Revisão a partir do AMSTAR 2 (debate):

Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis

Apresentadora: Júlia Santos
Debatedor: João Morais

Epidemiologia - Conceitos e Métodos III
Escola Nacional de Saúde Pública Sergio Arouca
Junho de 2025

Roteiro

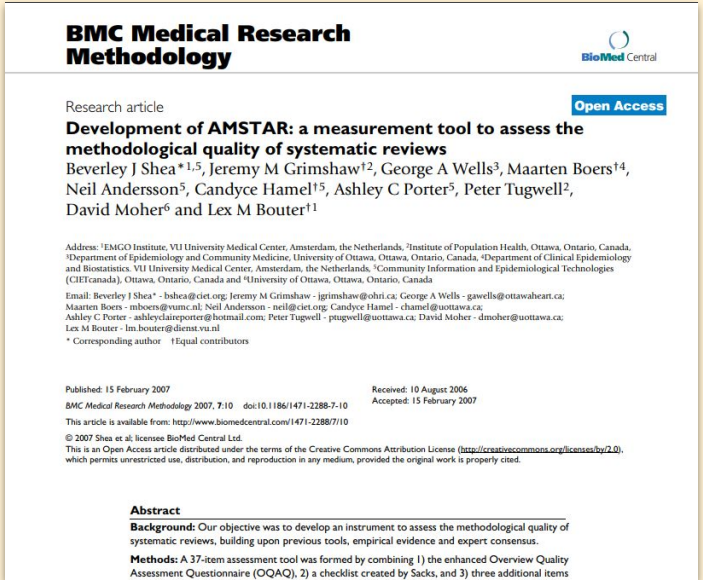
Realize uma **avalição geral da qualidade** da revisão sobre transtorno por consumo de álcool (McPheeters 2023), **identificando possíveis falhas** decorrentes de erros na condução da revisão.

Utilize o instrumento **AMSTAR 2** para essa avaliação, respondendo todas as 16 perguntas do checklist.

AMSTAR 2

- Avaliação da qualidade das Revisões Sistemáticas de intervenções em saúde

Shea *et al.*, 2007



BMC Medical Research Methodology

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Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews

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Abstract

Background: Our objective was to develop an instrument to assess the methodological quality of systematic reviews, building upon previous tools, empirical evidence and expert consensus.

Methods: A 37-item assessment tool was formed by combining 1) the enhanced Overview Quality Assessment Questionnaire (OQAQ), 2) a checklist created by Sacks, and 3) three additional items

Shea *et al.*, 2017

RESEARCH METHODS AND REPORTING

OPEN ACCESS

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both

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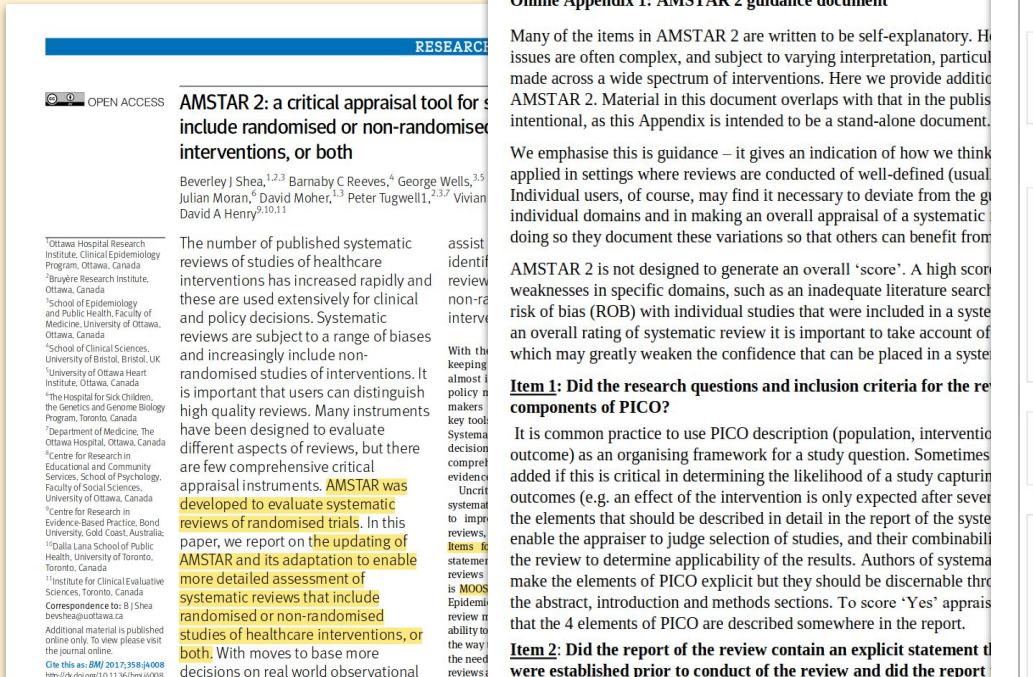
The number of published systematic reviews of studies of healthcare interventions has increased rapidly and these are used extensively for clinical and policy decisions. Systematic reviews are subject to a range of biases and increasingly include non-randomised studies of interventions. It is important that users can distinguish high quality reviews. Many instruments have been designed to evaluate different aspects of reviews, but there are few comprehensive critical appraisal instruments. AMSTAR was developed to evaluate systematic reviews of randomised trials. In this paper, we report on the updating of AMSTAR and its adaptation to enable more detailed assessment of systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. With moves to base more decisions on real world observational

assist decision makers in the identification of high quality systematic reviews, including those based on non-randomised studies of healthcare interventions.

With the rapid increase in biomedical publishing, keeping up with primary research has become almost impossible for healthcare practitioners and policy makers.[1] Consequently, healthcare decision makers rely on systematic reviews as one of the key tools for achieving evidence based healthcare.[2] Systematic reviews provide an opportunity to base decisions on accurate, succinct, credible, and comprehensive summaries of the best available evidence on a topic.[2]

Uncritically accepting the results of a single systematic review has risks. One of us (DM) led efforts to improve standards for reporting of systematic reviews, which led to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.[3] The reporting guide for systematic reviews of observational (non-randomised) studies is MOOSE (Meta-analysis of Observational Studies in Epidemiology).[4] The quality of reporting of a systematic review may, however, more accurately reflect authors' ability to write in a comprehensible manner rather than the way they conducted their review. This underscores the need for guidelines that evaluate the way in which reviews are planned and conducted.[5,6]

AMSTAR 2



RESEARCH

OPEN ACCESS

AMSTAR 2: a critical appraisal tool for s include randomised or non-randomised interventions, or both

Beverley J Shea,[1,2,3] Barnaby C Reeves,[4] George Wells,[3,5] Julian Moran,[6] David Moher,[1,3] Peter Tugwell1,[2,3,7] Vivian David A Henry[9,10,11]

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Online Appendix 1: AMSTAR 2 guidance document

Many of the items in AMSTAR 2 are written to be self-explanatory. H issues are often complex, and subject to varying interpretation, particul made across a wide spectrum of interventions. Here we provide additic AMSTAR 2. Material in this document overlaps with that in the publis intentional, as this Appendix is intended to be a stand-alone document.

We emphasise this is guidance – it gives an indication of how we think applied in settings where reviews are conducted of well-defined (usual Individual users, of course, may find it necessary to deviate from the gu individual domains and in making an overall appraisal of a systematic doing so they document these variations so that others can benefit from

AMSTAR 2 is not designed to generate an overall 'score'. A high scor weaknesses in specific domains, such as an inadequate literature search risk of bias (ROB) with individual studies that were included in a syste an overall rating of systematic review it is important to take account of which may greatly weaken the confidence that can be placed in a syste

Item 1: Did the research questions and inclusion criteria for the re components of PICO?

It is common practice to use PICO description (population, interventio outcome) as an organising framework for a study question. Sometimes added if this is critical in determining the likelihood of a study capturin outcomes (e.g. an effect of the intervention is only expected after sever the elements that should be described in detail in the report of the syste enable the appraiser to judge selection of studies, and their combinabili the review to determine applicability of the results. Authors of systema make the elements of PICO explicit but they should be discernable thro the abstract, introduction and methods sections. To score 'Yes' apprais that the 4 elements of PICO are described somewhere in the report.

Item 2: Did the report of the review contain an explicit statement t were established prior to conduct of the review and did the report

AMSTAR 2

1. Did the research questions and inclusion criteria for the review include the components of PICO?

For Yes:
- ☐ Population
- ☐ Intervention
- ☐ Comparator group
- ☐ Outcome

Optional (recommended)
- ☐ Timeframe for follow-up

☐ Yes
☐ No

2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

For Partial Yes:
The authors state that they had a written protocol or guide that included ALL the following:
- ☐ review question(s)
- ☐ a search strategy
- ☐ inclusion/exclusion criteria
- ☐ a risk of bias assessment
- ☐ a meta-analysis/synthesis plan, if appropriate, *and*
- ☐ a plan for investigating causes of heterogeneity
- ☐ justification for any deviations from the protocol

For Yes:
As for partial yes, plus the protocol should be registered and should also have specified:

☐ Yes
☐ Partial Yes
☐ No

3. Did the review authors explain their selection of the study designs for inclusion in the review?

For Yes, the review should satisfy ONE of the following:
- ☐ *Explanation for* including only RCTs
- ☐ OR *Explanation for* including only NRSI
- ☐ OR *Explanation for* including both RCTs and NRSI

☐ Yes
☐ No

4. Did the review authors use a comprehensive literature search strategy?

For Partial Yes (all the following):
- ☐ searched at least 2 databases (relevant to research question)
- ☐ provided key word and/or search strategy
- ☐ justified publication restrictions (eg, language)

For Yes, should also have (all the following):
- ☐ searched the reference lists/bibliographies of included studies
- ☐ searched trial/study registries
- ☐ included/consulted content experts in the field

☐ Yes
☐ Partial Yes
☐ No

1. As perguntas de pesquisa e o critério de inclusão para o estudo incluíram os componentes PICO?

População:

Intervenção:

Comparação:

Desfecho:

◆ Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis ◆

Research

JAMA | Original Investigation

Pharmacotherapy for Alcohol Use Disorder
A Systematic Review and Meta-Analysis

Melissa McPheeters, PhD, MPH; Elizabeth A. O'Connor, PhD; Sean Riley, MSc, MA; Sara M. Kennedy, MPH; Christiane Voisin, MSLS; Kaitlin Kuznacic, PharmD; Cory P. Coffey, PharmD; Mark D. Edlund, MD, PhD; Georgiy Bobashev, PhD; Daniel E. Jonas, MD, MPH

IMPORTANCE Alcohol use disorder affects more than 28.3 million people in the United States and is associated with increased rates of morbidity and mortality.

OBJECTIVE To compare efficacy and comparative efficacy of therapies for alcohol use disorder.

DATA SOURCES PubMed, the Cochrane Library, the Cochrane Central Trials Registry, PsycINFO, CINAHL, and EMBASE were searched from November 2012 to September 9, 2022 Literature was subsequently systematically monitored to identify relevant articles up to August 14, 2023, and the PubMed search was updated on August 14, 2023.

STUDY SELECTION For efficacy outcomes, randomized clinical trials of at least 12 weeks' duration were included. For adverse effects, randomized clinical trials and prospective cohort studies that compared drug therapies and reported health outcomes or harms were included.

DATA EXTRACTION AND SYNTHESIS Two reviewers evaluated each study, assessed risk of bias, and graded strength of evidence. Meta-analyses used random-effects models. Numbers needed to treat were calculated for medications with at least moderate strength of evidence for benefit.

MAIN OUTCOMES AND MEASURES The primary outcome was alcohol consumption. Secondary outcomes were motor vehicle crashes, injuries, quality of life, function, mortality, and harms.

RESULTS Data from 118 clinical trials and 20 976 participants were included. The numbers needed to treat to prevent 1 person from returning to any drinking were 11 (95% CI, 1-32) for acamprosate and 18 (95% CI, 4-32) for oral naltrexone at a dose of 50 mg/d. Compared with placebo, oral naltrexone (50 mg/d) was associated with lower rates of return to heavy drinking, with a number needed to treat of 11 (95% CI, 5-41). Injectable naltrexone was associated with fewer drinking days over the 30-day treatment period (weighted mean difference, −4.99 days; 95% CI, −9.49 to −0.49 days) Adverse effects included higher gastrointestinal distress for acamprosate (diarrhea: risk ratio, 1.58; 95% CI, 1.27-1.97) and naltrexone (nausea: risk ratio, 1.73; 95% CI, 1.51-1.98; vomiting: risk ratio, 1.53; 95% CI, 1.23-1.91) compared with placebo.

Supplemental content

CME Quiz at jamacmelookup.com

1. As perguntas de pesquisa e o critério de inclusão para o estudo incluíram os componentes PICO?

População: Adultos (18 anos ou mais) com Transtorno por Uso de Álcool (TUA).

Intervenção:

Comparação:

Desfecho:

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Study Selection

[...] "Studies that enrolled adults with alcohol use disorder and evaluated an FDA-approved medication (acamprosate, disulfiram, or naltrexone) or any of 6 off-label medications [...] were eligible for inclusion."

1. As perguntas de pesquisa e o critério de inclusão para o estudo incluíram os componentes PICO?

População: Adultos (18 anos ou mais) com Transtorno por Uso de Álcool (TUA).

Intervenção: Medicamentos (Aprovados FDA ou "*off label*") para prevenção de recaída.

Comparação:

Desfecho:

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Study Selection

[..] "Studies that enrolled adults with alcohol use disorder and evaluated an FDA-approved medication (acamprosate, disulfiram, or naltrexone) or any of 6 off-label medications (baclofen, gabapentin, varenicline, topiramate, prazosin, and ondansetron) for at least 12 weeks of treatment in an outpatient setting were eligible for inclusion."

1. As perguntas de pesquisa e o critério de inclusão para o estudo incluíram os componentes PICO?

População: Adultos (18 anos ou mais) com Transtorno por Uso de Álcool (TUA).

Intervenção: Medicamentos (Aprovados FDA ou "*off label*") para prevenção de recaída.

Comparação: Placebo ou outro medicamento.

Desfecho:

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Study Selection

[..] "For efficacy outcomes, double-blind randomized clinical trials (RCTs) that compared 1 of the FDA-approved or off-label medications listed above with placebo or with another medication were eligible for inclusion."

1. As perguntas de pesquisa e o critério de inclusão para o estudo incluíram os componentes PICO?

População: Adultos (18 anos ou mais) com Transtorno por Uso de Álcool (TUA).

Intervenção: Medicamentos (Aprovados FDA ou "*off label*") para prevenção de recaída.

Comparação: Placebo ou outro medicamento.

Desfecho:

- ➢ Retorno ao consumo
- ➢ Desfechos de saúde
- ➢ Efeitos adversos

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Study Selection

[..] "Eligible studies were required to assess 1 of the following outcomes: (1) alcohol consumption, consisting of return to any drinking, return to heavy drinking, percentage of drinking days, percentage of heavy drinking days (≥4 drinks per day for women; ≥5 drinks per day for men), or number of drinks per drinking day; (2) health outcomes—motor vehicle crashes, injuries, quality of life, function, or mortality; or (3) adverse events."

1. As perguntas de pesquisa e o critério de inclusão para o estudo incluíram os componentes PICO?

População: Adultos (18 anos ou mais) com Transtorno por Uso de Álcool (TUA).

