frontiers | Frontiers in Psychiatry

TYPE Study Protocol
PUBLISHED 04 September 2025
DOI 10.3389/fpsyt.2025.1667614

OPEN ACCESS

EDITED BY
David Crockford,
University of Calgary, Canada

REVIEWED BY
Michela (micky) Marinelli,
The University of Texas at Austin, United States
Heidar Sharafi,
University of Montreal Hospital Center (CRCHUM), Canada

*CORRESPONDENCE
Gustavo A. Angarita
gustavo.angarita@yale.edu

†These authors have contributed equally to this work and share first authorship

RECEIVED 16 July 2025
ACCEPTED 19 August 2025
PUBLISHED 04 September 2025

CITATION
Oliva HNP, Pulido-Saavedra A, Paredes-Naveda A, Forselius E, Potenza MN, Jegede OO and Angarita GA (2025) Pharmacotherapies for stimulant use disorder and co-occurring attention deficit hyperactivity disorder: protocol for a systematic review and a meta-analysis. *Front. Psychiatry* 16:1667614. doi: 10.3389/fpsyt.2025.1667614

Pharmacotherapies for stimulant use disorder and co-occurring attention deficit hyperactivity disorder: protocol for a systematic review and a meta-analysis

Henrique N. P. Oliva[1,2,3†], Alejandra Pulido-Saavedra[1,2,3†], Alisson Paredes-Naveda[1,2,4], Emerson Forselius[5], Marc N. Potenza[1,6,7,8,9], Oluwole O. Jegede[1,2] and Gustavo A. Angarita[1,2,3*]

[1]Department of Psychiatry, Yale University School of Medicine, New Haven, CT, United States, [2]Connecticut Mental Health Center, New Haven, CT, United States, [3]Clinical Neuroscience Research Unit, Connecticut Mental Health Center, New Haven, CT, United States, [4]Southern Connecticut State University (SCSU), New Haven, CT, United States, [5]Syracuse University, Syracuse, NY, United States, [6]Child Study Center, Yale University School of Medicine, New Haven, CT, United States, [7]Department of Neuroscience, Yale University, New Haven, CT, United States, [8]Connecticut Council on Problem Gambling, Wethersfield, CT, United States, [9]Wu Tsai Institute, Yale University, New Haven, CT, United States

Background: Stimulant use disorder (StUD) and attention-deficit/hyperactivity disorder (ADHD) frequently co-occur. This comorbidity complicates treatment and worsens clinical outcomes. Despite the high prevalence, shared vulnerability and clinical relevance of this comorbidity, evidence on effective pharmacotherapies among individuals with this dual diagnosis remains limited.
Materials and methods: This systematic review protocol is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statement and will include randomized controlled trials involving adults with comorbid StUD (cocaine, amphetamines, or methamphetamines) and ADHD. The following databases will be searched: PubMed, Embase, Scopus, and Web of Science. *Covidence* will be used to support independent screening and data extraction. Two reviewers will independently screen studies (title/abstract and full text). One author will extract data, which will be independently verified by a second reviewer. Quality assessment of included articles will be assessed using the Cochrane Risk of Bias instrument, and certainty of the evidence for each outcome will be assessed using Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methodology. Primary outcomes include duration of continuous abstinence, odds of stimulant-negative urine samples, ADHD symptom changes, and medication adverse events. Where feasible, meta-analyses will be conducted using random-effects models.
Significance and dissemination: This review will synthesize existing evidence on the efficacy of pharmacotherapies (stimulants and non-stimulants) for individuals with co-occurring StUD and ADHD. The results of this study will likely inform clinical practice by evaluating outcomes such as reduction in stimulant use and

abstinence, and improvement in ADHD symptoms. Findings will be disseminated through peer-reviewed publication and presentations to reach both clinical and academic audiences.
Systematic review registration: PROSPERO, CRD420250655356.

KEYWORDS

stimulant use disorder, attention deficit hyperactivity disorder, cocaine, methamphetamine, co-occurring disorder

Introduction

Attention-deficit hyperactivity disorder (ADHD) frequently co-occurs with substance use disorders (SUDs), particularly stimulant use disorder (StUD) involving cocaine, methamphetamine, or prescription stimulants (1). The prevalence of ADHD among individuals with cocaine and methamphetamine use disorder is approximately 20% (1–3), markedly higher than the estimated 6.8% prevalence in the general adult population (4). Conversely, ADHD increases the risk of developing StUD, potentially due to overlapping neurobiological vulnerabilities and self-medication with stimulants (5). The comorbidity is linked to worse treatment outcomes, including reduced retention, lower abstinence rates, greater morbidity, and higher healthcare utilization (6–8).

