Como elaborar uma metanálise?

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METANÁLISE

Revisão sistemática

Análise quantitativa (metanálise)

- 1. Buscar literatura
- 2. Avaliar a metodologia e extrair as informações
- 3. Descrição estatística e combinação dos efeitos
- 4. Diagnóstico e apresentação dos resultados

1

Literatura. Onde buscar? Como buscar?

Onde buscar?

Scopus











Por que consultar em +1 banco de dados?

↑ chance de extrair registros relevantes↓ variabilidade da indexação dos bancos de dados

Como buscar?

Estratégia	Descrição	Exemplo	
Truncagem	Inclui palavras com um mesmo radical	depress*	
Wildcards	Endereça variações na ortografia	analy?e	
Restrição de campos	Restringe a busca a campos como Abstract, Título	TITLE-ABS-KEY() [ti], [au]	
Frases	Inclui termos que aparecem próximos (" ") ou frase exata ({ })	"zika dengue" {oxidative stress}	
Booleanos	Restringem, expandem ou excluem um termo de busca	gato AND rato gato OR cachorro gato NOT rato	

Por que utilizar estratégias de busca?

↑ recall | ↑ precision

Gerenciamento









- Encontrar duplicatas
- Triagem



DEMONSTRAÇÃO

2

Extração de informações e Qualidade metodológica dos estudos

Eligibilidade

Table 5.3 Examples of Published Conceptual Breakdowns

Acronym	Concepts	Usage	
PICO/PECO (European Food Safety Authority 2010; Lefebvre et al. 2011)	Population, intervention or exposure, comparator, outcomes	Reviews evaluating the effects of an intervention or exposure	
PIT (de Vet et al. 2008; European Food Safety Authority 2010)	Population, index test, target condition	Reviews of test accuracy	
PO (European Food Safety Authority 2010)	Population, outcome	Reviews that aim to answer descriptive questions: questions about prevalence, occurrence, consumption, and incidence	
PICOT-D (Elias et al. 2015)	Population, intervention/exposure, comparator, outcomes + time + data	Reviews with measures of outcomes of interest, for example, blood glucose tests or hba1c levels	
PICOCs (Petticrew and Roberts 2006)	Population, intervention or exposure, comparator, outcomes + context + study design	Reviews in the social sciences	
ECLIPSE (Wildridge and Bell 2002)	Expectation, client group, location, impact, professionals, service	Reviews of service change	
SPIDER (Cooke et al. 2012)	Sample, phenomenon of interest, design, evaluation, research type	Reviews of qualitative and mixed method studies	
SPICE (Booth 2006)	Setting, perspective, intervention, comparison, evaluation	Reviews in which perspectives of the intervention need to be captured and the impact of the evaluation is important	

P: depressão maior

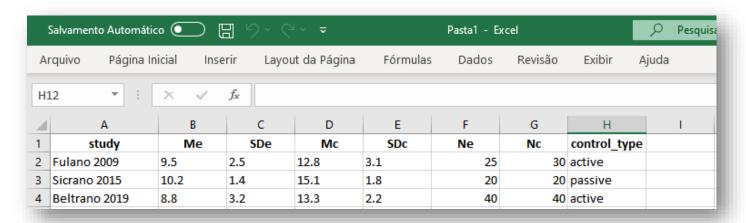
I: terapia cognitivo-comportamental

C: controle saudável

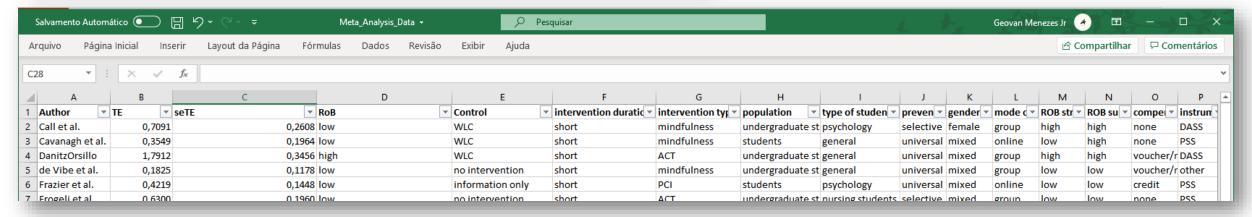
O: escala HAM-D

S: ensaios clínicos randomizados controlados

Extração das informações



Média, SD, N...



Tamanho de efeito, erro padrão do TE...

Escalas de avaliação da qualidade

Table A1 Jadad scale for reporting randomized controlled trials.

