Systematic review with meta-analysis: An overview

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Overview

- What is a systematic review?
- What are the differences b/ a SR and other types of literature reviews?
- Components of a SR
- What is a meta-analysis?
- Components of a MA
- Summary of key points

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What is a systematic review?

Focusses on a clearly formulated question that uses systematic and reproducible methods to identify, select and critically appraise all relevant research, and to collect and analyse data from the studies that are included in the review.

A systematic review

- Answers a focused research question.
- Employs a comprehensive, reproducible search strategy.
- Identifies ALL relevant studies (both published and unpublished).
- Assesses all results for inclusion/exclusion, and for quality.
- Presents an unbiased, balanced summary of findings.
- Involves a team of researchers looking at a complex research question.
- Takes months, or even years, to complete.

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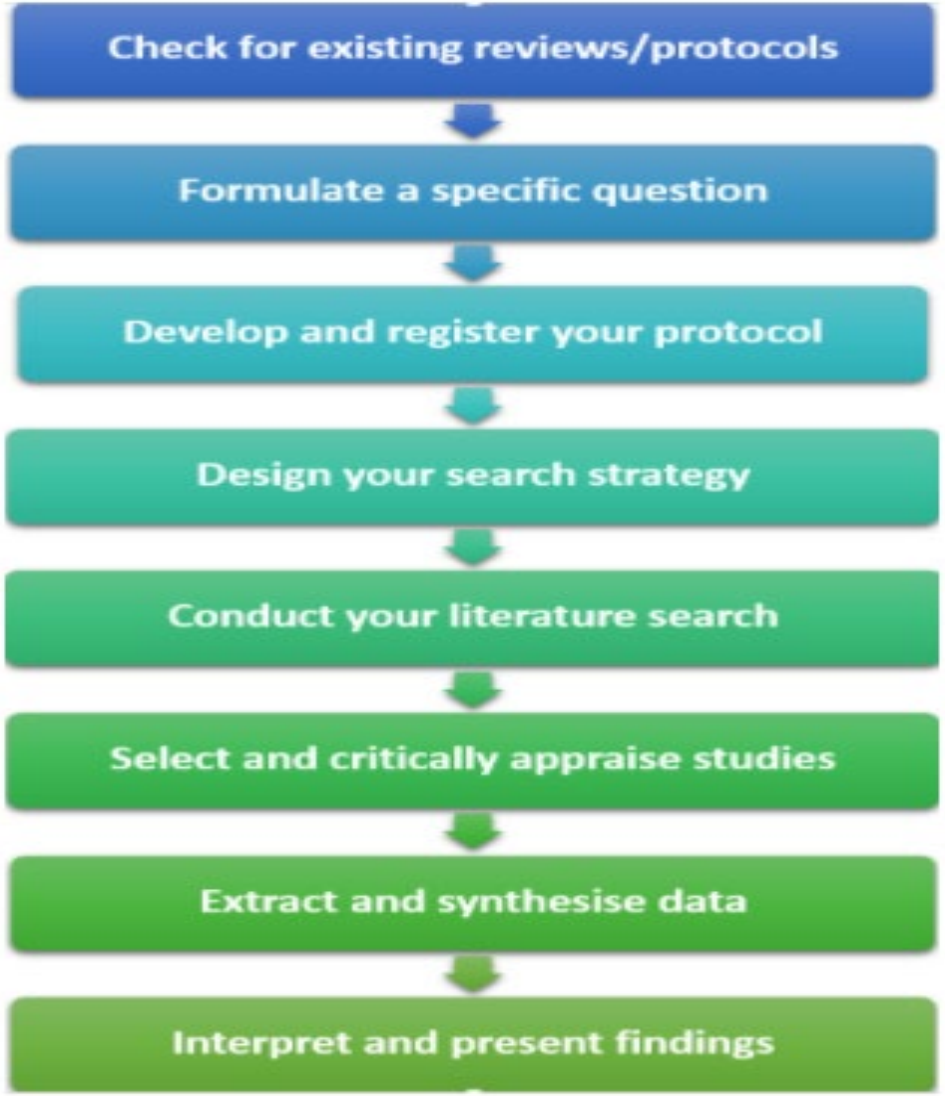
Types of systematic reviews

- A quantitative systematic review includes studies that have numerical data.
- A qualitative systematic review derives data from observation, interviews, or verbal interactions and focuses on the meanings and interpretations of the participants. It will include focus groups, interviews, observations and diaries.



Source: https://libguides.library.curtin.edu.au/systematic-reviews

What are the differences b/ a SR and other types of literature reviews?

	Systematic review	Literature review
Question	Focused on a single question	Not necessarily focused on a single question, but may describe an overview
Protocol	Includes a peer review protocol or plan	No protocol is included
Background	Provides summaries of the available literature on a topic	Provides summaries of the available literature on a topic
Objectives	Clear objectives are identified	Objectives may or may not be identified
Inclusion/exclusion criteria	Criteria is stated before review is conducted	Criteria not specific or may not be specified
Search strategy	Comprehensive search conducted in a systematic way	Strategy not explicitly stated
Article selection	Process clear, explicit and replicable	Not always clearly described
Process of evaluating articles	Comprehensive evaluation of study quality	Evaluation of study quality may or may not be included
Results and data synthesis	Clear summaries based on high quality evidence	Summary based on studies where the quality of the articles may not be specified. May also be influenced by the reviewer's theories, needs and beliefs
Discussion	Written by an expert or group of experts with a detailed and well established knowledge of the issues	Written by an expert or group of experts with a well established knowledge of the issues

Adapted based on: https://libguides.library.curtin.edu.au/systematic-reviews

Steps in a systematic review

1. Check for existing reviews/protocols. If a systematic review answering question has been conducted, or is being undertaken, you may need to amend or refine your question
2. Formulate a specific research question that is clear and focused. Use the PICO tool
3. Develop and register your protocol, including the rationale for the review, and eligibility criteria.
4. Design a robust search strategy that is explicit and reproducible. Assistance from a health librarian with search terms and database searches is invaluable
5. Conduct a comprehensive search of the literature by searching the relevant databases and other sources.
6. Select and critically appraise the quality of included studies. Cochrane 'Risk of bias' tool.
7. Extract relevant data from individual studies and use established methods to synthesise the data. If meta-analysis is appropriate, then include based on PICO question.
8. Interpret results, write a comprehensive report on all aspects of the systematic review. Present findings relative to their translation into clinical practice.

