folkehelseinstituttet

GRADE

The Grading of Recommendations Assessment, Development and Evaluation (short GRADE)

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Plan

- Introduction to GRADE
- GRADE domains
- Summary of findings table
- Certainty of evidence

Definition of certainty of evidence

- “the ratings of the certainty of evidence reflect the extent of our confidence that the estimates of the effect are correct”

- “not rating certainty in point estimates, but rather certainty that the true effect lies in a particular rang”

M. Hultcrantz et al. / Journal of Clinical Epidemiology 87 (2017) 4-13

GRADE

- assessing the certainty of the evidence
- structured and transparent
- criteria for downgrading and upgrading the certainty in evidence

Face-to-face interventions for informing or educating parents about early childhood vaccination (Review)

GRADE – SoF

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Face-to-face interventions directed to parents for informing or educating parents about early childhood vaccination, as compared with control

Patient or population: parents of preschool-aged children or expectant parents
Settings: clinics, antenatal classes, or the mother's home
Intervention: face-to-face information or educational interventions
Comparison: control (no education, other education, or control not described)

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed (baseline) risk	Corresponding (intervention) risk				
	Control (no face-to-face information or education)	Face-to-face information or education				
Vaccination status Final time point (3, 6, or 12 months post-intervention)	55 per 100[1]	66 per 100 (57 to 75)	**RR 1.20** (1.04 to 1.37)	3004 (7 studies)	⊕⊕◯◯ **low**[2]	The results for this outcome were variable, so the true result may be substantially higher or lower than this estimate

Formulate question

Select outcomes

Rate importance

Outcomes across studies

Create evidence profile with GRADEpro

Rate quality of evidence for each outcome

P	Outcome — Critical
I	Outcome — Critical
C	Outcome — Important
O	Outcome — Not important

Summary of findings & estimate of effect for each outcome

High	⊕⊕⊕⊕
Moderate	⊕⊕⊕◯
Low	⊕⊕◯◯
Very low	⊕◯◯◯

Grade down

1. Risk of bias
2. Inconsistency
3. Indirectness
4. Imprecision
5. Publication bias

Grade up

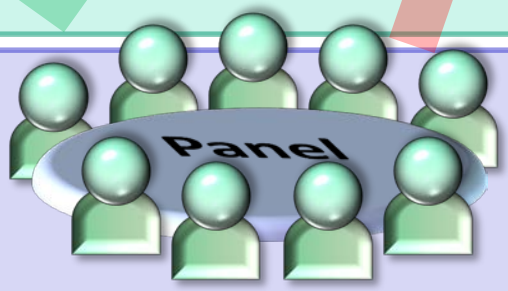
1. Large effect
2. Dose response
3. Opposing bias & Confounders

Randomization increases initial quality

Evidence synthesis

Input

Recommendation



Grade overall quality of evidence across outcomes based on lowest quality of ***critical*** outcomes

Grade recommendations

- For or against (direction) ↓↑
- Strong or conditional/weak (strength)

By considering balance of:

- ❑ Quality of evidence
- ❑ Balance benefits/harms
- ❑ Values and preferences

Revise if necessary by considering:

- ❑ Resource use (cost)

Guideline

Formulate Recommendations (↓↑ | ⊕…)

- "The panel recommends that ….should…" (↑↑ | ⊕…)
- "The panel suggests that ….should…" (↑? | ⊕…)
- "The panel suggests to **not** …" (↓? | ⊕…)
- "The panel recommends to **not**…" (↓↓ | ⊕…)

Start of GRADEing

- formulate question
- decide critical outcomes
- decide importance of outcome
- identify systematic reviews/studies

Framing the question

P: parents of preschool-aged children or expectant parents

S: clinics, antenatal classes, or the mother's home

I: face-to-face information or educational interventions

C: control (no education, other education, or control not described)

O: outcome

Cochrane Library

Cochrane Database of Systematic Reviews

Face-to-face interventions for informing or educating parents about early childhood vaccination (Review)

Kaufman J, Ryan R, Walsh L, Horey D, Leask J, Robinson P, Hill S

Objectives

To assess the effects of face-to-face interventions for informing or educating parents about early childhood vaccination on vaccination status and parental knowledge, attitudes and intention to vaccinate.

