http://doi.org/10.47626/1516-4446-2022-2979
Efficacy of bupropion and cognitive behavioral therapy in the treatment of methamphetamine use disorder: a systematic review and meta-analysis - Apuy LFM et al.

Figure S1 PRISMA flow diagram for systematic review and meta-analysis

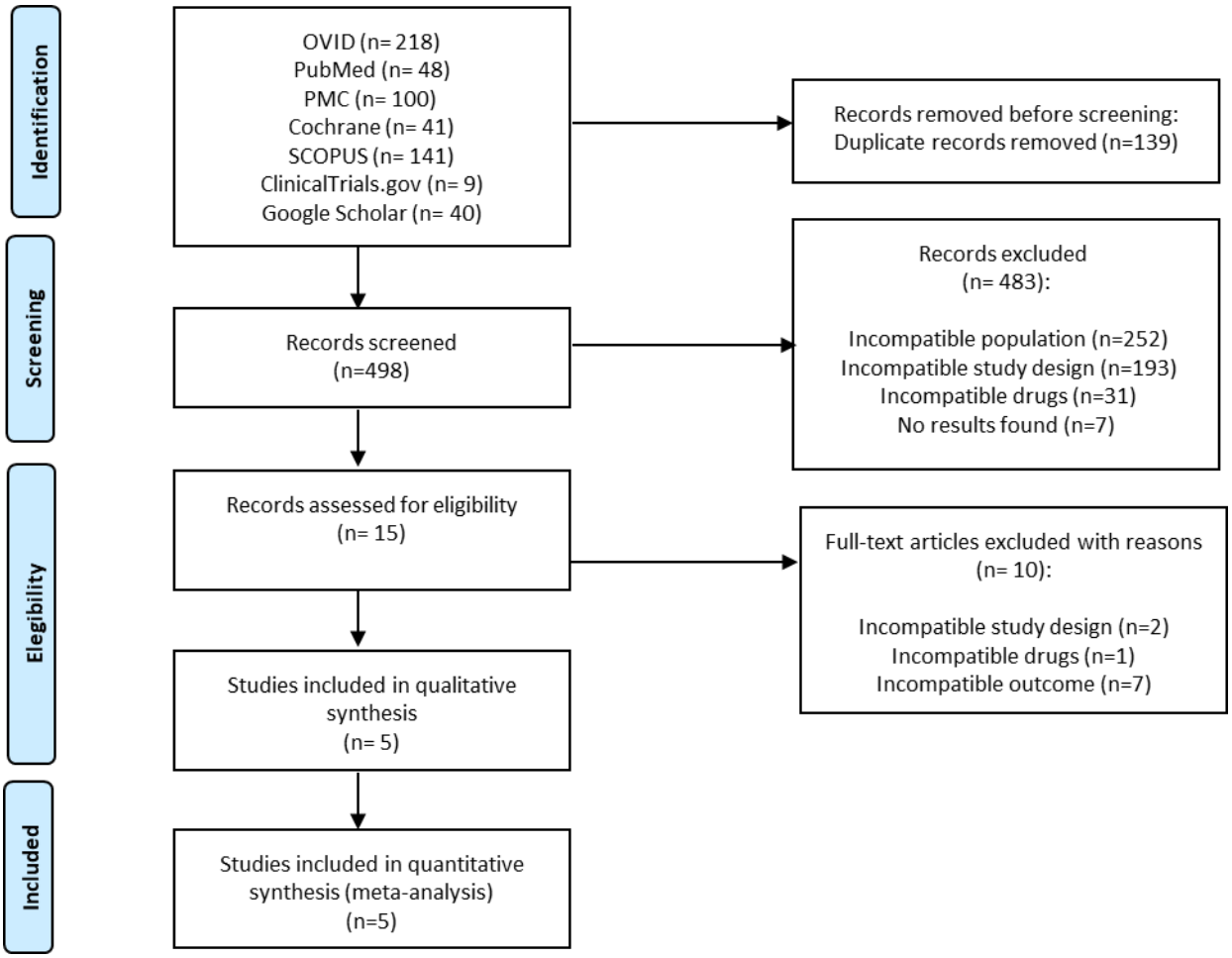
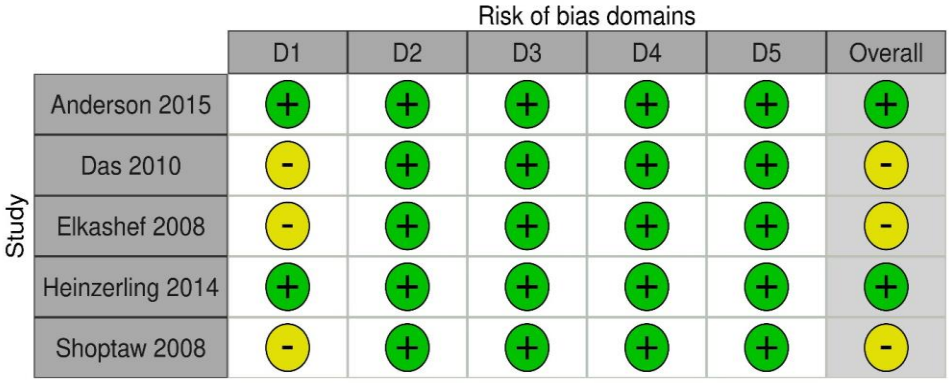