PICO question

- Population
- Intervention
- Comparator
- Outcome(s)

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Example of a PICO question

Review objective: to assess the clinical effectiveness of repositioning regimens on the prevention of pressure injuries (PI) in adults, regardless of risk in any setting.

Population – any adult, without an existing PI, admitted to any healthcare setting.

Intervention(s) – comparisons b/ frequencies of repositioning, e.g., -2,-3,-4 hourly, different positions for repositioning, e.g., tilts.

Comparator – comparisons with standard practice, however defined by study authors.

Outcome – primary outcome cumulative incidence of PI

What is bias?

- A systematic error or deviation from the truth, in results or inferences.
- Biases can operate in either direction: different biases can lead to underestimation or overestimation of the true intervention effect.
- Biases can vary in magnitude: some are small (and trivial compared with the observed effect) and some are substantial.
- Even a particular source of bias may vary in direction: bias due to a particular design flaw (e.g. lack of allocation concealment), may lead to over estimation of effect.
- Because the results of a study may in fact be unbiased despite a methodological flaw, it is more appropriate to consider risk of bias.

https://handbook-5-1.cochrane.org/chapter_8/8_assessing_risk_of_bias_in_included_studies.htm

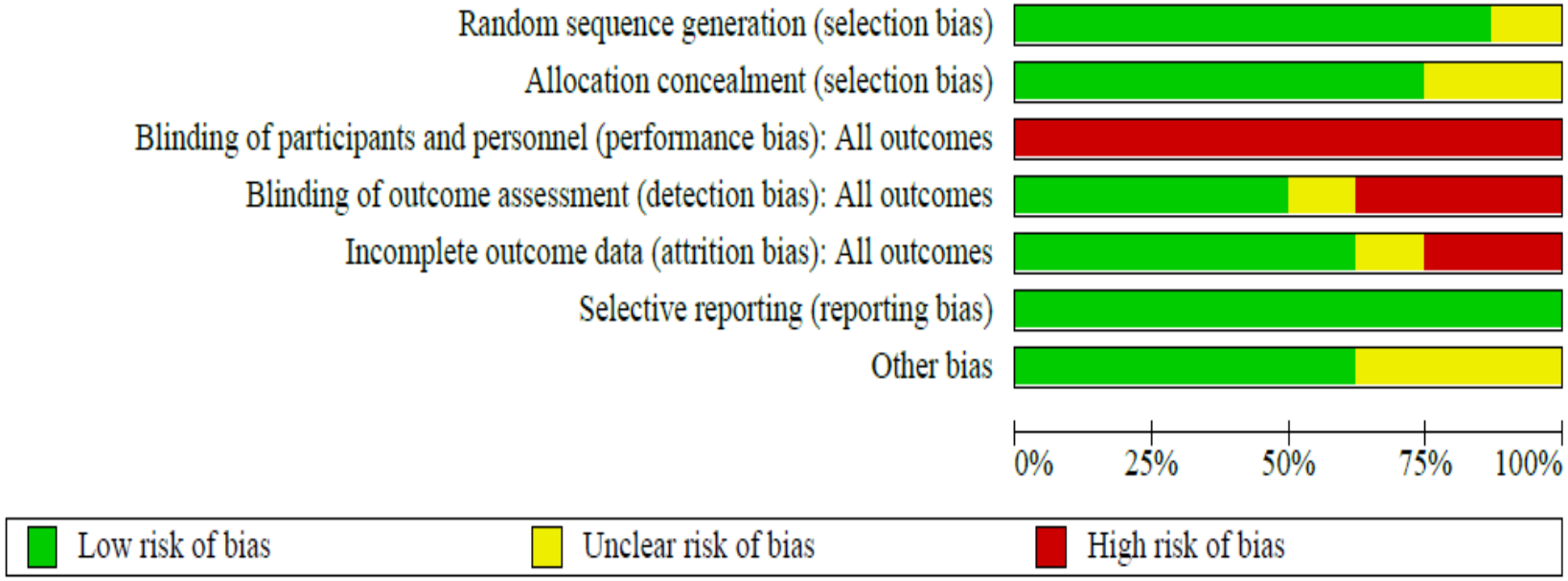
Assessing research quality in included papers

