METANÁLISE
META- ANÁLISIS
META-ANALYSIS

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METANÁLISE

META- ANÁLISIS

META-ANALYSIS

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CHECKLISTS FOR REPORTING SYSTEMATIC REVIEWS

The PRISMA Statement

- http://www.prisma-statement.org/
  The Preferred Reporting Items for Systematic Reviews and Meta-Analyses is an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses.
- PRISMA may also be useful for critical appraisal of published systematic reviews, although it is not a quality assessment instrument to gauge the quality of a systematic review.
- PRISMA-P is a 17-item checklist for elements considered essential in protocol for a systematic review or meta-analysis.

MOOSE Guidelines

- Meta-analysis of Observational Studies in Epidemiology checklist contains specifications for reporting of meta-analyses of observational studies in epidemiology.
- It refers to the Newcastle-Ottawa Scale for assessing the quality of non-randomized studies, a method of rating each observational study in your meta-analysis.
- Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA. 2000; 283(15):2008-2012.

https://www.prisma-statement.org/

PRISMA

PRISMA 2020 PRISMA extensions Translations Endorsement

Welcome to the PRISMA website

PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) is a guideline designed to improve the reporting of systematic reviews. PRISMA provides authors with guidance and examples of how to completely report why a systematic review was done, what methods were used, and what results were found. The main PRISMA reporting guideline (PRISMA 2020) primarily provides guidance for the reporting of systematic reviews evaluating the effects of interventions. PRISMA 2020 is complemented by various PRISMA extensions, which provide guidance for the reporting of different types or aspects of systematic reviews and other types of evidence synthesis (e.g. scoping reviews).

Key PRISMA 2020 documents

- Checklist
- Expanded checklist
- Flow diagram
- Statement paper
- Explanation and elaboration paper

PRISMA

The PRISMA 2020 statement: an updated guideline for reporting systematic reviews

Matthew J Page,[1] Joanne E McKenzie,[1] Patrick M Bossuyt,[2] Isabelle Boutron,[3] Tammy C Hoffmann,[4] Cynthia D Mulrow,[5] Larissa Shamseer,[6] Jennifer M Tetzlaff,[7] Elie A Akl,[8] Sue E Brennan,[1] Roger Chou,[9] Julie Glanville,[10] Jeremy M Grimshaw,[11] Asbjørn Hróbjartsson,[12] Manoj M Lalu,[13] Tianjing Li,[14] Elizabeth W Loder,[15] Evan Mayo-Wilson,[16] Steve McDonald,[1] Luke A McGuinness,[17] Lesley A Stewart,[18] James Thomas,[19] Andrea C Tricco,[20] Vivian A Welch,[21] Penny Whiting,[17] David Moher[22]

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http://dx.doi.org/10.1136/bmj.n71

Accepted: 4 January 2021

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement, published in 2009, was designed to help systematic reviewers transparently report why the review was done, what the authors did, and what they found. Over the past decade, advances in systematic review methodology and terminology have necessitated an update to the guideline. The PRISMA 2020 statement replaces the 2009 statement and the revised flow diagrams for original and updated reviews.

Systematic reviews serve many critical roles. They can provide syntheses of the state of knowledge in a field, from which future research priorities can be identified; they can address questions that otherwise could not be answered by individual studies; they can identify problems in primary research that should be rectified in future studies; and they can generate or evaluate theories about how or why phenomena occur. Systematic reviews therefore generate various types of knowledge for different users of reviews (such as patients, healthcare providers, researchers, and policy makers).[1 2] To ensure a systematic review is valuable to users, authors should prepare a transparent, complete

PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews

Matthew J Page,[1] David Moher,[2] Patrick M Bossuyt,[3] Isabelle Boutron,[4] Tammy C Hoffmann,[5] Cynthia D Mulrow,[6] Larissa Shamseer,[7] Jennifer M Tetzlaff,[8] Elie A Akl,[9] Sue E Brennan,[1] Roger Chou,[10] Julie Glanville,[11] Jeremy M Grimshaw,[12] Asbjørn Hróbjartsson,[13] Manoj M Lalu,[14] Tianjing Li,[15] Elizabeth W Loder,[16] Evan Mayo-Wilson,[17] Steve McDonald,[1] Luke A McGuinness,[18] Lesley A Stewart,[19] James Thomas,[20] Andrea C Tricco,[21] Vivian A Welch,[22] Penny Whiting,[18] Joanne E McKenzie[1]

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Additional material is published online only. To view please visit the journal online.

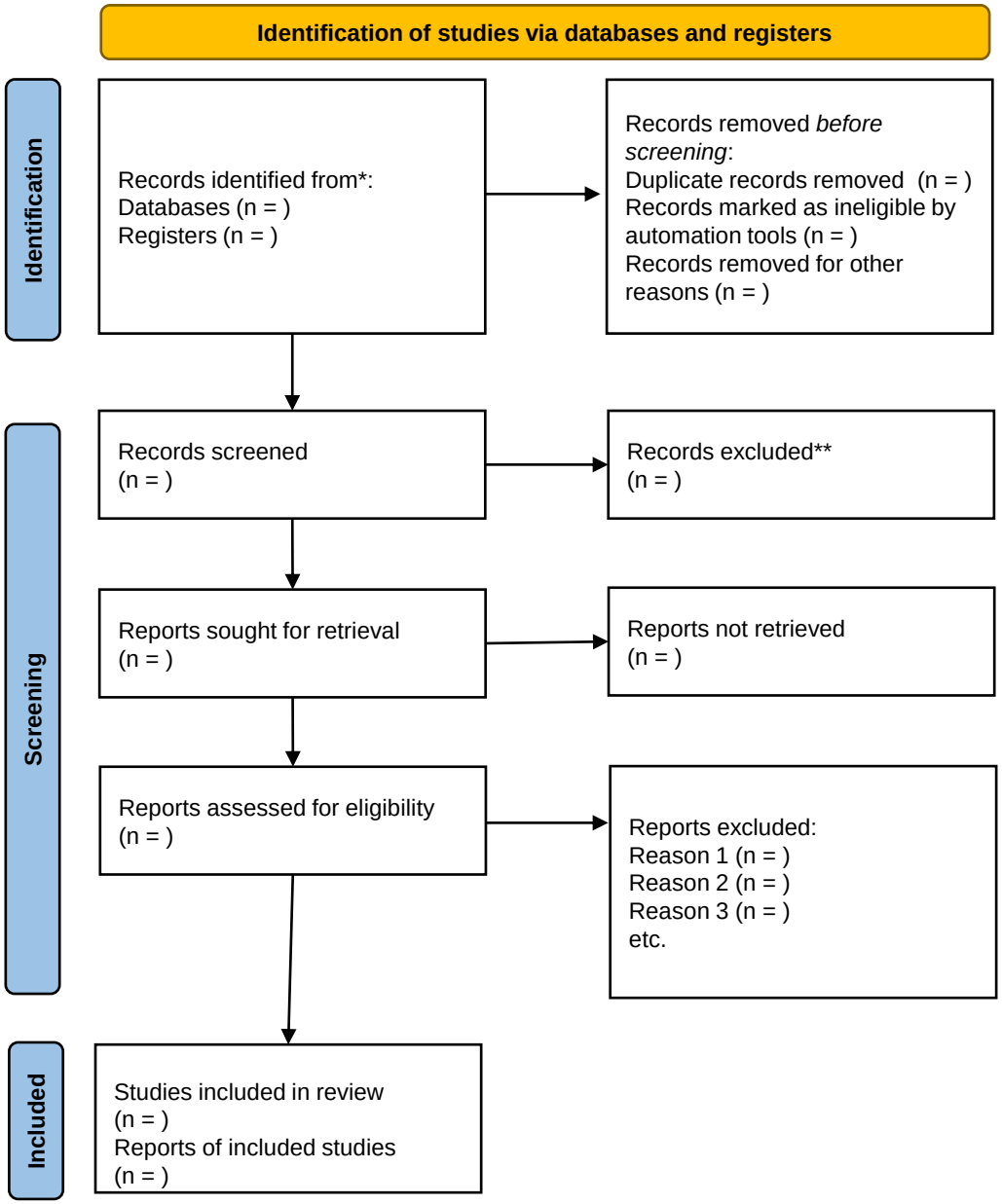
Cite this as: *BMJ* 2021;372:n160
http://dx.doi.org/10.1136/bmj.n160

Accepted: 4 January 2021

The methods and results of systematic reviews should be reported in sufficient detail to allow users to assess the trustworthiness and applicability of the review findings. The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement was developed to facilitate transparent and complete reporting of systematic reviews and has been updated (to PRISMA 2020) to reflect recent advances in systematic review

makers, who would otherwise be confronted by an overwhelming volume of research on which to base their decisions. To allow decision makers to assess the trustworthiness and applicability of review findings, reports of systematic reviews should be transparent and complete. Furthermore, such reporting should allow others to replicate or update reviews. The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement published in 2009 (hereafter referred to as PRISMA 2009)[1-12] was designed to help authors prepare transparent accounts of their reviews, and its recommendations have been widely endorsed and adopted.[13] We have updated the PRISMA 2009 statement (to PRISMA 2020) to ensure currency and relevance and to reflect advances in systematic review methodology and terminology.