Pharmacological options for ADHD include both stimulant (e.g., methylphenidate, amphetamines) and non-stimulant agents (e.g., atomoxetine, guanfacine, clonidine, viloxazine), alongside several off-label treatments such as bupropion and modafinil (9, 10). No medications are FDA-approved for StUD, but off-label agents – including bupropion, modafinil, disulfiram, and topiramate – are sometimes used (11, 12). The overlap in off-label agents for ADHD and StUD supports the hypothesis of shared pathophysiological mechanisms (7).

Evidence suggests that both disorders share alterations in dopaminergic, cholinergic, and GABAergic signaling (13–19), as well as structural and functional brain changes – particularly in prefrontal and anterior cingulate regions involved in executive control, reward processing, and impulse regulation (20–23). Such overlap may help explain anecdotal reports of therapeutic stimulant effects in individuals with ADHD and StUD (24–26) and the growing research interest in using stimulant medications for StUD (27).

While there is substantial literature on the treatment of ADHD and StUD individually, these studies may not fully capture the breadth of neurobiological alterations or the range of potentially effective pharmacological strategies when these conditions co-occur. Several randomized controlled trials (RCTs) have evaluated medications targeting either ADHD or StUD (28–30), and some of these have been synthesized in systematic reviews and meta-analyses (27). However, the field remains limited by a relative scarcity of double-blind RCTs specifically focused on dual-diagnosis populations. Existing reviews often aggregate findings from heterogeneous samples, making it difficult to draw definitive conclusions about efficacy or generalizability in individuals with co-occurring ADHD and StUD. As such, further targeted trials and meta-analytic efforts are needed to clarify treatment efficacy in this understudied group.

This protocol describes the methodology for a systematic review and meta-analysis of RCTs evaluating pharmacological treatments in adults with co-occurring ADHD and StUD. By synthesizing efficacy and safety data, the review aims to identify promising treatment strategies and inform future research.

Methods

Study registration

This protocol is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (PRISMA-P) statement and registered in the PROSPERO database under the registration number CRD420250655356.

Eligibility criteria

We will include RCTs that evaluate pharmacological interventions for adults (aged 18 years and older) with a dual diagnosis of StUD, including cocaine, methamphetamine, or prescription stimulant misuse, and ADHD. Eligible studies must have enrolled participants formally diagnosed with both conditions. Pharmacological interventions of interest will include stimulants (e.g., methylphenidate, amphetamines) and non-stimulants (e.g., atomoxetine, disulfiram, modafinil, topiramate).

A preliminary pilot search in PubMed yielded a small number of potentially eligible trials, confirming the feasibility of identifying studies meeting our criteria while also highlighting the scarcity of evidence in this specific comorbid population.

To be eligible, studies must have included individuals with co-occurring ADHD and StUD and reported at least one of the following outcomes: (1) treatment outcomes, including abstinence from stimulant use, measured via self-report, biologically verified

abstinence (e.g., urine metabolites), and/or improvements in ADHD symptoms (e.g., hyperactivity, impulsivity, inattention) assessed through validated instruments such as the Adult ADHD Rating Scale (AARS), Clinical Global Impression (CGI), or Conners' Adult ADHD Rating Scales (CAARS); and (2) safety outcomes, such as adverse events, side effects, or treatment tolerability. While other outcomes such as quality-of-life measures (e.g., World Health Organization Quality of Life Brief Version [WHOQOL-BREF] or 36-Item Short Form Health Survey [SF-36]) would provide valuable insights into functional outcomes, our preliminary search identified no trials reporting such data for StUD populations in this dual-diagnosis context. Should any eligible studies emerge during full screening that include quality of life measures, we will document and analyze these findings descriptively. No language restrictions will be applied.

We will exclude studies involving participants with primary diagnoses of SUDs other than StUD and studies that do not report outcomes based on pharmacotherapy treatments in individuals with co-occurring ADHD and StUD. Additional exclusion criteria will include animal studies, qualitative research, reviews, case reports, conference abstracts, and proceedings.