Intervenção: Medicamentos (Aprovados FDA ou "*off label*") para prevenção de recaída.

Comparação: Placebo ou outro medicamento.

Desfecho

- ➢ Retorno ao consumo
- ➢ Desfechos de saúde
- ➢ Efeitos adversos

Tempo de observação: ao menos 12 semanas.

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Study Selection

[..] "Studies that enrolled adults with alcohol use disorder and evaluated an FDA-approved medication [...] or any of 6 off-label medications [...] for at least 12 weeks of treatment in an outpatient setting were eligible for inclusion. Twelve weeks of treatment were required because longitudinal studies reported that shorter treatment may yield misleading conclusions about efficacy due to fluctuations in drinking behavior."

1. As perguntas de pesquisa e o critério de inclusão para o estudo incluíram os componentes PICO?

População: Adultos (18 anos ou mais) com Transtorno por Uso de Álcool (TUA).

Intervenção: Medicamentos (Aprovados FDA ou "*off label*") para prevenção de recaída.

Comparação: Placebo ou outro medicamento.

Desfecho

- ➢ Retorno ao consumo
- ➢ Desfechos de saúde
- ➢ Efeitos adversos

Tempo de observação: ao menos 12 semanas.

◆ AMSTAR 2 ◆

1. **PICO**

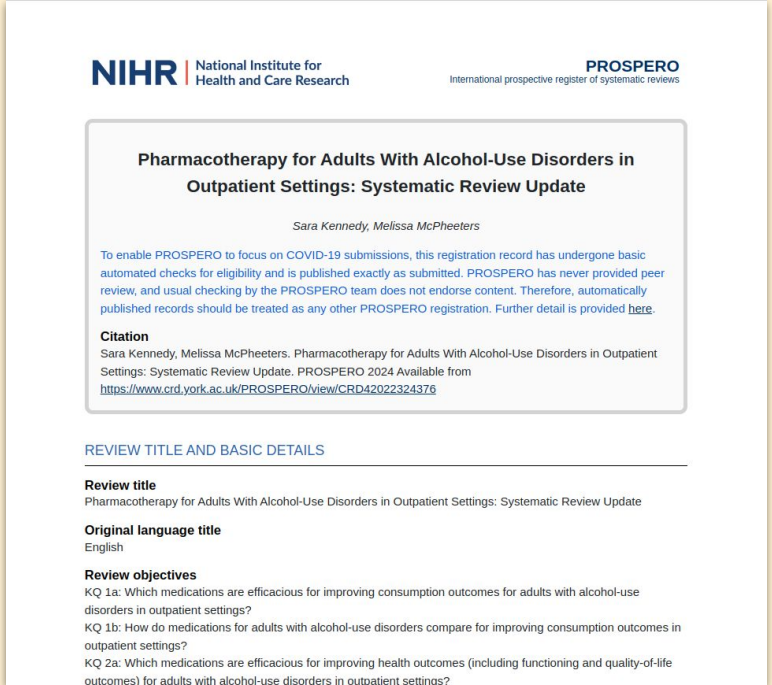
For yes:
☑️ Population
☑️ Intervention
☑️ Comparator group
☑️ Outcome
☑️ Timeframe for follow-up (optional)

☑️ **Yes**
☐ No

2. ★ O relato da revisão **declarou explicitamente** que os métodos de revisão foram estabelecidos **previamente à condução** da revisão e **justificou qualquer desvio** relevante do protocolo?

2. ★ O relato da revisão **declarou explicitamente** que os métodos de revisão foram estabelecidos **previamente à condução** da revisão e **justificou qualquer desvio** relevante do protocolo?

Protocolo **PROSPERO** (CRD42022324376)



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PROSPERO
International prospective register of systematic reviews

Pharmacotherapy for Adults With Alcohol-Use Disorders in Outpatient Settings: Systematic Review Update

Sara Kennedy, Melissa McPheeters

To enable PROSPERO to focus on COVID-19 submissions, this registration record has undergone basic automated checks for eligibility and is published exactly as submitted. PROSPERO has never provided peer review, and usual checking by the PROSPERO team does not endorse content. Therefore, automatically published records should be treated as any other PROSPERO registration. Further detail is provided here.

Citation
Sara Kennedy, Melissa McPheeters. Pharmacotherapy for Adults With Alcohol-Use Disorders in Outpatient Settings: Systematic Review Update. PROSPERO 2024 Available from https://www.crd.york.ac.uk/PROSPERO/view/CRD42022324376

REVIEW TITLE AND BASIC DETAILS

Review title
Pharmacotherapy for Adults With Alcohol-Use Disorders in Outpatient Settings: Systematic Review Update

Original language title
English

Review objectives
KQ 1a: Which medications are efficacious for improving consumption outcomes for adults with alcohol-use disorders in outpatient settings?
KQ 1b: How do medications for adults with alcohol-use disorders compare for improving consumption outcomes in outpatient settings?
KQ 2a: Which medications are efficacious for improving health outcomes (including functioning and quality-of-life outcomes) for adults with alcohol-use disorders in outpatient settings?

2. ★ O relato da revisão **declarou explicitamente** que os métodos de revisão foram estabelecidos **previamente à condução** da revisão e **justificou qualquer desvio** relevante do protocolo?

Protocolo **PROSPERO** (CRD42022324376)

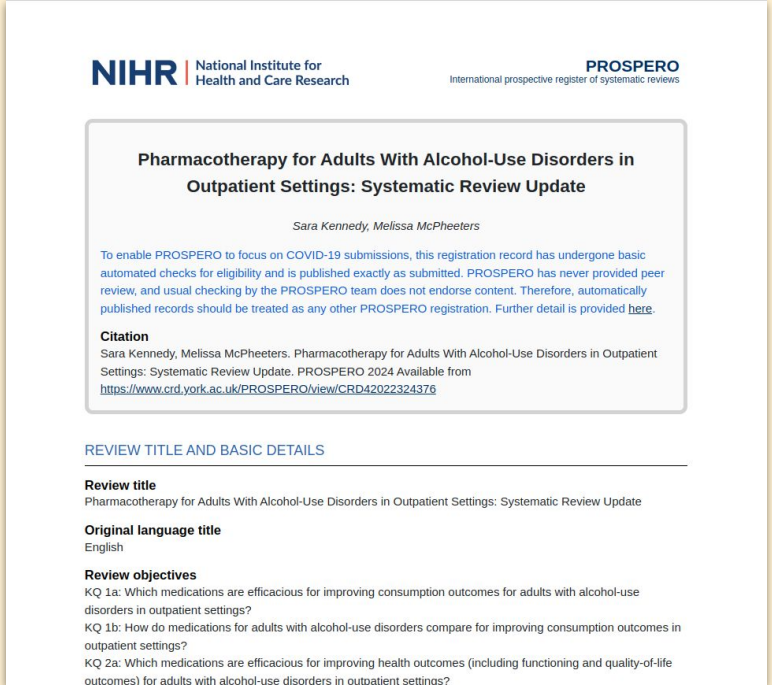
Para um **parcialmente sim**:

☐ Pergunta(s) de revisão

☐ Estratégia de busca

☐ Critérios de inclusão e exclusão

☐ Avaliação de Risco de Viés (RoB)



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☑️ Pergunta(s) de revisão

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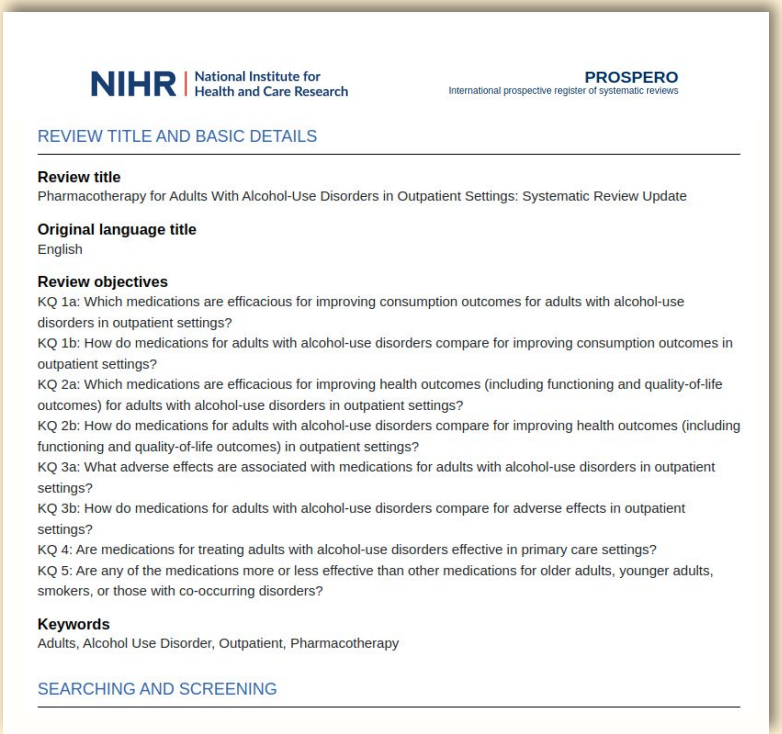
☐ Critérios de inclusão e exclusão

☐ Avaliação de Risco de Viés (RoB)



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KQ 2a: Which medications are efficacious for improving health outcomes (including functioning and quality-of-life outcomes) for adults with alcohol-use disorders in outpatient settings?
KQ 2b: How do medications for adults with alcohol-use disorders compare for improving health outcomes (including functioning and quality-of-life outcomes) in outpatient settings?
KQ 3a: What adverse effects are associated with medications for adults with alcohol-use disorders in outpatient settings?
KQ 3b: How do medications for adults with alcohol-use disorders compare for adverse effects in outpatient settings?
KQ 4: Are medications for treating adults with alcohol-use disorders effective in primary care settings?
KQ 5: Are any of the medications more or less effective than other medications for older adults, younger adults, smokers, or those with co-occurring disorders?

Keywords
Adults, Alcohol Use Disorder, Outpatient, Pharmacotherapy

SEARCHING AND SCREENING

2. ★ O relato da revisão **declarou explicitamente** que os métodos de revisão foram estabelecidos **previamente à condução** da revisão e **justificou qualquer desvio** relevante do protocolo?

Protocolo **PROSPERO** (CRD42022324376)

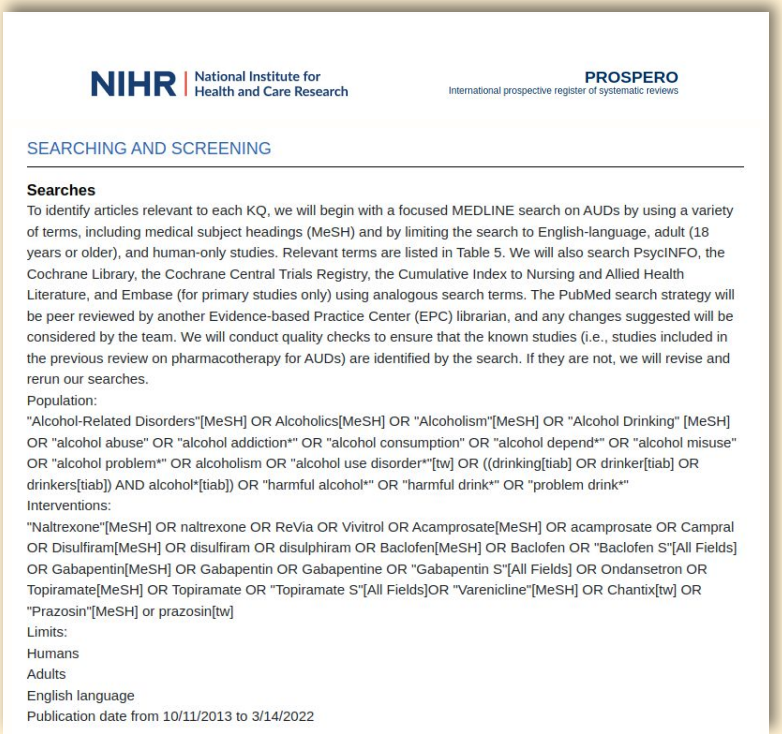
Para um **parcialmente sim**:

☑️ Pergunta(s) de revisão

☑️ Estratégia de busca

☐ Critérios de inclusão e exclusão

☐ Avaliação de Risco de Viés (RoB)



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SEARCHING AND SCREENING

Searches

To identify articles relevant to each KQ, we will begin with a focused MEDLINE search on AUDs by using a variety of terms, including medical subject headings (MeSH) and by limiting the search to English-language, adult (18 years or older), and human-only studies. Relevant terms are listed in Table 5. We will also search PsycINFO, the Cochrane Library, the Cochrane Central Trials Registry, the Cumulative Index to Nursing and Allied Health Literature, and Embase (for primary studies only) using analogous search terms. The PubMed search strategy will be peer reviewed by another Evidence-based Practice Center (EPC) librarian, and any changes suggested will be considered by the team. We will conduct quality checks to ensure that the known studies (i.e., studies included in the previous review on pharmacotherapy for AUDs) are identified by the search. If they are not, we will revise and rerun our searches.

Population:

"Alcohol-Related Disorders"[MeSH] OR Alcoholics[MeSH] OR "Alcoholism"[MeSH] OR "Alcohol Drinking" [MeSH] OR "alcohol abuse" OR "alcohol addiction*" OR "alcohol consumption" OR "alcohol depend*" OR "alcohol misuse" OR "alcohol problem*" OR alcoholism OR "alcohol use disorder*"[tw] OR ((drinking[tiab] OR drinker[tiab] OR drinkers[tiab]) AND alcohol*[tiab]) OR "harmful alcohol*" OR "harmful drink*" OR "problem drink*"

Interventions:

"Naltrexone"[MeSH] OR naltrexone OR ReVia OR Vivitrol OR Acamprosate[MeSH] OR acamprosate OR Campral OR Disulfiram[MeSH] OR disulfiram OR disulphiram OR Baclofen[MeSH] OR Baclofen OR "Baclofen S"[All Fields] OR Gabapentin[MeSH] OR Gabapentin OR Gabapentine OR "Gabapentin S"[All Fields] OR Ondansetron OR Topiramate[MeSH] OR Topiramate OR "Topiramate S"[All Fields]OR "Varenicline"[MeSH] OR Chantix[tw] OR "Prazosin"[MeSH] or prazosin[tw]

Limits:

Humans

Adults

English language

Publication date from 10/11/2013 to 3/14/2022

2. ★ O relato da revisão **declarou explicitamente** que os métodos de revisão foram estabelecidos **previamente à condução** da revisão e **justificou qualquer desvio** relevante do protocolo?

Protocolo **PROSPERO** (CRD42022324376)

Para um **parcialmente sim**:

☑️ Pergunta(s) de revisão

☑️ Estratégia de busca

☑️ Critérios de inclusão e exclusão

☐ Avaliação de Risco de Viés (RoB)

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Study selection / Searching and Screening

"Studies that enrolled adults with alcohol use disorder and evaluated an FDA-approved medication [...] or any of 6 off-label medications [...] for at least 12 weeks of treatment in an outpatient setting were eligible for inclusion. [...] and by limiting the search to English-language, adult (18 years or older), and human-only studies."

2. ★ O relato da revisão **declarou explicitamente** que os métodos de revisão foram estabelecidos **previamente à condução** da revisão e **justificou qualquer desvio** relevante do protocolo?