Critical outcomes and importance Kaufman 2018

Worksheet

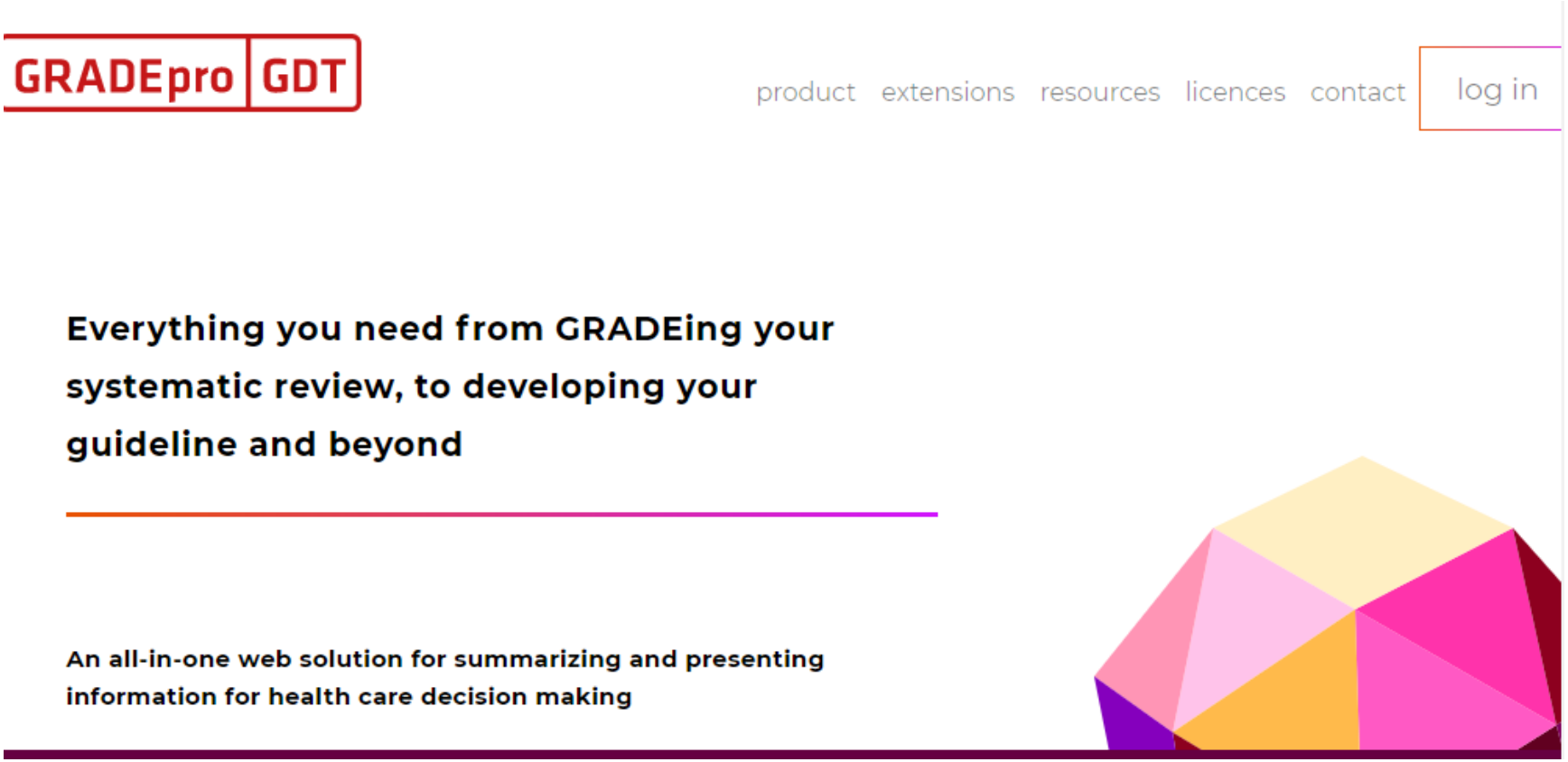
Exercise 1

Selecting and rating the importance of outcomes

1. Children: vaccination status of child (i.e. vaccination status up-to-date, or receipt of one or more vaccines, as defined by study authors); outcome domain: vaccination status and behaviours
2. Parents: knowledge or understanding of vaccination; outcome domain: knowledge or understanding
3. Parents: attitudes or beliefs about vaccination; outcome domain: attitudes or beliefs
4. Parents: intention to vaccinate child; outcome domain: attitudes or beliefs
5. All categories: adverse effects; outcome domain: any