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only

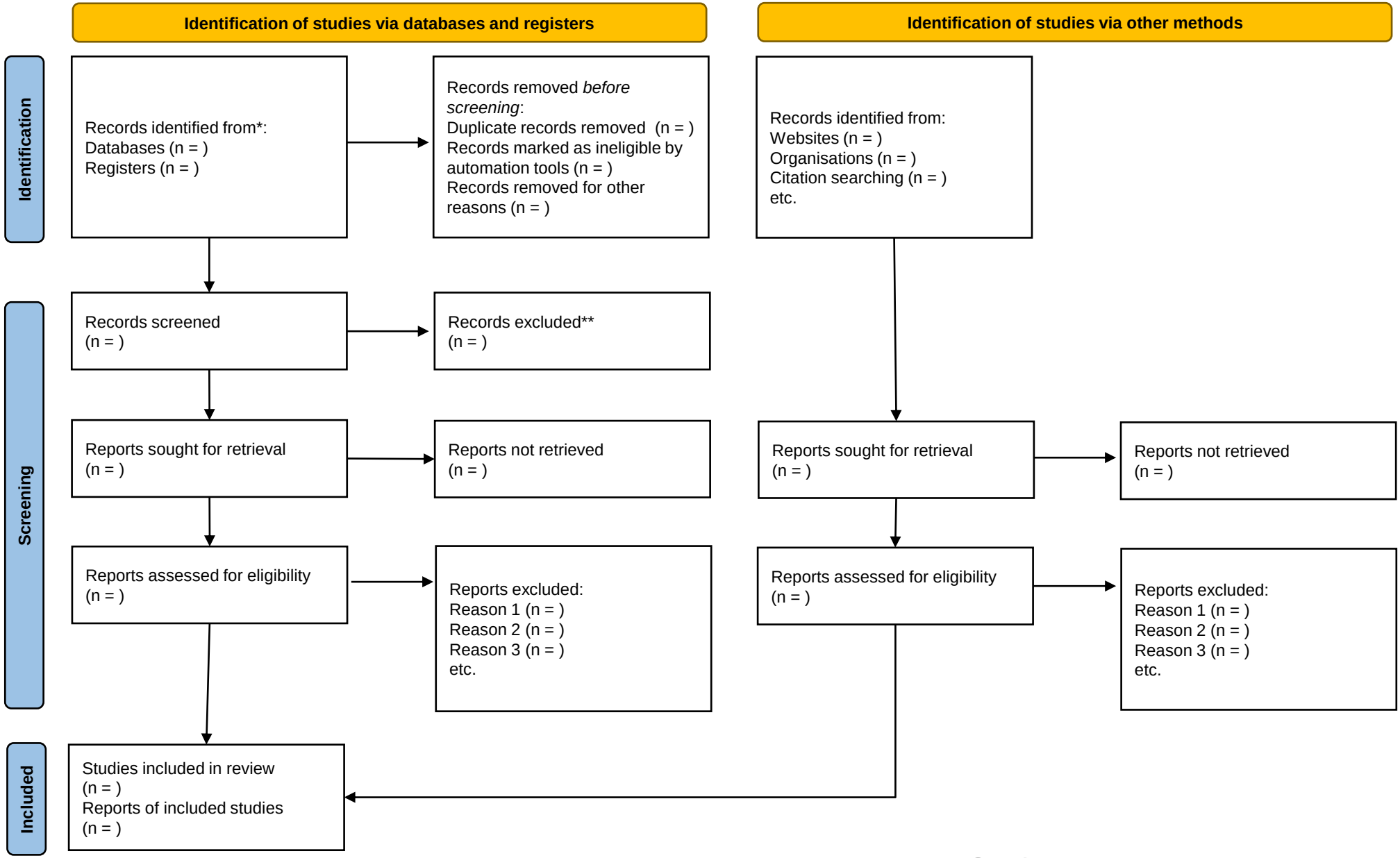


*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources



Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

PRISMA

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	

PRISMA

Section and Topic	Item #	Checklist item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	
Study characteristics	17	Cite each included study and present its characteristics.	
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	
	23b	Discuss any limitations of the evidence included in the review.	
	23c	Discuss any limitations of the review processes used.	
	23d	Discuss implications of the results for practice, policy, and future research.	
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	
Competing interests	26	Declare any competing interests of review authors.	
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

https://www.prisma-statement.org/extensions

PRISMA extensions

Several extensions to PRISMA have been developed to cover aspects of reporting not captured in the main PRISMA statement. These extensions provide reporting guidance for reviews that, for example, address particular review questions (e.g. diagnostic test accuracy), or use particular data sources (e.g. individual participant data). Click on the relevant extension below for more information.

- PRISMA for Abstracts
- PRISMA for Acupuncture
- PRISMA for Chinese Herbal Medicines
- PRISMA for Complex Interventions
- PRISMA-COSMIN for Outcome Measurement Instruments
- PRISMA for Diagnostic Test Accuracy
- PRISMA for EcoEvo
- PRISMA Equity
- PRISMA Harms
- PRISMA Individual Participant Data
- PRISMA for Living Systematic Reviews
- PRISMA Moxibustion
- PRISMA for Network Meta-Analyses
- PRISMA for Protocols
- PRISMA for Scoping Reviews
- PRISMA Search

MOOSE GUIDELINES

Meta-analysis of Observational Studies in Epidemiology

A Proposal for Reporting

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Ingram Olkin, PhD
G. David Williamson, PhD
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David Moher, MSc
Betsy J. Becker, PhD
Theresa Ann Sipe, PhD
Stephen B. Thacker, MD, MSc
for the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) Group

Objective Because of the pressure for timely, informed decisions in public health and clinical practice and the explosion of information in the scientific literature, research results must be synthesized. Meta-analyses are increasingly used to address this problem, and they often evaluate observational studies. A workshop was held in Atlanta, Ga, in April 1997, to examine the reporting of meta-analyses of observational studies and to make recommendations to aid authors, reviewers, editors, and readers.

Participants Twenty-seven participants were selected by a steering committee, based on expertise in clinical practice, trials, statistics, epidemiology, social sciences, and biomedical editing. Deliberations of the workshop were open to other interested scientists. Funding for this activity was provided by the Centers for Disease Control and Prevention.

Evidence We conducted a systematic review of the published literature on the conduct and reporting of meta-analyses in observational studies using MEDLINE, Educational Research Information Center (ERIC), PsycLIT, and the Current Index to Statistics. We also examined reference lists of the 32 studies retrieved and contacted experts in the field. Participants were assigned to small-group discussions on the subjects of bias, searching and abstracting, heterogeneity, study categorization, and statistical methods.

Consensus Process From the material presented at the workshop, the authors developed a checklist summarizing recommendations for reporting meta-analyses of ob-

MOOSE GUIDELINES

Reporting of background should include

- Problem definition
- Hypothesis statement
- Description of study outcome(s)
- Type of exposure or intervention used
- Type of study designs used
- Study population

Reporting of search strategy should include

- Qualifications of searchers (eg, librarians and investigators)
- Search strategy, including time period included in the synthesis and keywords
- Effort to include all available studies, including contact with authors
- Databases and registries searched
- Search software used, name and version, including special features used (eg, explosion)
- Use of hand searching (eg, reference lists of obtained articles)
- List of citations located and those excluded, including justification
- Method of addressing articles published in languages other than English
- Method of handling abstracts and unpublished studies
- Description of any contact with authors

MOOSE GUIDELINES

Reporting of methods should include

- Description of relevance or appropriateness of studies assembled for assessing the hypothes is to be tested
- Rationale for the selection and coding of data (eg, sound clinical principles or convenience)
- Documentation of how data were classified and coded (eg, multiple raters, blinding, and interrater reliability)
- Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)
- Assessment of study quality, including blinding of quality assessors; stratification or regression on possible predictors of study results
- Assessment of heterogeneity
- Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated
- Provision of appropriate tables and graphics

MOOSE GUIDELINES

Reporting of results should include

- Graphic summarizing individual study estimates and overall estimate
- Table giving descriptive information for each study included
- Results of sensitivity testing (eg, subgroup analysis)
- Indication of statistical uncertainty of findings

Reporting of discussion should include

- Quantitative assessment of bias (eg, publication bias)
- Justification for exclusion (eg, exclusion of non–English-language citations)
- Assessment of quality of included studies

Reporting of conclusions should include

- Consideration of alternative explanations for observed results
- Generalization of the conclusions (ie, appropriate for the data presented and within the domainof the literature review)
- Guidelines for future research
- Disclosure of funding source

VANTAGENS DA REVISÃO SISTEMÁTICA
VENTAJAS DE LAS REVISIONES SISTEMÁTICAS
ADVANTAGES OF SYSTEMATIC REVIEW

- Pode antecipar o resultado de grandes ensaios clínicos.
- Pode aumentar a “acurácia” dos resultados.
- Direciona futuros estudos a áreas carentes de evidências.
- Economia de recursos em pesquisa clínica.
- Auxílio a decisões de políticas de saúde.

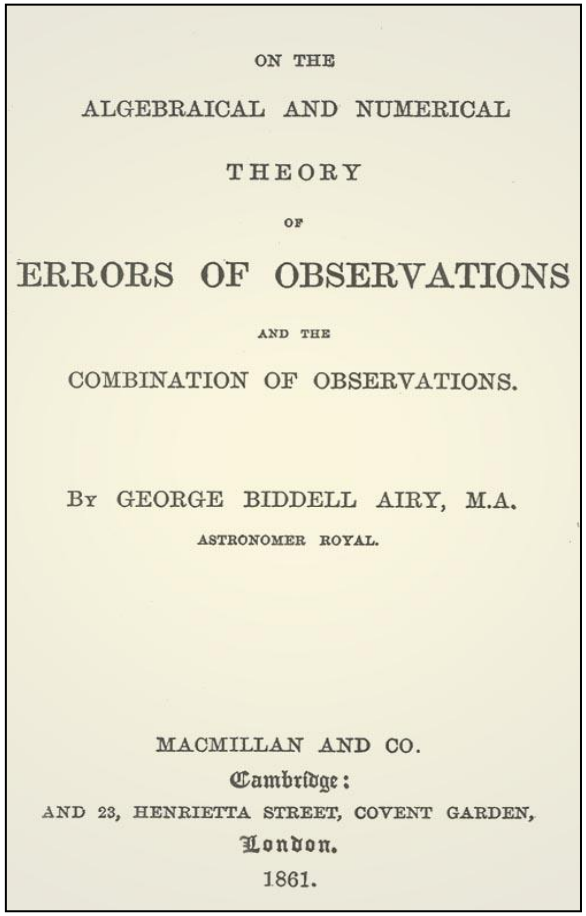


DEFINIÇÕES DE METANÁLISE
DEFINICIONES DE META-ANÁLISIS
DEFINITIONS OF META-ANALYSIS

- Análise estatística que combina ou integra os resultados de diversos ensaios clínicos independentes, considerados “combináveis” pelo especialista (Huque, 1988).
- Uso de técnicas estatísticas que combinam em uma medida resumo os resultados de estudos independentes voltados a uma única questão (Villar, 2001).

ORIGENS DA METANÁLISE
ORÍGENES DE LA META- ANÁLISIS
ORIGINS OF THE META-ANALYSIS

- Aplicações em astronomia
- Em 1861,o astrônomo britânico George Airy, publicou um ‘manual’ para astrônomos no qual ele descrevia os métodos usados para o processo de síntese quantitativa.



ON THE

ALGEBRAICAL AND NUMERICAL

THEORY

OF

ERRORS OF OBSERVATIONS

AND THE

COMBINATION OF OBSERVATIONS.

By GEORGE BIDDELL AIRY, M.A.

ASTRONOMER ROYAL.

MACMILLAN AND CO.

Cambridge:

AND 23, HENRIETTA STREET, COVENT GARDEN,

London.

1861.

ORIGENS DA METANÁLISE
ORÍGENES DE LA META- ANÁLISIS
ORIGINS OF THE META-ANALYSIS

- Pearson K. Report on certain enteric fever inoculation statistics. *BMJ* 1904; 3:1243-6.
- Em 1976, o termo *meta-analysis* aparece pela primeira vez, em um artigo do psicólogo Gene Glass.
- Uso na pesquisa em enfermagem, pesquisa social, educação, medicina...