Figure S2 Risk of bias assessment



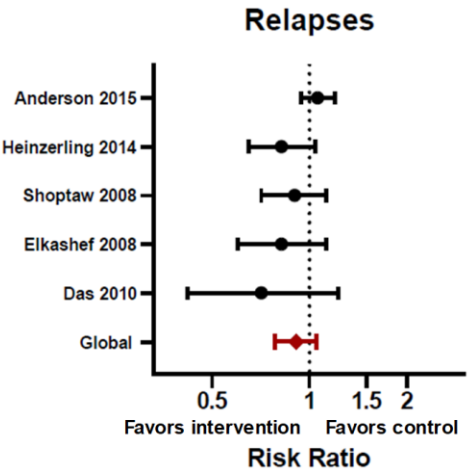
D1 = bias arising from the randomization process; D2 = bias due to deviations from the intended intervention; D3 = bias due to missing outcome data; D4 = bias in measurement of the outcome; D5 = bias in selection of the reported result; - = risk of bias with some concerns; + = low risk of bias

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Figure S3 Forest plot of relapse (primary outcome) and adherence (secondary outcome)

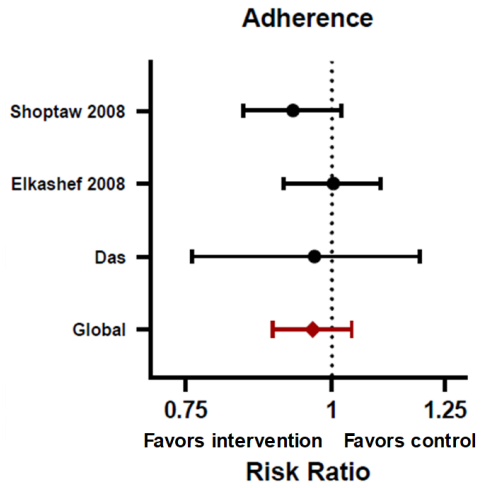
	Intervention		Control			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H Random 95% CI
Anderson 2015	86	100	84	104	35.2%	1.06 [0.94-1.20]
Heinzerling 2014	29	41	37	43	21.9%	0.82 [0.65-1.04]
Shoptaw 2008	27	36	31	37	21.4%	0.90 [0.71-1.13]
Elkashef 2008	36	79	40	72	14.9%	0.82 [0.60-1.13]
Das 2010	10	18	7	9	6.5%	0.71 [0.42-1.23]
Total	188	274	199	265	100%	0.91 [0.78-1.05]

Heterogeneity: Chi^2 = 7.47; df = 4 (p=0.11); I^2 = 46%
Test for overall effect: Z = 1.26 (p= 0.21)



	Intervention		Control			Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H Fixed 95% CI
Shoptaw 2008	85	100	92	100	37.7%	0.92 [0.84-1.02]
Elkashef 2008	90	100	90	100	36.9%	1.00 [0.91-1.10]
Das 2010	59	100	62	100	25.4%	0.95 [0.76-1.19]
Total	188	300	199	300	100%	0.96 [0.89-1.04]

