamada K. Methamphetamine use causes cognitive impairment and altered decision-making. Neurochem Int. 2019;124: 106-13.
12 Sitte HH, Freissmuth M. Amphetamines, new psychoactive drugs and the monoamine transporter cycle. Trends Pharmacol Sci. 2015;36: 41-50.
13 Meyer JH, Goulding VS, Wilson AA, Hussey D, Christensen BK, Houle S. Bupropion occupancy of the dopamine transporter is low during clinical treatment. Psychopharmacology (Berl). 2002;163:102-5.
14 Elkashef AM, Rawson RA, Anderson AL, Li SH, Holmes T, Smith EV, et al. Bupropion for the treatment of methamphetamine dependence. Neuropsychopharmacology. 2008;33:1162-70.
15 Newton TF, Roache JD, De La Garza R 2nd, Fong T, Wallace CL, Li SH, et al. Safety of intravenous methamphetamine administration during treatment with bupropion. Psychopharmacology (Berl). 2005; 182:426-35.
16 Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. Cochrane Database Syst Rev. 2013;2013:CD009329.
17 Castells X, Cunill R, Pérez-Mañá C, Vidal X, Capellà D. Psychostimulant drugs for cocaine dependence. Cochrane Database Syst Rev. 2016;9:CD007380.
18 Han DH, Renshaw PF. Bupropion in the treatment of problematic online game play in patients with major depressive disorder. J Psychopharmacol. 2012;26:689-96.
19 Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ. 2021;372:n160.
20 American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). Arlington: American Psychiatric Publishing; 2013.
21 Roy Rosenzweig Center for History and New Media. Zotero. https://rrchnm.org/portfolio-item/zotero/
22 Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan – a web and mobile app for systematic reviews. Syst Rev. 2016;5:210.
23 The Cochrane Collaboration. Review Manager (RevMan). https://training.cochrane.org/online-learning/core-software/revman
24 Kale N. Urine drug tests: ordering and interpreting results. Am Fam Physician. 2019;99:33-9.
25 Das M, Santos D, Matheson T, Santos GM, Chu P, Vittinghoff E, et al. Feasibility and acceptability of a phase II randomized pharmacologic intervention for methamphetamine dependence in high-risk men who have sex with men. AIDS. 2010;24:991-1000.
26 Shoptaw S, Heinzerling KG, Rotheram-Fuller E, Steward T, Wang J, Swanson AN, et al. Randomized, placebo-controlled trial of bupropion for the treatment of methamphetamine dependence. Drug Alcohol Depend. 2008;96:222-32.
27 Heinzerling KG, Swanson AN, Hall TM, Yi Y, Wu Y, Shoptaw SJ. Randomized, placebo-controlled trial of bupropion in methamphetamine-dependent participants with less than daily methamphetamine use. Addiction. 2014;109:1878-86.
28 Cochrane Methods Bias. RoB 2: a revised Cochrane risk-of-bias tool for randomized trials. [cited 2022 Sep 21]. https://methods.cochrane.org/bias/resources/rob-2-revised-cochrane-risk-bias-tool-randomized-trials
29 McGuinness LA, Higgins JPT. Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. Res Synth Methods. 2021;12:55-61.
30 Deeks JJ, Higgins JPT, Altman DG. Chapter 10: Analysing data and undertaking meta-analyses. https://training.cochrane.org/handbook/current/chapter-10
31 GraphPad Software. GraphPad Prism. https://www.graphpad.com/features
32 Jamovi. The Jamovi Project. https://www.jamovi.org/about.html
33 The Pan American Health Organization (OPS-OMS). Epidat: program for epidemiological data analysis. 2003. https://www.sergas.es/Saude-publica/EPIDAT?idioma=es
34 McMaster University. GRADEpro. https://www.gradepro.org/
35 Anderson AL, Li SH, Markova D, Holmes TH, Chiang N, Kahn R, et al. Bupropion for the treatment of methamphetamine dependence in non-daily users: a randomized, double-blind, placebo-controlled trial. Drug Alcohol Depend. 2015;150:170-4.
36 Muley MP, Joshi MA, Manekar MS. Effect of bupropion on dopamine and 5-hydroxytryptamine-mediated behaviour in mice. J Pharm Pharmacol. 1984;36:208-10.
37 Marek GJ, Vosmer G, Seiden LS. Dopamine uptake inhibitors block long-term neurotoxic effects of methamphetamine upon dopaminergic neurons. Brain Res. 1990;513:274-9.
38 Schindler CW, Gilman JP, Panlilio LV, McCann DJ, Goldberg SR. Comparison of the effects of methamphetamine, bupropion, and methylphenidate on the self-administration of methamphetamine by rhesus monkeys. Exp Clin Psychopharmacol. 2011;19:1-10.
39 Trivedi MH, Walker R, Ling W, Dela Cruz A, Sharma G, Carmody T, et al. Bupropion and Naltrexone in Methamphetamine Use Disorder. N Engl J Med. 2021;384:140-53.
40 Tiihonen J, Krupitsky E, Verbitskaya E, Blokhina E, Mamontova O, Föhr J, et al. Naltrexone implant for the treatment of polydrug dependence: a randomized controlled trial. Am J Psychiatry. 2012;169:531-6.
41 Winchell C, Rappaport BA, Roca R, Rosebraugh CJ. Reanalysis of methamphetamine dependence treatment trial. CNS Neurosci Ther. 2012;18:367-8.
42 McCann DJ, Li SH. A novel, nonbinary evaluation of success and failure reveals bupropion efficacy versus methamphetamine dependence: reanalysis of a multisite trial. CNS Neurosci Ther. 2012;18:414-8.
43 Newton TF, Roache JD, De La Garza R 2nd, Fong T, Wallace CL, Li SH, et al. Bupropion reduces methamphetamine-induced subjective effects and cue-induced craving. Neuropsychopharmacology. 2006;31:1537-44.
44 Chan B, Freeman M, Ayers C, Korthuis PT, Paynter R, Kondo K, et al. A systematic review and meta-analysis of medications for stimulant use disorders in patients with co-occurring opioid use disorders. Drug Alcohol Depend. 2020;216:108193.
45 Siefried KJ, Acheson LS, Lintzeris N, Ezard N. Pharmacological treatment of methamphetamine/amphetamine dependence: a systematic review. CNS Drugs. 2020;34:337-65.
46 Hermanstyne KA, Santos GM, Vittinghoff E, Santos D, Colfax G, Coffin P. Event-level relationship between methamphetamine use significantly associated with non-adherence to pharmacologic trial medications in event-level analyses. Drug Alcohol Depend. 2014;143:277-80.
47 AshaRani PV, Hombali A, Seow E, Ong WJ, Tan JH, Subramaniam M. Non-pharmacological interventions for methamphetamine use disorder: a systematic review. Drug Alcohol Depend. 2020;212:108060.
48 Okafor CN, Stein DJ, Dannatt L, Ipser J, van Nunen LJ, Lake MT, et al. Contingency management treatment for methamphetamine use disorder in South Africa. Drug Alcohol Rev. 2020;39:216-22.
49 Maneesang W, Hengpraprom S, Kalayasiri R. Effectiveness of mindfulness-based therapy and counseling programs (MBTC) on relapses to methamphetamine dependence at a substance dependency treatment center. Psychiatry Res. 2022;317:114886.