METANÁLISE DE ENSAIOS CLÍNICOS
META-ANÁLISIS DE ENSAYOS CLÍNICOS
META-ANALYSIS OF CLINICAL TRIALS

- No campo dos ensaios clínicos controlados, um grande salto para a utilização da metanálise foi o depoimento de Archie Cochrane, médico e epidemiologista britânico, em 1979:
- *"Seguramente a maior crítica à nossa profissão é que nós não temos resumos críticos organizados e atualizados periodicamente, por especialidades ou subespecialidades, de todos os ensaios clínicos controlados randomizados relevantes."* .

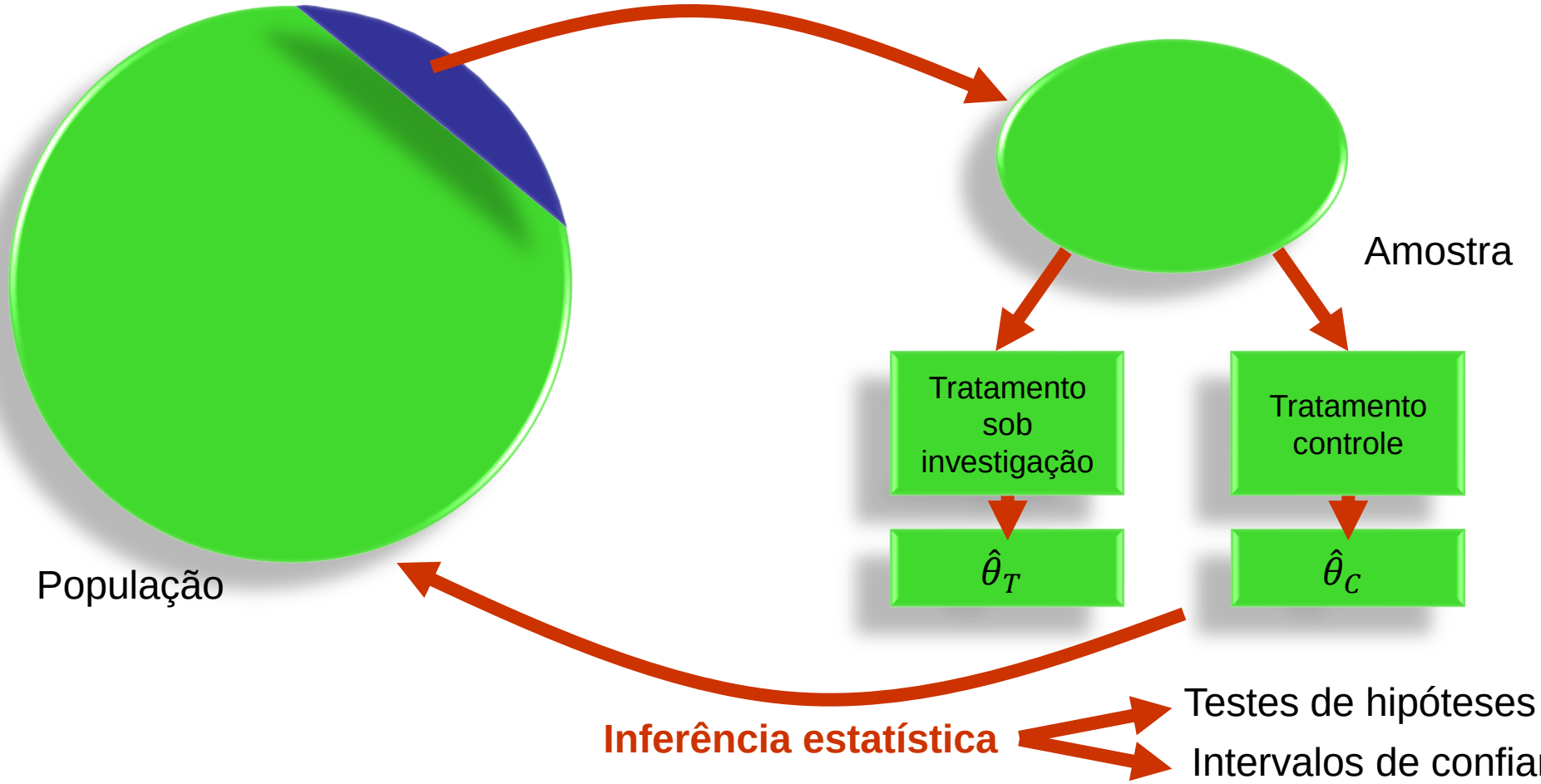
COLABORAÇÃO COCHRANE
COLABORACIÓN COCHRANE
COCHRANE COLLABORATION

THE COCHRANE COLLABORATION®

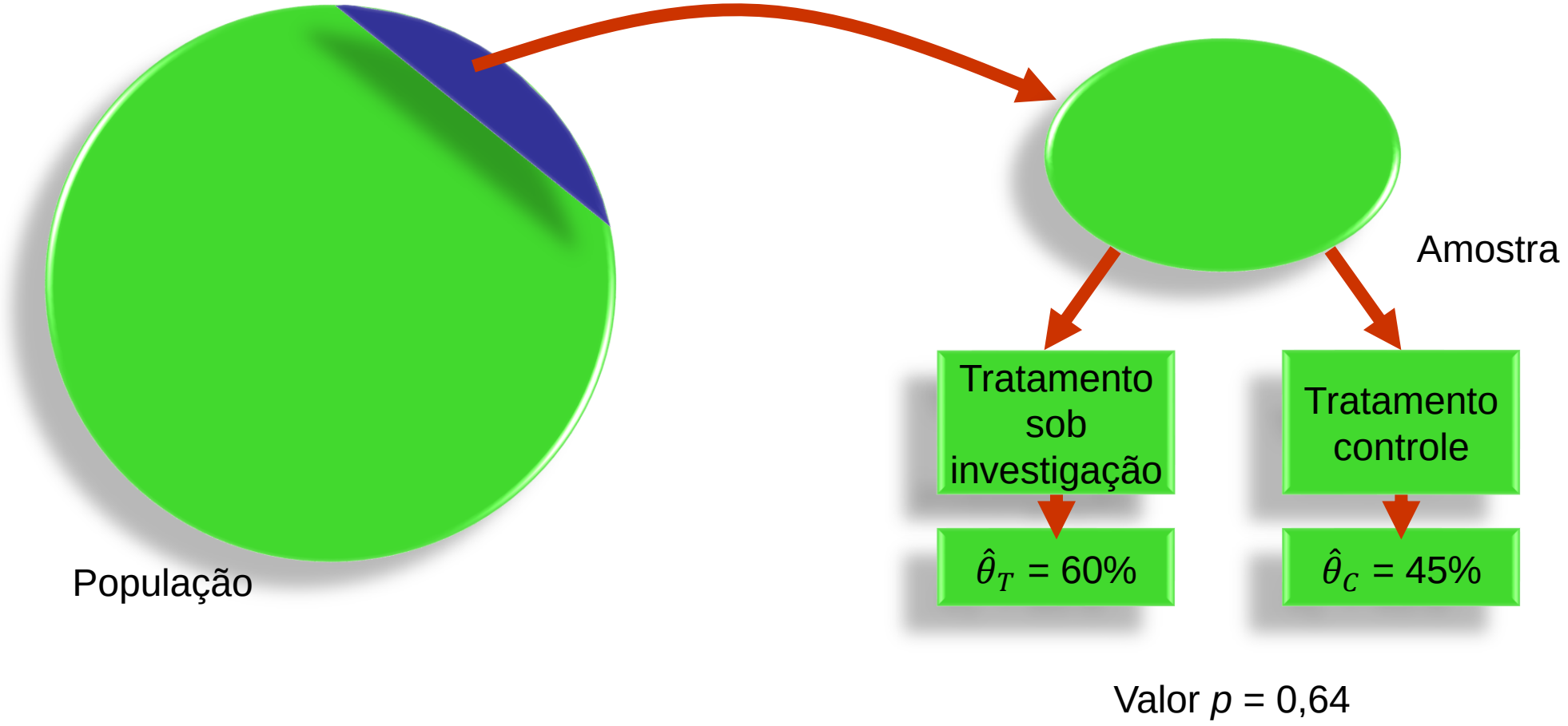
1992: Colaboração Cochrane (http://www.cochrane.org), realiza, auxilia e dissemina revisões sistemáticas de intervenções em saúde.

1997: Centro Cochrane do Brasil (http://brazil.cochrane.org/).

ANÁLISE ESTATÍSTICA – ENSAIOS CLÍNICOS
ANÁLISIS ESTADÍSTICO - ENSAYOS CLÍNICOS
STATISTICAL ANALYSIS - RCT



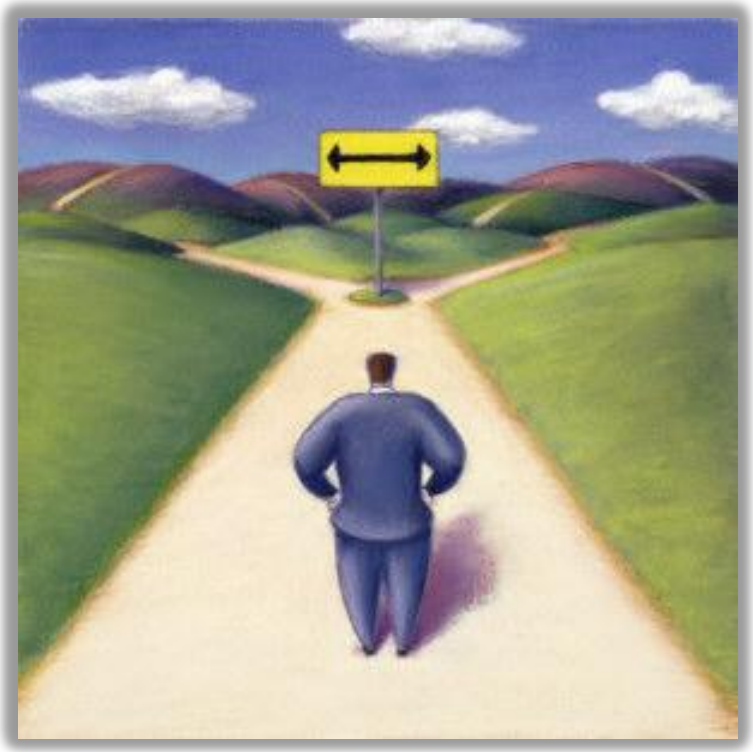
ANÁLISE ESTATÍSTICA – ENSAIOS CLÍNICOS
ANÁLISIS ESTADÍSTICO - ENSAYOS CLÍNICOS
STATISTICAL ANALYSIS - RCT



Valor p = 0,64

UM NOVO OLHAR PARA...
UNA NUEVA MIRADA PARA...
A NEW LOOK AT...

- Hipóteses nula e alternativa
- Erros tipo I e II
- Nível de significância
- Poder
- *P* valor, valor-*p*, *p*-value



O QUE É UM VALOR *P* ?
¿QUÉ ES UN VALOR DE P?
WHAT IS A P-VALUE?

(a) É a probabilidade da hipótese nula de um teste ser verdadeira.

