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Introducing ROB-ME: a tool for assessing risk of non-reporting biases in systematic reviews with meta-analysis

Matthew Page[1], Julian Higgins[2], Jonathan Sterne[2]

[1]Monash University, Australia; [2]University of Bristol, UK

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ROB-ME contributors

Core group: Matthew Page, Jonathan Sterne, Julian Higgins

Working group:

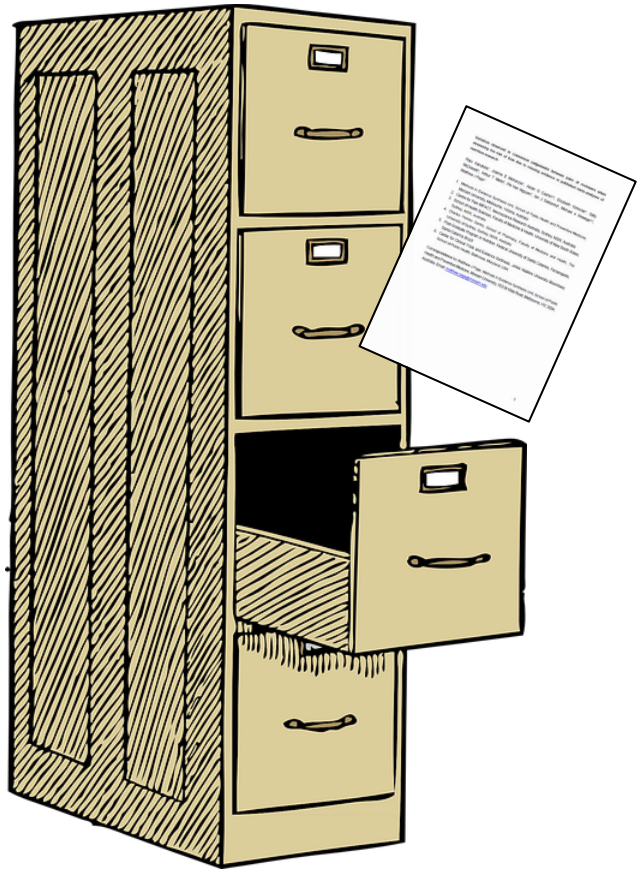
Isabelle Boutron
Asbjørn Hróbjartsson
Jamie Kirkham
Tianjing Li
Andreas Lundh
Evan Mayo-Wilson
Joanne McKenzie
Lesley Stewart
Alex Sutton
Lisa Bero
Adam Dunn
Kerry Dwan
Roy Elbers
Raju Kanukula
Joerg Meerpohl
Erick Turner

Non-reporting bias

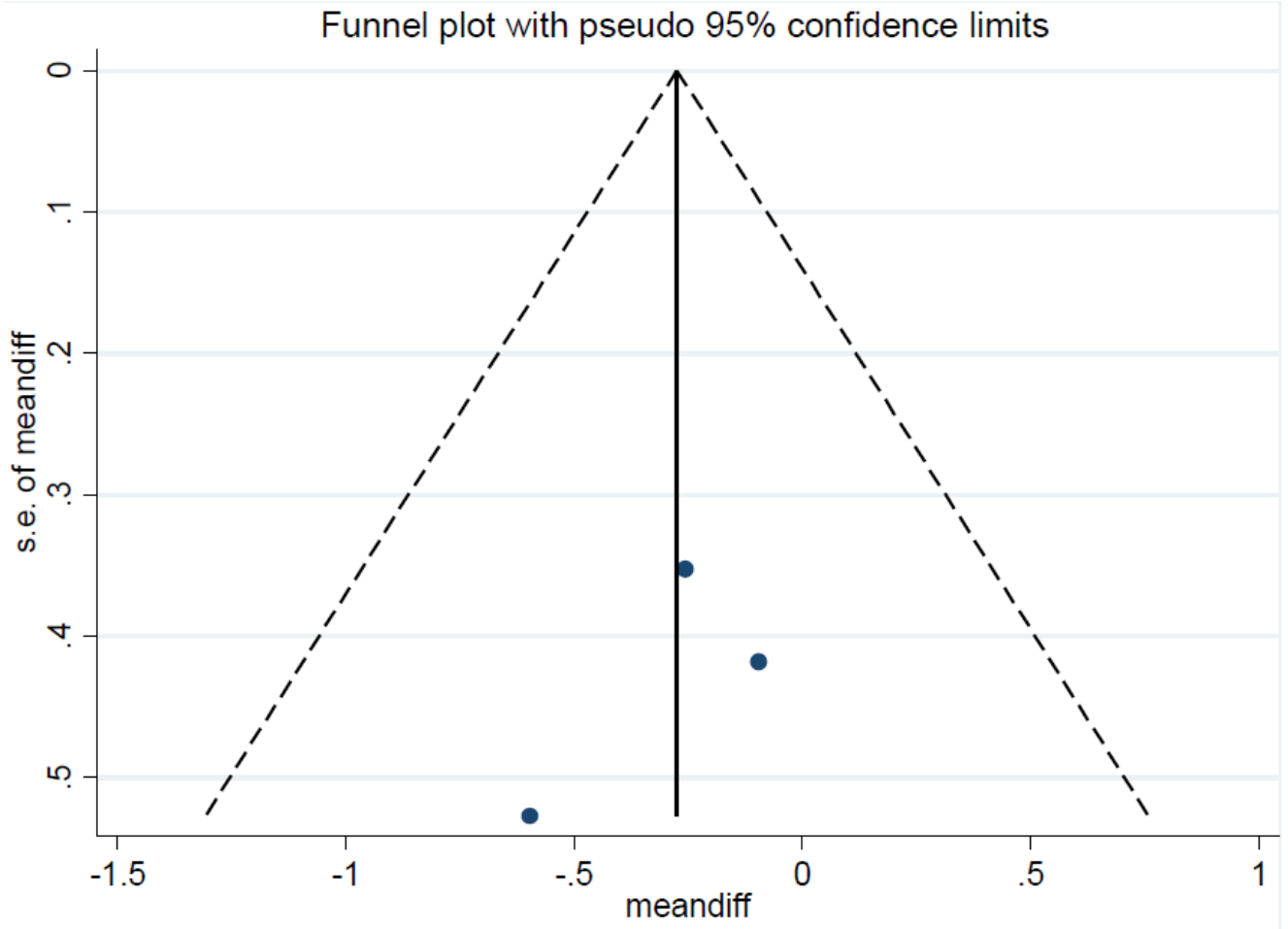
Arises when decisions about *whether*, *when*, *where* or *how* to report results of eligible studies are influenced by the P value, magnitude or direction of the results

Typically involves suppression of statistically non-significant studies or results