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Risk of bias (quality) assessment

We will use predefined criteria based on the **AHRQ Methods Guide for Comparative Effectiveness Reviews**, including questions to assess selection bias, confounding, performance bias, detection bias, and attrition bias [...]. We plan to include studies of any risk-of-bias rating in our main data synthesis and main analyses; we will conduct sensitivity analyses that remove studies deemed high risk of bias.

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Protocolo **PROSPERO** (CRD42022324376)

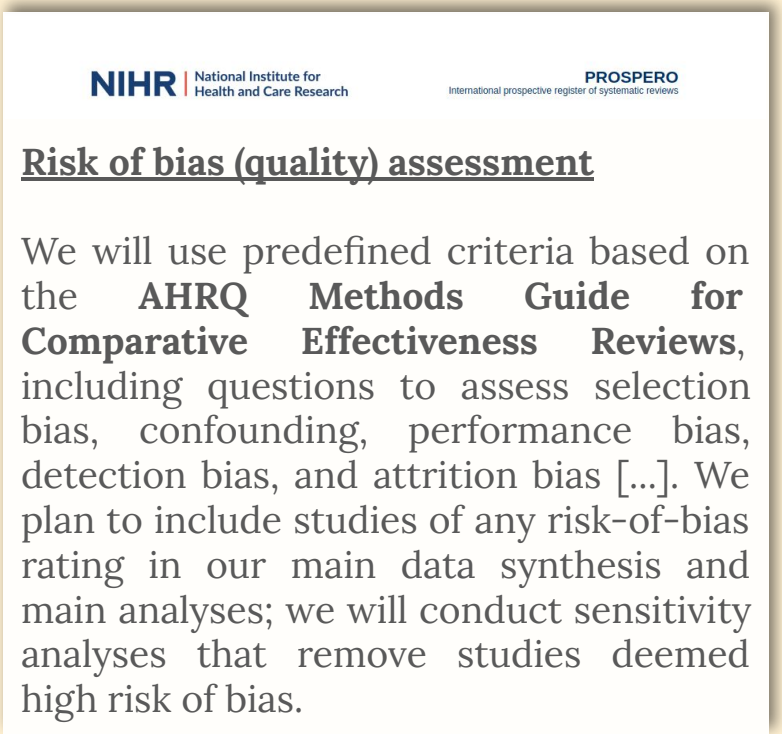
Parcialmente sim ✅

Para um **sim**:

☐ Plano de meta-análise, caso se aplique

☐ Plano para investigação de possíveis causas de heterogeneidade

☐ Justificativas para quaisquer desvios de protocolo



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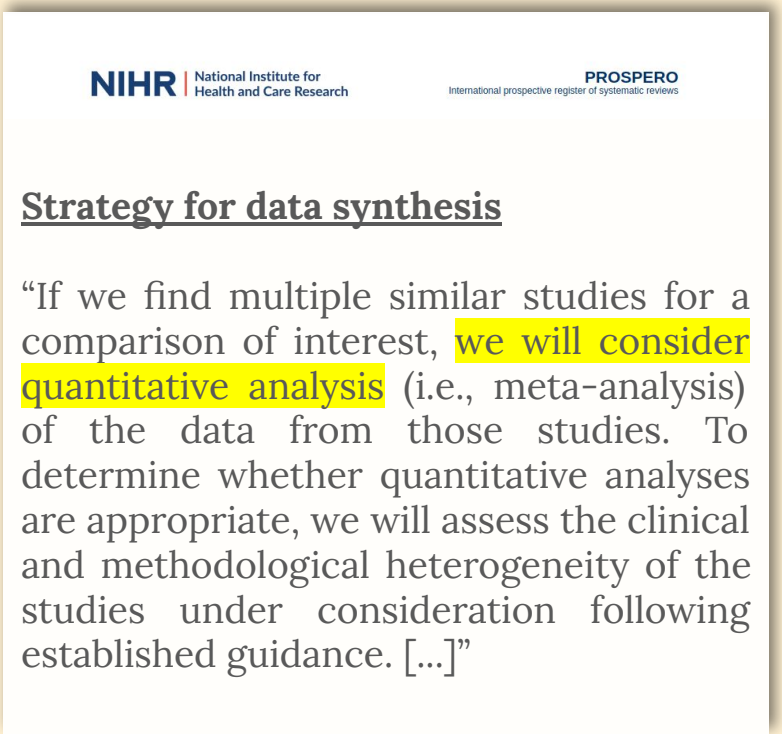
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Strategy for data synthesis

"If we find multiple similar studies for a comparison of interest, we will consider quantitative analysis (i.e., meta-analysis) of the data from those studies. To determine whether quantitative analyses are appropriate, we will assess the clinical and methodological heterogeneity of the studies under consideration following established guidance. [...]"

2. ★ O relato da revisão **declarou explicitamente** que os métodos de revisão foram estabelecidos **previamente à condução** da revisão e **justificou qualquer desvio** relevante do protocolo?

Protocolo **PROSPERO** (CRD42022324376)

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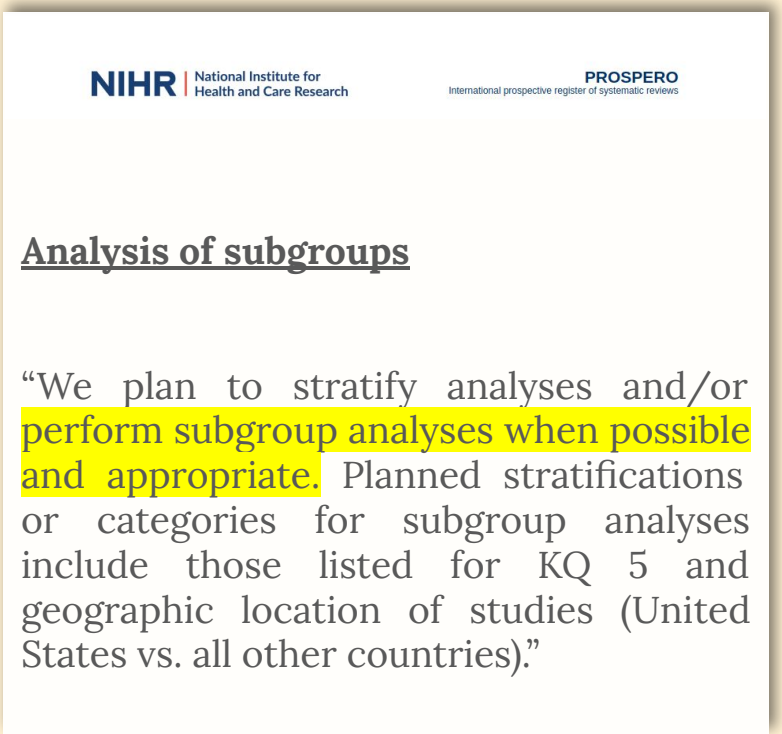

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Analysis of subgroups

"We plan to stratify analyses and/or perform subgroup analyses when possible and appropriate. Planned stratifications or categories for subgroup analyses include those listed for KQ 5 and geographic location of studies (United States vs. all other countries)."

2. ★ O relato da revisão **declarou explicitamente** que os métodos de revisão foram estabelecidos **previamente à condução** da revisão e **justificou qualquer desvio** relevante do protocolo?

Protocolo **PROSPERO** (CRD42022324376)

Parcialmente sim ✅

Para um **sim**:

☑️ Plano de meta-análise, caso se aplique

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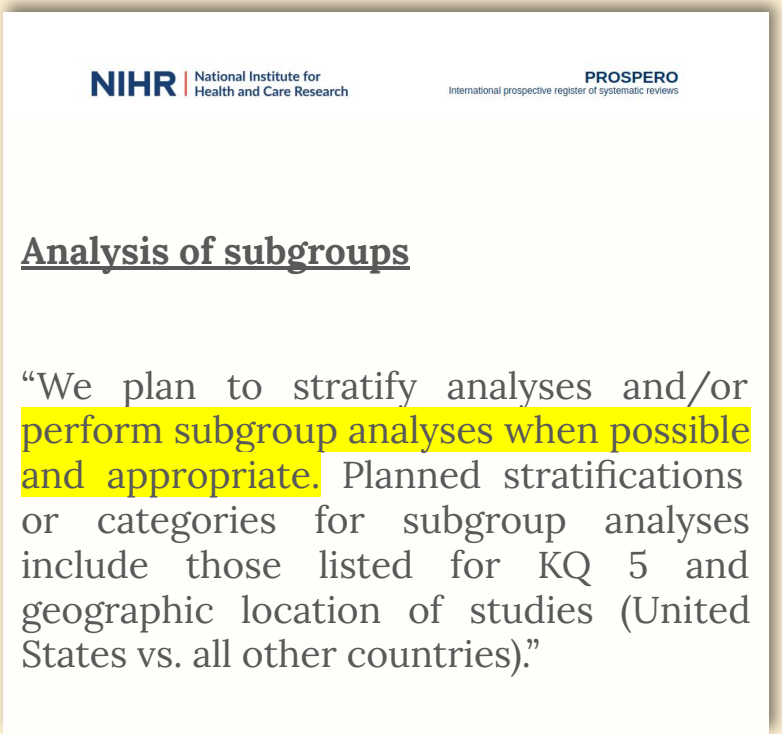
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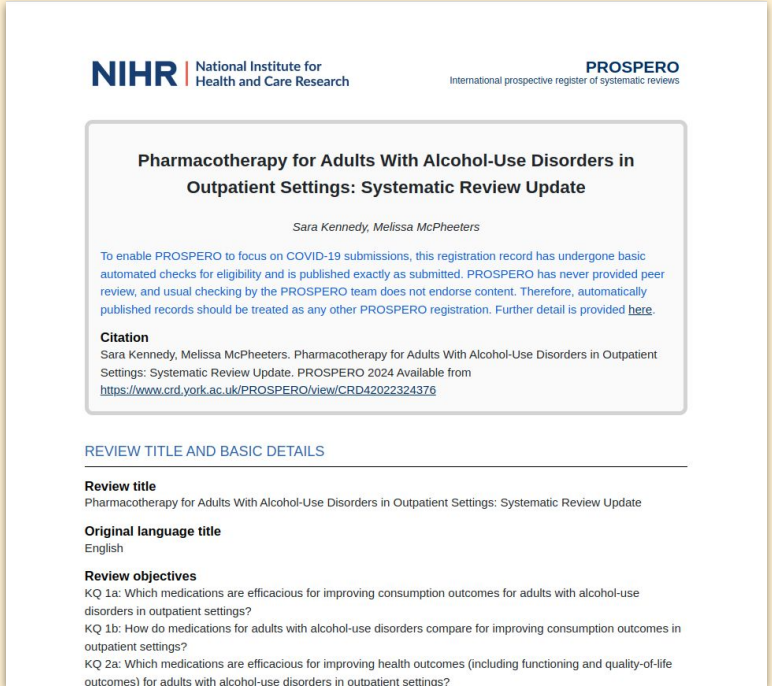
Protocolo **PROSPERO** (CRD42022324376)

Parcialmente sim ✅

Sim ✅

✅



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Pharmacotherapy for Adults With Alcohol-Use Disorders in Outpatient Settings: Systematic Review Update

Sara Kennedy, Melissa McPheeters

To enable PROSPERO to focus on COVID-19 submissions, this registration record has undergone basic automated checks for eligibility and is published exactly as submitted. PROSPERO has never provided peer review, and usual checking by the PROSPERO team does not endorse content. Therefore, automatically published records should be treated as any other PROSPERO registration. Further detail is provided here.

Citation
Sara Kennedy, Melissa McPheeters. Pharmacotherapy for Adults With Alcohol-Use Disorders in Outpatient Settings: Systematic Review Update. PROSPERO 2024 Available from https://www.crd.york.ac.uk/PROSPERO/view/CRD42022324376

REVIEW TITLE AND BASIC DETAILS

Review title
Pharmacotherapy for Adults With Alcohol-Use Disorders in Outpatient Settings: Systematic Review Update

Original language title
English

Review objectives
KQ 1a: Which medications are efficacious for improving consumption outcomes for adults with alcohol-use disorders in outpatient settings?
KQ 1b: How do medications for adults with alcohol-use disorders compare for improving consumption outcomes in outpatient settings?
KQ 2a: Which medications are efficacious for improving health outcomes (including functioning and quality-of-life outcomes) for adults with alcohol-use disorders in outpatient settings?

3. Os autores explicam a escolha dos delineamentos selecionados para a revisão?

◆ Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis ◆

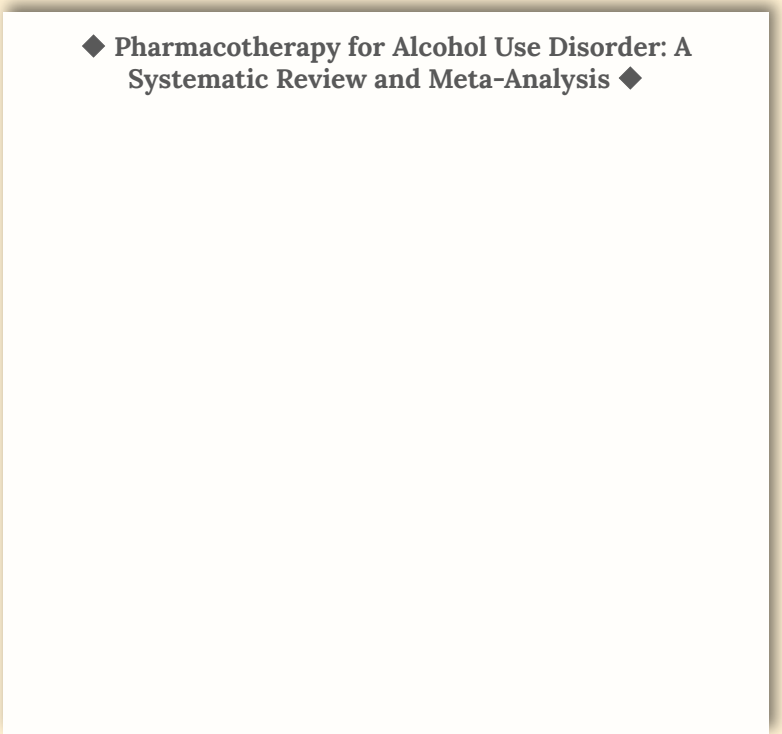
3. Os autores explicam a escolha dos delineamentos selecionados para a revisão?

Para **sim,** satisfazer uma das condições:

☐ Explicação para incluir RCTs apenas

☐ Explicação para incluir NRSI apenas

☐ Explicação para incluir RCTs e NSRI



3. Os autores explicam a escolha dos delineamentos selecionados para a revisão?

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☐ Explicação para incluir RCTs apenas

☐ Explicação para incluir NRSI apenas

☐ Explicação para incluir RCTs e NSRI

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Study Selection

[..] "For adverse effects, in addition to the double-blind RCTs included for efficacy, studies with the following designs were eligible if they compared 2 drugs of interest: nonrandomized or open-label trials, subgroup analyses from trials, prospective cohort studies, and case-control studies. Nonrandomized and observational studies were included to address harms because RCTs had insufficient sample sizes and duration to identify rare harms."