(b) É a probabilidade de um dado resultado, como a diferença entre dois grupos, ter sido obtido de um "acaso".

(c) É a probabilidade da hipótese nula ter sido enganosamente rejeitada.

(d) É a significância de um efeito observado.

(e) É a probabilidade de se obter uma estatística de teste igual ou mais extrema quanto aquela observada em uma amostra, assumindo verdadeira a hipótese nula.

Neyman e Pearson (1933)

1-) Estabelecemos a nossa hipótese, baseada em nossa crença.

A % de respostas (θ_T) do grupo de tratamento é superior à % de respostas (θ_C) do grupo controle/placebo.

2-) Esta hipótese é a hipótese alternativa (H_A)

$$H_A: \theta_T > \theta_C$$

3-) Busco a negação de minha hipótese alternativa, que será a hipótese nula (H_0)

$$H_0: \theta_T \leq \theta_C$$

4-) Tenho a hipótese nula como a verdadeira, e busco em uma amostra evidências favoráveis a esta hipótese.

5-) Se encontro uma "contradição", rejeito H_0 e tenho H_A como a verdadeira.

AUSÊNCIA DE EVIDÊNCIA DE EFEITO
AUSENCIA DE EVIDENCIA DE UN EFECTO
ABSENCE OF EVIDENCE OF TREATMENT EFFECT

- Hipóteses

$$H_0: \theta_T = \theta_C$$
$$H_A: \theta_T \neq \theta_C$$

Rejeito H_0: evidência de efeito de tratamento

Não rejeito H_0: ausência de evidência de efeito de tratamento

Ausência de evidência de efeito de tratamento
≠
Evidência de ausência de efeito de tratamento

Testes de hipóteses

- Hipóteses $H_0: \theta_T = \theta_C$

  $H_A: \theta_T \neq \theta_C$

Rejeito H_0: evidência de efeito de tratamento

Não rejeito H_0: ausência de evidência de efeito de tratamento

Nível de significância:

$\alpha = P(\text{rejeitar } H_0 \mid H_0 \text{ verdadeira})$

$= P(\text{evidência de efeito} \mid \text{tratamento = controle})$

Testes de hipóteses

- Hipóteses $H_0: \theta_T = \theta_C$

  $H_A: \theta_T \neq \theta_C$

Nível de significância:

$\alpha = P(\text{rejeitar } H_0 \mid H_0 \text{ verdadeira})$

$= P(\text{evidência de efeito} \mid \text{tratamento = controle})$

Valor *p*: menor valor que poderíamos ter escolhido para α, de modo que o teste trouxesse uma evidência de efeito de tratamento.

VALORES *P* E TAMANHOS AMOSTRAIS
VALOR DE *P* Y EL TAMAÑO DE LA MUESTRA
P VALUES AND SAMPLE SIZE

- *V*alores *p*: efeito de tamanho amostral
- Quanto maior o tamanho amostral, menor tende a ser o valor *p*
- Quanto menor o tamanho amostral, maior tende a ser o valor *p*

	n	Respostas	*Valor p*
Tratamento	50	12 (24%)	0,20
Controle	50	7 (14%)	

	n	Respostas	*Valor p*
Tratamento	100	24 (24%)	0,07
Controle	100	14 (14%)	

	n	Respostas	*Valor p*
Tratamento	150	36 (24%)	0,03
Controle	150	21 (14%)	



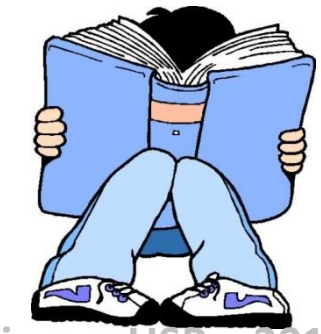
ELEMENTOS ESSENCIAIS DOS TESTES DE HIPÓTESES
ELEMENTOS ESENCIALES DE LAS PRUEBAS DE HIPOTESIS
ESSENTIAL ELEMENTS OF AN HYPOTHESIS TEST

- Erro tipo I: rejeitamos H_0, mas H_0 é verdadeira.
- Erro tipo II: não rejeitamos H_0, mas H_0 é falsa.
- Nível de significância: é a probabilidade de cometermos um erro tipo I, denotada por α e geralmente fixada em 5%.
- Poder (visão "simplista"): é a probabilidade de não cometermos um erro tipo II, denotada por $1 - \beta$, geralmente fixada em 5%, 10% ou 20%.

Leituras

- Altman DG, Bland JM. Absence of evidence is not evidence of absence. BMJ. 1995;311(7003): 485.

- Altman D, Bland JM. Confidence intervals illuminate absence of evidence. BMJ. 2004;328(7446):1016-7.



MEDIDAS DE EFEITO DE TRATAMENTOS
MEDICIONES DEL EFECTO DEL TRATAMIENTO
TREATMENT EFFECT MEASUREMENTS

Absolute risk reduction (*ARR*)

$$ARR = \theta_C - \theta_T$$

Relative risk (*RR*)

$$RR = \frac{\theta_T}{\theta_C}$$

Relative risk reduction (*RRR*)

$$RRR = (1 - RR)100\% = \left(\frac{\theta_C - \theta_T}{\theta_C}\right)100\%$$

Number needed to treat (*NNT*)

$$NNT = \frac{1}{ARR}$$

REDUÇÃO ABSOLUTA DE RISCO
REDUCCIÓN ABSOLUTA DEL RIESGO
ABSOLUTE RISK REDUCTION

	Major cardiovascular event		
	Yes	No	**Total**
Aspirin	477	19,457	**19,934**
Placebo	522	19,420	**19,942**

Ridker et al. (2005), DOI: 10.1056/NEJMoa050613

$$\hat{\theta}_C = \frac{522}{19{,}942} = 0{,}026176 \qquad \hat{\theta}_T = \frac{477}{19{,}934} = 0{,}023929$$

Absolute risk reduction (ARR) $\widehat{ARR} = \hat{\theta}_C - \hat{\theta}_T = 0{,}00225$

RISCO RELATIVO
RIESGO RELATIVO
RELATIVE RISK

	Major cardiovascular event		
	Yes	No	**Total**
Aspirin	477	19,457	**19,934**
Placebo	522	19,420	**19,942**

Ridker et al. (2005), DOI: 10.1056/NEJMoa050613

$$\hat{\theta}_C = \frac{522}{19{,}942} = 0{,}026176 \qquad \hat{\theta}_T = \frac{477}{19{,}934} = 0{,}023929$$

Relative risk (RR) $\quad \widehat{RR} = \frac{\hat{\theta}_T}{\hat{\theta}_C} \approx 0{,}91 \qquad \widehat{RR} = \frac{\hat{\theta}_C}{\hat{\theta}_T} \approx 1{,}09$

REDUÇÃO RELATIVA DE RISCO
REDUCCIÓN RELATIVA DEL RIESGO
RELATIVE RISK REDUCTION

	Major cardiovascular event		
	Yes	No	**Total**
Aspirin	477	19,457	**19,934**
Placebo	522	19,420	**19,942**

Ridker et al. (2005), DOI: 10.1056/NEJMoa050613

$$\hat{\theta}_C = \frac{522}{19{,}942} = 0{,}026176 \qquad \hat{\theta}_T = \frac{477}{19{,}934} = 0{,}023929$$

Relative risk reduction (RRR)

$$\widehat{RRR} = \left(1 - \widehat{RR}\right)100\% = 8.58\%$$

NÚMERO NECESSÁRIO PARA TRATAR
NÚMERO NECESARIO PARA TRATAR
NUMBER NEEDED TO TREAT

	Major cardiovascular event		
	Yes	No	**Total**
Aspirin	477	19,457	**19,934**
Placebo	522	19,420	**19,942**

Ridker et al. (2005), DOI: 10.1056/NEJMoa050613

$$\hat{\theta}_C = \frac{522}{19{,}942} = 0{,}026176 \qquad \hat{\theta}_T = \frac{477}{19{,}934} = 0{,}023929$$

Number needed to treat (NNT)

$$\widehat{NNT} = \frac{1}{\widehat{ARR}} \approx 445$$

ODDS RATIO
RAZÓN DE ODDS
ODDS RATIO

	Major cardiovascular event		
	Yes	No	**Total**
Aspirin	477	19,457	**19,934**
Placebo	522	19,420	**19,942**

Ridker et al. (2005), DOI: 10.1056/NEJMoa050613

$$\hat{\theta}_C = \frac{522}{19{,}942} = 0{,}026176 \qquad \hat{\theta}_T = \frac{477}{19{,}934} = 0{,}023929$$

Relative risk (RR)

$$\widehat{RR} = \frac{\hat{\theta}_C}{\hat{\theta}_T} \approx 1{,}094$$

Odds ratio (OR)

$$\widehat{OR} = \frac{522 \times 19{,}457}{477 \times 19{,}420} \approx 1{,}096$$

RISCO RELATIVO E ODDS RATIO
RIESGO RELATIVO Y RAZÓN DE ODDS
RELATIVE RISK AND ODDS RATIO

	Event of interest		
	Yes	No	**Total**
Treatment	a	b	$a+b$
Control	c	d	$c+d$

Ridker et al. (2005), DOI: 10.1056/NEJMoa050613

$$\hat{\theta}_C = \frac{c}{c+d} \qquad \hat{\theta}_T = \frac{a}{a+b}$$

Relative risk (RR)

$$\widehat{RR} = \frac{a(c+d)}{c(a+b)}$$

Odds ratio (OR)

$$\widehat{OR} = \frac{a \times d}{c \times b}$$

MEDIDAS DE EFEITO DE TRATAMENTOS
MEDICIONES DEL EFECTO DEL TRATAMIENTO
TREATMENT EFFECT MEASUREMENTS

O tratamento proposto traz resultados estatisticamente significantes ($x^2 = 29,8$, $P = 0,0001$) para a redução das taxas de mortalidade devida à doença.

A taxa de mortalidade observada para os indivíduos doentes submetidos ao tratamento proposto equivale a 1/3 da taxa de mortalidade observada para os não tratados.