Item	Maximum points	Description	Examples
Randomization	2	1 point if randomization is mentioned	"The patients were randomly assigned into two groups"
		1 additional point if the method of randomization is appropriate	The randomization was accomplished using a computer- generated random number list, coin toss or well-shuffled envelopes
		Deduct 1 point if the method of randomization is inappropriate (minimum 0)	The group assignment was accomplished by alternate assignment, by birthday, hospital number or day of the week
Blinding	2	1 point if blinding is mentioned	"The trial was conducted in a double-blind fashion"
		1 additional point if the method of blinding is appropriate	Use of identical tablets or injectables, identical vials Use of tablets with similar looks but different taste
		Deduct 1 point if the method of blinding is inappropriate (minimum 0)	Incomplete masking
An account of all patients	1	The fate of all patients in the trial is known. If there are no data the reason is stated	"There were 40 patients randomized but the data from 1 patient in the treatment group and 2 in the control were eliminated because of a break in protocol"

Halpern, S. H., & Douglas, M. J. (2005). Appendix: Jadad scale for reporting randomized controlled trials. *Evidence-based Obstetric Anesthesia*. *Oxford, UK: Blackwell Publishing Ltd*, 237-8.

Review > J Evid Based Med. 2015 Feb;8(1):2-10. doi: 10.1111/jebm.12141.

The methodological quality assessment tools for preclinical and clinical studies, systematic review and meta-analysis, and clinical practice guideline: a systematic review

Xiantao Zeng ¹, Yonggang Zhang, Joey S W Kwong, Chao Zhang, Sheng Li, Feng Sun, Yuming Niu, Liang Du

Affiliations + expand

PMID: 25594108 DOI: 10.1111/jebm.12141



DESCRIÇÃO E ANÁLISE ESTATÍSTICA

Tamanho de efeito Modelos fixos e aleatórios Heterogeneidade

Tamanho de efeito

Magnitude e direção de relacionamento entre duas variáveis ou de diferença entre duas populações

Considerações

- Invariante
- Interpretável
- Calculado com base em medidas geralmente relatadas
- Boas propriedades técnicas

Tamanho de efeito

Famílias

- Comparação de médias
 - Diferença não padronizada das médias (D)
 - Diferença padronizada das médias (d, g)
- Correlação
 - Coeficiente de correlação (r)
- Desfechos binários (categóricos)
 - Risco relativo (RR)
 - Odds ratio (OR) ou razão de chances

Diferença não padronizada (D)

	Grupos independentes	Grupos pareados
Diferença	$D = \bar{Y_1} - \bar{Y_2}$	$D = \bar{Y}_1 - \bar{Y}_2$
Variância	$V_D = \frac{S_1^2}{n_1} + \frac{S_2^2}{n_2}$	$V_D = \frac{S_{Diff}^2}{n}$
	$V_D = \frac{n_1 + n_2}{n_1 n_2} S_{Pooled}^2$	$V_D = \frac{S_{Diff}^2}{n}$
Erro padrão	$SE_D = \sqrt{V_D}$	$SE_D = \sqrt{V_D}$

•
$$S_{Pooled}^2 = \frac{(n_1 - 1)S_1^2 + (n_2 - 1)S_2^2}{n_1 + n_2 - 2}$$

•
$$S_{Diff} = \sqrt{S_1^2 + S_2^2 - 2 \times r \times S_1^2 \times S_2^2}$$
 ou $S_{Diff} = \sqrt{2 \times S_{Pooled}^2 (1 - r)}$

Diferença padronizada d de Cohen

Grupos independentes

Grupos pareados

$$d = \frac{Y_1 - Y_2}{S_{Pooled}}, v = \frac{n_1 + n_2}{n_1 n_2} + \frac{d^2}{2(n_1 + n_2)}$$

$$d = \left(\frac{\overline{Y}_1 - \overline{Y}_2}{S_{Difference}}\right) \sqrt{2(1-r)}, v = \left(\frac{1}{n} + \frac{d^2}{2n}\right) 2(1-r)$$

Diferença padronizada de Cohen

Table 11.1 Computing d, Independent Groups

Reported	Computation of Needed Quantities	
$\overline{Y}_1, \ \overline{Y}_2 \ S_{Pooled}, \ n_I, \ n_2$	$d = \frac{Y_1 - Y_2}{S_{Pooled}}, v = \frac{n_1 + n_2}{n_1 n_2} + \frac{d^2}{2(n_1 + n_2)}$	
t, n_1, n_2	$d = t\sqrt{\frac{n_1 + n_2}{n_1 n_2}}, v = \frac{n_1 + n_2}{n_1 n_2} + \frac{d^2}{2(n_1 + n_2)}$	
F, n_1, n_2	$d = \pm \sqrt{\frac{F(n_1 + n_2)}{n_1 n_2}}, v = \frac{n_1 + n_2}{n_1 n_2} + \frac{d^2}{2(n_1 + n_2)}$	
p (one-tailed), n_1 , n_2	$d = \pm t^{-1}(p)\sqrt{\frac{n_1 + n_2}{n_1 n_2}}, v = \frac{n_1 + n_2}{n_1 n_2} + \frac{d^2}{2(n_1 + n_2)}$	
$p(\text{two-tailed}), n_1, n_2$	$d = \pm t^{-1} \left(\frac{p}{2}\right) \sqrt{\frac{n_1 + n_2}{n_1 n_2}}, v = \frac{n_1 + n_2}{n_1 n_2} + \frac{d^2}{2(n_1 + n_2)}$	