3. Os autores explicam a escolha dos delineamentos selecionados para a revisão?

Para **sim,** satisfazer uma das condições:

☐ Explicação para incluir RCTs apenas

☐ Explicação para incluir NRSI apenas

☐ Explicação para incluir RCTs e NSRI

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Study Selection

"For efficacy outcomes, double-blind randomized clinical trials (RCTs) that compared 1 of the FDA-approved or offlabel medications listed above with placebo or with another medication were eligible for inclusion [..] For adverse effects, [...]"

3. Os autores explicam a escolha dos delineamentos selecionados para a revisão?

Para **sim,** satisfazer uma das condições:

☐ Explicação para incluir RCTs apenas

☐ Explicação para incluir NRSI apenas

☑️ Explicação para incluir RCTs e NSRI

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Study Selection

"For efficacy outcomes, double-blind randomized clinical trials (RCTs) that compared 1 of the FDA-approved or offlabel medications listed above with placebo or with another medication were eligible for inclusion [..] For adverse effects, [...]"

4. ★ Os autores usaram uma estratégia de busca na literatura compreensível?

◆ Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis ◆

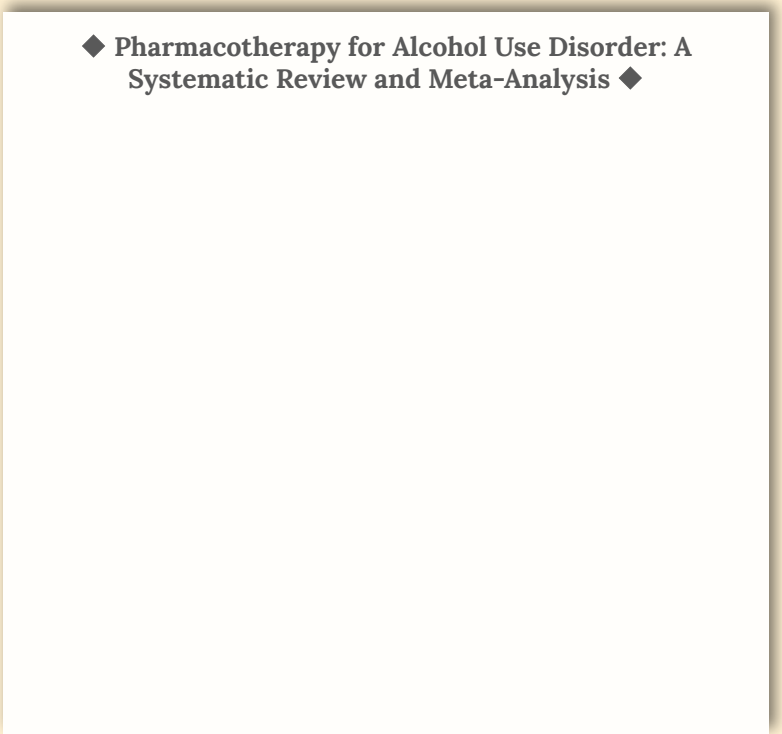
4. ★ Os autores usaram uma estratégia de busca na literatura compreensível?

Para **parcialmente sim,** satisfazer todas:

☐ Buscaram ao menos duas bases de dados

☐ Forneceram palavras-chave e/ou estratégia de busca

☐ Justificaram restrições de publicações (ex.: idioma)



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◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Data Sources and Searches

"PubMed, the Cochrane Library, the Cochrane Central Trials Registry, PsycINFO, CINAHL, and EMBASE were searched for English-language studies of adults aged 18 years or older from November 1, 2012, to September 9, 2022;"

4. ★ Os autores usaram uma estratégia de busca na literatura compreensível?

Para **parcialmente sim,** satisfazer todas:

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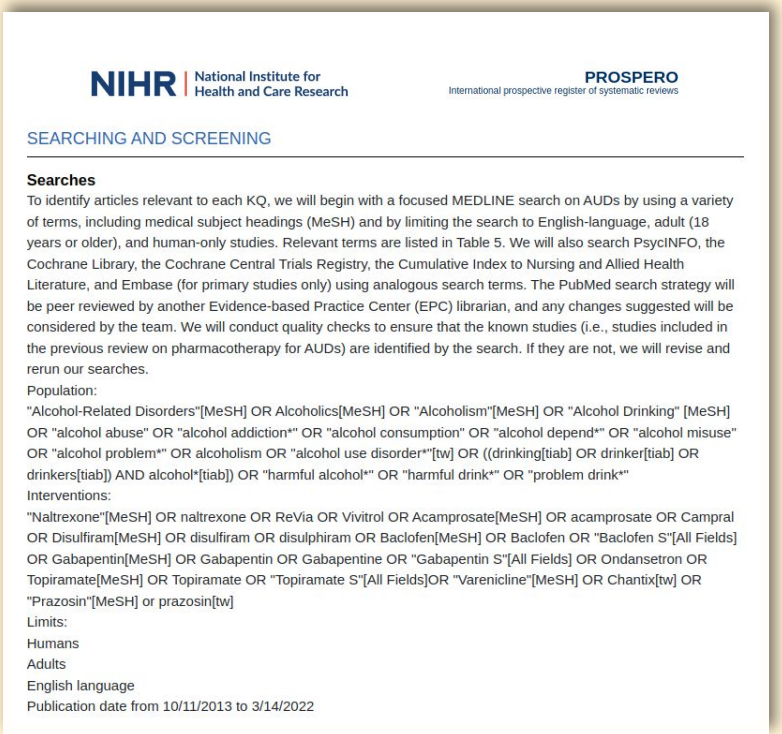

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SEARCHING AND SCREENING

Searches

To identify articles relevant to each KQ, we will begin with a focused MEDLINE search on AUDs by using a variety of terms, including medical subject headings (MeSH) and by limiting the search to English-language, adult (18 years or older), and human-only studies. Relevant terms are listed in Table 5. We will also search PsycINFO, the Cochrane Library, the Cochrane Central Trials Registry, the Cumulative Index to Nursing and Allied Health Literature, and Embase (for primary studies only) using analogous search terms. The PubMed search strategy will be peer reviewed by another Evidence-based Practice Center (EPC) librarian, and any changes suggested will be considered by the team. We will conduct quality checks to ensure that the known studies (i.e., studies included in the previous review on pharmacotherapy for AUDs) are identified by the search. If they are not, we will revise and rerun our searches.

Population:

"Alcohol-Related Disorders"[MeSH] OR Alcoholics[MeSH] OR "Alcoholism"[MeSH] OR "Alcohol Drinking" [MeSH] OR "alcohol abuse" OR "alcohol addiction*" OR "alcohol consumption" OR "alcohol depend*" OR "alcohol misuse" OR "alcohol problem*" OR alcoholism OR "alcohol use disorder*"[tw] OR ((drinking[tiab] OR drinker[tiab] OR drinkers[tiab]) AND alcohol*[tiab]) OR "harmful alcohol*" OR "harmful drink*" OR "problem drink*"

Interventions:

"Naltrexone"[MeSH] OR naltrexone OR ReVia OR Vivitrol OR Acamprosate[MeSH] OR acamprosate OR Campral OR Disulfiram[MeSH] OR disulfiram OR disulphiram OR Baclofen[MeSH] OR Baclofen OR "Baclofen S"[All Fields] OR Gabapentin[MeSH] OR Gabapentin OR Gabapentine OR "Gabapentin S"[All Fields] OR Ondansetron OR Topiramate[MeSH] OR Topiramate OR "Topiramate S"[All Fields]OR "Varenicline"[MeSH] OR Chantix[tw] OR "Prazosin"[MeSH] or prazosin[tw]

Limits:

Humans

Adults

English language

Publication date from 10/11/2013 to 3/14/2022

4. ★ Os autores usaram uma estratégia de busca na literatura compreensível?

Para **parcialmente sim,** satisfazer todas:

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☐ Justificaram restrições de publicações (ex.: idioma)

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Data Sources and Searches

"PubMed, the Cochrane Library, the Cochrane Central Trials Registry, PsycINFO, CINAHL, and EMBASE were searched for English-language studies of adults aged 18 years or older from November 1, 2012, to September 9, 2022;"

PROSPERO:
[...] and by limiting the search to English-language, adult (18 years or older), and human-only studies.

AMS VAR 2

4. ⭐ de busca na literatura co

Para **parcialmente sim,** satisfazer todas:

☑️ Buscaram ao menos duas bases de dados

☑️ Forneceram palavras-chave e/ou estratég busca

☐ Justificaram restrições de publicações (ex.: idioma)

AMSTAR 2

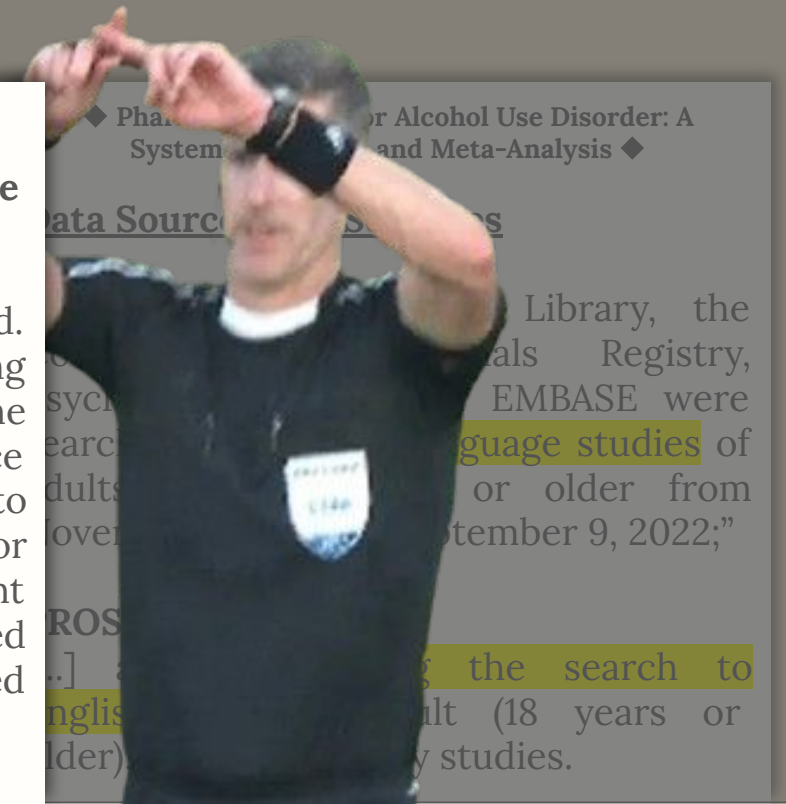
4. ✓ de busca na literatura
co

Para **parcialmente sim,** satisfazer todas:

◆ AMSTAR 2: Online Appendix 1. ◆

Item 4: Did the review authors use a comprehensive literature search strategy?

"At least two bibliographic databases should be searched. [...] Searches should be supplemented by checking published reviews, specialized registers, or experts in the particular field of study, and by reviewing the reference list from the studies found. Sometimes it is necessary to approach authors of original studies to clarify results or obtain updates or corrections. Publications in all relevant languages should be sought and a justification provided when there are language restrictions. We have highlighted the need for searching the grey literature in some cases."



◆ Pha r Alcohol Use Disorder: A System and Meta-Analysis ◆

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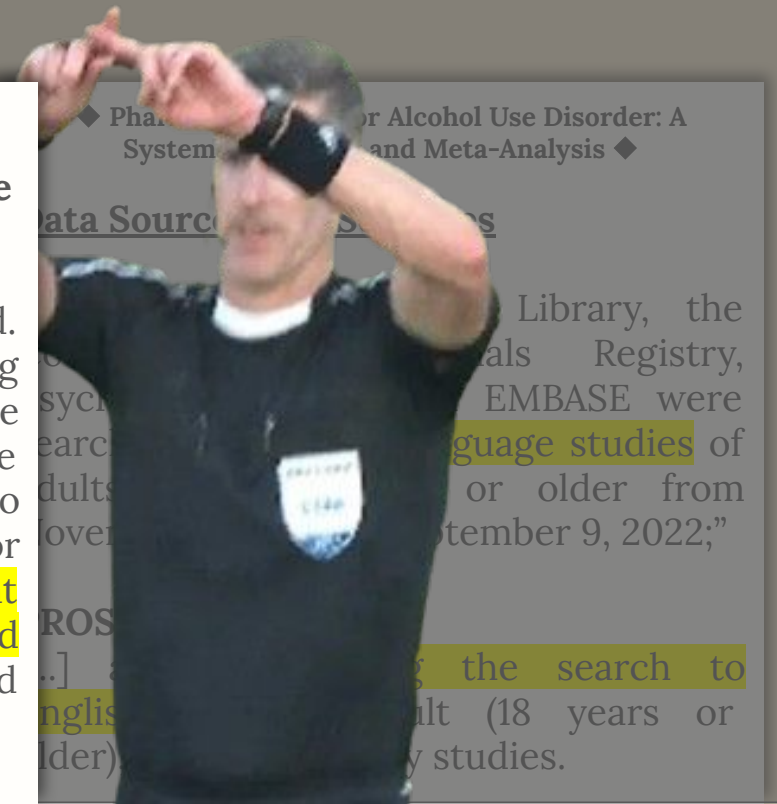

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☐ **Justificaram restrições de publicações (ex.: idioma)**

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

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PROSPERO:
[...] and by limiting the search to English-language, adult (18 years or older), and human-only studies.

4. ★ Os autores usaram uma estratégia de busca na literatura compreensível?

Para **sim,** satisfazer também:

☑️ Buscaram listas de referências e bibliografias dos estudos inclusos

☑️ Buscaram em registros de ensaios clínicos

☑️ Incluíran/consultaram especialistas na área

☑️ Conduziram buscas dentro de 24 meses do término da revisão

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Data Sources and Searches

"PubMed, the Cochrane Library, the Cochrane Central Trials Registry, PsycINFO, CINAHL, and EMBASE were searched [...] Reference lists of pertinent reviews and trials were manually searched for additional relevant citations."

"After September 9, 2022, an ongoing systematic monitoring of the literature was conducted through article alerts."

4. ★ Os autores usaram uma estratégia de busca na literatura compreensível?

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5. Os autores realizaram seleção dos estudos em dupla?

◆ Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis ◆

5. Os autores realizaram seleção dos estudos em dupla?

Para **sim,** marcar um:

☐ Ao menos dois revisores independemente acordaram na seleção de estudos elegíveis e atingiram consenso sobre quais estudos incluir

☐ Dois revisores selecionaram uma amostra de estudos elegíveis e atingiram boa concordância (80% ao menos) com o restante selecionado por um revisor

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Study selection

"Two investigators independently reviewed each title and abstract. Studies marked for possible inclusion by either reviewer underwent independent full-text review by 2 reviewers. If the reviewers disagreed, they resolved conflicts by discussion and consensus or by consulting a third, senior member of the team."

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6. Os autores realizaram extração de dados em dupla?

◆ Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis ◆

6. Os autores realizaram extração de dados em dupla?

Para **sim,** marcar um:

☐ Ao menos dois revisores atingiram consenso sobre quais dados extrair dos estudos inclusos

☐ Dois revisores extraíram dados de uma amostra de estudos elegíveis e atingiram uma boa concordância (ao menos 80%), com o restante sendo extraído por um revisor

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Data Extraction, Risk-of-Bias Assessment, and Strength of Evidence

"Structured data extraction forms were used to gather relevant data from each article. At least 2 investigators reviewed all data extractions for completeness and accuracy."