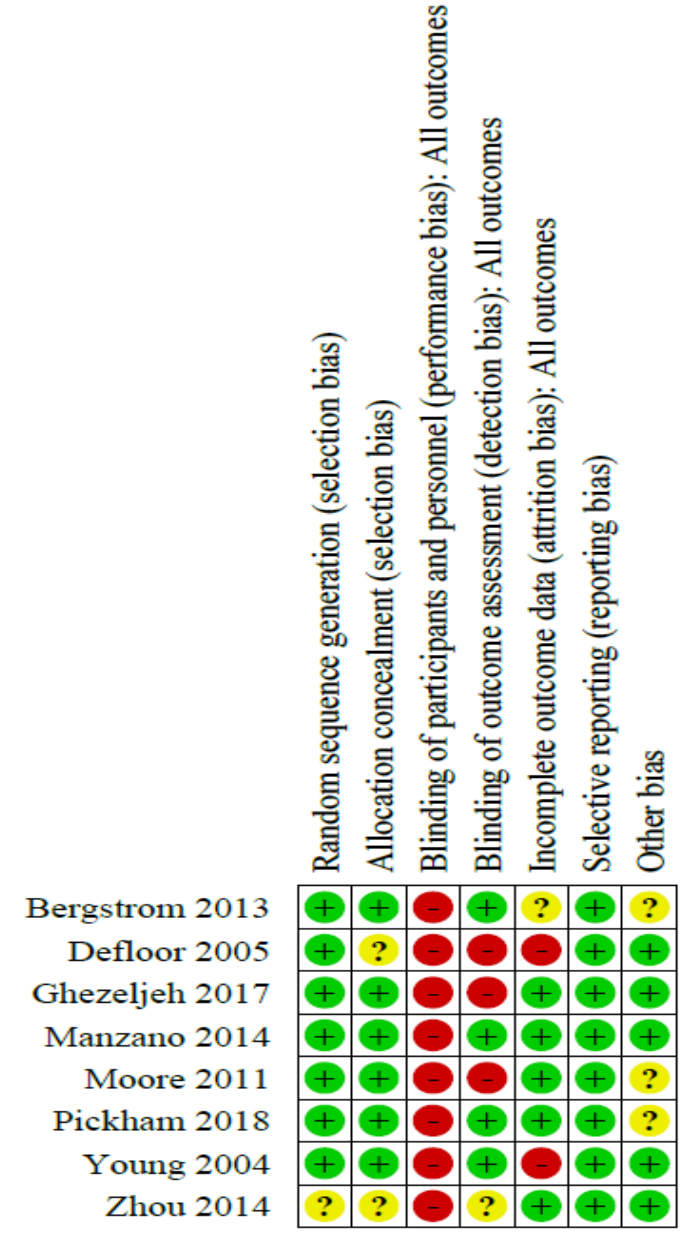
- Various tools for assessing risk of bias, e.g., Cochrane RoB tool for RCT(i.e., randomisation, allocation concealment, blinding, incomplete data, selective reporting, other bias)
- Risk of Bias (RoB) tools for non-randomised studies, e.g., ROBINS-I ("Risk Of Bias In Non-randomised Studies - of Interventions")

https://www.nhmrc.gov.au/guidelinesforguidelines/develop/assessing-risk-bias

Example of RoB assessment

Figure 4. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included clinical studies.

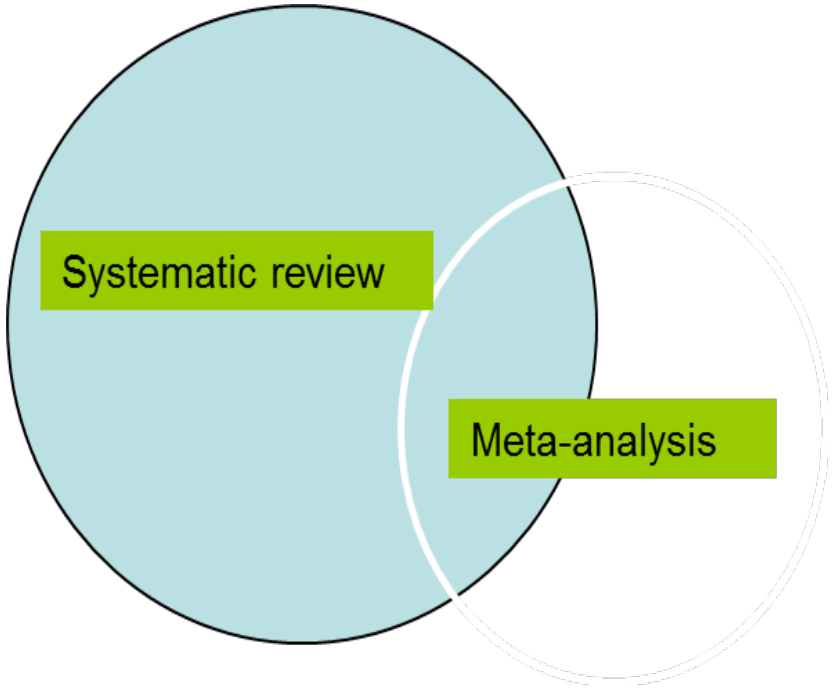




Gillespie BM et al Repositioning for pressure injury prevention in adults. Cochrane Database of Systematic Reviews 2020, Issue 6. Art. No.: CD009958. DOI10.1002/14651858.CD009958.pub3.

Optional components of a systematic review

Studies must be examining the same intervention against the same comparators, measuring the same outcome in the same population, using the same study design.



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META-ANALYSIS

What is a meta-analysis?

- Combines the results of two or more studies
- Estimates a common or average treatment effect across studies