Collection and analysis of the data

Information sources

We will search PubMed, Embase, Scopus, Web of Science, and CINAHL (via the EBSCOhost platform) to identify relevant studies. Additionally, we will search ClinicalTrials.gov to capture unpublished and ongoing trials. To ensure comprehensive coverage, we will also manually screen the reference lists of included studies and relevant systematic reviews or meta-analyses to identify additional eligible publications not captured through the primary searches.

Search strategy

The search strategy was developed using a combination of relevant keywords and medical subject headings related to stimulant use disorder, attention-deficit hyperactivity disorder, comorbidity, pharmacotherapy, and specific medications of interest. Filters will be applied for clinical trials as the publication type. The strategy will be adapted for each database to ensure appropriate syntax and indexing. The complete search syntax for PubMed and Scopus are provided in the Supplementary Table 1.

Study selection process

Two independent reviewers will screen all titles and abstracts identified by the search. Studies meeting the inclusion criteria will undergo full-text review by two authors. Disagreements between reviewers will be resolved through discussion or by involving a third reviewer. The inclusion and exclusion process will be documented, with reasons for exclusion noted.

Data extraction

Data will be extracted by two independent reviewers using a standardized data extraction form. Extracted information will include:

- Study Characteristics: author(s), publication year, country, study design, sample size, participant demographics.
- Interventions: type of pharmacotherapy (e.g., medication name, dosage, administration).
- Outcomes: measures of efficacy (e.g., abstinence from stimulants, improvements in ADHD symptoms), and other relevant secondary outcomes such as safety (e.g., adverse events).

Quality assessment

The risk of bias of the included studies will be assessed using the Cochrane risk of bias tool for randomized trials (RoB2) (31). Each study will be evaluated across several domains, including selection bias, performance bias, detection bias, and reporting bias. We also assess publication bias using funnel plots and Egger's test if ≥10 studies are available. Any potential sources of bias will be documented.

The quality of evidence for all outcomes will be evaluated using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methodology. This systematic approach examines five key domains: risk of bias, precision, directness, consistency across studies, and potential publication bias to determine the overall confidence in the estimated effects (32).

Outcomes

For substance use, primary outcomes will include (1) abstinence duration (measured as longest continuous stimulant-free period via biologically verified methods like urine toxicology, to be pooled as standardized mean differences [SMDs]) and (2) odds of stimulant-negative urine samples during treatment (pooled as odds ratios [ORs]).

For ADHD, primary outcomes will comprise (1) symptom severity (measured by validated scales such as the AARS or CAARS, pooled as SMDs) and (2) clinical improvement (proportion of participants rating improvement on the CGI scale, pooled as ORs).

Secondary outcomes will focus on safety, including treatment-emergent adverse events and withdrawal rates. The comparisons will be performed between active treatment vs. placebo within each drug group. If feasible, depending on the number of included studies, we will also compare efficacy across drug classes (stimulants vs. non-stimulants). Continuous outcomes will be analyzed as SMDs with 95% CIs and dichotomous outcomes as ORs with 95% CIs. Where operational definitions diverge (e.g., abstinence criteria), separate analyses will be conducted if sufficient data are available.

Data synthesis

Data from eligible studies will be synthesized qualitatively when appropriate. In addition, a narrative description will summarize study characteristics, medication types, and outcome measures for all included trials, providing context for the quantitative findings. We will summarize intervention characteristics, participant populations, outcome measures, and direction and magnitude of effects, highlighting consistencies and discrepancies across studies. Where applicable, findings will be organized into thematic domains (e.g., treatment outcome, safety) and presented in a summary table to aid comparison. If studies are sufficiently homogeneous, a meta-analysis will be performed using fixed or random-effects models, as appropriate, to estimate pooled effect sizes for the primary outcomes. Heterogeneity will be assessed using the I^2 statistic. Because the included pharmacotherapies may vary in mechanism of action, we will address this potential source of heterogeneity by conducting subgroup analyses stratified by medication class (e.g., stimulants vs. non-stimulants) and, where data permit, by individual agents. Additionally, we plan to conduct leave-one-out analyses and analyses excluding high-risk-of-bias studies to evaluate the robustness of pooled estimates and identify whether individual studies exert a disproportionate influence on the overall findings. To address the biological and clinical relevance of effect sizes, we will interpret pooled results in the context of established minimally important differences (when available) and recognized benchmarks for meaningful change in stimulant use and ADHD symptomatology. Where such thresholds are not well established, we will consider the magnitude of observed changes alongside their potential impact on functional outcomes, safety, and patient-centered measures, thereby ensuring that statistical significance is evaluated within a clinically meaningful framework. The completed PRISMA-P table is available in Supplementary Table 2.