6. Os autores realizaram extração de dados em dupla?

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◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Data Extraction, Risk-of-Bias Assessment, and Strength of Evidence

"Structured data extraction forms were used to gather relevant data from each article. At least 2 investigators reviewed all data extractions for completeness and accuracy."

7. ★ Os autores forneceram uma lista de estudos excluídos e justificaram a exclusão?

◆ Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis ◆

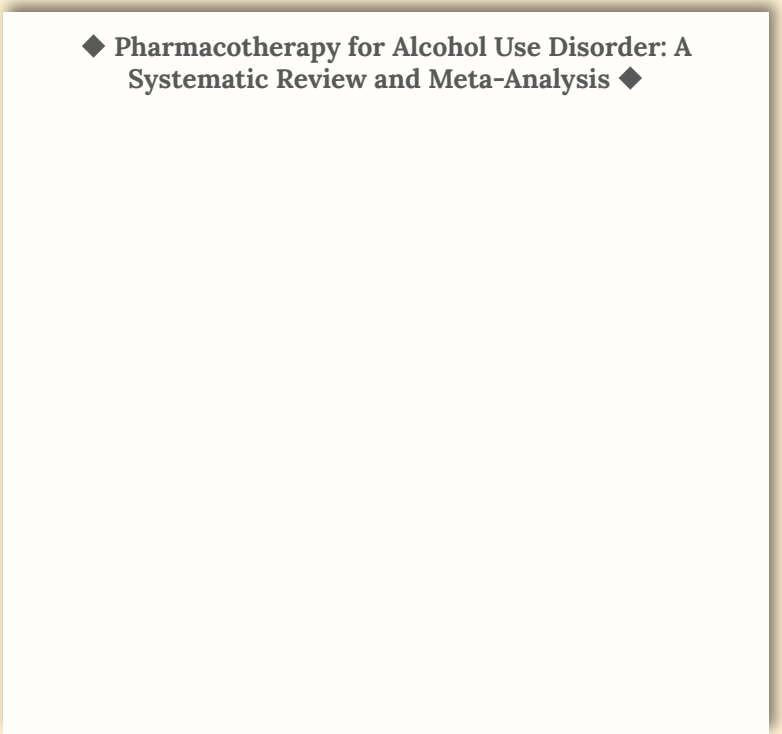
7. ★ Os autores forneceram uma lista de estudos excluídos e justificaram a exclusão?

Para **parcialmente sim**:

☐ Forneceram uma lista de todos os estudos potencialmente relevantes que foram lidos em texto completo mas excluídos da revisão

Para **sim**:

☐ Justificaram as exclusões da revisão de cada estudo potencialmente relevante



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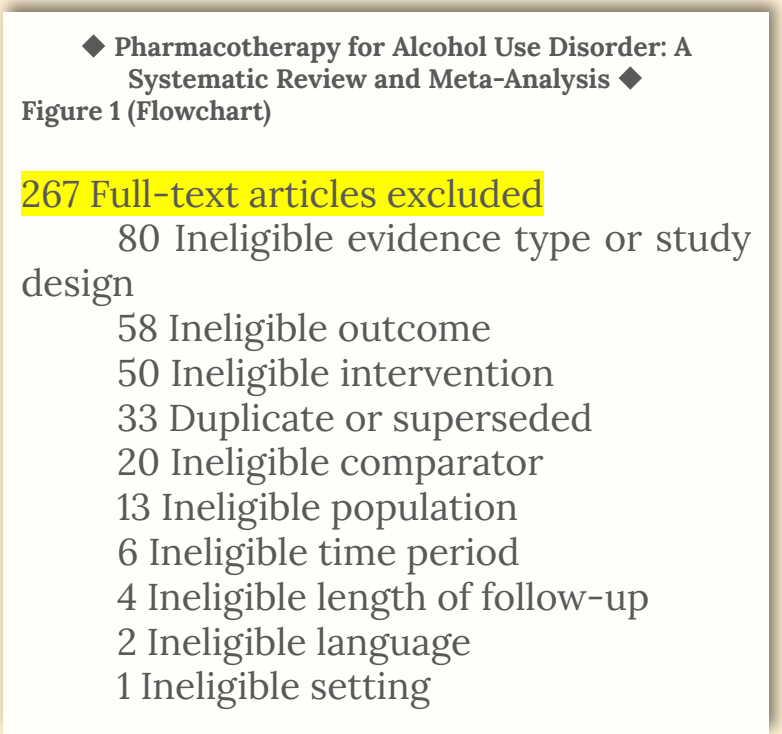
Para **sim**:

☐ Justificaram as exclusões da revisão de cada estudo potencialmente relevante



◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆
Figure 1 (Flowchart)

267 Full-text articles excluded
80 Ineligible evidence type or study design
58 Ineligible outcome
50 Ineligible intervention
33 Duplicate or superseded
20 Ineligible comparator
13 Ineligible population
6 Ineligible time period
4 Ineligible length of follow-up
2 Ineligible language
1 Ineligible setting

AMS VAR 2

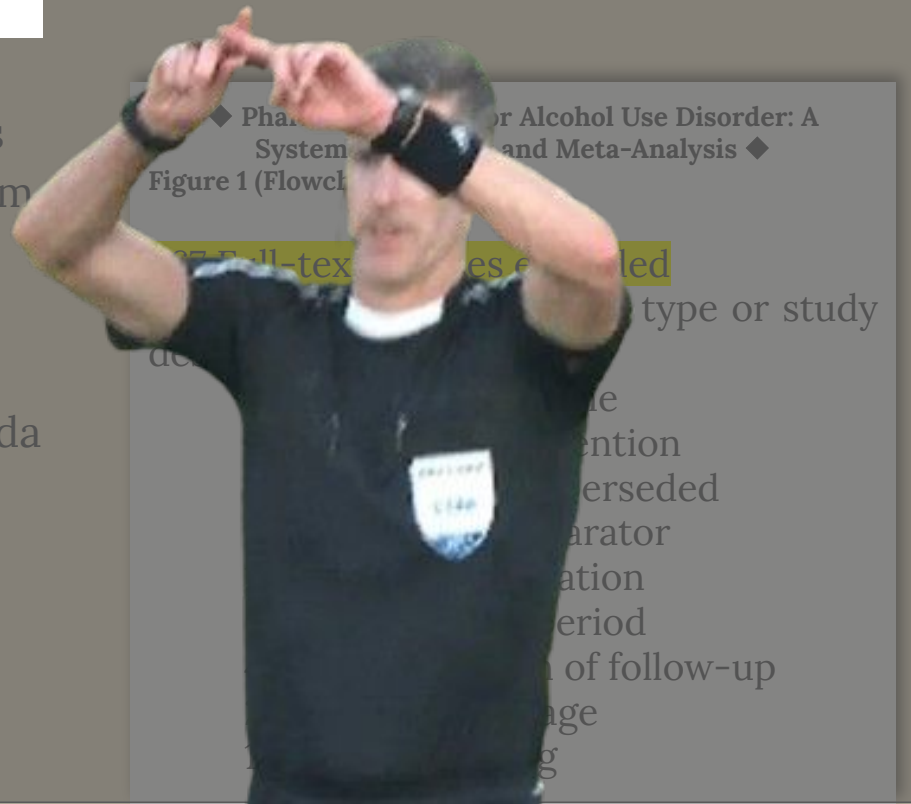
7. ★ ...e estudos excluídos e justificaram a exc...

Para **parcialmente sim**:

☐ Forneceram uma lista de todos os estudos potencialmente relevantes que foram lidos em texto completo mas excluídos da revisão

Para **sim**:

☐ Justificaram as exclusões da revisão de cada estudo potencialmente relevante



AMS VAR 2

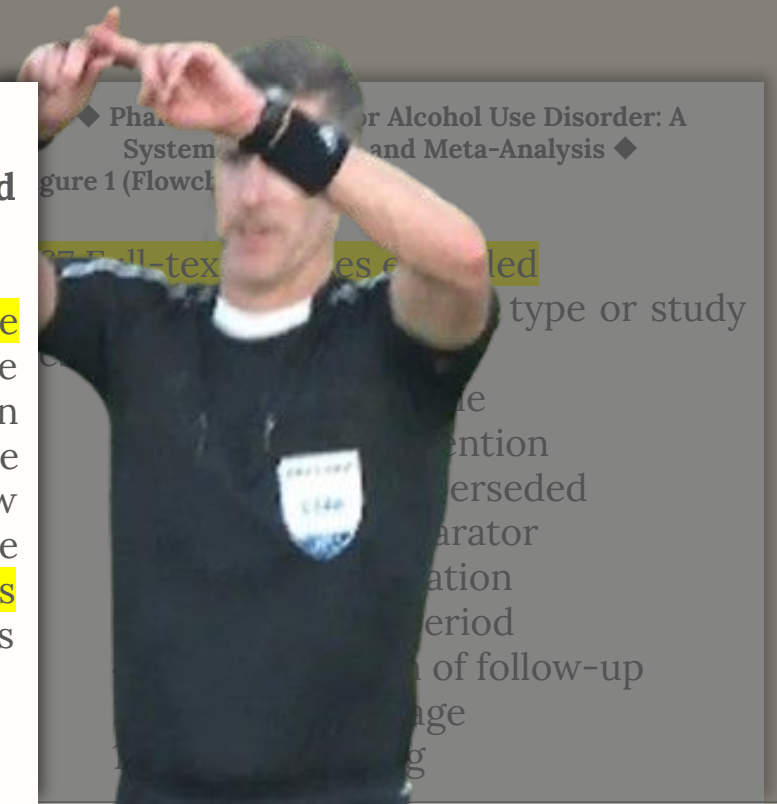
7. ★ ...e estudos excluídos e justificaram a exc...

Para **parcialmente sim**:

◆ AMSTAR 2: Online Appendix 1. ◆

<u>Item 7:</u> Did the review authors provide a list of excluded studies and justify the exclusions?

"This item requires review authors to provide a complete list of potentially relevant studies with justification for the exclusion of each. [...] Exclusion should not be based on risk of bias, which is dealt with separately and later in the review process. Unjustified exclusion may bias the review findings and we encourage an inclusive approach in the early stages of a review. This item requires review authors to provide a complete list of potentially relevant studies with justification for the exclusion of each one."



7. ★ Os autores forneceram uma lista de estudos excluídos e justificaram a exclusão?

Para **parcialmente sim**:

☐ Forneceram uma lista de todos os estudos potencialmente relevantes que foram lidos em texto completo mas excluídos da revisão

Para **sim**:

☐ Justificaram as exclusões da revisão de cada estudo potencialmente relevante

"This item requires review authors to **provide a complete list** of potentially relevant studies with justification for the exclusion of each."

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆
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- 13 Ineligible population
- 6 Ineligible time period
- 4 Ineligible length of follow-up
- 2 Ineligible language
- 1 Ineligible setting

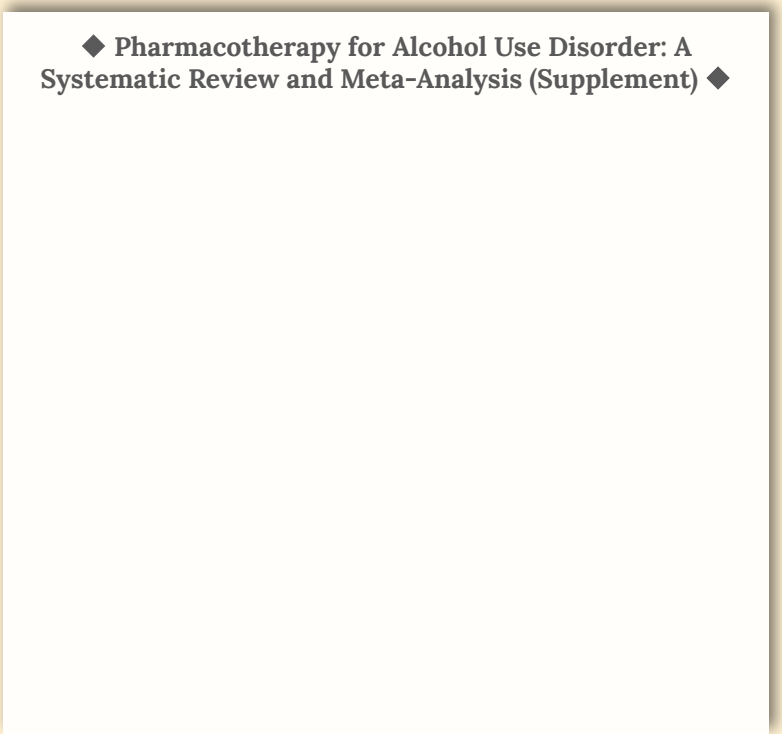
8. Os autores descreveram os estudos incluídos em detalhamento adequado?

Para **parcialmente sim**:

☐ Descrever população
☐ Descrever intervenções
☐ Descrever comparadores
☐ Descrever desfechos
☐ Descrever delineamentos

Para **sim**:

☐ Descrever população detalhadamente
☐ Descrever intervenções e comparadores em detalhe
☐ Descrever contexto
☐ Descrever tempo de acompanhamento



8. Os autores descreveram os estudos incluídos em detalhamento a

Pa
- ☐
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Pa
- ☐
- ☐

de
- ☐
- ☐ Descrever tempo de acompanhamento

eTable 4. Characteristics of Included Studies

Author, Year Trial Name	Arm Dose, mg/day (N)	Rx Duration, Weeks (Follow-up)	Setting	Recruitment Method	Age, Years	% Non-White	% Female	% With Co-occurring Condition	Co-intervention	Risk of Bias
Addolorato, 2007[11]	BAC 30 (42) Placebo (42)	12	University treatment and research center	People contacting alcohol treatment unit	49	NR	0	Liver cirrhosis 100 Hepatitis B 15 Hepatitis C 29	Routine psychological support	Medium
Anton, 1999[12]; Anton, 2001[13]	NTX 50 (68) Placebo (63)	12	US, Outpatient academic research center	Ads, referrals for treatment seekers	41 to 44	11 to 18	27 to 31	0	CBT	Medium
Anton, 2003[14] COMBINE pilot DBRCT	ACA 3000 + CBI + MM (9) ACA 3000 + MM (9) NTX 100 + CBI + MM (9) NTX 100 + MM (9) Placebo + CBI + MM (9) Placebo + MM (8)[a]	16	11 US academic sites	Ads, community resources, clinical referrals at 11 academic sites	38 to 42	17 to 22	22 to 33	NR	As randomized	Medium
Anton, 2005[15]	NTX 50 + CBT (39) NTX 50 + MET	12	US, Outpatient	Ads, referred to clinical service	43 to 45	8 to 23	21 to 27	NR	CBT and MET as randomized	Medium