Diferença padronizada de Cohen

Table 11.2 Computing *d*, Matched Groups

Reported	Computation of Needed Quantities
\overline{Y}_1 , \overline{Y}_2 $S_{\text{Difference}}$, r , n (number of pairs)	$d = \left(\frac{\overline{Y}_1 - \overline{Y}_2}{S_{Difference}}\right) \sqrt{2(1-r)}, v = \left(\frac{1}{n} + \frac{d^2}{2n}\right) 2(1-r)$
t (from paired t-test), r, n	$d = t\sqrt{\frac{2(1-r)}{n}}, v = \left(\frac{1}{n} + \frac{d^2}{2n}\right)2(1-r)$
F (from repeated measures ANOVA), r , n	$d = \pm \sqrt{\frac{2F(1-r)}{n}}, v = \left(\frac{1}{n} + \frac{d^2}{2n}\right) 2(1-r)$
p (one-tailed), r , n	$d = \pm t^{-1}(p)\sqrt{\frac{2(1-r)}{n}}, v = \left(\frac{1}{n} + \frac{d^2}{2n}\right)2(1-r)$
p (two-tailed), r , n	$d = \pm t^{-1} \left(\frac{p}{2}\right) \sqrt{\frac{2(1-r)}{n}}, v = \left(\frac{1}{n} + \frac{d^2}{2n}\right) 2(1-r)$

Diferença padronizada g de Hedges

$$J(df) = 1 - \frac{3}{4df - 1}$$

$$g = J(df)d$$

$$V_g = \left[J(df)\right]^2 V_d$$

Correlação

r, r_{pbis}

Table 11.5 Computing r

Reported	Computation of Needed Quantities
r, n	$v_r = \frac{(1-r^2)^2}{n-1}, z = 0.5 \ln\left(\frac{1+r}{1-r}\right), v_z = \frac{1}{n-3}$
<i>t</i> , <i>n</i>	$r = \pm \sqrt{\frac{t^2}{t^2 + n - 2}}, v_r = \frac{(1 - r^2)^2}{n - 1}, z = 0.5 \ln\left(\frac{1 + r}{1 - r}\right), v_z = \frac{1}{n - 3}$
t, r	$n = t^2 \left(\frac{1-r^2}{r^2}\right) - 2$, $v_r = \frac{(1-r^2)^2}{n-1}$, $z = 0.5 \ln\left(\frac{1+r}{1-r}\right)$, $v_z = \frac{1}{n-3}$
p(one-tailed), r	$n = \left[t^{-1}(p)\right]^2 \left(\frac{1-r^2}{r^2}\right) - 2, v_r = \frac{(1-r^2)^2}{n-1}, z = 0.5 \ln\left(\frac{1+r}{1-r}\right), v_z = \frac{1}{n-3}$
p(two-tailed), r	$n = \left[t^{-1}\left(\frac{p}{2}\right)\right]^2 \left(\frac{1-r^2}{r^2}\right) - 2, v_r = \frac{(1-r^2)^2}{n-1}, z = 0.5\ln\left(\frac{1+r}{1-r}\right), v_z = \frac{1}{n-3}$

Risco Relativo

_	Evento	Sem evento	Total
Grupo 1	А	В	A + B (n ₁)
Grupo 2	С	D	C + D (n ₂)

$$p_1 = A/n_1$$
 $p_2 = C/n_2$

$$RR = p_1/p_2 \rightarrow ln(RR)$$

Risco Relativo

Table 11.9 Computing Risk Ratio, Independent Groups in Prospective Study

Reported	Computation of Needed Quantities	
A, B, C, D	$RR = \frac{A/n_1}{C/n_2}, lnRR = \ln(RR)V_{lnRR} = \frac{1}{A} - \frac{1}{n_1} + \frac{1}{C} - \frac{1}{n_2}$	
p_1, p_2, n_1, n_2	$RR = \frac{P_1}{P_2} \ln RR = \ln(RR) V_{lnRR} = \frac{1 - P_1}{n_1 P_1} + \frac{1 - P_2}{n_2 P_2}$	
$RR, UD_{RD}, LL_{RD}, Cl_{Level}$	$RR = \text{Given } \ln RR = \ln(RR) \ LL_{lnRR} = \ln(LL_{RR}) \ UL_{lnRR} = \ln(\text{UL}_{RR})$	
	$V_{lnRR} = \left(\frac{UL_{lnRR} - LL_{lnRR}}{2Z}\right)^2 \text{ or } \left(\frac{UL_{lnRR} - lnRR}{Z}\right)^2 \text{ or } \left(\frac{lnRR - LL_{lnRR}}{Z}\right)^2$	