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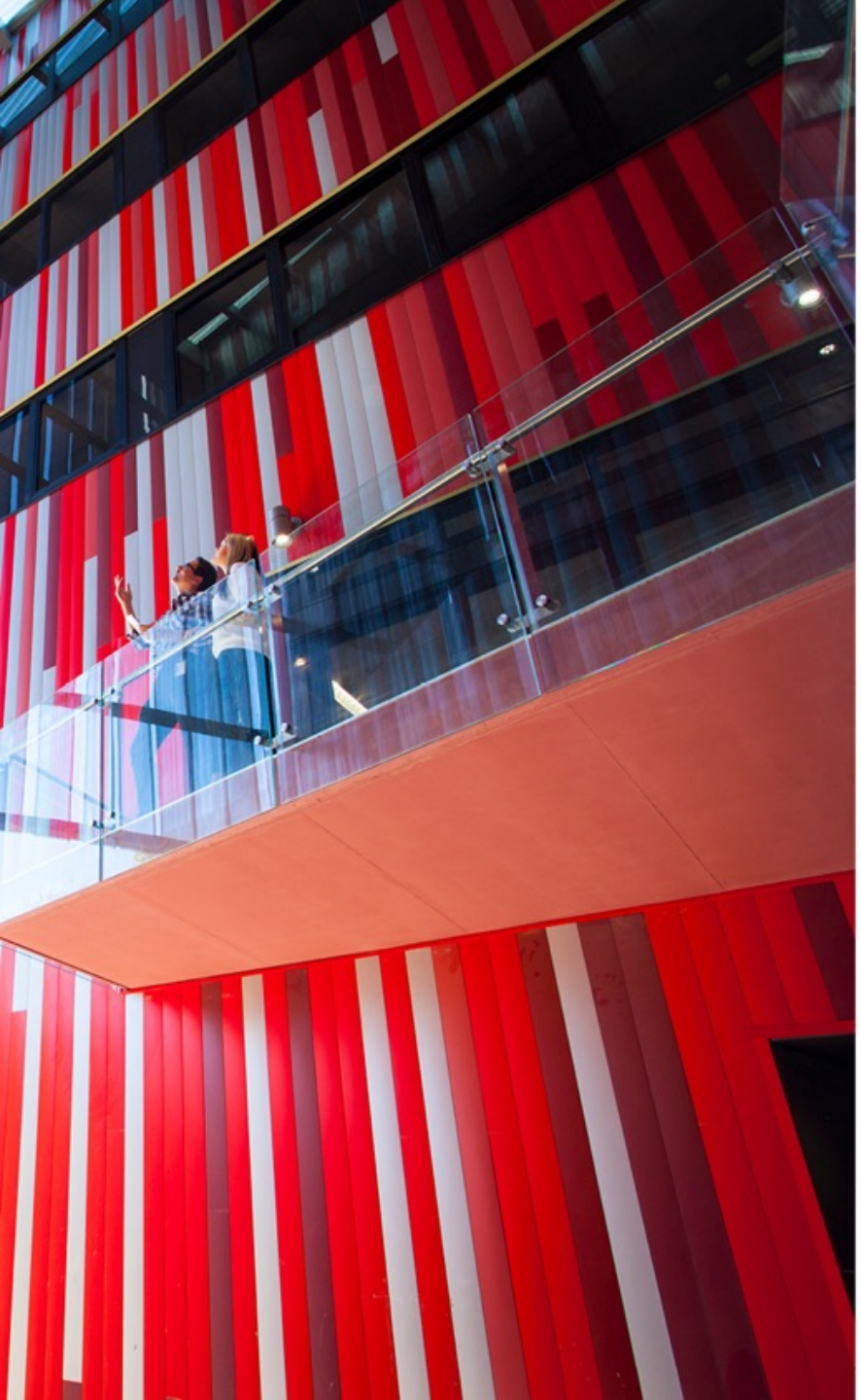

Why do a meta-analysis?

- Quantify treatment effects and their uncertainty
- Increase power
- Increase precision, larger sample size
- Explore differences between studies
- Settle controversies between studies
- Generate hypotheses

For example

- Eight trials studying the effect of different positioning regimens on the prevention of PI in adults.

- How can we summarise the effect of different positioning regimens across these trials?

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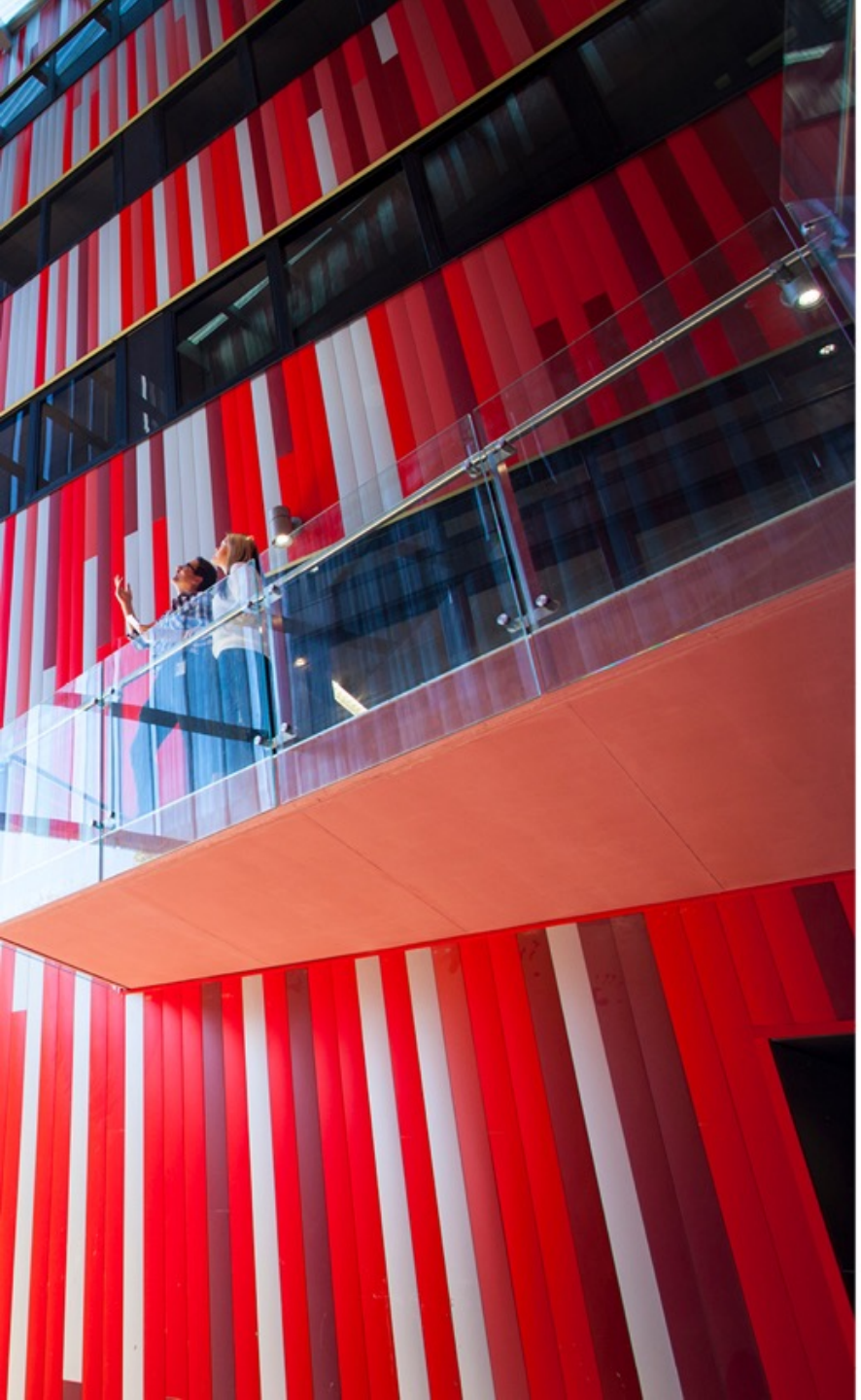
When should you do a meta-analysis

- When more than one study has provided results about the same question
- When there are minimal differences across studies
- When the same outcome has been measured
- When data in each study are available



Some issues

- Only summary statistic available (e.g., p = 0.01) or OR 2.1 (95% CI 1.0 – 4.6).
- When more than one intervention has been used, e.g., turning regimen and support surfaces)
- When the outcome has been measured by different instruments, e.g., pain, QoL

When not to do a meta-analysis
Garbage in = garbage out!