8. Os autores descreveram os estudos incluídos em detalhamento adequado?

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◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis (Supplement)** ◆

eTable 4. Characteristics of Included Studies

- Author (year), trial name
- Invervention and dosage
- Follow-up in weeks
- Setting
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- % non white, % female, % with co-occuring condition
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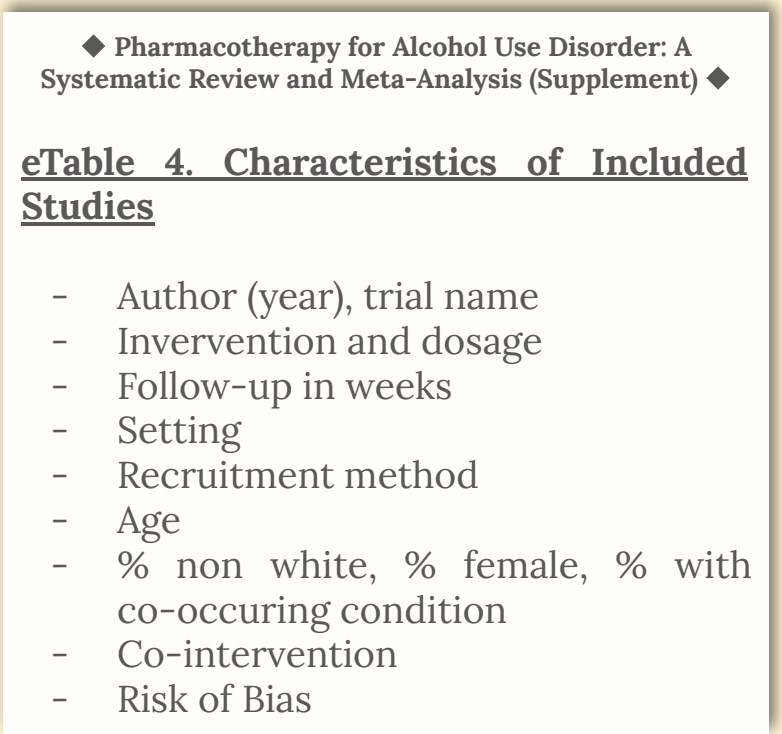

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Para **sim**:
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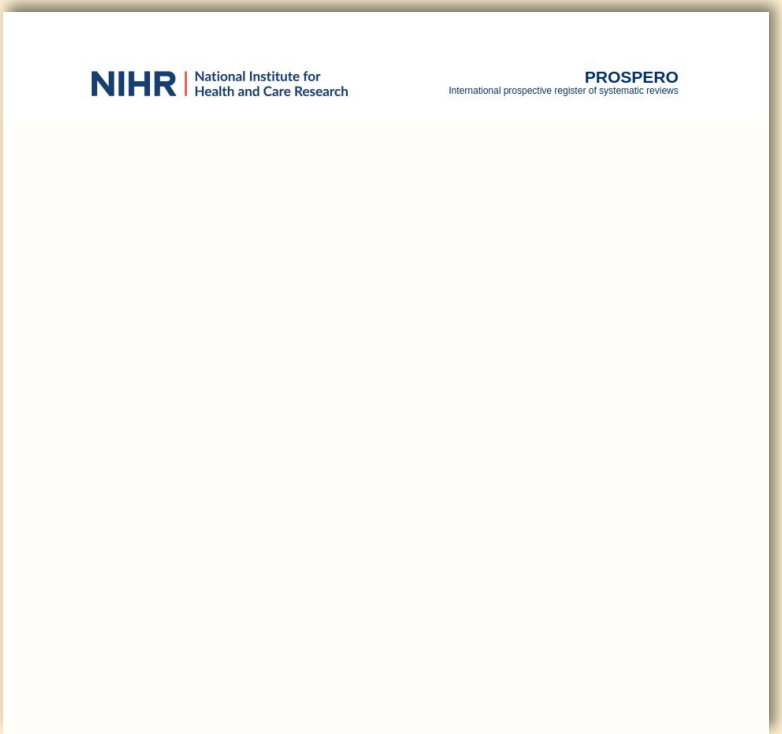
9. Os autores usaram uma técnica adequada de verificação de risco de viés (RoB) nos estudos incluídos na revisão?

Para **parcialmente sim**, teriam de ter avaliado o risco de viés de:
☐ Ausência de sigilo da alocação
☐Falta de cegamento de pacientes e avaliadores ao mensurar os desfechos

Para **sim**, também devem ter considerado:
☐ sequência de alocação não verdadeiramente aleatória
☐ seleção dos resultados reportados dentre múltiplas mensurações ou análises de um desfecho



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Risk of bias (quality) assessment

"[...] criteria based on AHRQ [...] including questions to assess selection bias, confounding, performance bias, detection bias, and attrition bias (i.e., those about adequacy of randomization, allocation concealment, similarity of groups at baseline, masking, attrition, whether intention-to-treat analysis was used, method of handling dropouts and missing data, validity and reliability of outcome measures, and treatment fidelity)."

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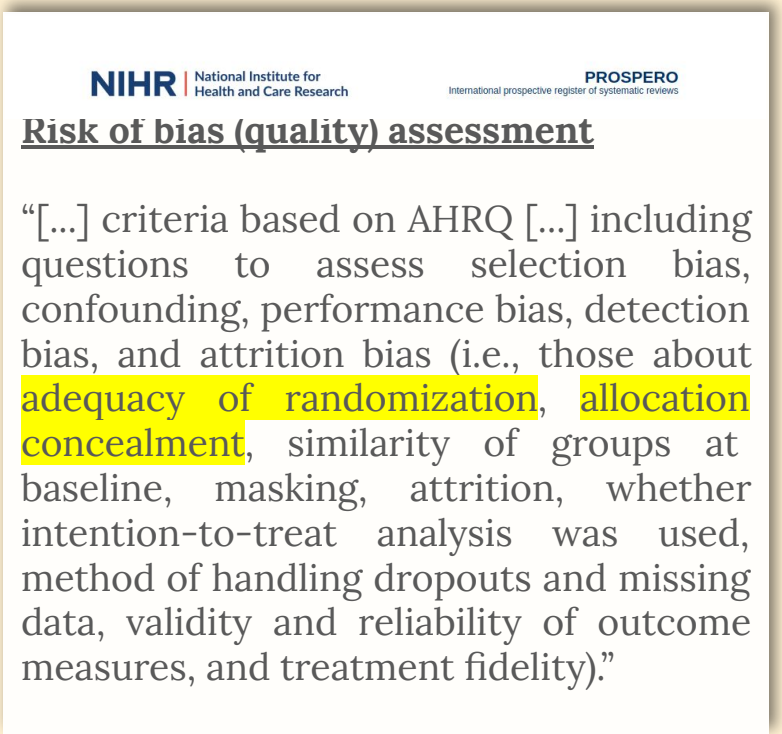
NIHR | National Institute for Health and Care Research

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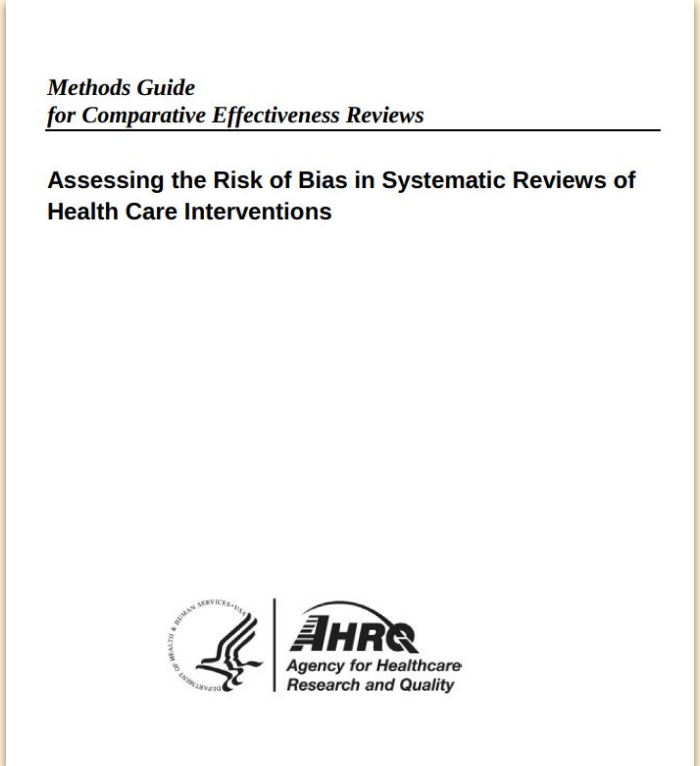

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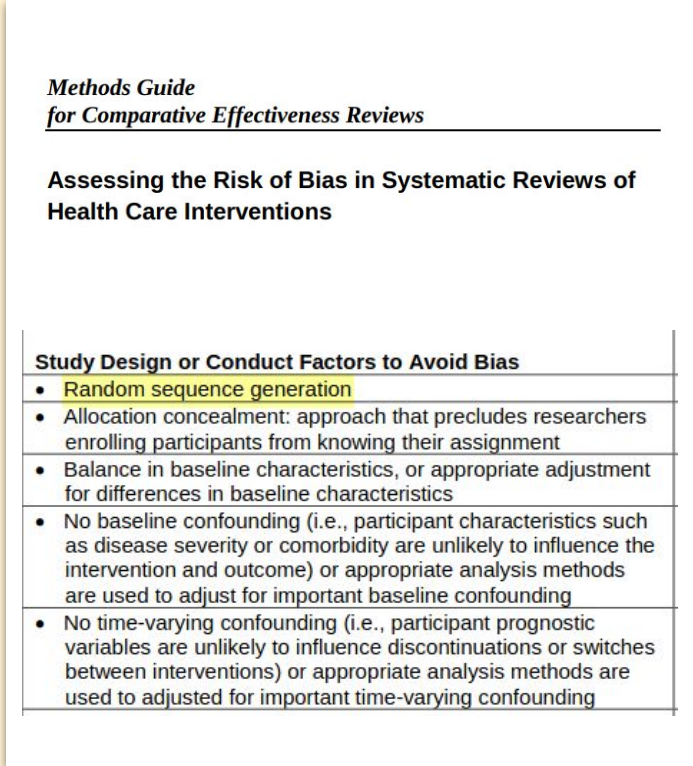

Methods Guide
for Comparative Effectiveness Reviews

Assessing the Risk of Bias in Systematic Reviews of Health Care Interventions

Study Design or Conduct Factors to Avoid Bias
• Random sequence generation
• Allocation concealment: approach that precludes researchers enrolling participants from knowing their assignment
• Balance in baseline characteristics, or appropriate adjustment for differences in baseline characteristics
• No baseline confounding (i.e., participant characteristics such as disease severity or comorbidity are unlikely to influence the intervention and outcome) or appropriate analysis methods are used to adjust for important baseline confounding
• No time-varying confounding (i.e., participant prognostic variables are unlikely to influence discontinuations or switches between interventions) or appropriate analysis methods are used to adjusted for important time-varying confounding

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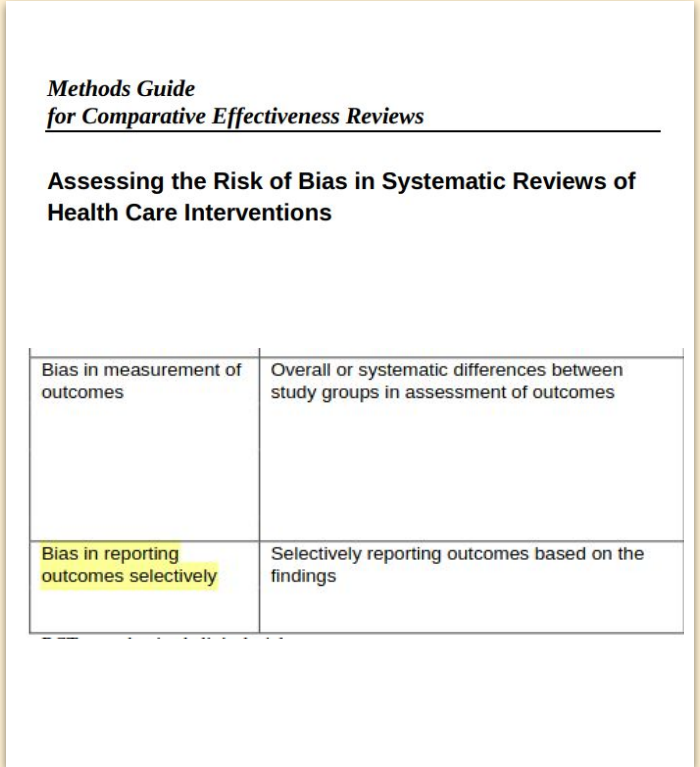


Methods Guide
for Comparative Effectiveness Reviews

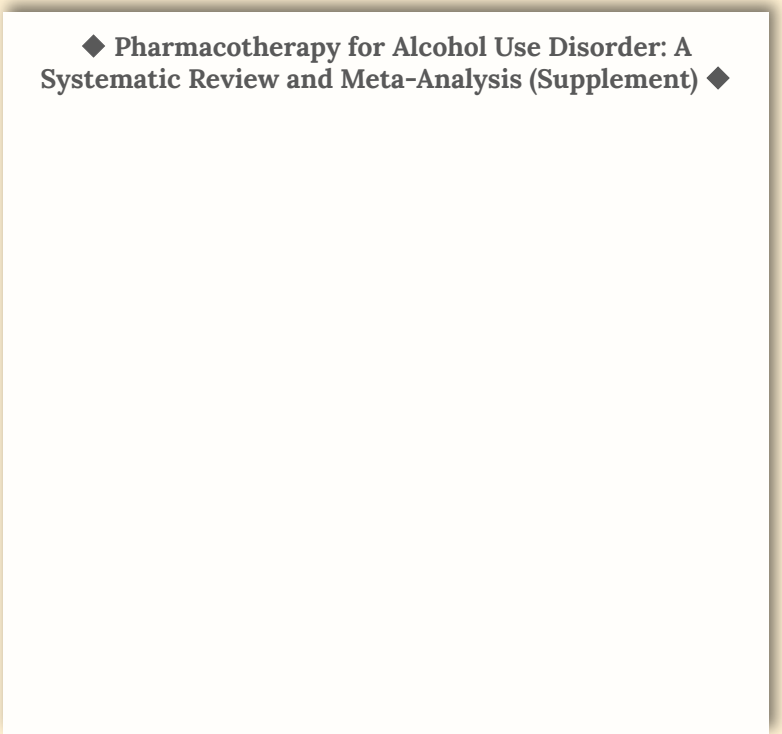
Assessing the Risk of Bias in Systematic Reviews of Health Care Interventions

Bias in measurement of outcomes	Overall or systematic differences between study groups in assessment of outcomes
Bias in reporting outcomes selectively	Selectively reporting outcomes based on the findings

10. Os autores reportaram as fontes de financiamento dos estudos incluídos na revisão?

Para **sim**:

☐ Devem ter reportado sobre as fontes de financiamento dos estudos incluídos na revisão. Reportar que os revisores consideraram essa informação, mas não foi reportada também entra em consideração.



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◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis (Supplement)** ◆

❌ Não relatam sobre fontes de financiamento dos estudos na lista de estudos incluídos.