Razão de chances (odds ratio)

_	Evento	Sem evento	Total
Grupo 1	Α	В	A + B (n ₁)
Grupo 2	С	D	C + D (n ₂)

$$p_1 = A/n_1$$
 $p_2 = C/n_2$

Odds ratio

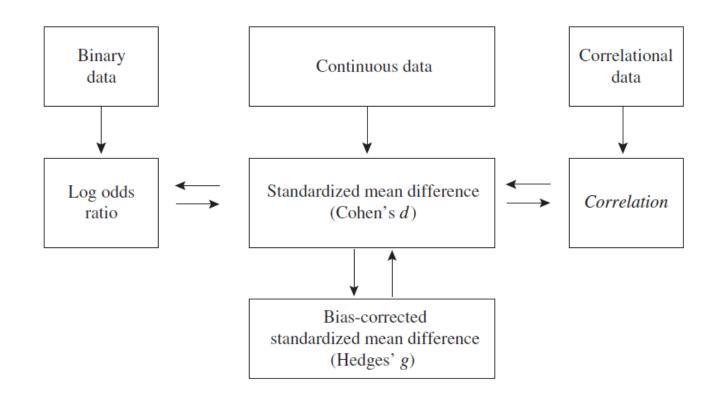
OR =
$$\frac{p_1/(1-p_1)}{p_2/(1-p_2)} \to \ln(OR)$$

Razão de chances (odds ratio)

Table 11.10 Computing Odds Ratio, Independent Groups in a Prospective Study

Reported	Computation of Needed Quantities
A, B, C, D	$OR = \frac{AD}{BC}, lnOR = \ln(OR) V_{lnOR} = \frac{1}{A} + \frac{1}{B} + \frac{1}{C} + \frac{1}{D}$
p_1, p_2, n_1, n_2	$OR = \frac{P_1 \left(1 - P_2 \right)}{P_2 \left(1 - P_1 \right)} lnOR = \ln \left(OR \right) V_{lnOR} = \frac{1}{n_1 P_1} + \frac{1}{n_1 \left(1 - P_1 \right)} + \frac{1}{n_2 P_2} + \frac{1}{n_2 \left(1 - P_2 \right)}$
$OR, UD_{OR}, LL_{OR}, Cl_{Level}$	$OR = \text{Given } lnOR = \ln(OR) \ LL_{lnOR} = \ln(LL_{OR}) \ UL_{\ln OR} = \ln(\text{UL}_{OR})$
	$V_{lnOR} = \left(\frac{UL_{lnOR} - LL_{lnOR}}{2Z}\right)^2 \text{ or } \left(\frac{UL_{lnOR} - lnOR}{Z}\right)^2 \text{ or } \left(\frac{lnOR - LL_{lnOR}}{Z}\right)^2$

Conversão entre tamanhos de efeito



Conversão entre tamanhos de efeito

$$d = \frac{\ln(OR)\sqrt{3}}{\pi} \Leftrightarrow \ln(OR) = \frac{\pi d}{\sqrt{3}} \qquad V_d = \frac{3V_{ln(OR)}}{\pi^2} \qquad V_{ln(OR)} = \frac{\pi^2 v_d}{3}$$

$$V_d = \frac{3V_{ln(OR)}}{\pi^2}$$

$$V_{ln(OR)} = \frac{\pi^2 v_d}{3}$$

$$d = \frac{2r}{\sqrt{1 - r^2}} \iff r = \frac{d}{\sqrt{d^2 + a}} \qquad v_d = \frac{4v_r}{(1 - r^2)^3} \qquad v_r = \frac{a^2 v_d}{(d^2 + a)^3}$$

$$a = \frac{(n_1 + n_2)^2}{n_1 n_2}$$

$$v_d = \frac{4v_r}{(1 - r^2)^3}$$

$$v_r = \frac{a^2 v_d}{(d^2 + a)^3}$$

General Article

CONTRASTS AND CORRELATIONS IN EFFECT-SIZE ESTIMATION

By Ralph L. Rosnow, 1 Robert Rosenthal, 2 and Donald B. Rubin 3

E se alguma medida não for relatada no artigo?