CONSORT 2010

- CONsolidated Standards of Reporting Trials.
- Conjunto mínimo de recomendações para a apresentação dos resultados de ensaios clínicos controlados aleatorizados.
- *Check-list* de 25 itens
- Fluxograma.
- http://www.consort-statement.org/

CONSORT 2010

RESEARCH METHODS & REPORTING

CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomised trials

David Moher,[1] Sally Hopewell,[2] Kenneth F Schulz,[3] Victor Montori,[4] Peter C Gøtzsche,[5] P J Devereaux,[6] Diana Elbourne,[7] Matthias Egger,[8] Douglas G Altman[2]

[1]Ottawa Methods Centre, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa

Medicine, London

ABSTRACT

Overwhelming evidence shows the quality of reporting of randomised controlled trials (RCTs) is not optimal. Without
aders cannot judge the reliability and validity of trial findings nor extract information for systematic
ological analyses indicate that inadequate reporting and design are associated with biased estimates
h systematic error is seriously damaging to RCTs, which are considered the gold standard for
because of their ability to minimise or avoid bias.
l editors developed the CONSORT (Consolidated Standards of Reporting Trials) statement to improve
f RCTs. It was first published in 1996 and updated in 2001. The statement consists of a checklist
uthors can use for reporting an RCT. Many leading medical journals and major international editorial
he CONSORT statement. The statement facilitates critical appraisal and interpretation of RCTs.
RT revision, it became clear that explanation and elaboration of the principles underlying the
uld help investigators and others to write or appraise trial reports. A CONSORT explanation and
ublished in 2001 alongside the 2001 version of the CONSORT statement.
n January 2007, the CONSORT statement has been further revised and is published as the CONSORT
date improves the wording and clarity of the previous checklist and incorporates recommendations
e only recently received recognition, such as selective outcome reporting bias.
This explanatory and elaboration document—intended to enhance the use, understanding, and dissemination of the
CONSORT statement—has also been extensively revised. It presents the meaning and rationale for each new and updated

> Almost all methods of analysis yield an estimate of the treatment effect, which is a contrast between the outcomes in the comparison groups. Authors should accompany this by a confidence interval for the estimated effect, which indicates a central range of uncertainty for the true treatment effect. The confidence interval may be interpreted as the range of values for the treatment effect that is compatible with the observed data. It is customary to present a 95% confidence interval, which gives the range expected to include the true value in 95 of 100 similar studies.

CONSORT 2025

CONSORT 2025 statement: updated guideline for reporting randomised trials

Sally Hopewell, An-Wen Chan, Gary S Collins, Asbjørn Hróbjartsson, David Moher, Kenneth F Schulz, Ruth Tunn, Rakesh Aggarwal, Michael Berkwits, Jesse A Berlin, Nita Bhandari, Nancy J Butcher, Marion K Campbell, Runcie C W Chidebe, Diana Elbourne, Andrew Farmer, Dean A Fergusson, Robert M Golub, Steven N Goodman, Tammy C Hoffmann, John P A Ioannidis, Brennan C Kahan, Rachel L Knowles, Sarah E Lamb, Steff Lewis, Elizabeth Loder, Martin Offringa, Philippe Ravaud, Dawn P Richards, Frank W Rockhold, David L Schriger, Nandi L Siegfried, Sophie Staniszewska, Rod S Taylor, Lehana Thabane, David Torgerson, Sunita Vohra, Ian R White, Isabelle Boutron*

Well designed and properly executed randomised trials are considered the most reliable evidence on the benefits of healthcare interventions. However, there is overwhelming evidence that the quality of reporting is not optimal. The CONSORT (Consolidated Standards of Reporting Trials) statement was designed to improve the quality of reporting and provides a minimum set of items to be included in a report of a randomised trial. CONSORT was first published in 1996, then updated in 2001 and 2010. Here, we present the updated CONSORT 2025 statement, which aims to account for recent methodological advancements and feedback from end users. We conducted a scoping review of the literature and developed a project-specific database of empirical and theoretical evidence related to CONSORT, to generate a list of potential changes to the checklist. The list was enriched with recommendations provided by the lead authors of existing CONSORT extensions (Harms, Outcomes, Non-pharmacological Treatment), other related reporting guidelines (TIDieR) and recommendations from other sources (eg, personal communications). The list of potential changes to the checklist was assessed in a large, international, online, three-round Delphi survey involving 317 participants and discussed at a two-day online expert consensus meeting of 30 invited international experts. We have made substantive changes to the CONSORT checklist. We added seven new checklist items, revised three items, deleted one item, and integrated several items from key CONSORT extensions. We also restructured the CONSORT checklist, with a new section on open science. The CONSORT 2025 statement consists of a 30-item checklist of essential items that should be included when reporting the results of a randomised trial and a diagram for documenting the flow of participants through the trial. To facilitate implementation of CONSORT 2025, we have also developed an expanded version of the CONSORT 2025 checklist, with bullet points

Lancet 2025; 405: 1633–40

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Oxford Clinical Trials Research Unit, Centre for Statistics in Medicine, University of Oxford, Oxford UK (Prof S Hopewell DPhil, R Tunn DPhil); Department of Medicine, Women's College Research Institute, University of Toronto, Toronto, ON, Canada (Prof A-W Chan MD DPhil); UK EQUATOR Centre, Centre for Statistics in Medicine, University of Oxford, Oxford, UK (Prof G S Collins PhD); Centre for Evidence-Based Medicine

Lancet 2025; 405: 1633–40
https://doi.org/10.1016/S0140-6736(25)00672-5

CONSORT 2025

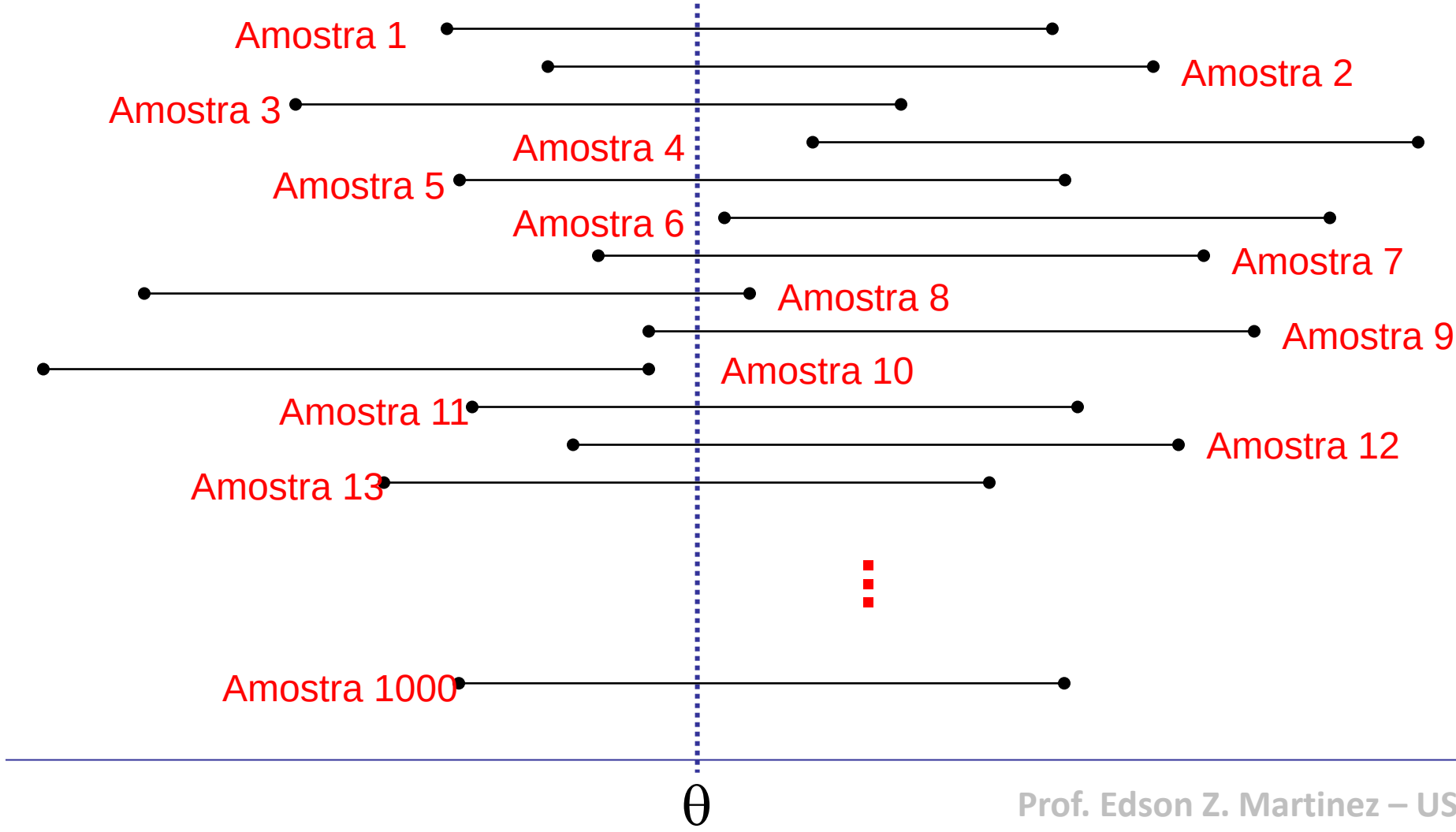
CONSORT 2025 statement: updated guideline for reporting randomised trials

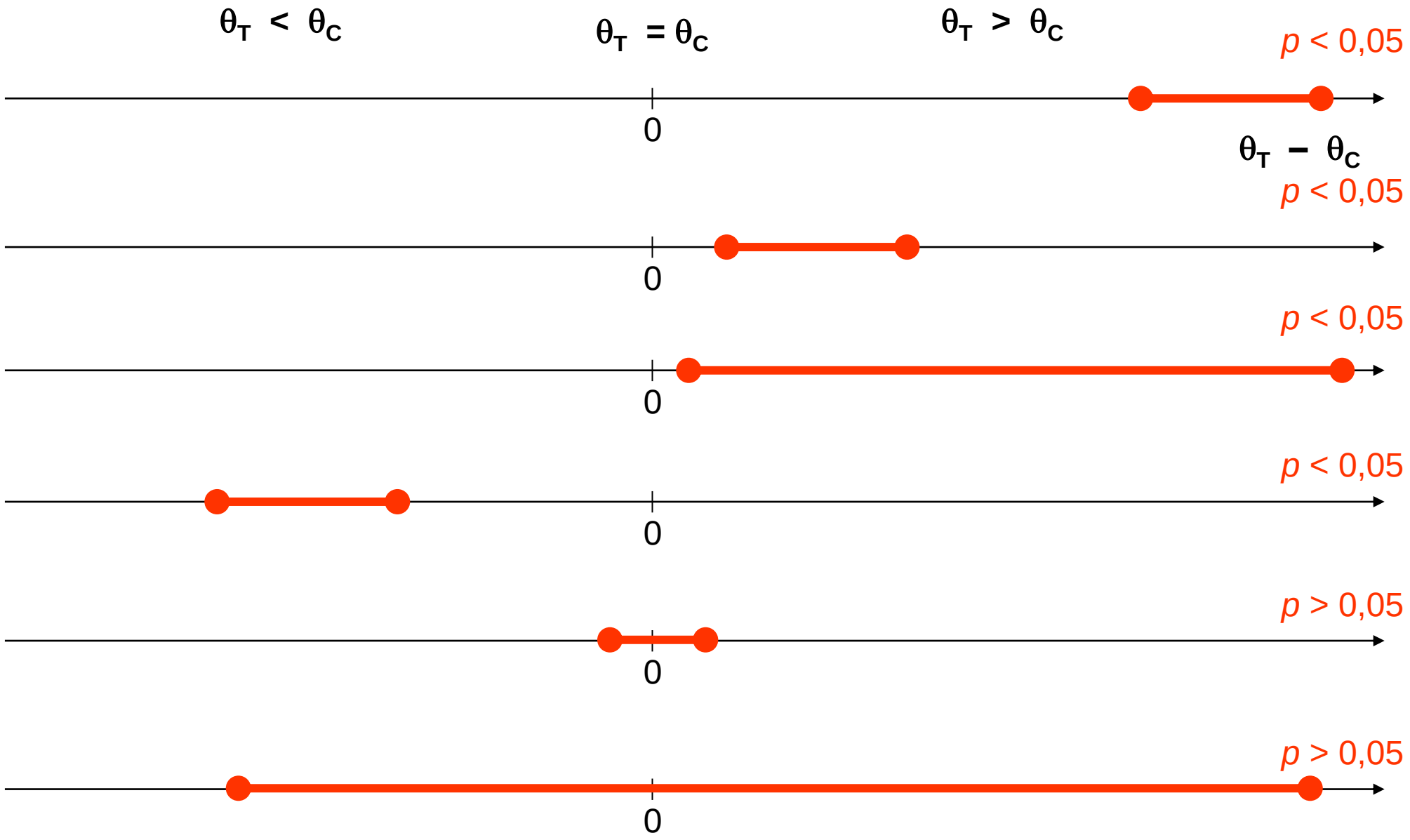
Sally Hopewell, An-Wen Chan, Gary S Collins, Asbjørn Hróbjartsson, David Moher, Kenneth F Schulz, Ruth Tunn, Rakesh Aggarwal, Michael Berkwits, Jesse A Berlin, Nita Bhandari, Nancy J Butcher, Marion K Campbell,Runcie C W Chidebe, Diana Elbourne, Andrew Farmer, Dean A Fergusson, Robert M Golub, Steven N Goodman, Tammy C Hoffmann, John P A Ioannidis, Brennan C Kahan, Rachel L Knowles, Sarah E Lamb, Steff Lewis, Elizabeth Loder, Martin Offringa, Philippe Ravaud, Dawn P Richards, Frank W Rockhold, David L Schriger,*