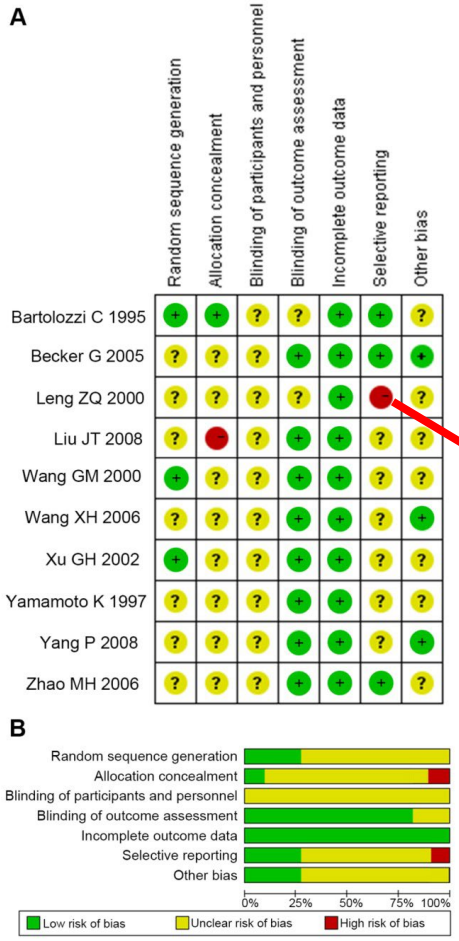
Can lead to bias in a meta-analysis

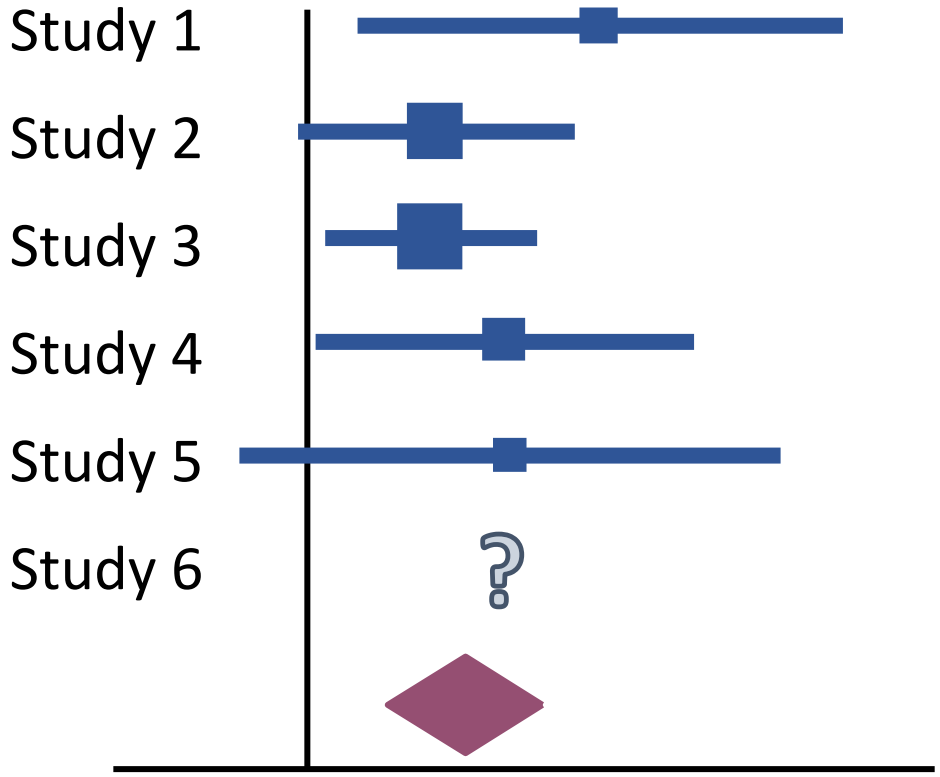


Too much focus on funnel plots



Too little focus on the impact of selective reporting





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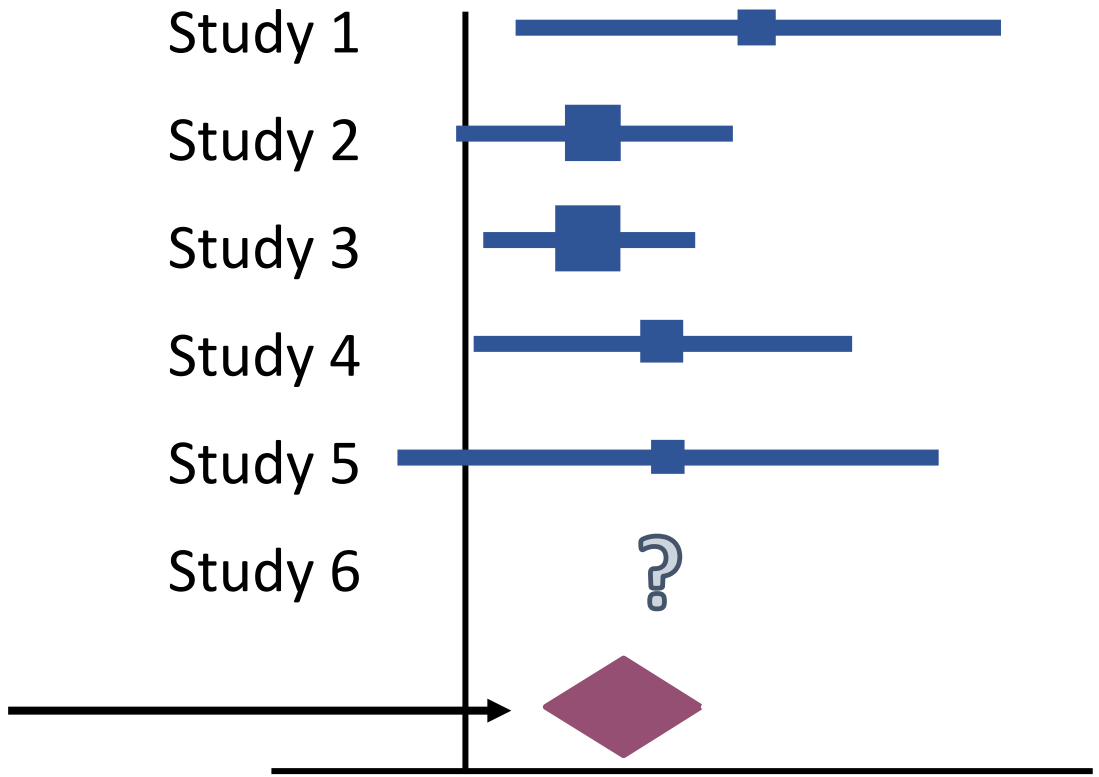
Risk of bias due to missing evidence



Low risk of bias?

Some concerns?

High risk of bias?

ROB-ME tool

ROB-ME = “Risk Of Bias due to Missing Evidence”, a new tool for integrating assessment of risk of bias in meta-analyses due to:

- missing studies (‘publication bias’)
- missing study results (‘selective reporting bias’)

Primarily designed to assess meta-analyses of the effects of interventions

Development informed by

- review of existing tools (Page et al. BMJ Open 2018)
- expert consensus
- piloting

ROB-ME: a tool for assessing risk of bias due to missing evidence in systematic reviews with meta-analysis

Matthew J Page,[1] Jonathan A C Sterne,[2,3,4] Isabelle Boutron,[5] Asbjørn Hróbjartsson,[6,7] Jamie J Kirkham,[8] Tianjing Li,[9] Andreas Lundh,[6,7,10] Evan Mayo-Wilson,[11] Joanne E McKenzie,[1] Lesley A Stewart,[12] Alex J Sutton,[13] Lisa Bero,[14] Adam G Dunn,[15] Kerry Dwan,[16] Roy G Elbers,[17] Raju Kanukula,[1] Joerg J Meerpohl,[18,19] Erick H Turner,[20,21] Julian P T Higgins[2,3]

For numbered affiliations see end of the article

Correspondence to: M Page
matthew.page@monash.edu
(ORCID 0000-0002-4242-7526)