- A meta-analysis is only as good as the studies in it.
- If included studies are biased

✓Meta analysis results will be incorrect

✓Will give more credibility and narrower confidence intervals

- If serious reporting biases are present

✓Unrepresentative set of studies may give misleading result

Combining data

Gillespie BM et al Repositioning for pressure injury prevention in adults. Cochrane Database of Systematic Reviews 2020, Issue 6. Art. No.: CD009958. DOI10.1002/14651858.CD009958.pub3.

- Weighting studies
- More weight to studies that give more information
- More participants, more events, narrower confidence intervals
- Calculated using the estimated effect and its variance

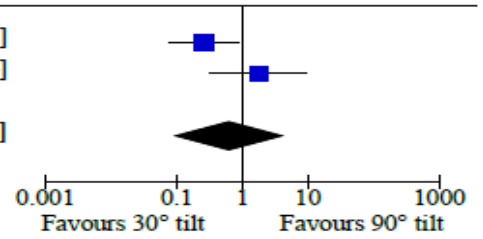
Comparison 2. 30° tilt 3-hourly overnight versus 90° tilt overnight

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Pressure injury occurrence (stage 1 to 4)	2	252	Risk Ratio (M-H, Random, 95% CI)	0.62 [0.10, 3.97]

Analysis 2.1. Comparison 2: 30° tilt 3-hourly overnight versus 90° tilt overnight, Outcome 1: Pressure injury occurrence (stage 1 to 4)

Study or Subgroup	30° tilt 3-hourly overnight Events	Total	90° tilt overnight Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Moore 2011	3	99	13	114	54.7%	0.27 [0.08 , 0.91]
Young 2004	3	18	2	21	45.3%	1.75 [0.33 , 9.34]
Total (95% CI)		**117**		**135**	**100.0%**	**0.62 [0.10 , 3.97]**
Total events:	6		15			

Heterogeneity: Tau² = 1.24; Chi² = 3.21, df = 1 (P = 0.07); I² = 69%
Test for overall effect: Z = 0.50 (P = 0.62)
Test for subgroup differences: Not applicable



Displaying results

Gillespie BM et al Repositioning for pressure injury prevention in adults. Cochrane Database of Systematic Reviews 2020, Issue 6. Art. No.: CD009958. DOI10.1002/14651858.CD009958.pub3.

- Forest plot
- Provides a ‘snapshot’ of statistical results
- Identifies heterogeneity
- Shows the effect of individual studies and the ‘summary’ effect across studies

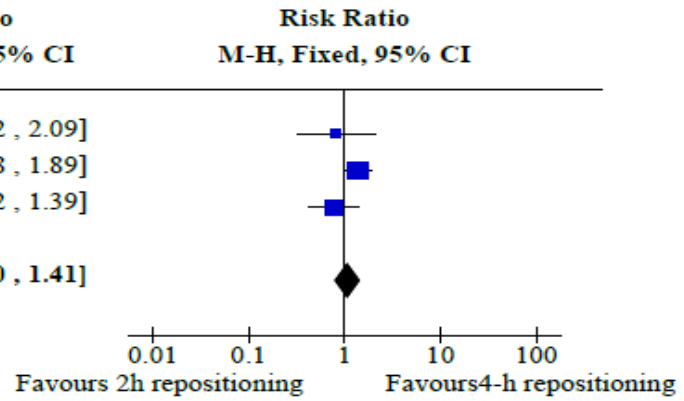
Analysis 1.1. Comparison 1: 2-hourly repositioning versus 4-hourly repositioning on any type of support surface, Outcome 1: Pressure injury occurrence (stage 1 to 4)

Study or Subgroup	2-hourly repositioning Events	Total	4-hourly repositioning Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Bergstrom 2013	8	321	9	295	15.4%	0.82 [0.32 , 2.09]
Defloor 2005	39	63	30	66	48.2%	1.36 [0.98 , 1.89]
Manzano 2014	17	165	22	164	36.3%	0.77 [0.42 , 1.39]
Total (95% CI)		**549**		**525**	**100.0%**	**1.06 [0.80 , 1.41]**
Total events:	64		61			

Heterogeneity: $Chi^2 = 3.65$, $df = 2$ ($P = 0.16$); $I^2 = 45\%$

Test for overall effect: $Z = 0.41$ ($P = 0.68$)

Test for subgroup differences: Not applicable



The label

Review: Use of repositioning regimes and positions to prevent pressure injuries

Comparison: 2 hourly and 4 hourly

Outcome: pressure injuries of any stage

Comparison 1. 2-hourly repositioning versus 4-hourly repositioning on any type of support surface

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Pressure injury occurrence (stage 1 to 4)	3	1074	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.80, 1.41]

Analysis 1.1. Comparison 1: 2-hourly repositioning versus 4-hourly repositioning on any type of support surface, Outcome 1: Pressure injury occurrence (stage 1 to 4)

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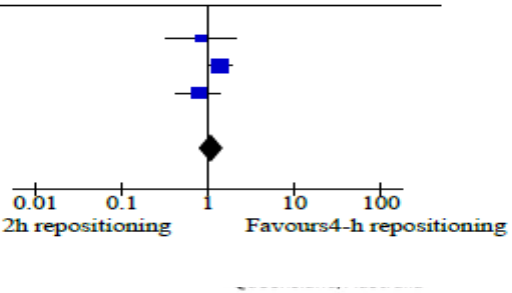

The scale

The horizontal line at the bottom is the scale measuring the treatment effect.