https://gdt.gradepro.org/app/handbook/handbook.html#h.1i2bwkm8zpjo

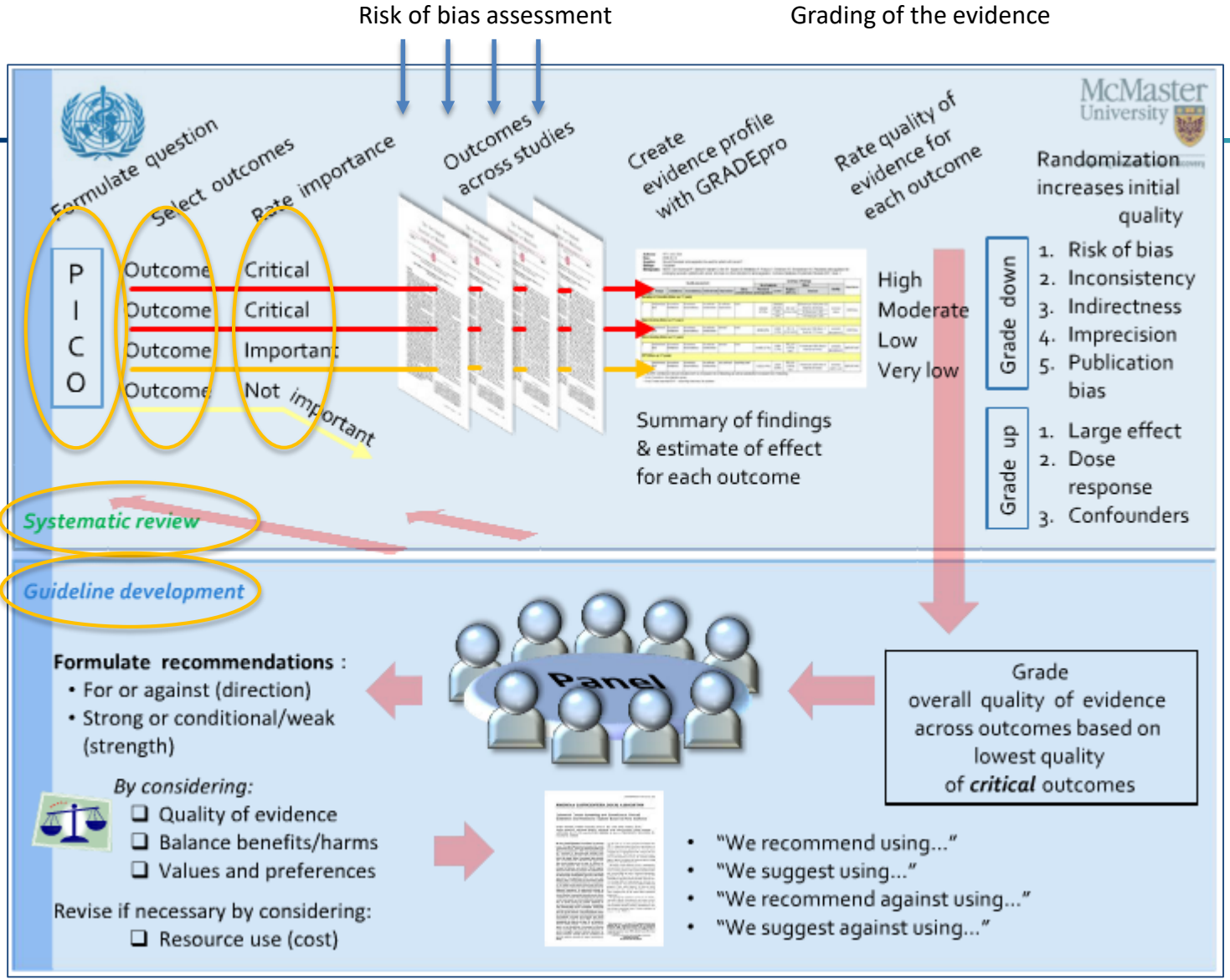
https://gradepro.org/product/#features



GRADE categories for the certainty of a body of evidence

Quality level	Symbol	Definition
High	⊕⊕⊕⊕	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	⊕⊕⊕◯	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	⊕⊕◯◯	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low	⊕◯◯◯	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

Population
Intervention
Comparison
Outcome



Determinants of certainty
5 factors that can lower certainty

1. Design limitations (risk of bias)
2. Inconsistency of results (heterogeneity)
3. Indirectness (applicability)