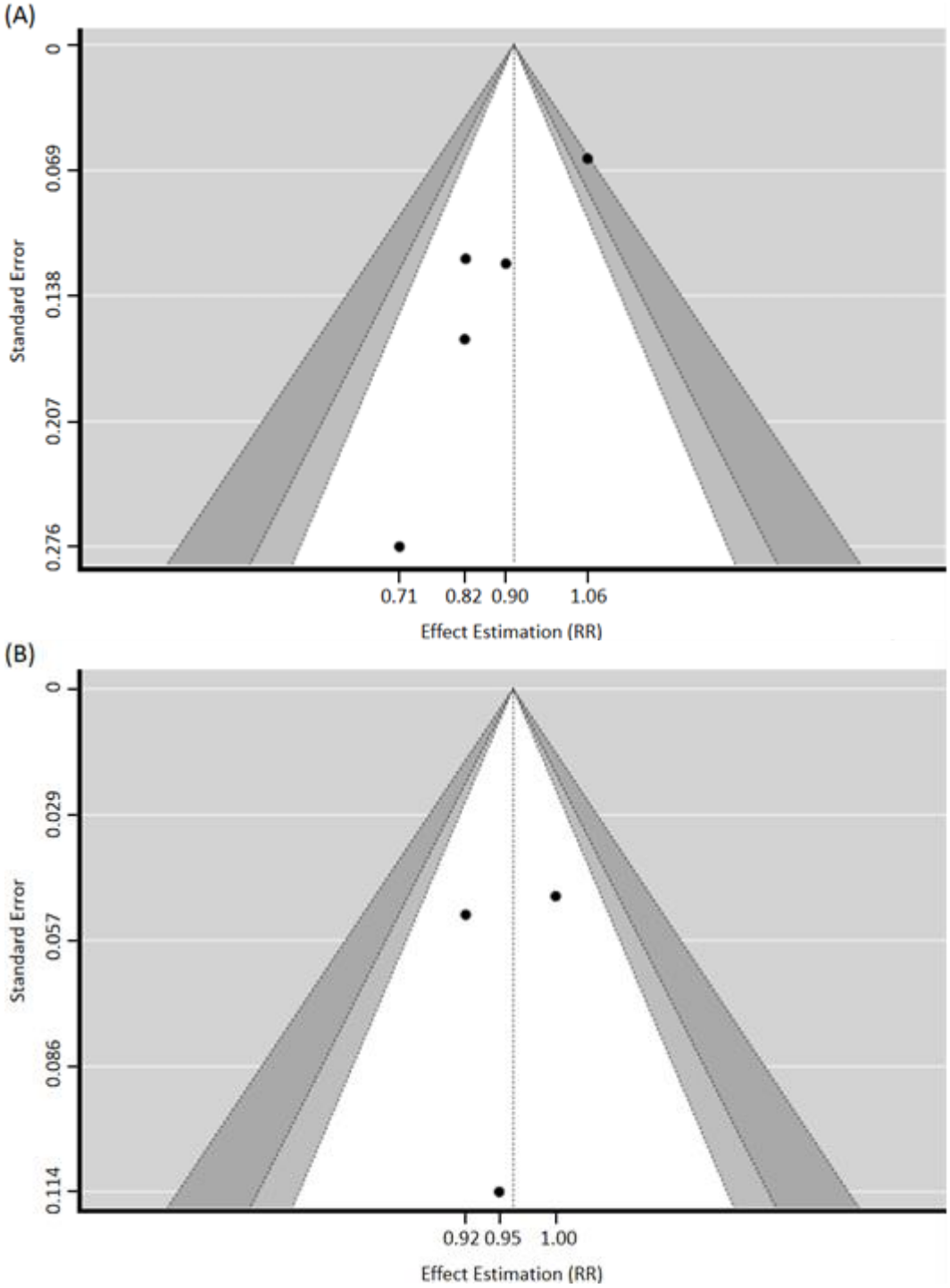
Heterogeneity: Chi^2 = 1.32; df = 2 (p=0.52); I^2 = 0%
Test for overall effect: Z = 1.08 (p= 0.28)



M-H = Mantel-Haenszel; Chi^2 = chi-square test; df = degrees of freedom; I^2 = heterogeneity.
* $p < 0.05$

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Figure S4 Funnel plot panel of relapse (primary outcome) and adherence (secondary outcome)



(A) = Funnel plot of relapse. (B) = Funnel plot of adherence.

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Table S1 Search strategy, terms, and descriptors used