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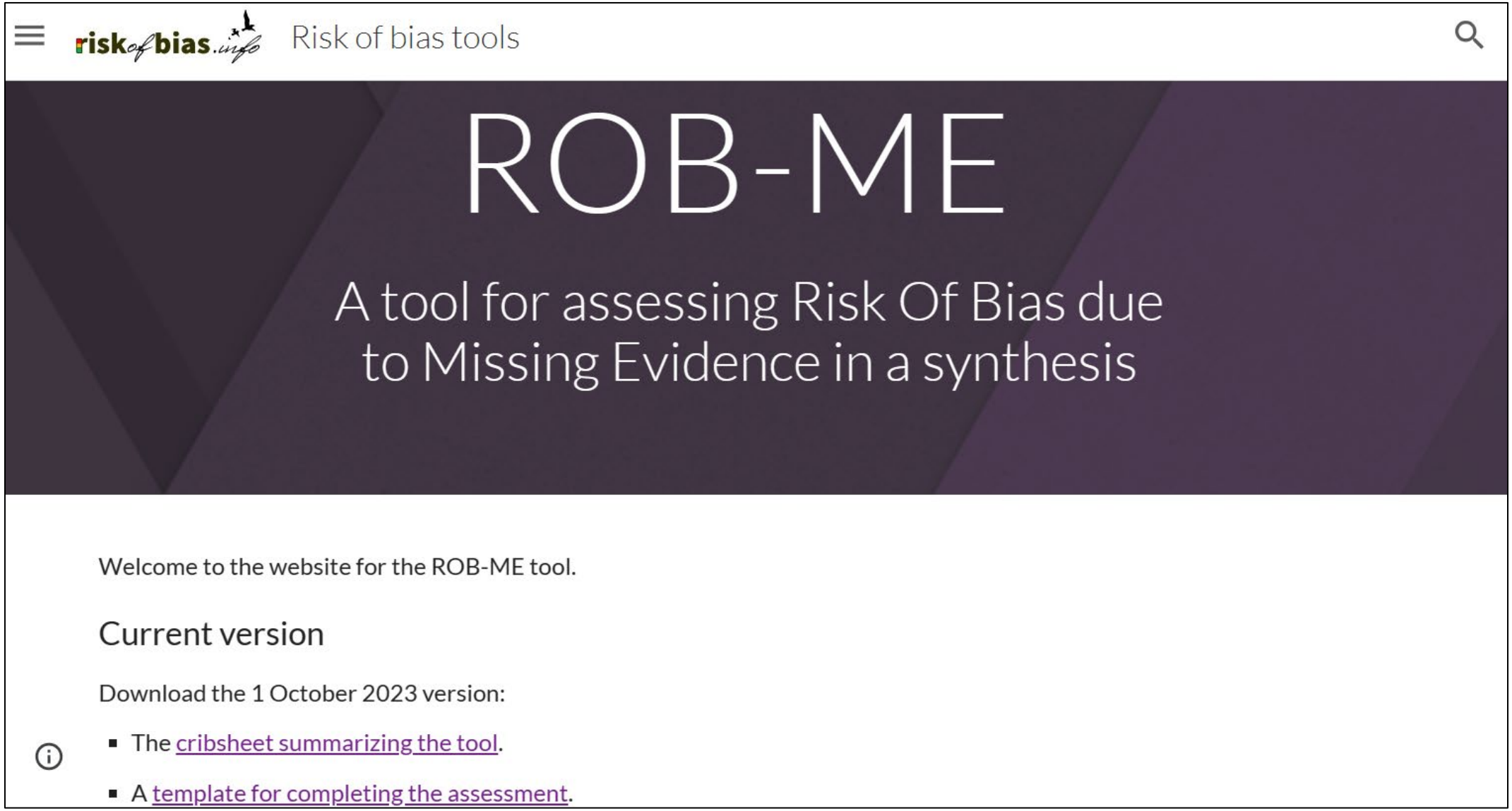
Various methods are available to help users assess whether selective non-publication of studies or selective non-reporting of study results has occurred, but not its impact on a meta-analysis. This limitation of existing methods leaves users to decide their risk of bias and interpret results appropriately.

A key feature of systematic reviews of quantitative research is the attempt to identify all studies that meet the review inclusion criteria and to include relevant data from all such studies in meta-analyses. This goal is compromised when reporting of primary studies is influenced by the P value, magnitude, or direction of



https://www.riskofbias.info

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Chapter 13: Assessing risk of bias due to missing evidence in a meta-analysis

Search Handbook

Matthew J Page, Julian PT Higgins, Jonathan AC Sterne

Key Points:

- Systematic reviews seek to identify all research that meets the eligibility criteria. However, this goal can be compromised by 'non-reporting bias': when decisions about how, when or where to report results of eligible studies are influenced by the P value, magnitude or direction of the results.
- There is convincing evidence for several types of non-reporting bias, reinforcing the need for review authors to search all possible sources where study reports and results may be located. It may be necessary to consult multiple bibliographic databases, trials registers, manufacturers, regulators and study authors or sponsors.
- Risk of bias in a meta-analysis result can arise when either an entire study report or a particular study result is unavailable selectively (e.g. because the P value, magnitude or direction of the results were considered unfavourable by the investigators). In each case, available evidence differs systematically from missing evidence.

https://training.cochrane.org/handbook/current/chapter-13

Overview of the ROB-ME tool

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ROB-ME tool

1. Select and define which meta-analyses will be assessed for risk of bias due to missing evidence

2. Determine which studies meeting the inclusion criteria for the meta-analyses have missing results and thus cannot contribute to the meta-analyses

3. Consider the potential for missing studies across the systematic review

4. Assess risk of bias due to missing evidence in each meta-analysis

ROB-ME tool: Step 1

Select which meta-analyses will be assessed for risk of bias:

- Strive to assess meta-analyses of outcomes that are most important for decision making (typically those in ‘Summary of findings’ tables)

Specify the PICO for each meta-analysis and type of study results eligible for inclusion (e.g. eligible measurement instruments, time points, methods of analysis)

ROB-ME tool: Step 1

Specify PICO for each meta-analysis

Specify eligible results for each meta-analysis

Step 1. Select and define meta-analyses that will be assessed for risk of bias due to missing evidence		
Meta-analysis ID	**Specify the PICO for all meta-analyses that will be assessed for risk of bias. For example:** ***Participants**: People with shoulder pain* ***Intervention**: Ibuprofen* ***Comparator**: Placebo* ***Outcome**: Pain intensity at short-term (0-12 weeks)* **Add/delete rows where necessary**	**For each meta-analysis, specify which study designs and results were eligible for inclusion, indicating whether the meta-analysis was restricted to particular:** • **study designs, and;** • **outcome definitions (e.g. measures, metrics, time points), and;** • **methods of analysis (e.g. analysis populations, crude or adjusted estimates).** **If such information is reported elsewhere in the systematic review, either indicate the relevant section of the review or copy the information here.** **For example:** ***Eligible study designs**: Randomized trials* ***Eligible outcome definitions**: Pain scores measured using any scale; up to 12 weeks post-randomization* ***Eligible methods of analysis**: Analyses of change from baseline values; intention-to-treat analysis sample; analyses adjusted for covariates*
1	**Participants:** **Intervention:** **Comparator:** **Outcome:**	**Eligible study designs:** **Eligible outcome definitions:** **Eligible methods of analysis:**
2	**Participants:** **Intervention:** **Comparator:** **Outcome:**	**Eligible study designs:** **Eligible outcome definitions:** **Eligible methods of analysis:**

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ROB-ME tool: Step 2

Assemble various sources of information about each study meeting the inclusion criteria of the review

- registration info
- protocol
- journal articles
- clinical study reports (CSRs) and other regulatory documents
- info from authors or sponsors

ROB-ME tool: Step 2

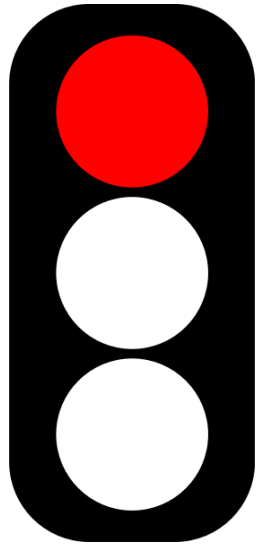
For each study meeting the inclusion criteria of the meta-analyses:

1. Compare information about outcomes that were measured with results that were available

2. Record whether results of interest were available for the study

3. If unavailable, consider whether this is because of the nature of the findings (e.g. statistical non-significance, unfavourable direction of effect) or some other reason (e.g. outcome not measured)

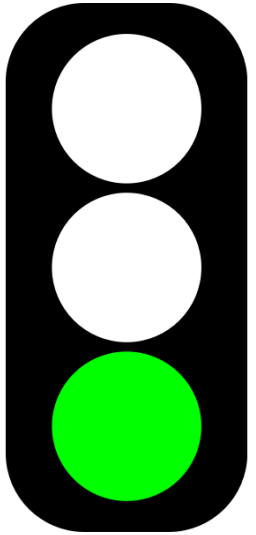
ROB-ME tool: Step 2



May be reasonable to suspect selective non-reporting if:

- outcome was pre-specified yet no result is available, and no explanation for its absence is provided
- outcome is almost certain to have been recorded but no results are available (refer to core outcome sets)
- authors have conflicts of interest that might have led them to withhold unfavourable results

ROB-ME tool: Step 2



Results might be unavailable for a reason other than selective non-reporting, e.g.