4. Imprecision (number of events and confidence intervals)
5. Publication bias

Risk of bias assessment

Review authors' judgement:

- **Was the allocation sequence adequately generated?**
- **Was allocation adequately concealed?**
- **Was knowledge of the allocated intervention adequately prevented during the study?**
  - Participants
  - Trial personnel
- **Were incomplete outcome data adequately addressed?**
- **Are reports of the study free of suggestion of selective outcome reporting?**
- **Was the study apparently free of other problems that could put it at a high risk of bias?**

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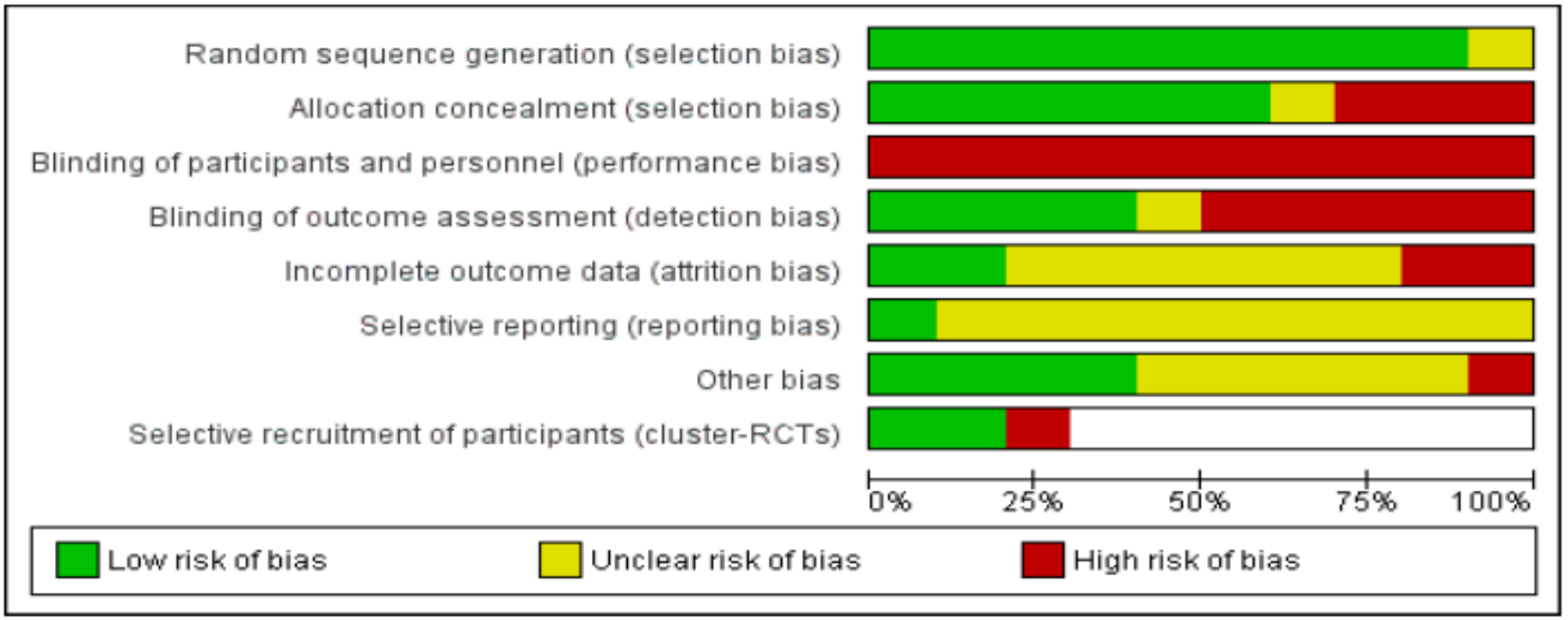
Domains from the Cochrane Handbook: http://handbook.cochrane.org/