Discussion

This protocol outlines the methodology for a systematic review and meta-analysis examining pharmacological treatments for individuals with co-occurring ADHD and StUD. Designed in accordance with PRISMA-P guidelines, the protocol aims to employ a comprehensive search strategy, clearly defined eligibility criteria, and standardized data extraction and quality assessment tools to ensure rigor and reproducibility. By focusing on RCTs, this study seeks to provide high-quality evidence in an area where clinical decision-making remains complex.

This study protocol is not without potential limitations. The exclusion of non-RCT studies may limit insights into real-world treatment effects, and high attrition rates in existing trials may reduce generalizability. Despite this constraint, the proposed review will address a significant gap in the literature by synthesizing data specific to populations with co-occurring ADHD and StUD.

While pharmacological interventions alone may have limited efficacy on substance use, their integration with targeted psychosocial treatments is widely recommended for optimal care; however, the study's focus on pharmacotherapies will exclude psychosocial treatments (27). Notwithstanding these limitations, this protocol builds on existing critical evidence-based work to generate a review aimed to guide future research and inform best practices for treating individuals with co-occurring ADHD and StUD.

Author's note

This publication does not express the views of the Department of Mental Health and Addiction Services or the State of Connecticut. The views and opinions expressed are those of the authors.

Author contributions

HO: Writing – review & editing, Project administration, Writing – original draft, Methodology, Conceptualization, Investigation. AP: Writing – original draft, Writing – review & editing, Investigation. AP: Writing – review & editing, Writing – original draft. EF: Writing – review & editing, Writing – original draft. MP: Supervision, Writing – review & editing, Writing – original draft. OJ: Methodology, Writing – review & editing, Writing – original draft. GA: Supervision, Conceptualization, Writing – review & editing, Methodology, Resources, Writing – original draft.

Funding

The author(s) declare financial support was received for the research and/or publication of this article. The work described in this article was funded in part by the State of Connecticut, Department of Mental Health and Addiction Services. This study will be supported in part by the National Institute on Drug Abuse (NIDA) grants R01 DA052454-03 and R33DA053592.

Conflict of interest

MP discloses that he has consulted for and advised Boehringer Ingelheim; has been involved in a patent application with Yale University and Novartis; has received research support from Mohegan Sun Casino and the Connecticut Council on Problem Gambling; has participated in surveys, mailings or telephone consultations related to drug addiction, internet use, impulse-control disorders or other health topics; has consulted for and/or advised gambling, non-profit, healthcare and legal entities on issues related to internet use, impulse control and addictive disorders; has performed grant reviews for research-funding agencies; has edited journals and journal sections; has given academic lectures in grand rounds, CME events and other clinical or scientific venues; and has generated books or book chapters for publishers of mental health texts. The authors alone are responsible for the content and writing of this paper.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

The author(s) declare that no Generative AI was used in the creation of this manuscript.

Any alternative text (alt text) provided alongside figures in this article has been generated by Frontiers with the support of artificial intelligence and reasonable efforts have been made to ensure accuracy, including review by the authors wherever possible. If you identify any issues, please contact us.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2025.1667614/full#supplementary-material

References

1. Rohner H, Gaspar N, Philipsen A, Schulze M. Prevalence of attention deficit hyperactivity disorder (ADHD) among substance use disorder (SUD) populations: meta-analysis. *Int J Environ Res Public Health*. (2023) 20. doi: 10.3390/ijerph20021275

2. Obermeit LC, Cattie JE, Bolden KA, Marquine MJ, Morgan EE, Franklin DR, et al. Attention-deficit/hyperactivity disorder among chronic methamphetamine users: Frequency, persistence, and adverse effects on everyday functioning. *Addictive Behav*. (2013) 38:2874–8. doi: 10.1016/j.addbeh.2013.08.010

3. Pérez de Los Cobos J, Siñol N, Puerta C, Cantillano V, López Zurita C, Trujols J. Features and prevalence of patients with probable adult attention deficit hyperactivity disorder who request treatment for cocaine use disorders. *Psychiatry Res*. (2011) 185:205–10. doi: 10.1016/j.psychres.2009.03.019