The outcome is PI, the right side of the scale is greater than 1, BUT the diamond crosses the line of 'no effect'.

Comparison 1. 2-hourly repositioning versus 4-hourly repositioning on any type of support surface

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Pressure injury occurrence (stage 1 to 4)	3	1074	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.80, 1.41]

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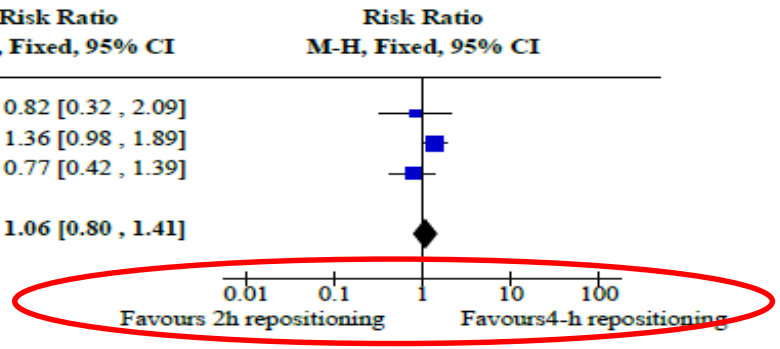
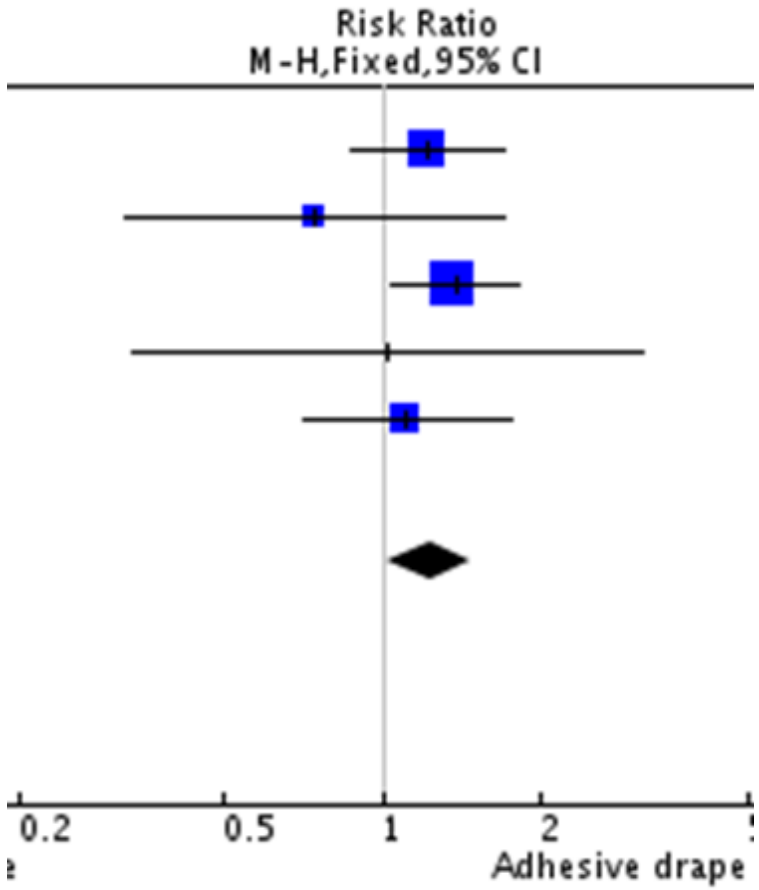


The line of no effect

- The vertical line in the middle is the line of no effect.
- Each horizontal line represents an individual study.
- If the horizontal line crosses the line of no effect, then there is no statistical difference between the treatment and control groups



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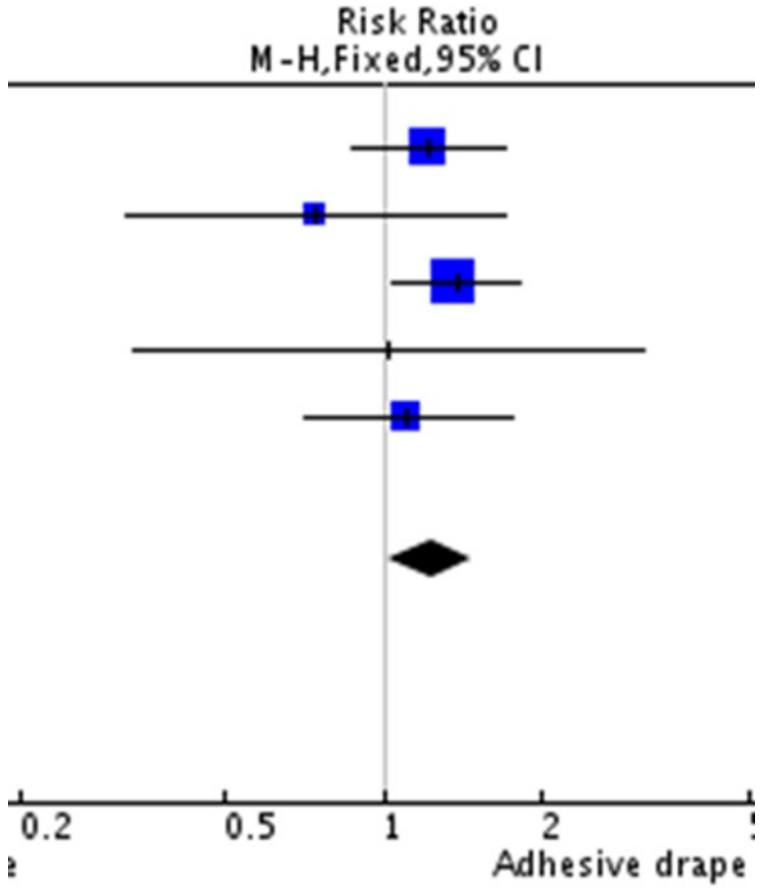
Individual trials

- Each study is given a square block representing the treatment effect.
- The size of the block is proportional to the weight given to that study
- The horizontal line is the confidence interval (CI)
- The wider the confidence interval, the less likely the treatment effect is the true effect.