Risk of bias summary for a body of evidence

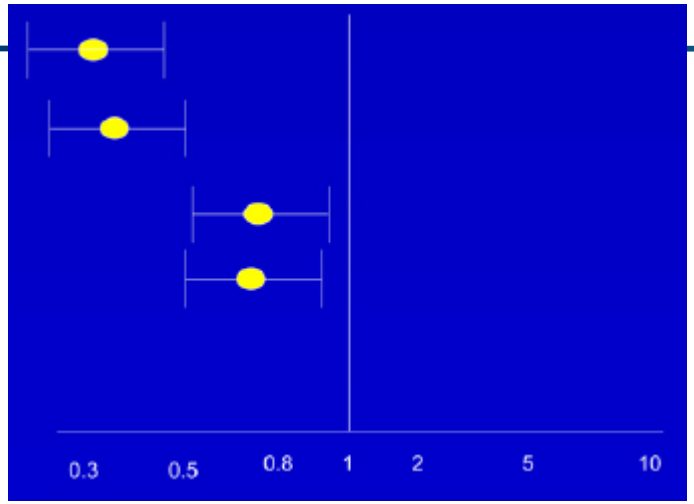
Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies



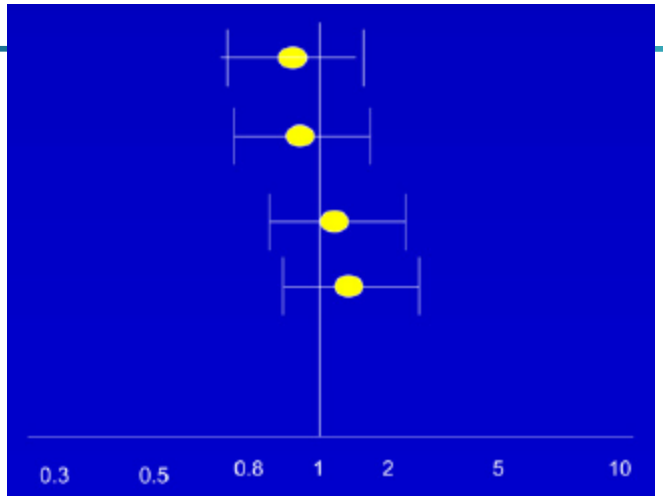
Kaufman 2018

«All studies had limitations in design. We downgraded evidence where the contributing studies were at high or unclear risk of bias for sequence generation (Jackson 2011), or allocation concealment (Hu 2017; Usman 2009; Usman 2011; Wood 1998)”