4. Song P, Zha M, Yang Q, Zhang Y, Li X, Rudan I. The prevalence of adult attention-deficit hyperactivity disorder: A global systematic review and meta-analysis. *J Glob Health*. (2021) 11:4009. doi: 10.7189/jogh.11.04009

5. Wilens TE, Faraone SV, Biederman J, Gunawardene S. Does stimulant therapy of attention-deficit/hyperactivity disorder beget later substance abuse? A meta-analytic review of the literature. *Pediatrics*. (2003) 111:179–85. doi: 10.1542/peds.111.1.179

6. Kast KA, Rao V, Wilens TE. Pharmacotherapy for attention-deficit/hyperactivity disorder and retention in outpatient substance use disorder treatment: A retrospective cohort study. *J Clin Psychiatry*. (2021) 82. doi: 10.4088/JCP.20m13598

7. Levin FR, Evans SM, Vosburg SK, Horton T, Brooks D, Ng J. Impact of attention-deficit hyperactivity disorder and other psychopathology on treatment retention among cocaine abusers in a therapeutic community. *Addict Behav*. (2004) 29:1875–82. doi: 10.1016/j.addbeh.2004.03.041

8. Oliva F, Mangiapane C, Nibbio G, Berchialla P, Colombi N, Vigna-Taglianti FD. Prevalence of cocaine use and cocaine use disorder among adult patients with attention-deficit/hyperactivity disorder: A systematic review and meta-analysis. *J Psychiatr Res*. (2021) 143:587–98. doi: 10.1016/j.jpsychires.2020.11.021

9. Clemow DB, Walker DJ. The potential for misuse and abuse of medications in ADHD: a review. *Postgrad Med*. (2014) 126:64–81. doi: 10.3810/pgm.2014.09.2801

10. Farhat LC, Flores JM, Avila-Quintero VJ, Polanczyk GV, Cipriani A, Furukawa TA, et al. Treatment outcomes with licensed and unlicensed stimulant doses for adults with attention-deficit/hyperactivity disorder: A systematic review and meta-analysis. *JAMA Psychiatry*. (2024) 81:157–66. doi: 10.1001/jamapsychiatry.2023.3985

11. Angarita GA, Hadizadeh H, Cerdena I, Potenza MN. Can pharmacotherapy improve treatment outcomes in people with co-occurring major depressive and cocaine use disorders? *Expert Opin Pharmacother*. (2021) 22:1669–83. doi: 10.1080/14656566.2021.1931684

12. Martins B, Rutland W, De Aquino JP, Kazer BL, Funaro M, Potenza MN, et al. Helpful or harmful? The therapeutic potential of medications with varying degrees of abuse liability in the treatment of substance use disorders. *Curr Addict Rep*. (2022) 9:647–59. doi: 10.1007/s40429-022-00432-9

13. Ashok AH, Mizuno Y, Volkow ND, Howes OD. Association of stimulant use with dopaminergic alterations in users of cocaine, amphetamine, or methamphetamine: A systematic review and meta-analysis. *JAMA Psychiatry*. (2017) 74:511–9. doi: 10.1001/jamapsychiatry.2017.0135

14. Edden RA, Crocetti D, Zhu H, Gilbert DL, Mostofsky SH. Reduced GABA concentration in attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry*. (2012) 69:750–3. doi: 10.1001/archgenpsychiatry.2011.2280

15. Johansson J, Landgren M, Fernell E, Lewander T, Venizelos N. Decreased binding capacity (Bmax) of muscarinic acetylcholine receptors in fibroblasts from boys with attention-deficit/hyperactivity disorder (ADHD). *Atten Defic Hyperact Disord*. (2013) 5:267–71. doi: 10.1007/s12402-013-0103-0

16. Malison RT, Best SE, van Dyck CH, McCance EF, Wallace EA, Laruelle M, et al. Elevated striatal dopamine transporters during acute cocaine abstinence as measured by [123I] beta-CIT SPECT. *Am J Psychiatry*. (1998) 155:832–4. doi: 10.1176/ajp.155.6.832

17. Schrantee A, Václavů L, Heijtel DF, Caan MW, Gsell W, Lucassen PJ, et al. Dopaminergic system dysfunction in recreational dexamphetamine users. *Neuropsychopharmacology*. (2015) 40:1172–80. doi: 10.1038/npp.2014.301