- the outcome was clearly not measured (based on an examination of the protocol or statistical analysis plan)
- the instrument or equipment needed to measure the outcome were not available at the time the study was conducted
- the data were not analysed owing to a fault in the measurement instrument, or substantial missing data

ROB-ME tool: Step 2

Key for Results Matrix

✓	A study result is available for inclusion in the meta-analysis.
~	No study result is available for inclusion in the meta-analysis, for a reason unrelated to the P value, magnitude or direction of the result.
?	Unclear whether an eligible study result was generated.
X	No study result is available for inclusion in the meta-analysis, likely because of the P value, magnitude or direction of the result generated. *Optional: Record any information known about the results (if available), such as the direction of effect (e.g. Favours intervention / Favours control), the statistical significance of the result (e.g. P > 0.05), or narrative descriptions (e.g. "No difference").*

Example of a completed Results Matrix

Study ID	Source(s) used	Number of participants analysed	Result available for inclusion in Meta-analysis 1	Result available for inclusion in Meta-analysis 2	Result available for inclusion in Meta-analysis 3	Result available for inclusion in Meta-analysis 4
Smith 2000	PMID: XXXXXXXX	455	✓	X	✓	?
Nyqvist 2017	None (not published)	67	X	X	~	~
Stylianos 2019	PMID: XXXXXXXX	87	?	✓	✓	X
Hozo 2014	PMID: XXXXXXXX	145	X	✓	X	✓
MacIntyre 2020	NCTXXXXXXXX	280	~	✓	X	~

Record availability of results for each study

ROB-ME tool: Step 3

Consider whether circumstances indicate potential for there to be **additional studies that were not identified** because of the P value, magnitude or direction of results generated

Less concerned when reviewing set of studies known to have been initiated, irrespective of their results

- e.g. prospective meta-analysis
- e.g. meta-analysis restricted to prospectively registered studies

ROB-ME tool: Step 3

More concerns about additional missing studies if:

- research area is not one for which all studies are expected to have been prospectively registered
- no study registers were searched
- search strategy designed to retrieve studies only if they reported a particular outcome

ROB-ME tool: Step 3

Answer questions

Step 3. Consider the potential for missing studies across the systematic review

Answer the following questions to determine whether circumstances indicate potential for some eligible studies not being identified because of the P value, magnitude or direction of the results generated. Answer these questions once, in relation to the systematic review as a whole.

Question	Response options
3.1. Were prospectively registered studies or studies identified for a prospective meta-analysis the only type of study eligible for inclusion in the review?	Y / N
3.2. If N to 3.1: Would you expect every eligible study to be identifiable regardless of its results?	NA / Y / PY / PN / N
3.3. If Y/PY to 3.2: Were you likely to have found all eligible studies regardless of their results?	NA / Y / PY / PN / N

Y: 'Yes'; PY: 'Probably yes'; PN: 'Probably no'; N: 'No'; NA: 'Not applicable'.

Check the box below if the response to 3.1 was 'No' and the response to 3.2 or 3.3 was 'No / Probably no'

☐ Circumstances indicate potential for some eligible studies not being identified because of the P value, magnitude or direction of the results generated

Provide any relevant information to support responses

Draw conclusion about potential for missing studies

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ROB-ME tool: Step 4

Assess risk of bias due to missing evidence in each meta-analysis

- Similar structure as RoB 2 and ROBINS-I

Signalling questions to facilitate risk of bias judgements

- Yes', 'Probably yes', 'Probably no', 'No', 'No information', 'Not applicable'

Risk of bias judgements follow from answers to signalling questions (can be over-ridden)

- 'Low risk of bias', 'Some concerns', 'High risk of bias'

ROB-ME tool: Step 4

Details of the meta-analysis being assessed for risk of bias	
Specify the meta-analysis	
Specify the meta-analysis result (e.g. summary effect estimate and 95% CI)	
Specify the number of included studies and participants	

Risk of bias assessment	
Signalling questions	**Response options**
The following questions relate to the within-study assessment of non-reporting bias ('known unknowns')	
4.1. Of the studies identified, was there any for which no result was available for inclusion in the meta-analysis, likely because of the P value, magnitude or direction of the result generated (refer to Step 2)?	Y / N
4.2. If Y to 4.1: Is it likely that there would be a notable change to the summary effect estimate if the omitted results had been included?	NA / Y / PY / PN / N / NI
4.3. Of the studies identified, was there any for which it was unclear whether an eligible result was generated (refer to Step 2)?	Y / N
4.4. If Y to 4.3: Is it likely that there would be a notable change to the summary effect estimate if the potentially omitted results had been included?	NA / Y / PY / PN / N / NI
The following questions relate to the across-study assessment of non-reporting bias ('unknown unknowns')	
4.5 Do circumstances (identified in Step 3) indicate potential for some eligible studies not being identified because of the P value, magnitude or direction of the results generated?	Y / N
4.6. If Y to 4.5: Is it likely that studies not identified had results that were eligible for inclusion in the meta-analysis?	NA / Y / PY / PN / N
4.7. If Y to 4.1, 4.3 or 4.5: Does the pattern of observed study results suggest that the meta-analysis is likely to be missing results that were systematically different (in terms of P value, magnitude or direction) from those observed?	NA / Y / PY / PN / N
4.8. If Y/PY/NI to 4.2, 4.4, 4.6 or 4.7: Did sensitivity analyses suggest that the summary effect estimate was biased due to missing results?	NA / Y / PY / PN / N
Risk of bias judgement	Low / High / Some concerns
Optional: What is the predicted direction of bias for this meta-analysis?	

Y: 'Yes'; PY: 'Probably yes'; PN: 'Probably no'; N: 'No'; NI: 'No information'

Answer signalling questions

Reach risk-of-bias judgement

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ROB-ME tool: Step 4 signalling questions

Are any of the studies identified missing or potentially missing from the meta-analysis because of the P value, magnitude or direction of the result?