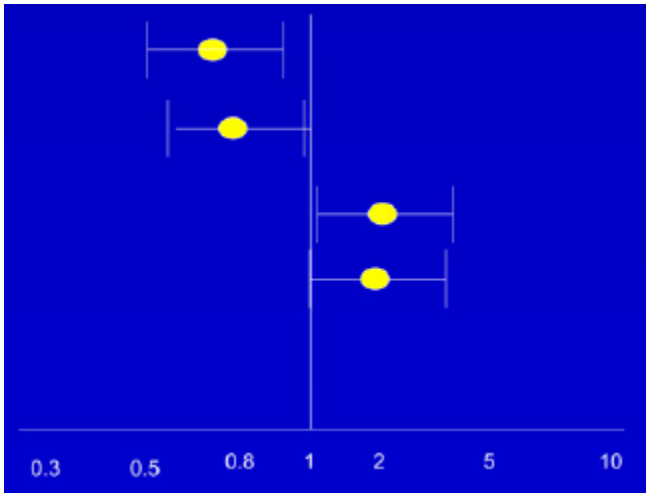
Inconsistency - Heterogeneity



No overlap,
same direction of effect



Overlap,
different directions of effect



No overlap,
different directions of effect

Inconsistency

Exercise 3

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Kaufman 2018

“We also downgraded the certainty of the evidence for vaccination status, due to inconsistency, which was clear from the high level of statistical heterogeneity.»

Indirectness

- Differences in population (applicability)
- Differences in interventions (applicability)
- Differences in outcomes measures (surrogate outcomes)
- Indirect Comparisons

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Kaufman 2018

“We downgraded the certainty of the evidence for attitudes due to indirectness, because the specific measures for this outcome (perceived diseases severity and vaccine benefits) were only part of what could be measured, and what was relevant to parents and other decision makers.»