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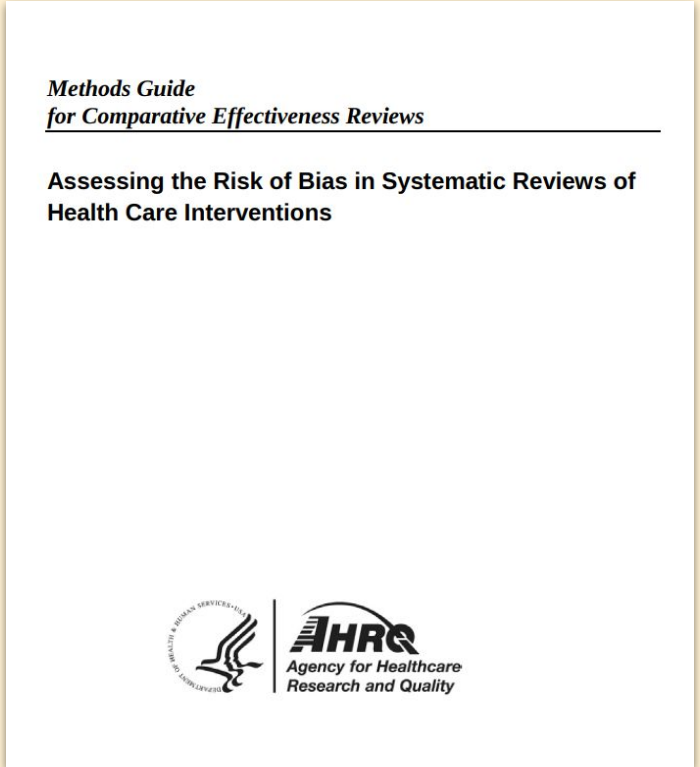

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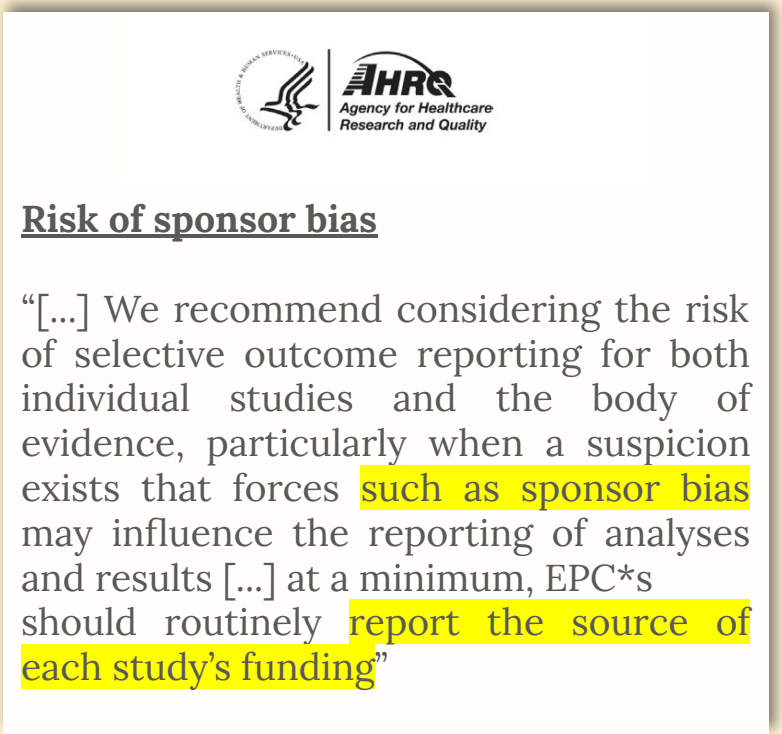

*EPC: Evidence-based practice center

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*EPC: Evidence-based practice center

AHRQ Agency for Healthcare Research and Quality

Risk of sponsor bias

"[...] We recommend considering the risk of selective outcome reporting for both individual studies and the body of evidence, particularly when a suspicion exists that forces such as sponsor bias may influence the reporting of analyses and results [...] at a minimum, EPC*s should routinely report the source of each study's funding"

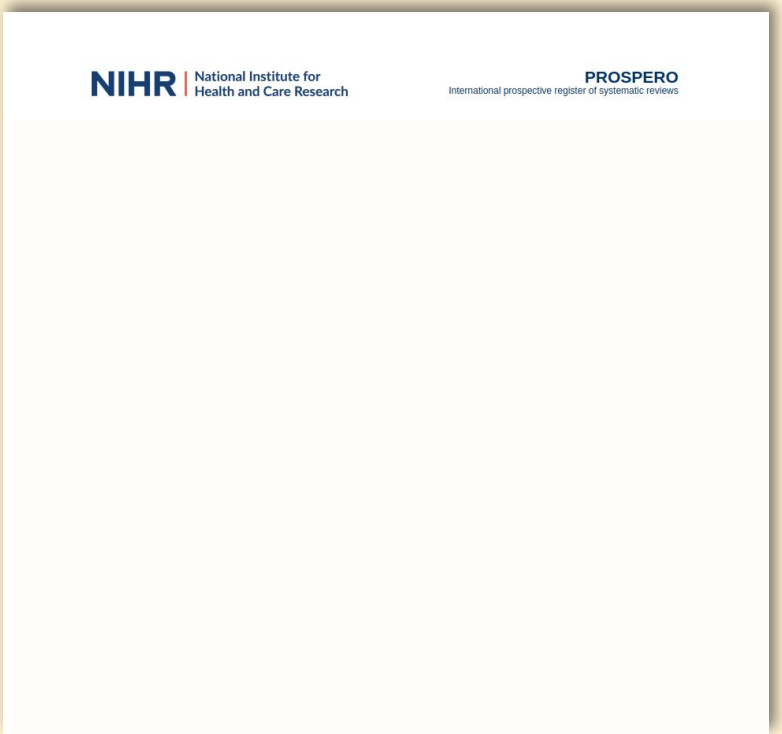
11. ★ Se uma meta-análise foi realizada, os autores da revisão usaram métodos apropriados para combinação estatística dos resultados?

Para **sim**:

☐ Os autores justificaram a combinação de dados através de meta-análise.

☐ Os autores usaram um método ponderado apropriado para combinar os resultados dos estudos e ajustar pela heterogeneidade, se presente.

☐ Os autores investigaram possíveis causas de heterogeneidade.



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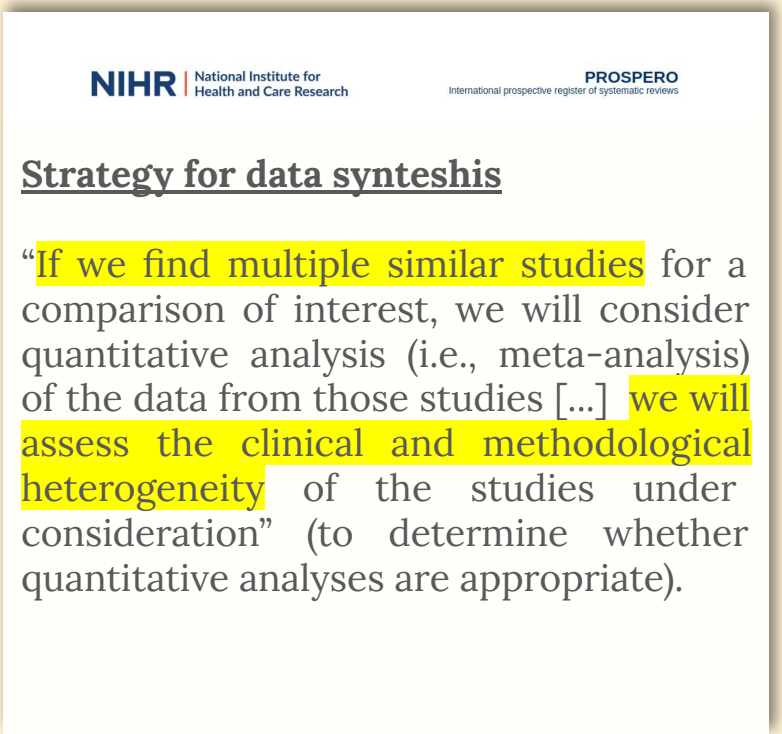

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Strategy for data synteshis

"If we find multiple similar studies for a comparison of interest, we will consider quantitative analysis (i.e., meta-analysis) of the data from those studies [...] we will assess the clinical and methodological heterogeneity of the studies under consideration" (to determine whether quantitative analyses are appropriate).

11. ★ Se uma meta-análise foi realizada, os autores da revisão usaram métodos apropriados para combinação estatística dos resultados?

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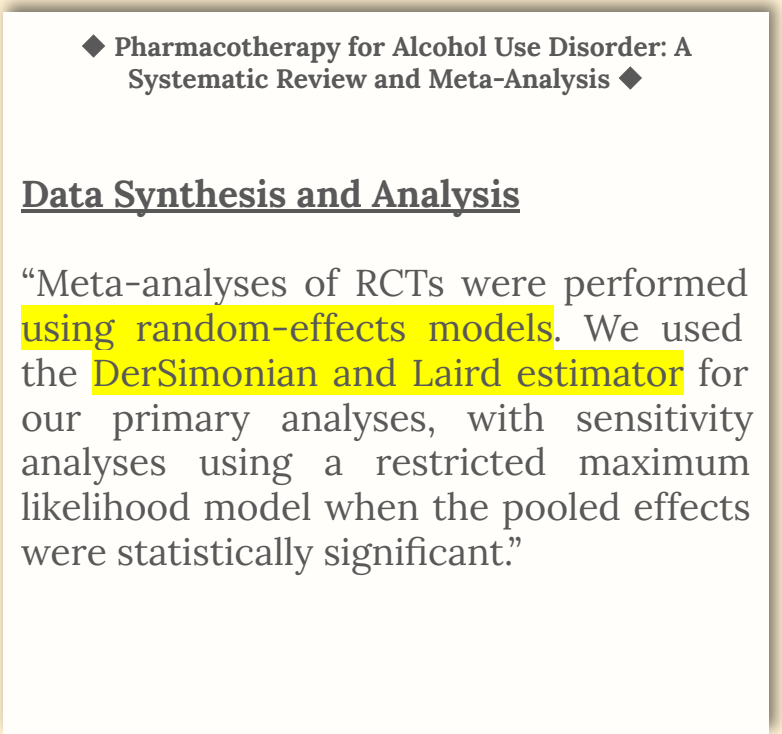

◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Data Synthesis and Analysis

"Meta-analyses of RCTs were performed using random-effects models. We used the DerSimonian and Laird estimator for our primary analyses, with sensitivity analyses using a restricted maximum likelihood model when the pooled effects were statistically significant."

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◆ **Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis** ◆

Data Synthesis and Analysis

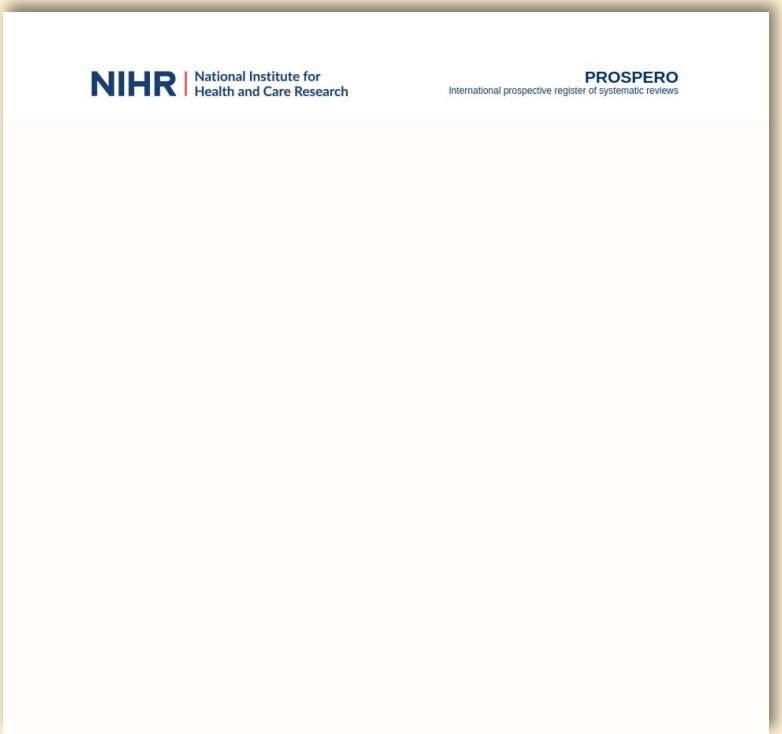
"Meta-analyses of RCTs were performed using random-effects models. We used the DerSimonian and Laird estimator for our primary analyses, with sensitivity analyses using a restricted maximum likelihood model when the pooled effects were statistically significant. [...] Potential sources of heterogeneity were examined by analyzing subgroups defined by patient population (eg, US vs non-US studies)."

12. Se uma meta-análise foi realizada, os autores avaliaram o potencial impacto do Risco de Viés (RoB) dos estudos no resultado da síntese?

Para **sim**:

☐ Devem ter incluído apenas estudos com “baixo” risco de viés, OU

☐ Devem ter realizado análises de performance para investigar possíves impactos do RoB nas medidas resumo de efeito



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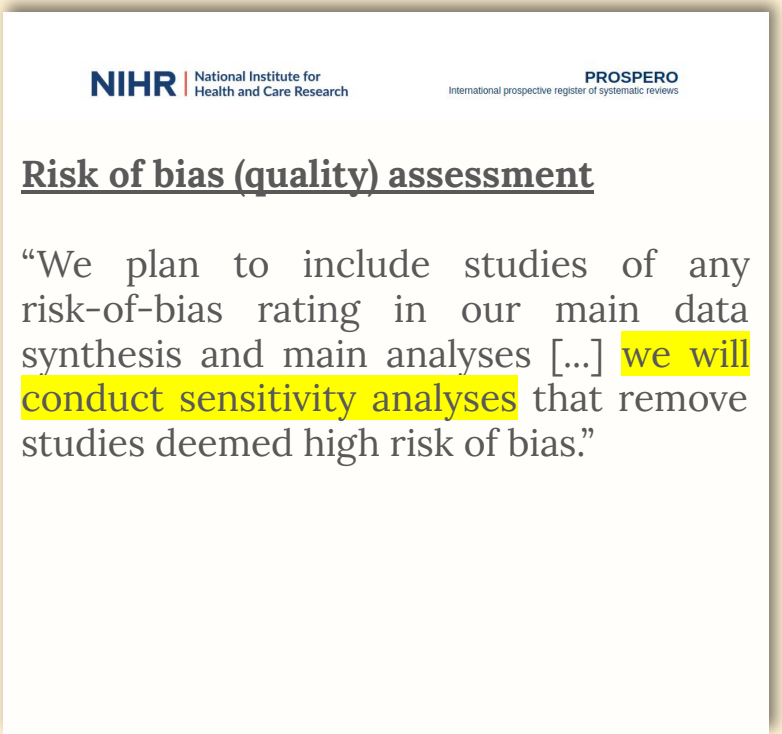