Commentary | Open Access | Published: 09 July 2014

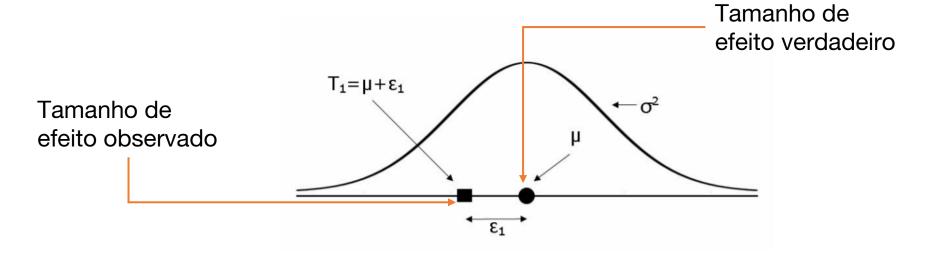
Systematic review automation technologies

Guy Tsafnat [™], Paul Glasziou, Miew Keen Choong, Adam Dunn, Filippo Galgani & Enrico Coiera

Systematic Reviews 3, Article number: 74 (2014) Cite this article

COMBINANDO TE

Combinando TE



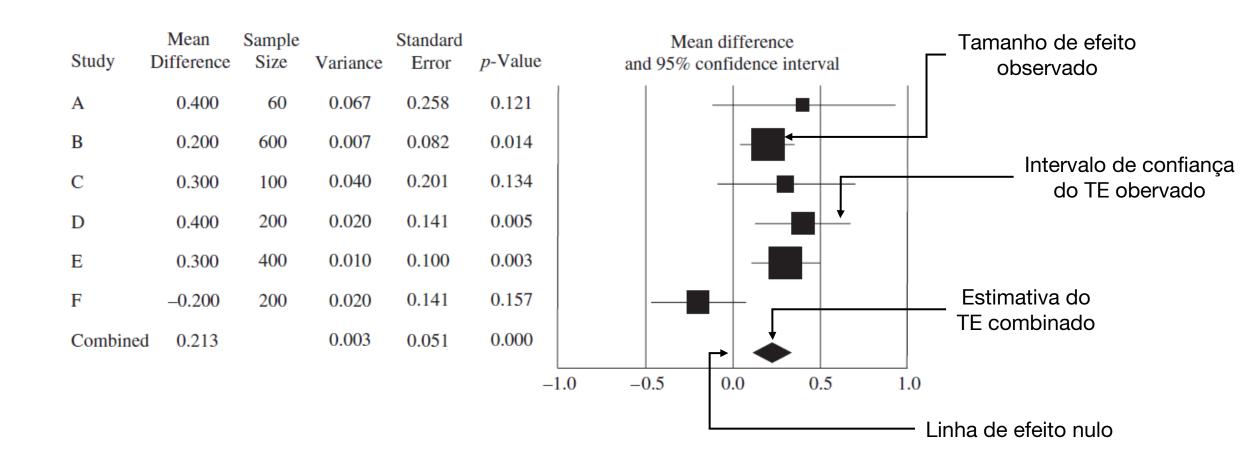
$$\overline{T}_{\bullet} = \frac{\sum_{i=1}^{k} w_i T_i}{\sum_{i=1}^{k} w_i} \qquad w_i = \frac{1}{v_i} \qquad v_{\bullet} = \frac{1}{\sum_{i=1}^{k} (1/v_i)}$$

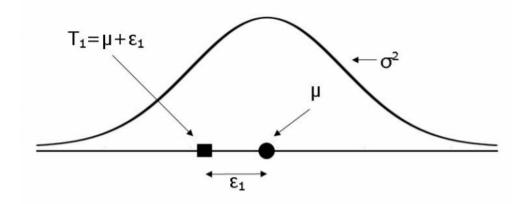
$$\overline{T}_{\bullet} - C_{\alpha} \le \theta \le \overline{T}_{\bullet} + C_{\alpha}$$
 $Z = \frac{|\overline{T}_{\bullet}|}{\sqrt{v_{\bullet}}}$

[0.56, 1.23]

[-0.15, 0.35]

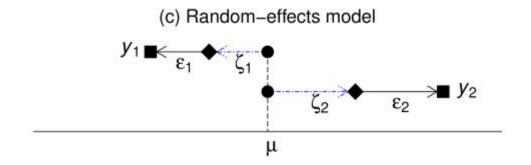
Forest plot



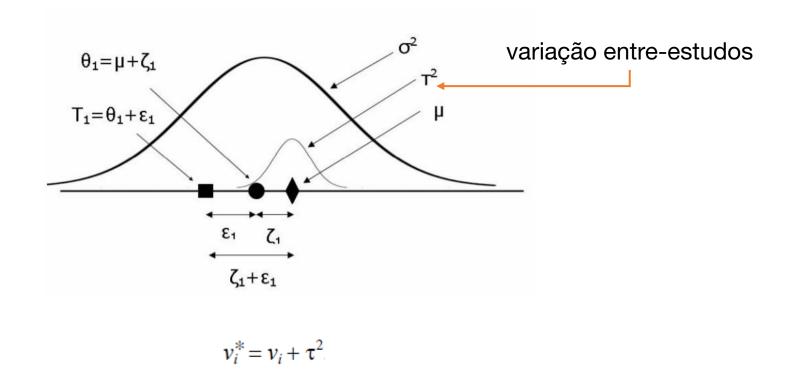


$$\overline{T}_{\bullet} = \frac{\sum_{i=1}^{k} w_i T_i}{\sum_{i=1}^{k} w_i} \qquad w_i = \frac{1}{v_i} \qquad v_{\bullet} = \frac{1}{\sum_{i=1}^{k} (1/v_i)} \qquad \overline{T}_{\bullet} - C_{\alpha} \le \theta \le \overline{T}_{\bullet} + C_{\alpha} \qquad Z = \frac{|\overline{T}_{\bullet}|}{\sqrt{v_{\bullet}}}$$