Imprecision

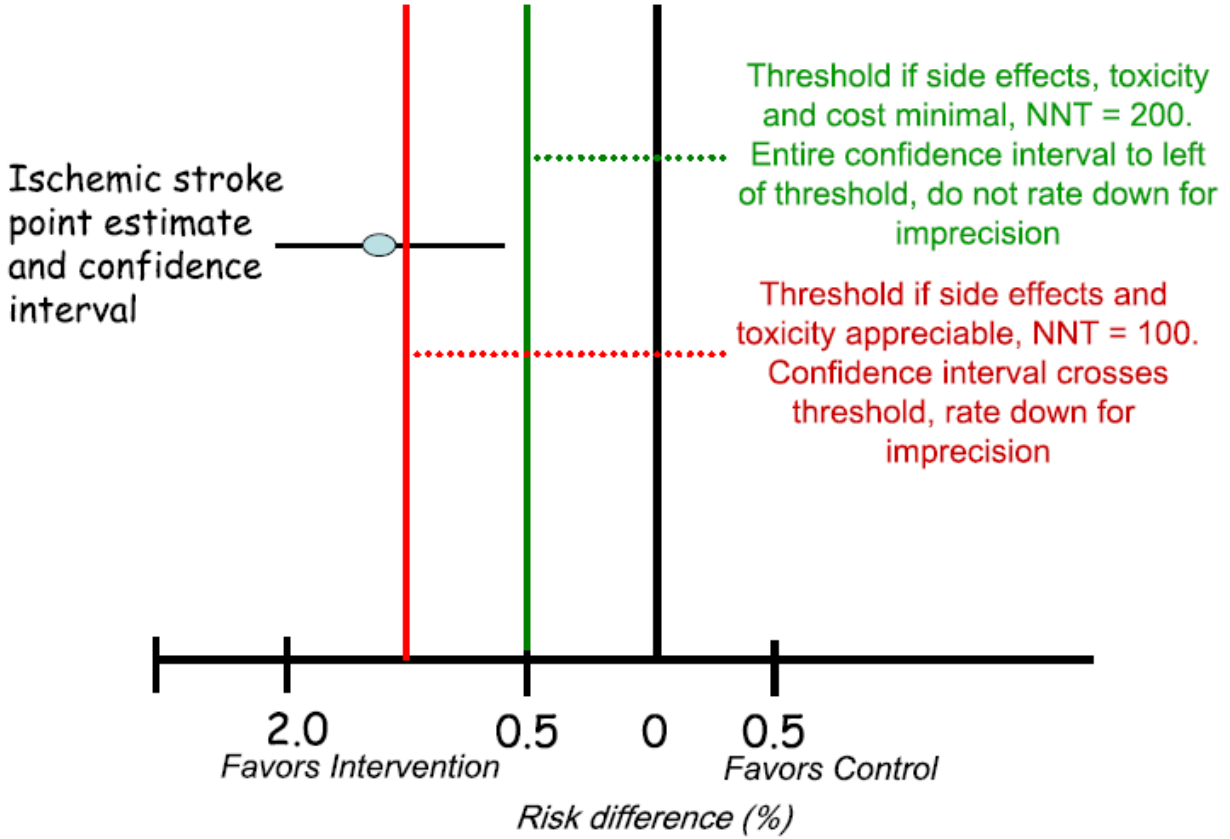

Fig. 1. Rating down for imprecision in guidelines: thresholds are key.

NNT: Number-Needed-to-Treat

Imprecision

- Exercise 4

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Kaufman 2018

«The certainty of the evidence for intention to vaccinate and adverse effects was downgraded for imprecision, due to the wide confidence intervals for the included studies.»

Publication bias

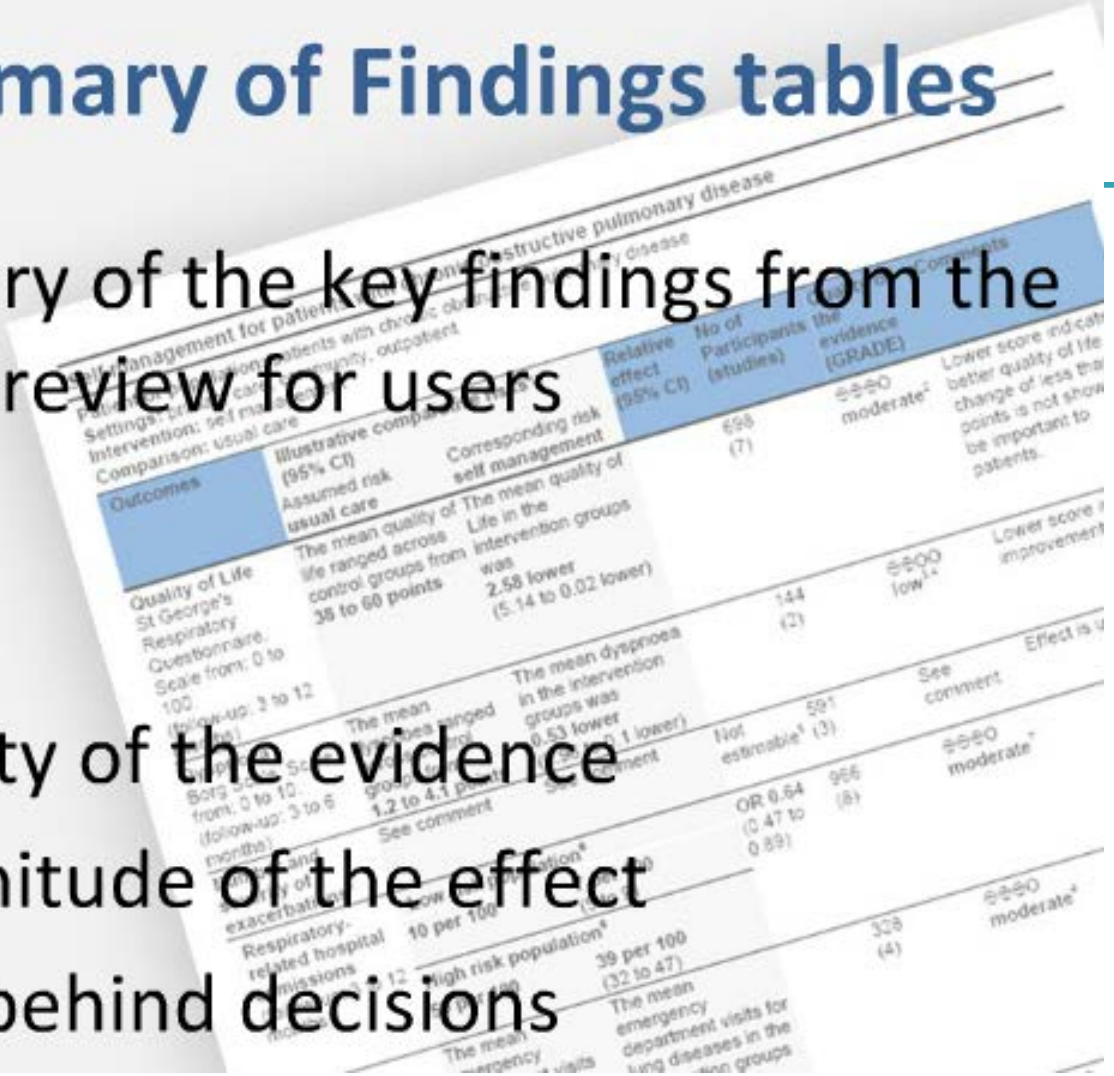
Publication bias is a systematic under-estimation or an over-estimation of the underlying beneficial or harmful effect due to the **selective publication of studies**. Confidence in the combined estimates of effects from a systematic review can be reduced when publication bias is suspected, even when the included studies themselves have a low risk of bias.