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Each study

- For each study there is an ID (first author & year)
- Data for each trial are divided into experimental and control
- This is the % of weight given to each study in the pooled analysis

	2-hourly repositioning		4-hourly repositioning			Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI

The summary statistic

- Data shown in the graph are also shown numerically
- The label above the graph indicates the summary statistic used

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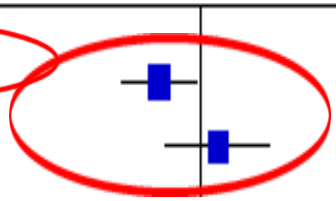

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The pooled result

- The diamond represents the treatment effect based on pooled results from the meta-analysis
- The point estimate is represented by the vertical height of the diamond (0.62)
- The confidence interval is represented by the horizontal width of the diamond (0.10 to 3.97)

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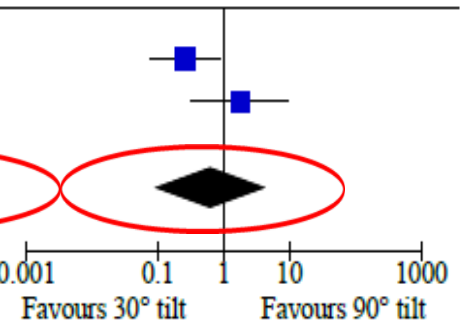

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Interpreting confidence intervals

Always present the confidence interval with the treatment effect estimate

Precision

✓The point estimate is the best guess of the effect of an intervention

✓ CI represents uncertainty – it is simply a range of values we can be reasonably sure contains the true effect

Significance

✓If the confidence interval contains a null value

✓It rarely means evidence of no effect

✓ It means effect cannot be confirmed or refuted by the available evidence

Consider what level of change is clinically important

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Interpretation

- The heterogeneity between studies is represented by the Chi^2 & the I^2 (or can be assessed visually)
- The statistical difference between treatments is represented by the Z score

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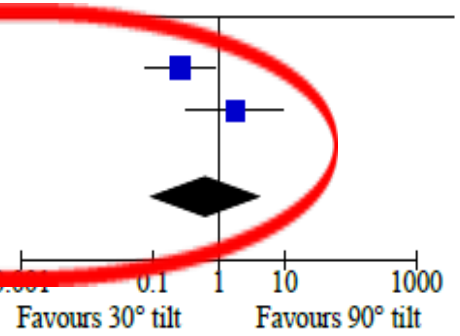

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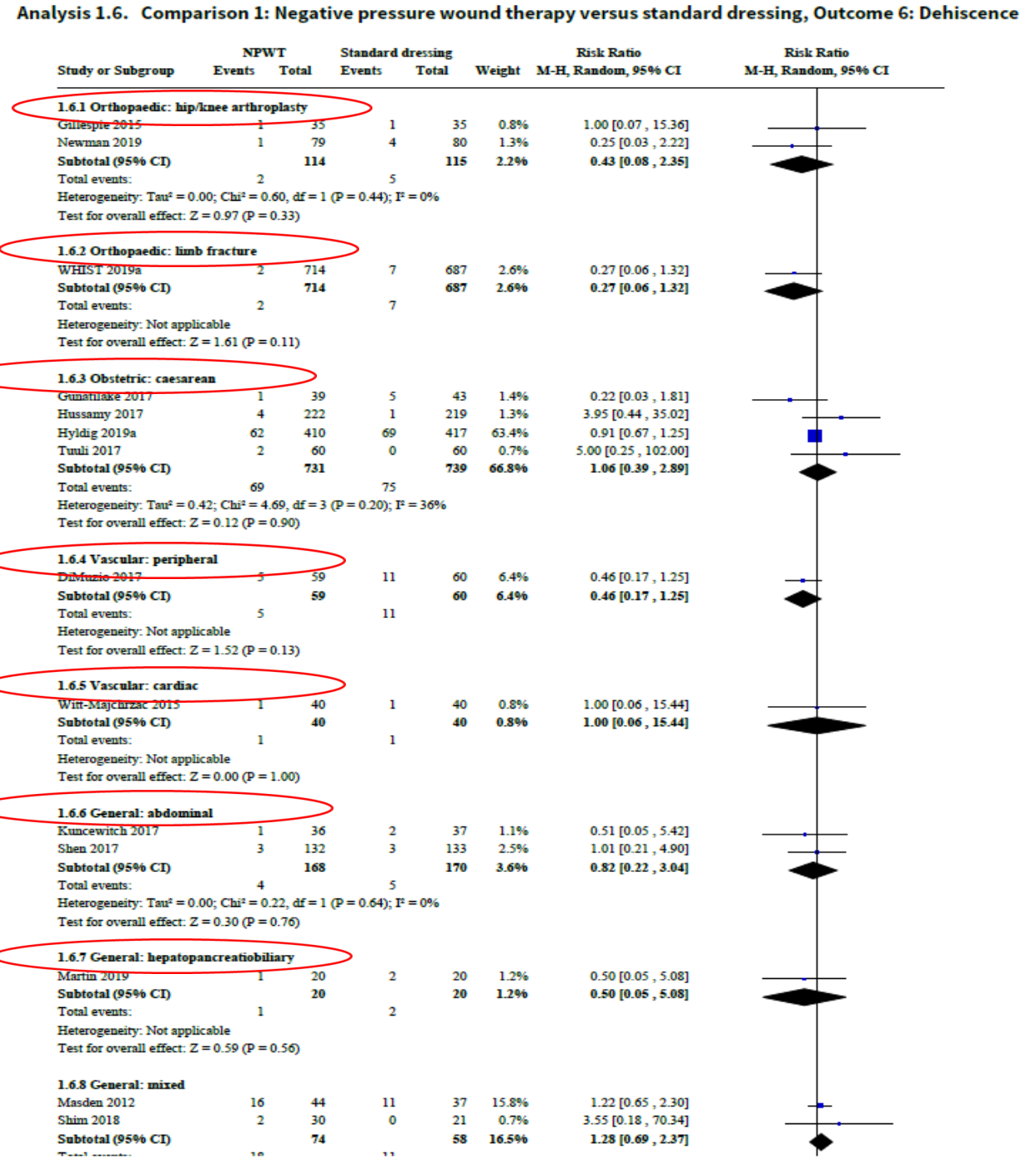
Subgroup analyses