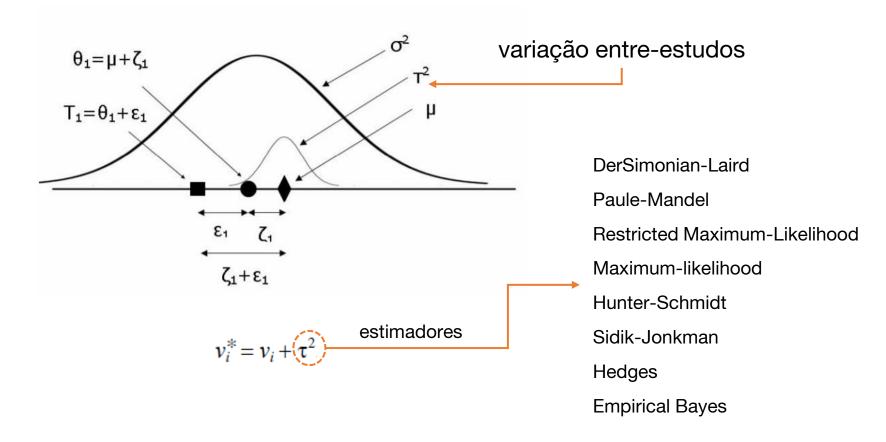
Modelo fixo: os estudos compartilham o mesmo tamanho de efeito verdadeiro



Modelo aleatório: existe uma distribuição de tamanhos de efeito verdadeiros

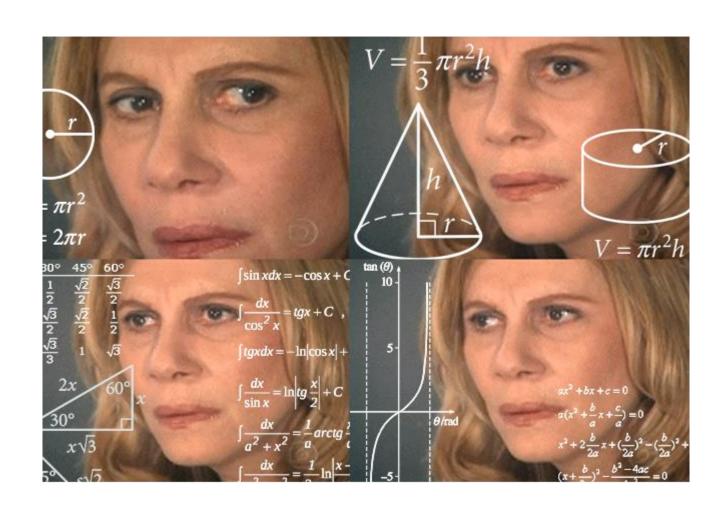


Modelo aleatório: existe uma distribuição de tamanhos de efeito verdadeiros



Modelo aleatório: existe uma distribuição de tamanhos de efeito verdadeiros

QUAL ESCOLHER?



Heterogeneidade

- Metodológica desenho experimental (randomização, cegamento, perda...)
- Clínica características dos participantes e da intervenção
- Desfecho instrumento de mensuração

Q de Cochran

$$Q = \sum_{i=1}^{k} \left[\left(T_{i} - \overline{T}_{\bullet} \right)^{2} / v_{i} \right] = \sum_{i=1}^{k} w_{i} \left(T_{i} - \overline{T}_{\bullet} \right)^{2}$$