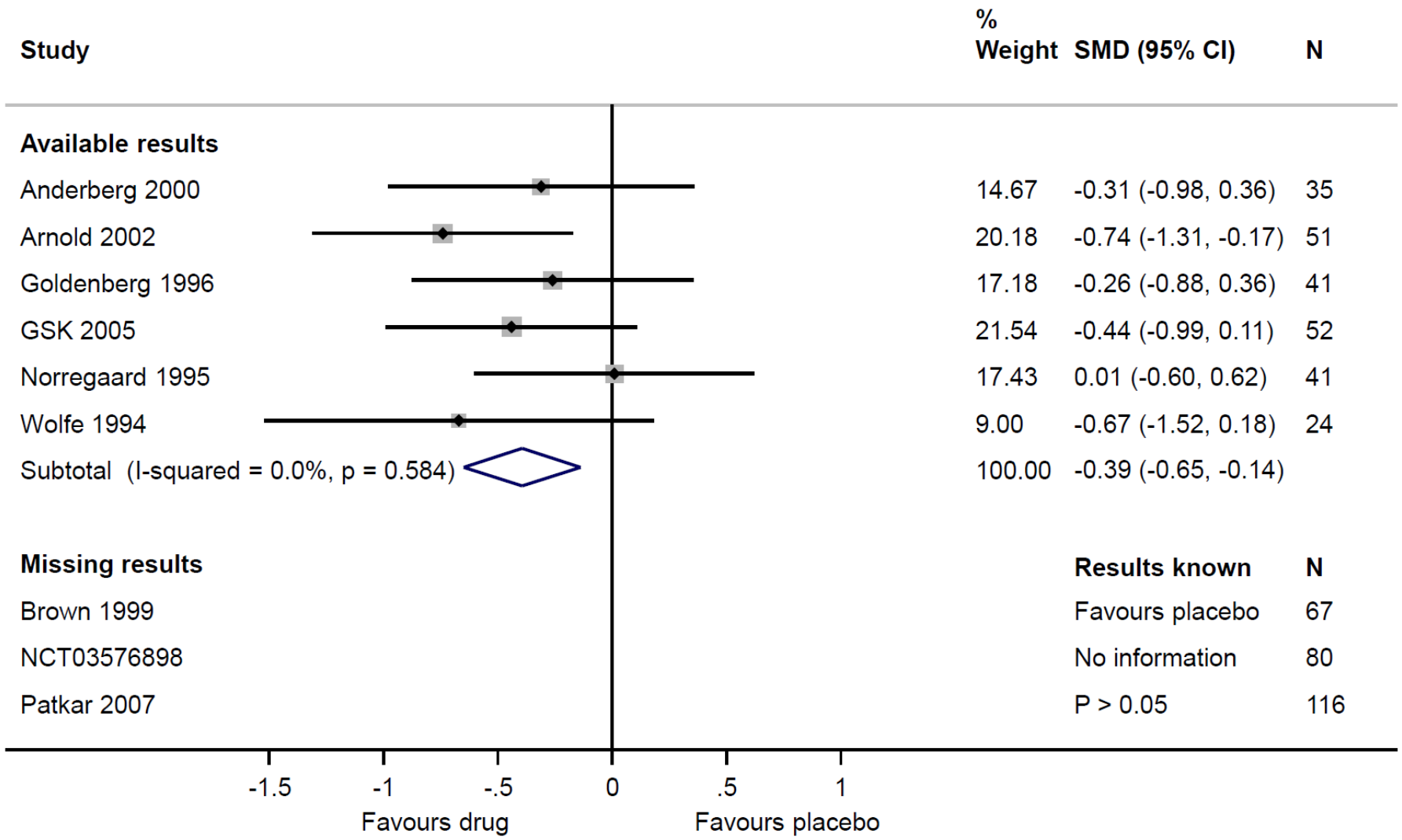
If so, would the summary effect estimate change notably if the omitted results had been included?

Do circumstances indicate potential for additional missing studies?

If so, are the additional missing studies likely to have had eligible results?

Does the pattern of study results suggest the meta-analysis is missing results that were systematically different from those observed?

Do sensitivity analyses suggest the summary effect estimate was biased due to missing results?


Study
% Weight
SMD (95% CI)
N
Available results
Anderberg 2000
14.67
-0.31 (-0.98, 0.36)
35
Arnold 2002
20.18
-0.74 (-1.31, -0.17)
51
Goldenberg 1996
17.18
-0.26 (-0.88, 0.36)
41
GSK 2005
21.54
-0.44 (-0.99, 0.11)
52
Norregaard 1995
17.43
0.01 (-0.60, 0.62)
41
Wolfe 1994
9.00
-0.67 (-1.52, 0.18)
24
Subtotal (I-squared = 0.0%, p = 0.584)
100.00
-0.39 (-0.65, -0.14)
Missing results
Results known
N
Brown 1999
Favours placebo
67
NCT03576898
No information
80
Patkar 2007
P > 0.05
116
-1.5
-1
-.5
0
.5
1
Favours drug
Favours placebo

ROB-ME tool: Step 4 signalling questions

Are any of the studies identified missing or potentially missing from the meta-analysis because of the P value, magnitude or direction of the result?

If so, would the summary effect estimate change notably if the omitted results had been included?

Do circumstances indicate potential for additional missing studies?

If so, are the additional missing studies likely to have had eligible results?

Does the pattern of study results suggest the meta-analysis is missing results that were systematically different from those observed?

Do sensitivity analyses suggest the summary effect estimate was biased due to missing results?

ROB-ME tool: Step 4 signalling questions

Are any of the studies identified missing or potentially missing from the meta-analysis because of the P value, magnitude or direction of the result?

If so, would the summary effect estimate change notably if the omitted results had been included?

Do circumstances indicate potential for additional missing studies?

If so, are the additional missing studies likely to have had eligible results?

Does the pattern of study results suggest the meta-analysis is missing results that were systematically different from those observed?

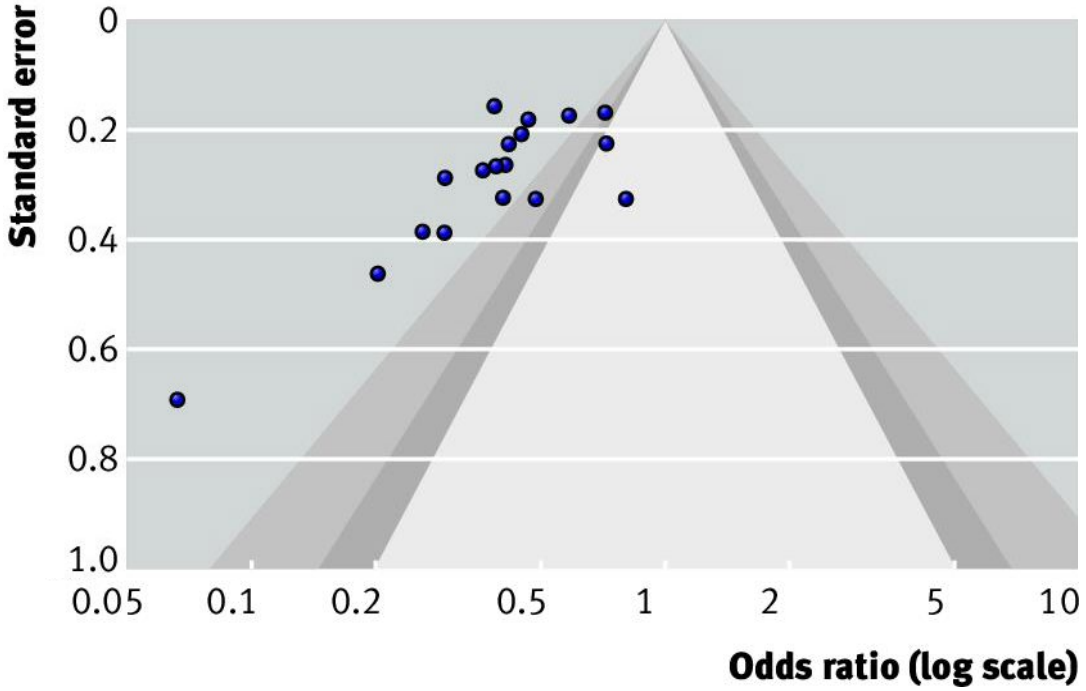
Do sensitivity analyses suggest the summary effect estimate was biased due to missing results?