- Involve splitting all participant data into subgroups to make comparisons between them.
- Subgroup analyses for subsets of participants, e.g., males/ females, or for subsets of studies, e.g., different geographical locations.
- Subgroup analyses to investigate heterogeneous results, or answer specific questions about particular patient groups, types of intervention or types of study.



Sensitivity analyses

- Analysis to determine how sensitive the results of a systematic review are to changes based on how it was done, e.g., one sensitivity analysis may explore the impact of using different meta-analysis models.
- Another sensitivity analysis may explore the impact of excluding or including studies in meta-analysis based on sample size, methodological quality, or variance. If results remain consistent across the different analyses, the results can be considered robust as even with different decisions they remain similar.
- Inclusion of studies based on quality or risk of bias can affect the pooled result of the meta-analysis
- E.g., sensitively analyses of studies at high risk of bias vs studies of low risk of bias

Other issues of interpretation

- Do the results make sense? i.e., biological plausibility.
- Do conclusions reflect findings? Avoid overstating inconclusive results.
- Applicability to clinical practice, the ‘so what’ question, external validity.

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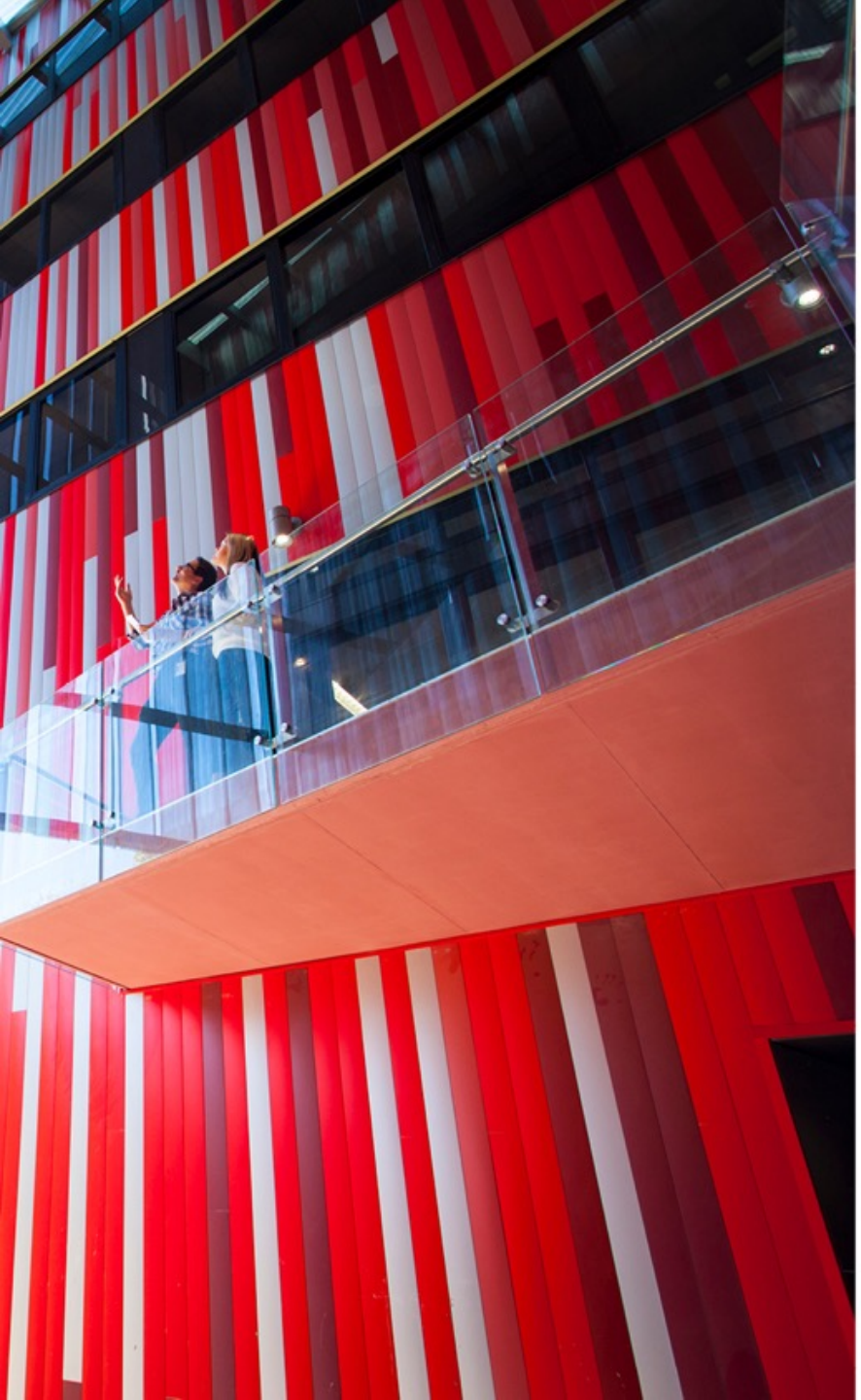

Summary of key points

- SR examine a focussed questions of clinical importance
- May or may not include meta-analysis, depending on how the outcomes were measured, levels of heterogeneity
- Require a research team where tasks can be allocated, +statistician if MA is included
- Decision to pool data influenced by degree of heterogeneity between studies.
- Conclusions must be supported by the results of the meta-analyses.
- Care in interpretation – sensitivity or sub-group analysis may be appropriate

THANK YOU

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