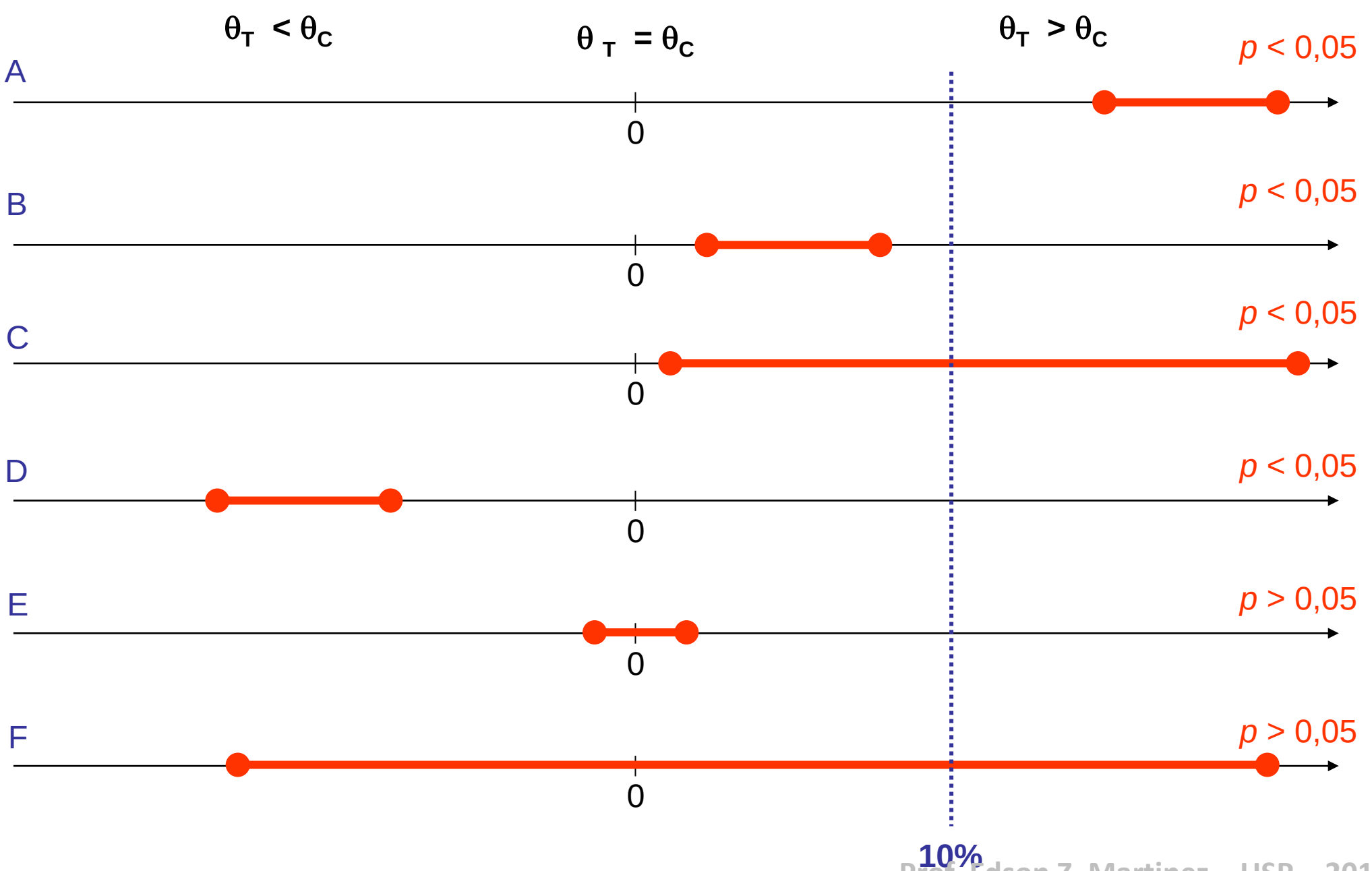
Statistical methods	21a	Statistical methods used to compare groups for primary and secondary outcomes, including harms	• Statistical methods for each analysis:
			  ○ Main analysis methods for statistical comparison
			  ○ Any deviation from the statistical analysis plan
			  ○ Distinction between prespecified and post-hoc analyses
			  ○ Effect measure (e.g., absolute risk) with confidence intervals
			  ○ Statistical significance level
			• For Bayesian analysis: choices of priors, computational choices, details of any modelling, effect measure with credible intervals
			• For adjusted analyses (if applicable):
			  ○ Rationale for adjusted analyses
			  ○ Whether adjusted analyses were pre-specified or post hoc
			  ○ Choice of covariates adjusted for
			  ○ Statistical methods (including how continuous covariates were handled)
			• Methods to account for multiplicity, if applicable
			• Software used for analyses

	21b	Definition of who is included in each analysis (e.g., all randomised participants), and in which group	• Who was included in the primary and other analyses (e.g., all randomised participants with either observed or imputed outcome data): ○ Any exclusions due to missing data or other reasons • Trial group in which participants were analysed (e.g., as-randomised)

Interpretação frequentista: se retirássemos da população um número grande de amostras tamanho *n*, 95% destas amostras iriam gerar intervalos de confiança que contém o parâmetro (populacional).

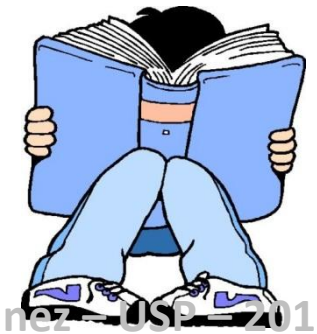



θT < θC
θT = θC
θT > θC
p < 0,05
0
θT − θC
p < 0,05
0
p < 0,05
0
p < 0,05
0
p > 0,05
0
p > 0,05
0



Leituras

- Turk DC. "Statistical significance and clinical significance are not synonyms!". *Clin J Pain*. 2000;16(3):185-7.
- Houle TT, Stump DA. Statistical significance versus clinical significance. *Semin Cardiothorac Vasc Anesth*. 2008;12(1):5-6.
- Braitman LE. Confidence intervals assess both clinical significance and statistical significance. *Ann Intern Med*. 1991; 114(6):515-7.

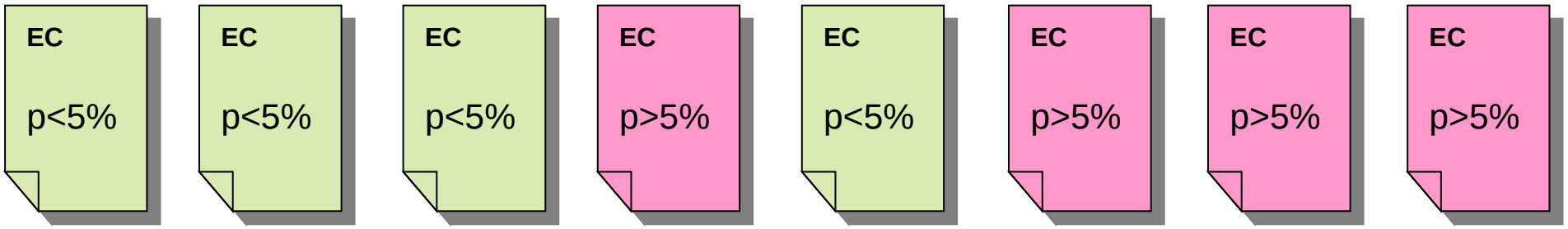




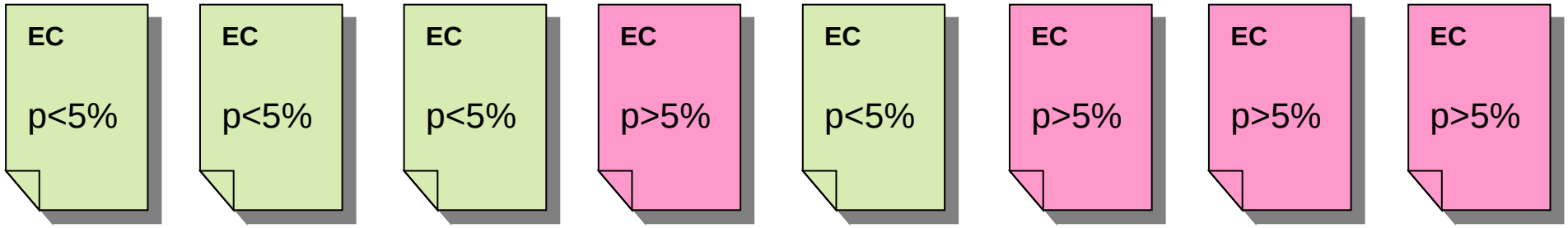
RECOMENDAÇÕES
RECOMENDACIONES
ADVICES

- Os valores *p*, se empregados, devem ser utilizados como complementos às medidas de tamanho de efeito de tratamento, que por sua vez, devem ser acompanhadas de seus intervalos de confiança.
- Evitar o rótulo “estatisticamente significante”, privilegiar a “significância clínica”.
- As relações entre tamanho amostral e evidência devem ser adequadamente exploradas.