ROB-ME tool: Step 4 signalling questions

Consider findings of graphical and statistical methods, when appropriate

- contour-enhanced funnel plots
- tests for funnel plot asymmetry
- sensitivity analyses

Consult a statistician before proceeding with tests and sensitivity analyses



Source: Sterne JAC, et al. BMJ 2011;342:d4002

ROB-ME tool: Step 4 signalling questions

Step 4. Assess risk of bi

Responses underlined i

Guidance for answering signalling questions available in cribsheet on riskofbias.info

Details of the meta-ar		
Specify the meta-analysis	For example, "Random-effects meta-analysis of the effect of ibuprofen versus placebo on pain intensity at short-term (0-12 weeks)"	
Specify the meta-analysis result (e.g. summary effect estimate and 95% CI)	For example, "Mean difference -15.00, 95% CI -23.99, -6.01"	
Specify the number of included studies and participants	For example, "10 studies (4,934 participants)"	
Risk of bias assessment		
Signalling questions	**Elaboration**	**Response options**
The following questions relate to the within-study assessment of non-reporting bias ('known unknowns')		
4.1. Of the studies identified, was there any for which no result was available for inclusion in the meta-analysis, likely because of the P value, magnitude or direction of the result generated (refer to Step 2)?	***Note: In software to be developed to implement the tool, responses to this question will be prefilled automatically based on what users enter into the Results Matrix (Step 2).*** **Answer 'Yes'** if any of the studies in the Results Matrix were marked with an 'X' for this particular meta-analysis.	Y / N
4.2. If Y to 4.1: Is it likely that there would be a notable change to the summary effect estimate if the omitted results had been included?	First, consider whether the amount of missing evidence is large enough that its omission is likely to lead to a notable change in the summary (combined) effect estimate observed (regardless of how large the observed estimate is). Second, consider the direction of effect (e.g. favours experimental intervention) for any studies missing from the meta-analysis, if such information is known (e.g. when study authors only report that "pain was lower in the drug group", without presenting summary statistics or effect estimates). It may be helpful to append any known studies that are missing from the meta-analysis to a forest plot, for example using the template presented in Figure 1. **Answer 'Yes / Probably yes'** if the amount of missing information is non-trivial and, if known, the direction of effect in omitted studies differs from the direction of effect for the meta-analysis, and hence the omission is likely to lead to a notable change in the magnitude of the summary effect estimate. If the meta-analysis was estimated using a fixed-effect model, consider the total weight of the studies missing from the meta-analysis. If the weight of missing studies was comparable to or greater than that of the	NA / Y / PY / PN / N / NI

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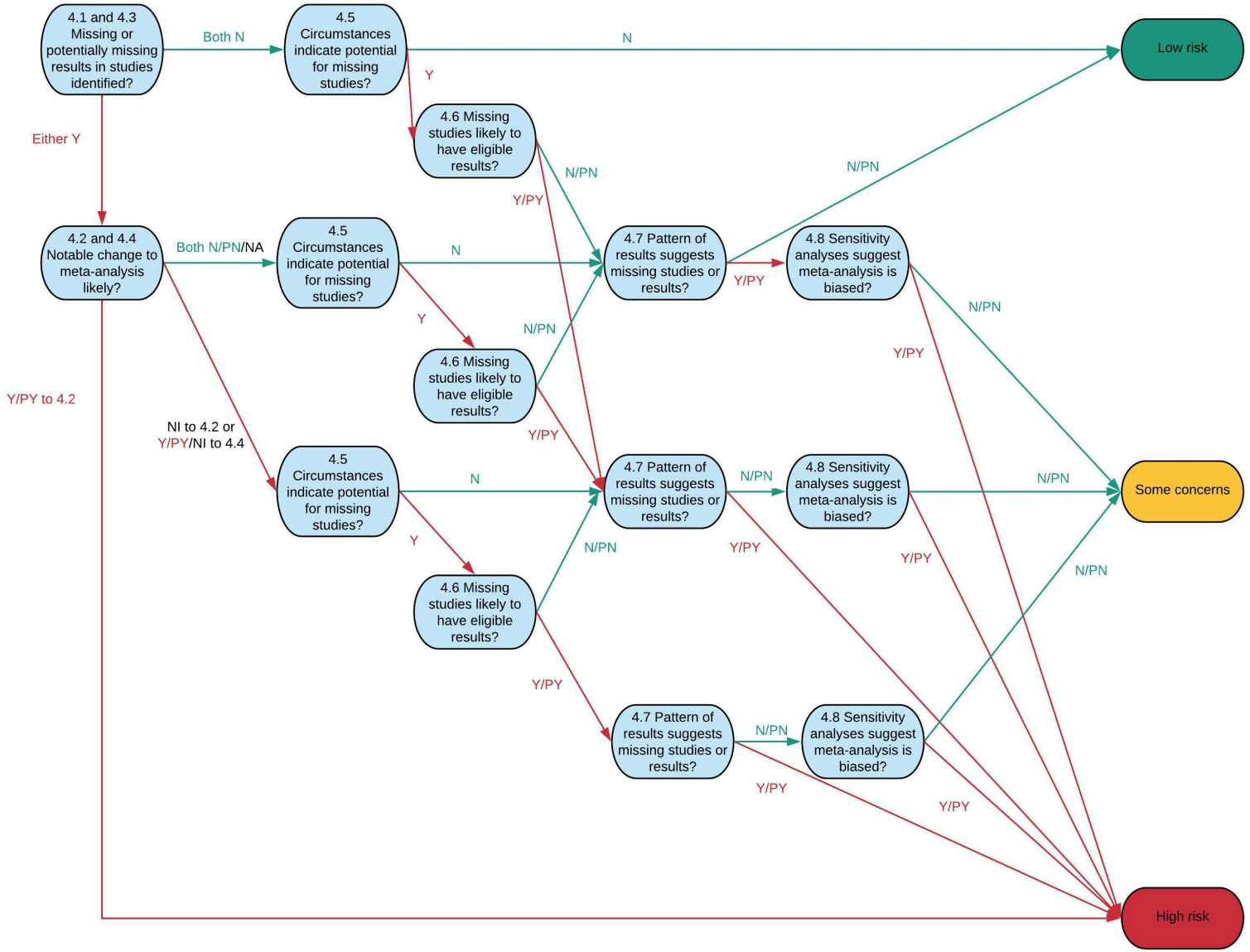
Algorithm for ROB-ME judgement



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ROB-ME algorithm: example

Consider the findings of each approach to reach an overall judgement of risk of bias due to missing evidence. For example, if:

- **selective non-reporting** of results was **not detected** in any of the studies identified…
- …but the **search strategy** was designed to retrieve studies only if they reported a particular outcome, or a **contour-enhanced funnel plot** suggests the meta-analysis is likely to be missing results that were systematically different from those observed…
- …the meta-analysis is at **high risk of bias**

Example

Original research

Effects of exercise training in people with non-small cell lung cancer before lung resection: a systematic review and meta-analysis

Francis-Edouard Gravier ,[1,2] Pauline Smondack,[1] Guillaume Prieur,[2,3] Clement Medrinal ,[3,4,5] Yann Combret ,[3] Jean-François Muir,[1,2] Jean-Marc Baste,[6,7] Antoine Cuvelier,[2,8] Fairuz Boujibar,[6,7] Tristan Bonnevie[1,2]

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/thoraxjnl-2021-217242).

[1]ADIR Association, University Hospital Centre Rouen, Rouen, France

ABSTRACT

Introduction Exercise training before lung resection for non-small cell lung cancer is believed to decrease postoperative complications (POC) by improving cardiorespiratory fitness. However, this intervention lacks a strong evidence base.

Aim To assess the effectiveness of preoperative exercise training compared with usual care on POC and other

Key messages

What is the key question?

► Does preoperative exercise training for people with scheduled lung resection surgery for non-small cell lung cancer reduce postoperative complications?