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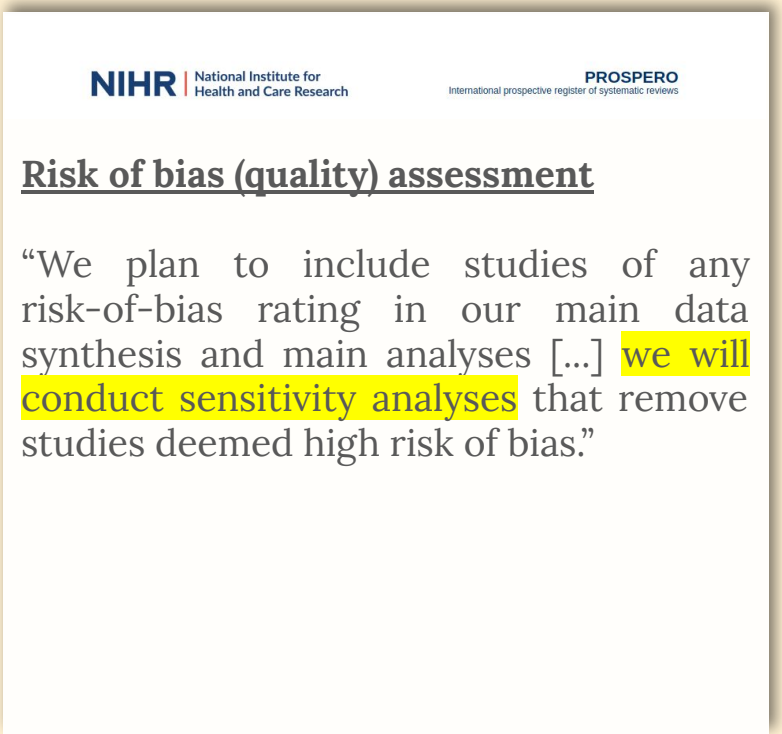

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Risk of bias (quality) assessment

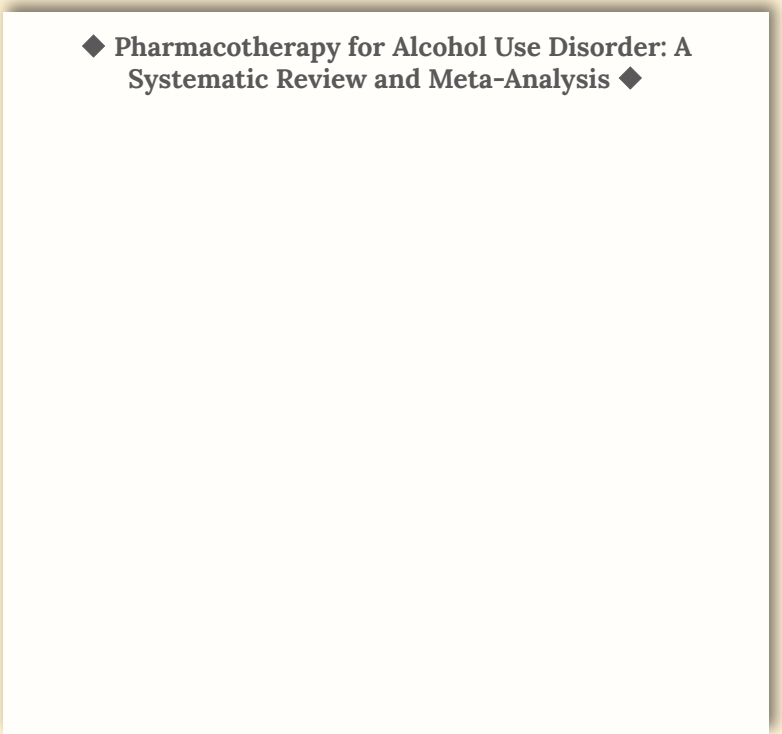
"We plan to include studies of any risk-of-bias rating in our main data synthesis and main analyses [...] we will conduct sensitivity analyses that remove studies deemed high risk of bias."

13. ★ Os autores levaram em conta o Risco de Viés (RoB) dos estudos ao interpretar/discutir os resultados da revisão?

Para **sim**:

☐ Devem ter incluído apenas estudos com “baixo” risco de viés, OU

☐ Se RCTs com risco moderado ou alto de viés foram incluídos, devem ter incluído uma discussão do impacto potencial do RoB nos resultados.



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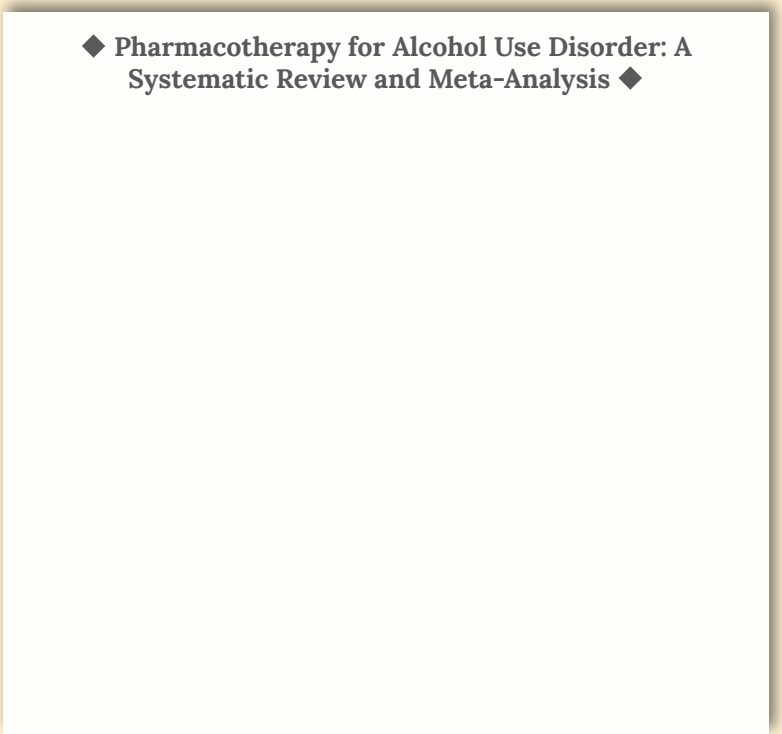
14. Os autores da revisão forneceram uma explicação/discussão satisfatória sobre qualquer heterogeneidade observada nos resultados da revisão?

Para **sim**:

☐ Não houve heterogeneidade nos resultados

☐ OU se houve heterogeneidade nos resultados, os autores forneceram uma investigação de possíveis fontes de heterogeneidade e discutiram o impacto de tal nos resultados da revisão.



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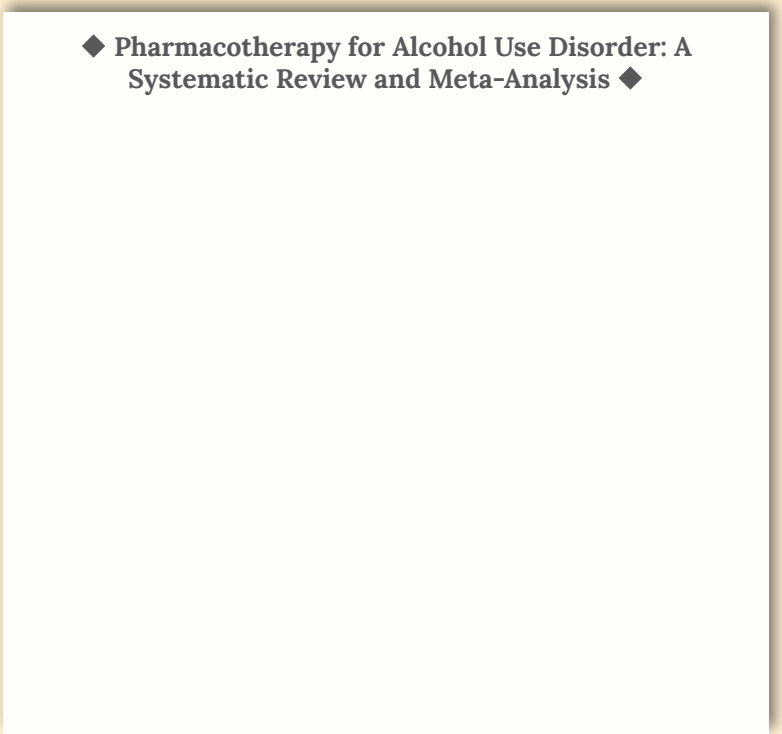
15. ★ Se houve síntese quantitativa, os autores da revisão propuseram uma investigação adequada de viés de publicação e discutiram seu impacto?

Para **sim**:

☐ realizaram testes gráficos ou estatísticos para viés de publicação e discutiram sua verossimilhança e magnitude do impacto do viés de publicação.



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Para **sim**:

☐ Autores demonstraram não haver conflito de interesse

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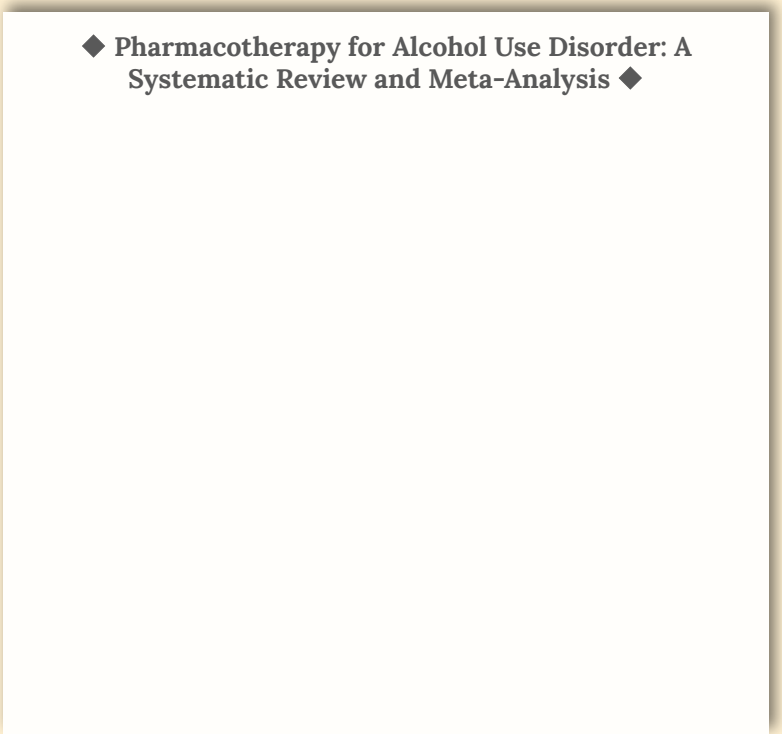

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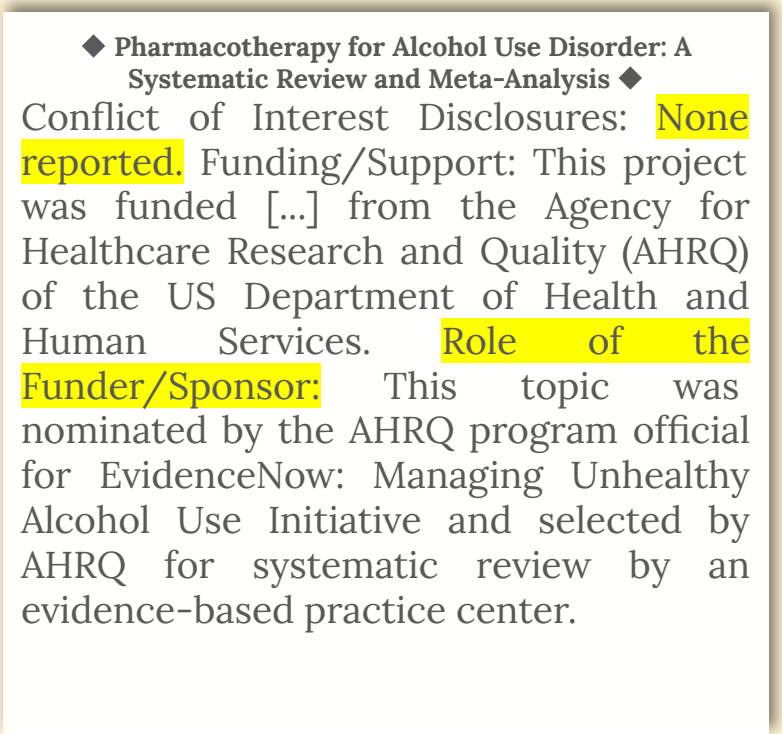

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Conflict of Interest Disclosures: None reported. Funding/Support: This project was funded [...] from the Agency for Healthcare Research and Quality (AHRQ) of the US Department of Health and Human Services. Role of the Funder/Sponsor: This topic was nominated by the AHRQ program official for EvidenceNow: Managing Unhealthy Alcohol Use Initiative and selected by AHRQ for systematic review by an evidence-based practice center.

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AMSTAR 2 - Checklist final

		Sim	Parcial	Não		Sim	Parcial	Não
1.	PICO	✅			9. ★ RoB	✅		
2.	★ Métodos de revisão	✅			10. Fontes de Financiamento	✅		
3.	Delineamentos incluídos	✅			11. ★ Meta-análise (métod.)	✅		
4.	★ Estratégia de busca			❌	12. RoB na Meta-análise	✅		
5.	Seleção em dupla	✅			13. ★ RoB na interpretação			❌
6.	Extração em dupla	✅			14. Heterogeneidade	✅		
7.	★ Estudos excluídos			❌	15. ★ Viés de publicação			❌
8.	Estudos incluídos			❌	16. Conflitos de interesse	✅		

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2.	★ Métodos de revisão	✅			10. Fontes de Financiamento	✅		
3.	Delineamentos incluídos	✅			11. ★ Meta-análise (métod.)	✅		
4.	★ Estratégia de busca			❌	12. RoB na Meta-análise	✅		
5.	Seleção em dupla	✅			13. ★ RoB na interpretação			❌
6.	Extração em dupla	✅			14. Heterogeneidade	✅		
7.	★ Estudos excluídos			❌	15. ★ Viés de publicação			❌
8.	Estudos incluídos			❌	16. Conflitos de interesse	✅		

⚠️ **1 fragilidade não crítica**

🚨 **4 falhas críticas**

AMSTAR

Box 2: Rating overall confidence in the results of the review

- **High**
- *No or one non-critical weakness*: the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest
- **Moderate**
- *More than one non-critical weakness**: the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review
- **Low**
- *One critical flaw with or without non-critical weaknesses*: the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest
- **Critically low**
- *More than one critical flaw with or without non-critical weaknesses*: the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies

*Multiple non-critical weaknesses may diminish confidence in the review and it may be appropriate to move the overall appraisal down from moderate to low confidence.

		Parcial	Não
1.	PICO		
2.	★ Métodos		
3.	Delineamen		
4.	★ Estratégi		
5.	Seleção em		❌
6.	Extração em		
7.	★ Estudos e		❌
8.	Estudos incl		

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2.	★ Métodos de revisão	✅			10. Fontes de Financiamento	✅		
3.	Delineamentos incluídos	✅			11. ★ Meta-análise (métod.)	✅		
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7.	★ Estudos excluídos			❌	15. ★ Viés de publicação			❌
8.	Estudos incluídos			❌	16. Conflitos de interesse	✅		

⚠️ **1 fragilidade não crítica**

🚨 **4 falhas críticas**

Confiança geral da revisão:

Extremamente baixa.

Conclusões

- Risco de viés **remanescente** do estudo anterior (Jonas *et al.*, 2014)
- Diversas fragilidades que podem ter propiciado **viés de seleção**
  - Transparência na lista de estudos relevantes: os critérios de inclusão e exclusão foram aplicados adequadamente?
  - Viés de **publicação** e viés de **idioma**
- RoB apenas ao classificar “força da evidência” das associações
- Seguindo o instrumento de avaliação AMSTAR 2, a Revisão de McPheeters (2023) apresentou falhas críticas e possui uma confiança de evidência **extremamente baixa**.

Obrigado!

joao.tlp@gmail.com