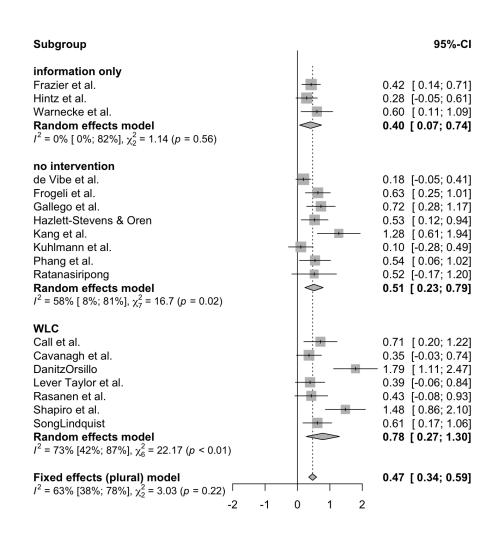
$$\chi^{2}; p < 0,10$$

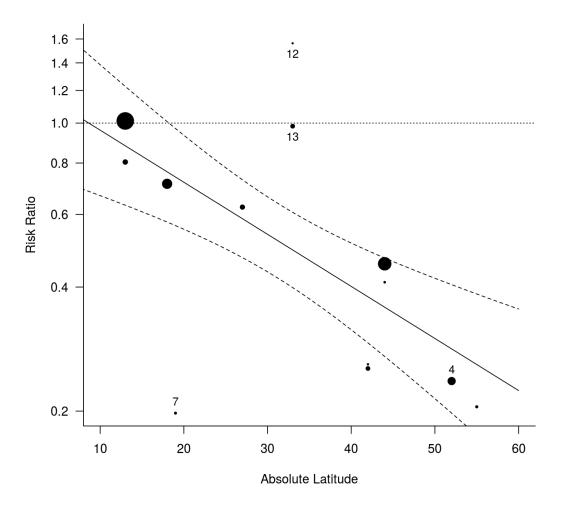
Proporção de variação que não é devido ao erro de amostragem

$$I^2 = 100\% * \left(\frac{Q - (k - 1)}{Q}\right)$$

- 25% pouca heterogeneidade
- 50% heterogeneidade moderada
- 75% alta heterogeneidade

Análise de subgrupo e metarregressão





4

DIAGNÓSTICO E APRESENTAÇÃO DOS RESULTADOS

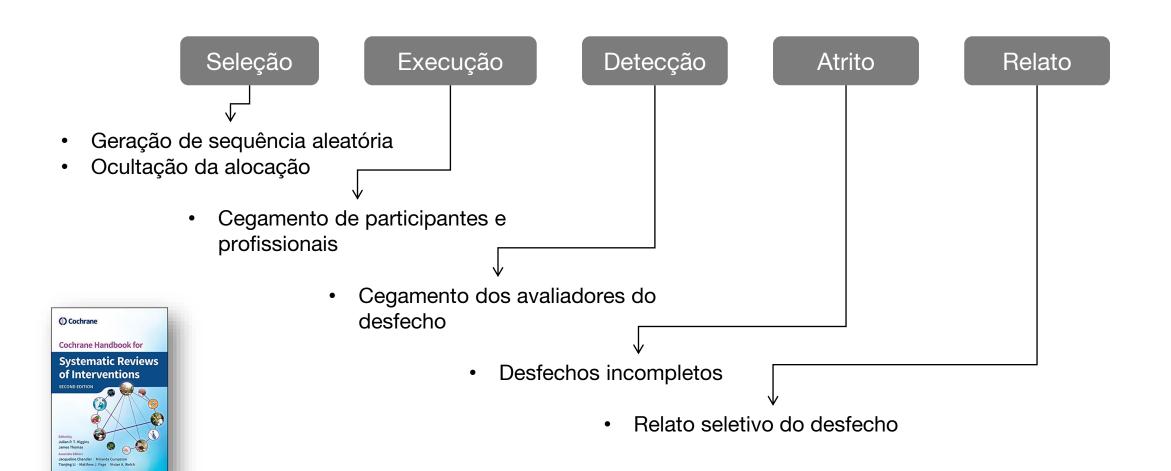
Viés de publicação

- Resultados significativos
- Resultados "positivos"

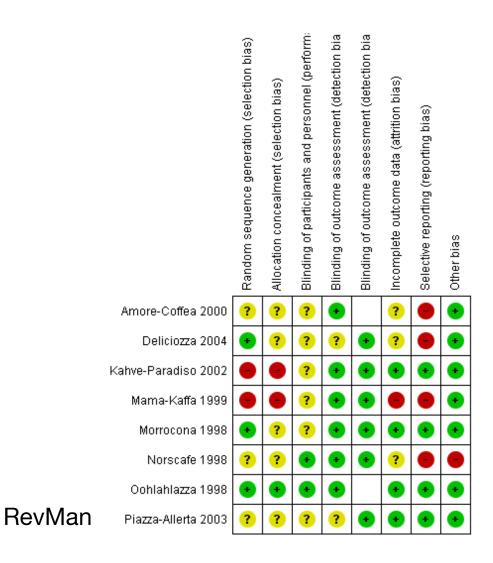
+ chances de ser publicado

- + rapidamente
- Em inglês
- Em periódico de maior impacto
 - + citações

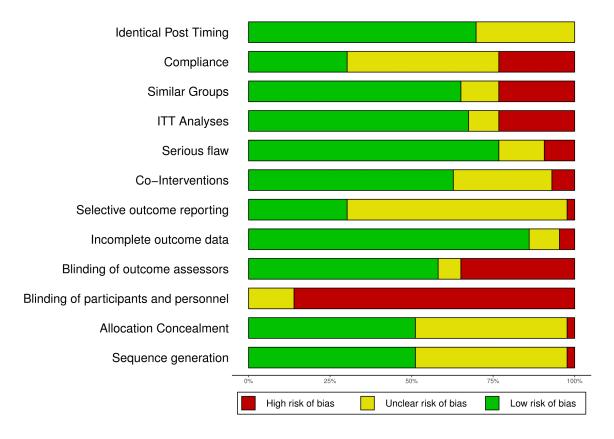
Fontes de Viés



Risco de viés



RevMan R (dmetar)