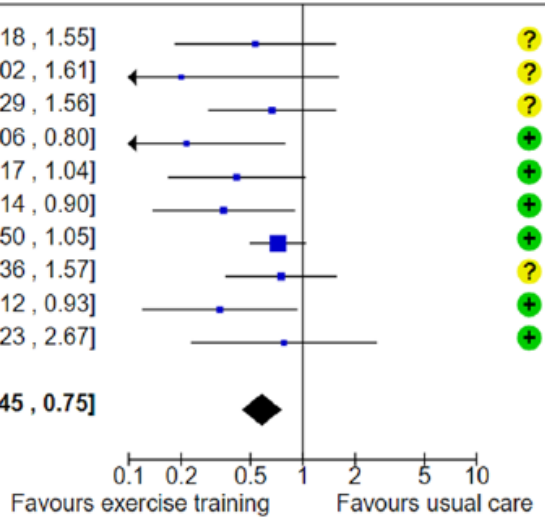
ROB-ME Step 1: Select meta-analyses to assess

Meta-analysis 1: Postoperative complications
RR 0.58, 95% CI 0.45 to 0.75 (10 studies, 617 participants)

A

Study or Subgroup	Exercise training Events	Total	Usual care Events	Total	Weight	Risk ratio M-H, Random, 95% CI
✓ Benzo 2011b	3	9	5	8	5.5%	0.53 [0.18 , 1.55]
✓ Pehlivan 2011	1	30	5	30	1.4%	0.20 [0.02 , 1.61]
✓ Fang 2013	6	22	9	22	8.7%	0.67 [0.29 , 1.56]
✓ Morano 2013	2	12	7	9	3.6%	0.21 [0.06 , 0.80]
✓ Huang 2017	5	30	12	30	7.5%	0.42 [0.17 , 1.04]
✓ Lai 2017	5	51	14	50	7.0%	0.35 [0.14 , 0.90]
✓ Licker 2017	27	74	39	77	44.9%	0.72 [0.50 , 1.05]
✓ Sebio Garcia 2017	5	10	8	12	11.5%	0.75 [0.36 , 1.57]
✓ Lai 2019	4	34	12	34	5.9%	0.33 [0.12 , 0.93]
✓ Liu 2020	4	37	5	36	4.1%	0.78 [0.23 , 2.67]
Total (95% CI)		**309**		**308**	**100.0%**	**0.58 [0.45 , 0.75]**
Total events:	62		116			

Heterogeneity: Tau² = 0.00; Chi² = 8.41, df = 9 (P = 0.49); I² = 0%
Test for overall effect: Z = 4.26 (P < 0.0001)
Test for subgroup differences: Not applicable



Gravier et al. Effects of exercise training in people with non-small cell lung cancer before lung resection: a systematic review and meta-analysis. Thorax 2022 May;77(5):486-496

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ROB-ME Step 1: Define PICO and eligible results

P: People with scheduled lung resection surgery for non-small cell lung cancer

I: Preoperative aerobically demanding types of exercise training

C: Usual care

O: Postoperative complications

Eligible study designs: Randomized trials

Eligible outcome definitions: Any postoperative complication

Eligible methods of analysis: No restrictions reported

ROB-ME Step 2: Results matrix

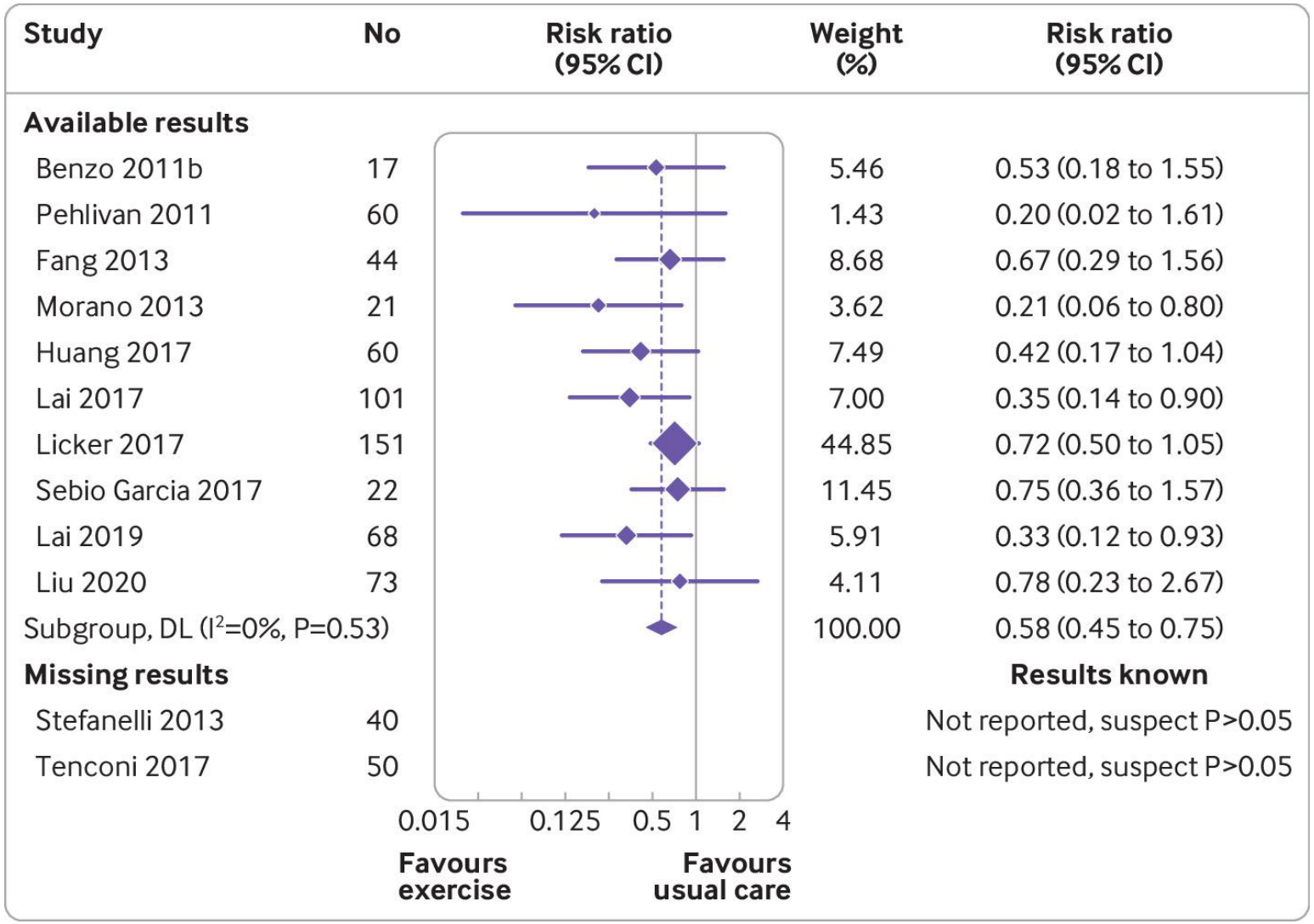
Study ID	Source(s) used	Number of participants analysed	Result available for inclusion in Meta-analysis 1
Benzo 2011b	PMID: 21663994	17	✓
Pehlivan 2011	PMID: 21881371	60	✓
Fang 2013	DOI: 10.3969/j.issn.1001-1242.2013.07.006	44	✓
Morano 2013	PMID: 22926460	21	✓
Huang 2017	PMID: 28839990	60	✓
Lai 2017	PMID: 28520962	101	✓
Licker 2017	PMID: 27771425	151	✓
Sebio Garcia 2017	PMID: 28730888	22	✓
Lai 2019	PMID: 31807526	68	✓
Liu 2020	PMID: 31348053	73	✓
Benzo 2011a	PMID: 21663994	9	~
Sommer 2016	PMID: 27151595	40	?
Stefanelli 2013	PMID: 23892298	40	X
Tenconi 2017	DOI: 10.1093/icvts/ivx280.091	50	X

ROB-ME Step 2: Results matrix

Study ID	Source(s) used	Number of participants analysed	Result available for inclusion in Meta-analysis 1
Benzo 2011b	PMID: 21663994	17	✓
	PMID: 21881371	60	✓
	DOI: 10.3969/j.issn.1001-1242.2013.07.006	44	✓
	PMID: 22926460	21	✓
	PMID: 288399	60	✓
	PMID: 285209	101	✓
	PMID: 277714	151	✓
Sebio Garcia 2017	PMID: 2873	22	✓
Lai 2019	PMID: 318 75	68	✓
Liu 2020	PMID: 13480	73	✓
Benzo 2011a	PM : 216639	9	~
Sommer 2016	MID: 27151595	40	?
Stefanelli 2013	PMID: 23892298	40	X
Tenconi 2017	DOI: 10.1093/icvts/ivx280.091	50	X

Postop complications not reported as an outcome. P value for **all** between-group and within-group differences were <0.05

Postop complications specified in protocol but not reported in conference abstract. P value for **all** outcomes in the abstract were <0.05



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MONASH University

ROB-ME tool: Step 4 signalling questions

Are any of the studies identified missing or potentially missing from the meta-analysis because of the P value, magnitude or direction of the result?