18. Volkow ND, Tomasi D, Wang GJ, Logan J, Alexoff DL, Jayne M, et al. Stimulant-induced dopamine increases are markedly blunted in active cocaine abusers. *Mol Psychiatry*. (2014) 19:1037–43. doi: 10.1038/mp.2014.58

19. Volkow ND, Wang GJ, Newcorn JH, Kollins SH, Wigal TL, Telang F, et al. Motivation deficit in ADHD is associated with dysfunction of the dopamine reward pathway. *Mol Psychiatry*. (2011) 16:1147–54. doi: 10.1038/mp.2010.97

20. Angarita GA, Worhunsky PD, Naganawa M, Toyonaga T, Nabulsi NB, Li CR, et al. Lower prefrontal cortical synaptic vesicle binding in cocaine use disorder: An exploratory (11) C-UCB-J positron emission tomography study in humans. *Addict Biol*. (2022) 27:e13123. doi: 10.1111/adb.13123

21. Hu Y, Salmeron BJ, Gu H, Stein EA, Yang Y. Impaired functional connectivity within and between frontostriatal circuits and its association with compulsive drug use and trait impulsivity in cocaine addiction. *JAMA Psychiatry*. (2015) 72:584–92. doi: 10.1001/jamapsychiatry.2015.1

22. Oliva HNP, Prudente TP, Nunes EJ, Cosgrove KP, Radhakrishnan R, Potenza MN, et al. Substance use and spine density: a systematic review and meta-analysis of preclinical studies. *Mol Psychiatry*. (2024) 29(9):2873-85. doi: 10.1038/s41380-024-02519-3

23. Schinz D, Schmitz-Koep B, Tahedl M, Teckenberg T, Schultz V, Schulz J, et al. Lower cortical thickness and increased brain aging in adults with cocaine use disorder. *Front Psychiatry*. (2023) 14:1266770. doi: 10.3389/fpsyt.2023.1266770

24. Carli G, Cavicchioli M, Martini AL, Bruscoli M, Manfredi A, Presotto L, et al. Neurobiological dysfunctional substrates for the self-medication hypothesis in adult individuals with attention-deficit hyperactivity disorder and cocaine use disorder: A fluorine-18-fluorodeoxyglucose positron emission tomography study. *Brain Connectivity*. (2023) 13:370–82. doi: 10.1089/brain.2022.0076

25. Khantzian EJ. The self-medication hypothesis of substance use disorders: a reconsideration and recent applications. *Harv Rev Psychiatry*. (1997) 4:231–44. doi: 10.3109/10673229709030550

26. Mariani JJ, Khantzian EJ, Levin FR. The self-medication hypothesis and psychostimulant treatment of cocaine dependence: an update. *Am J Addict*. (2014) 23:189–93. doi: 10.1111/j.1521-0391.2013.12086.x

27. Chan B, Kondo K, Freeman M, Ayers C, Montgomery J, Kansagara D. Pharmacotherapy for cocaine use disorder-a systematic review and meta-analysis. *J Gen Intern Med*. (2019) 34:2858–73. doi: 10.1007/s11606-019-05074-8

28. Mariani JJ, Pavlicova M, Bisaga A, Nunes EV, Brooks DJ, Levin FR. Extended-release mixed amphetamine salts and topiramate for cocaine dependence: A randomized controlled trial. *Biol Psychiatry*. (2012) 72:950–6. doi: 10.1016/j.biopsych.2012.05.032

29. McElroy SL, Hudson JI, Mitchell JE, Wilfley D, Ferreira-Cornwell MC, Gao J, et al. Efficacy and safety of lisdexamfetamine for treatment of adults with moderate to severe binge-eating disorder: a randomized clinical trial. *JAMA Psychiatry*. (2015) 72:235–46. doi: 10.1001/jamapsychiatry.2014.2162

30. Moran LM, Phillips KA, Kowalczyk WJ, Ghitza UE, Agage DA, Epstein DH, et al. Aripiprazole for cocaine abstinence: a randomized-controlled trial with ecological momentary assessment. *Behav Pharmacol*. (2017) 28:63–73. doi: 10.1097/fbp.0000000000000268

31. Sterne JA, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. (2019) 366. doi: 10.1136/bmj.l4898

32. Schünemann H, Brożek J, Guyatt G, Oxman A. *Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach*, Vol. 15. (2013).