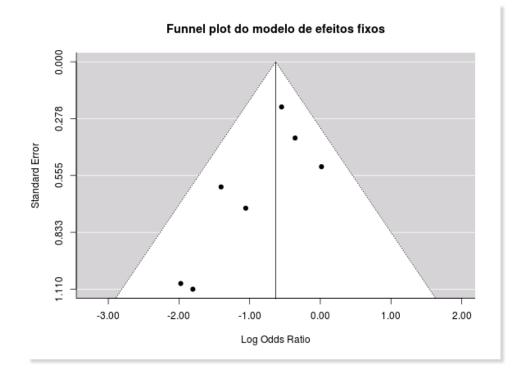
Avaliação do viés

- Funnel plot
- Egger's regression
- p-Curve e p-Uniform
- Trim and fill

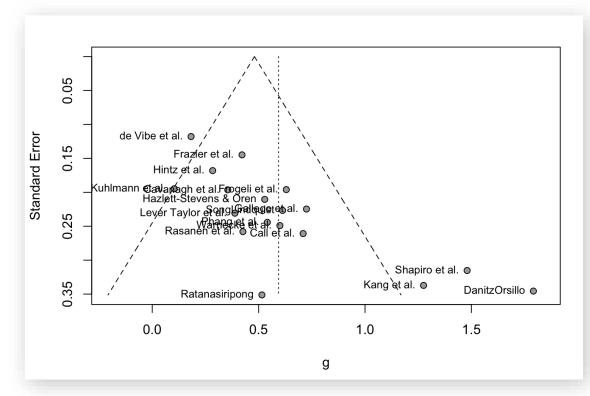
•

Funnel plot

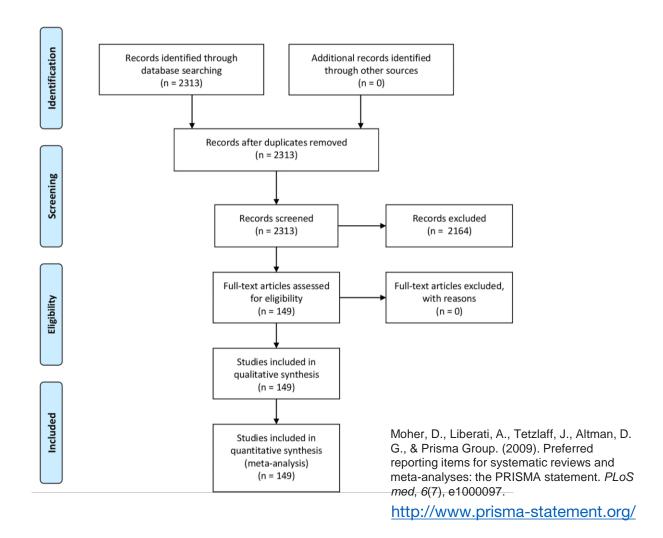
sem viés



com viés



PRISMA flow diagram & checklist



PRISMA 2009 Checklist

Section/topic		Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	1
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1-2
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	none
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	2
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	2-3
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	2
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	2-3
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	3
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	3
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	3
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	3-4
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ⁵) for each meta-analysis.	3

Page 1 of



PRISMA 2009 Checklist

Section/topic		Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	3
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	none
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	4
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	4
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	6
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	4-6
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	4
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	none
DISCUSSION	-		
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	6-8
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	8
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	8
FUNDING	-		
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	none

From: Moher D, Liberali A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

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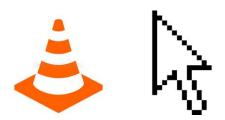
SOFTWARES





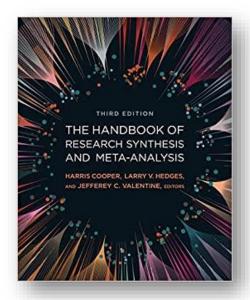


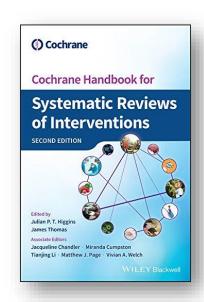
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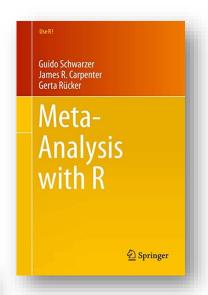
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Como elaborar uma metanálise?

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