Answer:

If Yes, would the summary effect estimate change notably if the omitted results had been included?

Answer:

ROB-ME tool: Step 4 signalling questions

Are any of the studies identified missing or potentially missing from the meta-analysis because of the P value, magnitude or direction of the result?

Answer: Yes. Two studies are missing from the meta-analysis

If Yes, would the summary effect estimate change notably if the omitted results had been included?

Answer: Probably yes. Inclusion of one or more studies with unfavourable results could shift the summary effect estimate

ROB-ME tool: Step 4 signalling questions

Do circumstances indicate potential for additional missing studies?

Answer:

If Yes/Probably yes, are the additional missing studies likely to have had eligible results?

Answer:

ROB-ME tool: Step 4 signalling questions

Do circumstances indicate potential for additional missing studies?

Answer: Yes. The review question is not one for which we would expect all trials conducted to be identifiable (e.g. registered publicly), and no trials registers were searched.

If Yes/Probably yes, are the additional missing studies likely to have had eligible results?

Answer: Probably yes. Postoperative complications are commonly measured in trials with a surgical component.

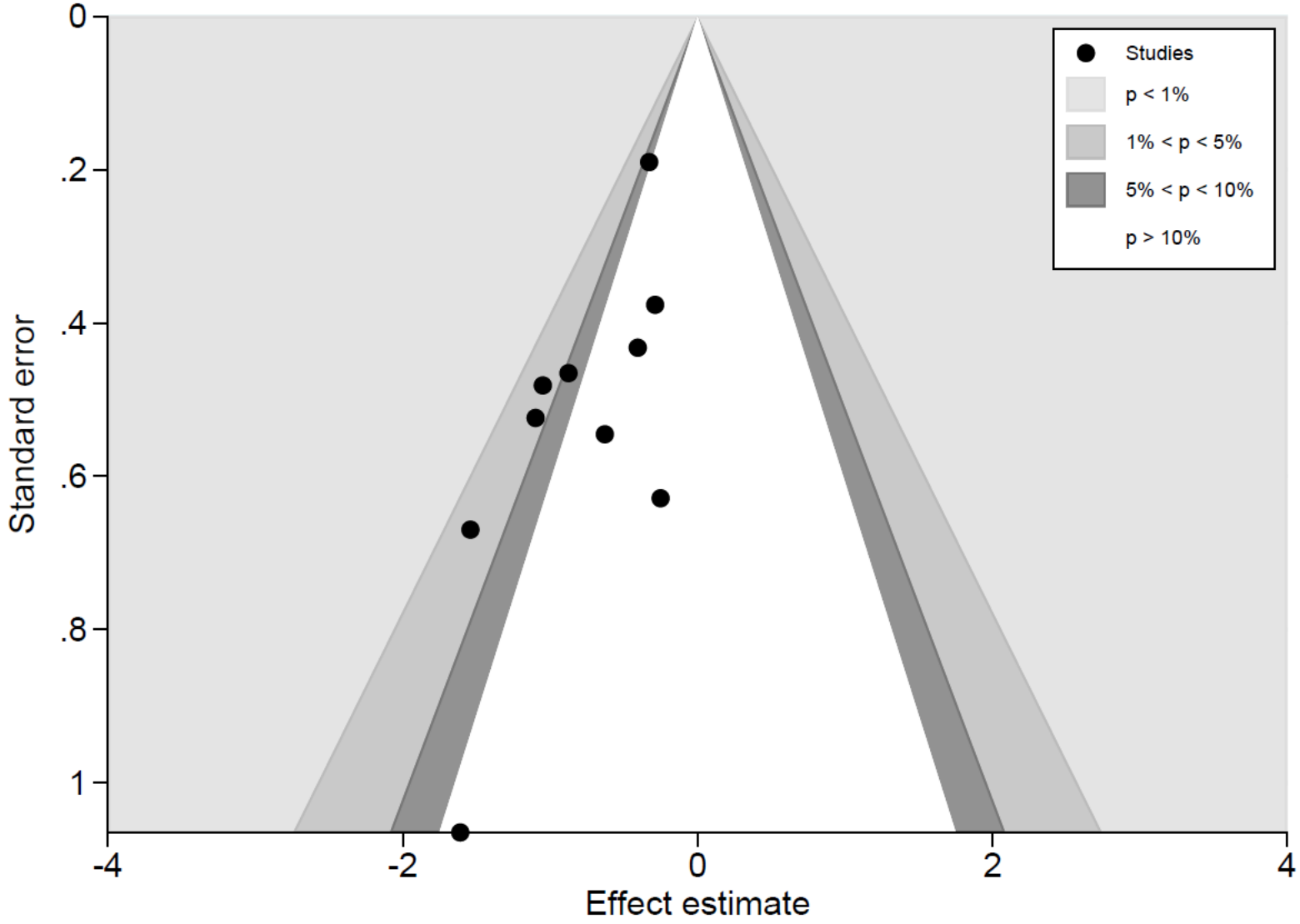
ROB-ME tool: Step 4 signalling questions

Does the pattern of study results suggest the meta-analysis is missing results that were systematically different from those observed?

Answer:

Do sensitivity analyses suggest the summary effect estimate was biased due to missing results?

Answer:


Studies
p < 1%
1% < p < 5%
5% < p < 10%
p > 10%
Standard error
0
.2
.4
.6
.8
1
-4
-2
0
2
4
Effect estimate

ROB-ME tool: Step 4 signalling questions

Does the pattern of study results suggest the meta-analysis is missing results that were systematically different from those observed?

Answer: Probably yes. There is slight asymmetry in the funnel plot (some studies missing from the area of statistical non-significance)

Do sensitivity analyses suggest the summary effect estimate was biased due to missing results?

Answer: No. No sensitivity analyses performed

ROB-ME tool: Overall assessment

Summary:

- There was evidence of selective non-reporting of results in some of the studies identified
- Inclusion of these missing results could change the summary estimate
- Circumstances indicate potential for additional missing studies with eligible results
- There is some evidence of funnel plot asymmetry due to non-reporting bias

ROB-ME tool: Overall assessment

Summary:

- There was evidence of selective non-reporting of results in some of the studies identified
- Inclusion of these missing results could change the summary estimate
- Circumstances indicate potential for additional missing studies with eligible results
- There is some evidence of funnel plot asymmetry due to non-reporting bias

ROB-ME judgement: Low risk of bias Some concerns High risk of bias

ROB-ME tool: Overall assessment

Summary:

- There was evidence of selective non-reporting of results in some of the studies identified
- Inclusion of these missing results could change the summary estimate
- Circumstances indicate potential for additional missing studies with eligible results
- There is some evidence of funnel plot asymmetry due to non-reporting bias

ROB-ME judgement: High risk of bias

Take home message

ROB-ME provides a framework for considering risk of bias due to missing evidence in meta-analyses included in your review

The ROB-ME tool should be used alongside other tools (e.g. RoB 2, TACIT) to facilitate appropriate interpretation of results

See https://www.riskofbias.info/welcome/rob-me-tool for more detail