VIÉS DE PUBLICAÇÃO
SESGO DE PUBLICACIÓN
PUBLICATION BIAS

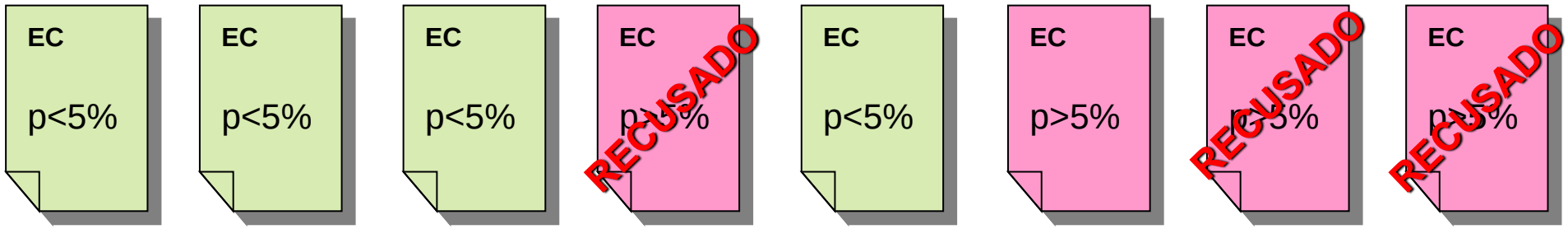


VIÉS DE PUBLICAÇÃO
SESGO DE PUBLICACIÓN
PUBLICATION BIAS



Fato: muitas revistas tendem a privilegiar os artigos com $p < 0,05$ quando tomam decisões de aceitá-los ou não para publicação.

VIÉS DE PUBLICAÇÃO
SESGO DE PUBLICACIÓN
PUBLICATION BIAS



Fato: muitas revistas tendem a privilegiar os artigos com $p < 0,05$ quando tomam decisões de aceitá-los ou não para publicação.

GRÁFICO DO FUNIL
GRÁFICO DEL EMBUDO
FUNNEL PLOT

Funnel plots - scatter plots in which the treatment effects estimated from individual studies on the horizontal axis are plotted against a measure of study precision on the vertical axis - have been proposed as a means of detecting publication bias in meta-analysis (Sterne and Egger, 2001).

Sterne, J. A., Egger, M. (2001). *Funnel plots for detecting bias in meta-analysis. Journal of Clinical Epidemiology, 54(10), 1046–1055.* doi:10.1016/s0895-4356(01)00377-8

GRÁFICO DO FUNIL
GRÁFICO DEL EMBUDO
FUNNEL PLOT

- Mortality results from 16 trials of intravenous magnesium in acute myocardial infarction (Sterne and Egger, 2001).

		Magnesium		Control	
Study	year	Deaths	Total no. of patients	Deaths	Total no. of patients
Morton	1984	1	40	2	36
Rasmussen	1986	9	135	23	135
Smith	1986	2	200	7	200
Abraham	1987	1	48	1	46
Feldstedt	1988	10	150	8	148
Schechter	1989	1	59	9	56
Ceremzynski	1989	1	25	3	23
Bertschat	1989	0	22	1	21
Singh	1990	6	76	11	75
Pereira	1990	1	27	7	27
Schechter	1991	2	89	12	80
Golf	1991	5	23	13	33
Thogersen	1991	4	130	8	122
LIMIT-2	1992	90	1159	118	1157
Schechter	1995	4	107	17	108
ISIS-4	1995	2216	29011	2103	29039



GRÁFICO DO FUNIL
GRÁFICO DEL EMBUDO
FUNNEL PLOT

```
> library(metafor)

> Dados <- read.csv2("https://codeberg.org/edsonzmartinez/Metanalise/raw/branch/main/Sterne_and_Egger.csv")

          study year   d1    n1   d0    n0
1        Morton 1984    1    40    2    36
2     Rasmussen 1986    9   135   23   135
3         Smith 1986    2   200    7   200
4       Abraham 1987    1    48    1    46
5     Feldstedt 1988   10   150    8   148
6     Schechter 1989    1    59    9    56
7   Ceremzynski 1989    1    25    3    23
8     Bertschat 1989    0    22    1    21
9         Singh 1990    6    76   11    75
10      Pereira 1990    1    27    7    27
11    Schechter 1991    2    89   12    80
12         Golf 1991    5    23   13    33
13    Thogersen 1991    4   130    8   122
14      LIMIT-2 1992   90  1159  118  1157
15    Schechter 1995    4   107   17   108
16       ISIS-4 1995 2216 29011 2103 29039

> meta <- rma.mh(ai=d1, bi=n1-d1, ci=d0, di=n0-d0, data=dados, measure="OR")
```



GRÁFICO DO FUNIL
GRÁFICO DEL EMBUDO
FUNNEL PLOT

```
> meta

Fixed-Effects Model (k = 16)

Test for Heterogeneity:
Q(df = 15) = 47.1401, p-val < .0001

Model Results (log scale):

estimate      se    zval    pval    ci.lb   ci.ub
  0.0061  0.0304  0.2004  0.8412  -0.0534  0.0656

Model Results (OR scale):

estimate   ci.lb   ci.ub
  1.0061  0.9480  1.0678

Cochran-Mantel-Haenszel Test:    CMH =  0.0343, df = 1,  p-val = 0.8530
Tarone's Test for Heterogeneity: X^2 = 56.2087, df = 15, p-val < 0.0001
```

GRÁFICO DO FUNIL
GRÁFICO DEL EMBUDO
FUNNEL PLOT

```
> meta <-rma.mh(ai=d1,
                bi=n1-d1,
                ci=d0,
                di=n0-d0,
                data=dados,
                measure="OR",
 slab=paste(study, year,
                     sep=", "))
> forest(meta)
> mtext("95%CI",side=3,at=10,
                       line=-1)
```

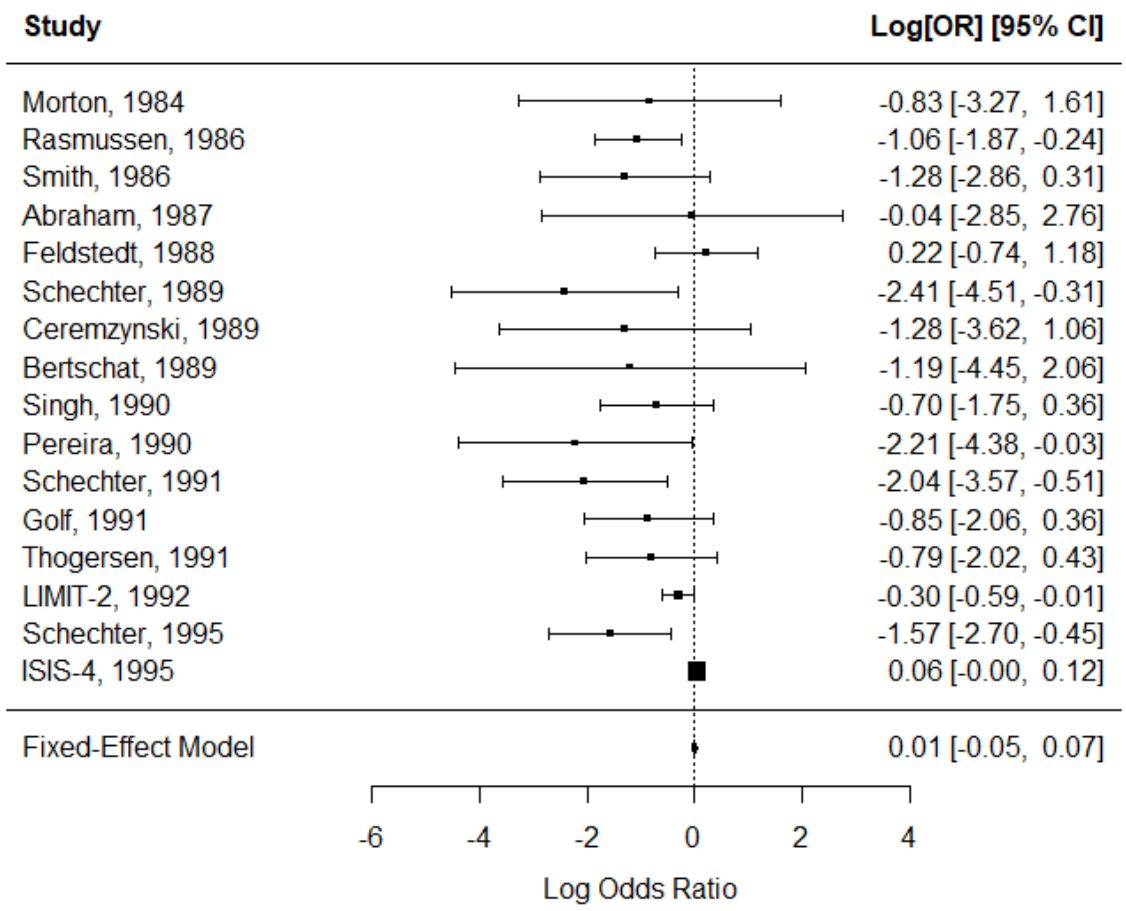


GRÁFICO DO FUNIL
GRÁFICO DEL EMBUDO
FUNNEL PLOT

```
> funnel(meta)
```

- Asymmetry in funnel plots may indicate publication bias in meta-analysis
- In the absence of bias the graph resembles a symmetrical inverted funnel because the treatment effect estimates from smaller studies scatter more widely at the bottom of the graph, with the spread narrowing with increasing precision among larger studies.