Databases	Search strategy	Results
SCOPUS	(TITLE-ABS-KEY (methamphetamine) OR TITLE-ABS-KEY (substance AND use AND disorders) AND TITLE-ABS-KEY (bupropion) OR TITLE-ABS-KEY (bupropion AND hydrochloride) OR TITLE-ABS-KEY (cognitive AND behavior AND therapy) AND TITLE-ABS-KEY (urine) OR TITLE-ABS-KEY (enzyme AND immunoassay))	141
PubMed	(((methamphetamine [MeSH Terms]) OR (substance related disorders [MeSH Terms])) OR (methamphetamine [Title/Abstract])) OR (substance related disorder [Title/Abstract]) AND ((bupropion [MeSH Terms]) OR (bupropion hydrochloride [MeSH Terms])) OR (bupropion [Title/Abstract]) AND ((enzyme immunoassay [MeSH Terms]) OR ((enzyme immunoassay [Title/Abstract])) OR (methamphetamine/urine [MeSH Terms]) OR (urine))	48
PubMed Central	(((((((methamphetamine [MeSH Terms]) OR methamphetamine [Title]) OR methamphetamine [Abstract]) OR substance related disorders [MeSH Terms]) OR substance related disorders [Title]) OR substance related disorders [Abstract])) AND ((((bupropion [MeSH Terms]) OR bupropion [Title]) OR bupropion [Abstract]) OR bupropion hydrochloride [MeSH Terms])) AND (((((urine) OR enzyme immunoassay [MeSH Terms]) OR enzyme immunoassay [Title]) OR enzyme immunoassay [Abstract]) OR methamphetamine/urine [MeSH Terms])	100
SciELO	(metamfetamina) OR (abuso de sustancias) AND (bupropión) OR (terapia cognitivo conductual) AND (orina) OR (metabolitos)	3
LILACS	(metamfetamina) OR (abuso de substâncias) AND (bupropiona) AND (urina) OR (metabólitos)	145
Search engines		
Ovid Medline	(methamphetamine.sh. or methamphetamine. ti. or methamphetamine.ab. or substance related disorders. sh. or substance related disorders. ti. or substance related disorders.ab.) and (bupropion.sh. or bupropion.ti. or bupropion.ab. or bupropion hydrochloride.sh.)	218
Cochrane Library	(MeSH descriptor: [Methamphetamine] explode all trees OR MeSH descriptor: [Substance-Related Disorders] explode all trees OR ("methamphetamine"): ti,ab,kw OR ("substance related disorder"): ti,ab,kw OR ("substance dependence"): ti,ab,kw) AND (MeSH descriptor: [Bupropion] explode all trees OR ("bupropion hydrochloride"): ti,ab,kw) AND (MeSH descriptor: [Immunoenzyme Techniques] explode all trees OR ("enzyme immunoassay"): ti,ab,kw OR ("enzyme immunochromatography"): ti,ab,kw OR (urine))	41
Google Scholar	“allintitle: Methamphetamine bupropion”	40
Clinical trial records		
Clinicaltrials.gov	"Methamphetamine dependence" as disease and "bupropion" as additional term	9
ICTRP	Methamphetamine and Bupropion as keywords	0

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Table S2 Characteristics of the studies included in the review

Study	Year of publication	Population size and groups	Pharmacological intervention	Primary outcome	Primary outcome results
Elkashef	2008	151 participants, 79 received bupropion 72 received placebo	Bupropion 150 mg for 3 days, then, 300 mg for 11 weeks, then 150 mg on the last 3 days	Percentage of participants who abstained from methamphetamine use during each week of treatment defined by methamphetamine-free urine	No significant difference between the bupropion and placebo groups for the probability of a methamphetamine-free week according to the generalized estimating equation model (54% bupropion vs 44% placebo, p = 0.09)
Anderson	2015	204 participants (report of minor daily methamphetamine use), 100 received bupropion 104 received placebo	Bupropion 150 mg for 3 days, then 300 mg for 11 weeks, then 150 mg on the last 3 days	The effectiveness of bupropion based on methamphetamine withdrawal	No significant difference between the bupropion and placebo groups regarding withdrawal success (≤ 2 negative urine samples at week 11 and 12), which was achieved in 14% of the bupropion group and 19% of the placebo group (χ^2, p = 0.32)
Shoptaw	2008	73 patients, 36 received bupropion 37 received placebo	Bupropion 150 mg twice daily	Percentage of participants who abstained from methamphetamine use during each week of treatment defined by methamphetamine-free urine	No significant difference between groups regarding the probability of a methamphetamine-free week (χ^2 = 0.004, df = 71, p = 0.95)
Heinzerling	2014	84 patients (reported minor daily methamphetamine use), 41 received bupropion 43 received placebo	Bupropion 150 mg for 3 days, then, 300 mg for 11 weeks, then 150 mg on the last 3 days	No positive urine test in the last 2 weeks, without missing > 1 out of 3 weekly tests	No significant difference in abstinence (29% bupropion vs 14% placebo, χ^2 = 2.92; p = 0.087)
Das	2010	30 men who have sex with men, 20 received bupropion 10 received placebo	One 150 mg bupropion tablet for 1 week and then 2 tablets every morning	Patient retention and adherence to pharmacological treatment	Adherence to the study drug was 60% (59% bupropion, 62% placebo; p = 0.98)