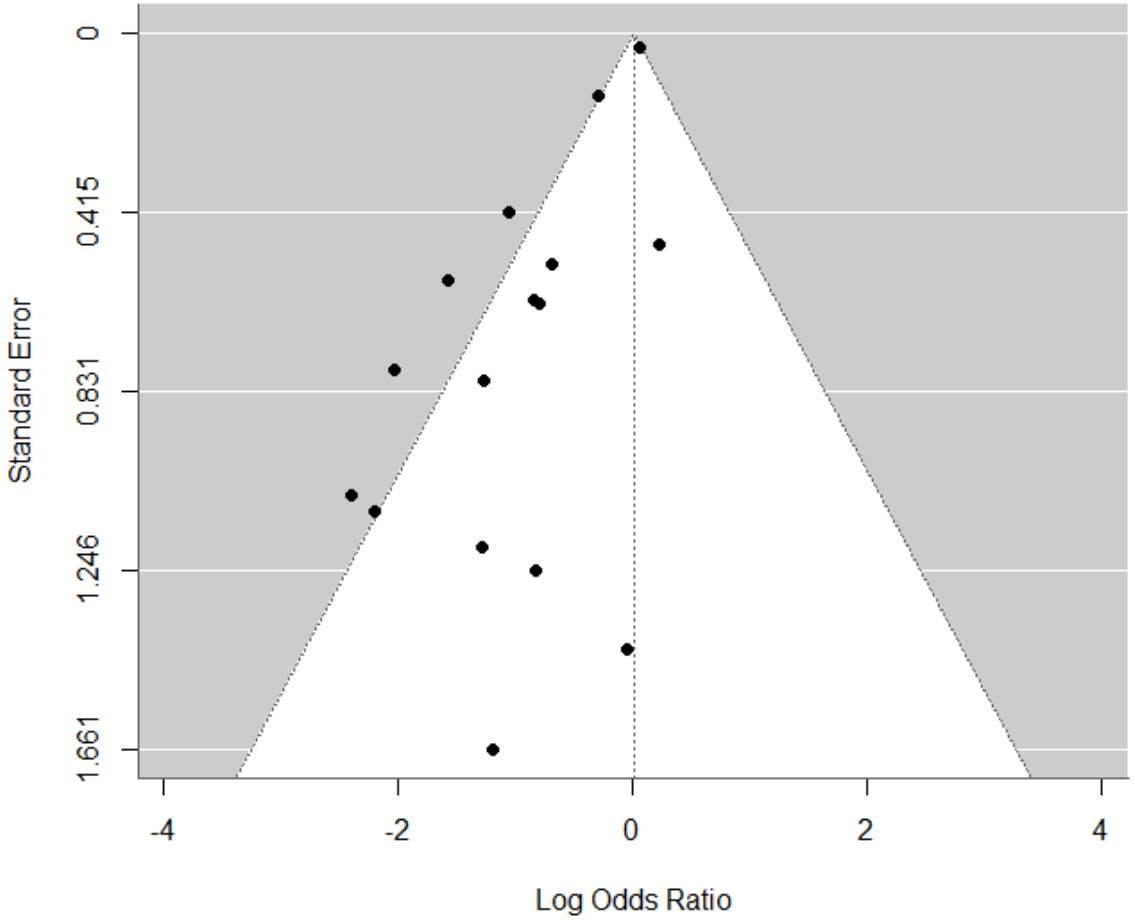
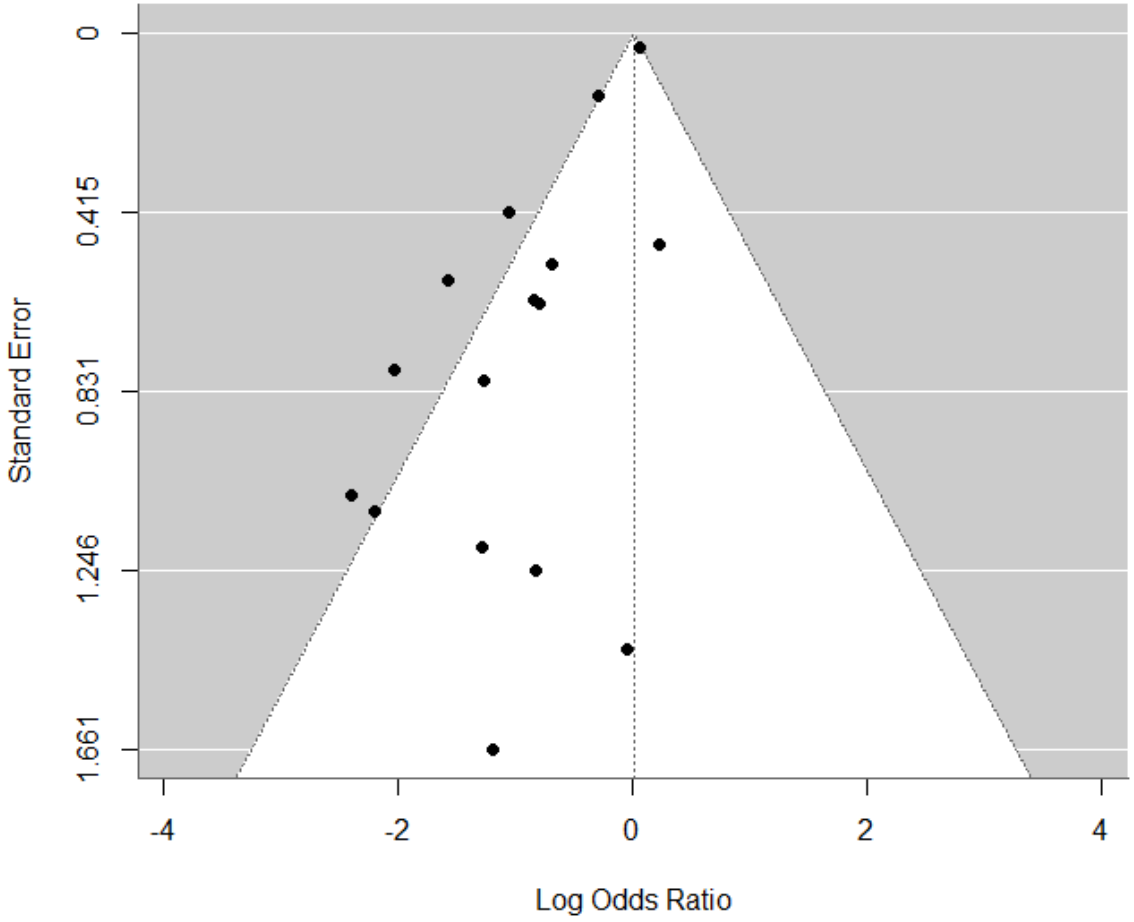


GRÁFICO DO FUNIL
GRÁFICO DEL EMBUDO
FUNNEL PLOT

- The largest studies have the smallest standard errors, so to place the largest trials at the top of the graph, the axis has to be inverted (standard error 0 at the top). The diagonal lines show the expected 95% confidence intervals around the summary estimate, i.e. [summary effect estimate – (1.96 SE)] and [summary effect estimate + (1.96 SE)] for each SE on the vertical axis. They indicate the extent of between-trial heterogeneity: in the absence of heterogeneity 95% of the trials should lie within the funnel defined by these straight lines.



GRÁF
GRÁF
FUNN

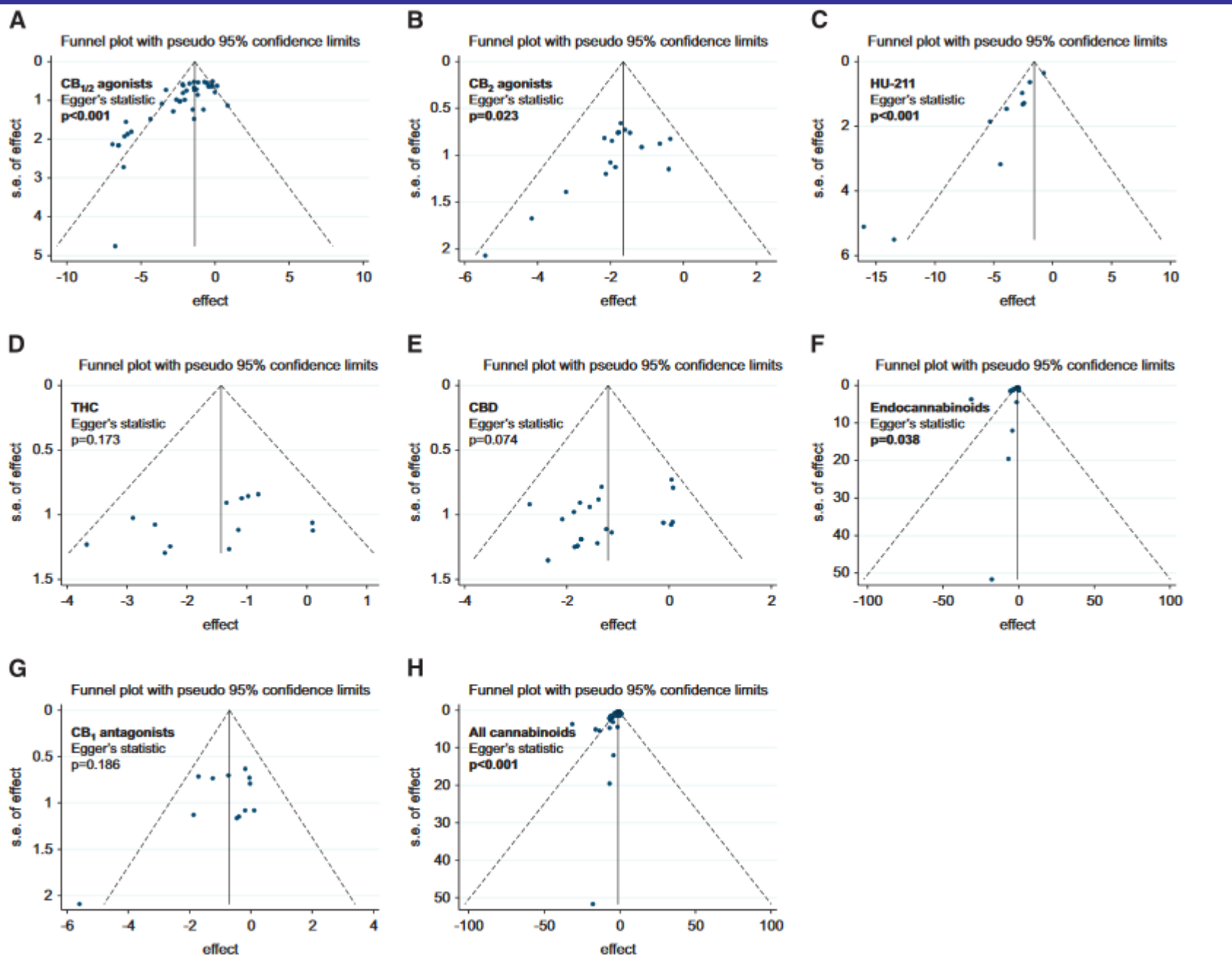


Figure 5. Funnel plots for all studies (**A**) and each cannabinoid (CB) subgroup (**B**–**H**) evaluating publication bias. Standard error of the standardized mean difference (SE (SMD), y axes) for each study is plotted against its effect size (SMD, horizontal axes)). CBD, cannabidiol; THC, Δ^9-Tetrahydrocannabinol.

England, T. J., Hind, W. H., Rasid, N. A., & O'sullivan, S. E. (2015). Cannabinoids in experimental stroke: a systematic review and meta-analysis. Journal of Cerebral Blood Flow & Metabolism, 35(3), 348-358. doi:10.1038/jcbfm.2014.218

METANÁLISE

META- ANÁLISIS

META-ANALYSIS

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