Kaufman 2018

«We did not downgrade any outcomes for issues of publication bias.»

The Summary of Findings tables

- Is a summary of the key findings from the systematic review for users
- Presents
  - the quality of the evidence
  - the magnitude of the effect
  - reasons behind decisions



Kaufman 2018

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Grading of Recommendations Assessment, Development and Evaluation

http://www.gradeworkinggroup.org/

Table: GRADE's approach to rating quality of evidence (aka confidence in effect estimates)

For each outcome based on a systematic review and across outcomes (lowest quality across the outcomes critical for decision making)

1. Establish initial level of confidence		2. Consider lowering or raising level of confidence		3. Final level of confidence rating
Study design	*Initial confidence in an estimate of effect*	*Reasons for considering lowering or raising confidence*		*Confidence in an estimate of effect across those considerations*
		↓ Lower if	↑ Higher if*	
Randomized trials →	High confidence	Risk of Bias Inconsistency Indirectness Imprecision Publication bias	Large effect Dose response All plausible confounding & bias • would reduce a demonstrated effect or • would suggest a spurious effect if no effect was observed	High ⊕⊕⊕⊕
				Moderate ⊕⊕⊕◯
Observational studies →	Low confidence			Low ⊕⊕◯◯
				Very low ⊕◯◯◯

*upgrading criteria are usually applicable to observational studies only.

Learning material - examples

- Cochrane interactive learning http://training.cochrane.org/interactivelearning
- GRADE https://cebgrade.mcmaster.ca/
- Equatornetwork http://www.equator-network.org/
- Testing treatments http://www.testingtreatments.org/

Peer review

- Prepare a short introduction to what the review is about
- Positive feedback
- Points to consider improving
- Preparation time apr. 45 min
- Each feedcak 14 min, max 7 min by opponent
- Group starts at 12.00
- Done by 13.30

Name	Tentative research question	Tutor	Opponent
Nazar	Breath analysis as a test for cancer screening: A systematic review and meta-analysis	Lillebeth	Israel
Israel Paul	What is the prevalence of hearing loss among noise-exposed workers in Africa?	Lillebeth	Olive
Olive	Severe illness among infants, a systematic reveiw	Lillebeth	Mari
Mari	To what degree do patients adhere to anticoagulation treatment in secondary prevention after cardioembolic stroke? Which factors may affect the level of adherence?	Lillebeth	Nazar

Name	Tentative research question	Tutor	Opponent
Melf	What do we know about the cost effectiveness of SMS reminders to increase adherence to preventive therapies in sub-Saharan Africa?	Eva	Tekle
Tekle Airgecho	Antimicrobial peptides are emerging topics of interest to fight against antimicrobial drug resistance. The bacterial toxin anti-toxin (TA) system, is less studied yet its promising results attracted attention of experts in the area. ''So, what is the TA system in bacteria: its biology, mechanism of action, possibilities and implication in public health intervention'' will be my topic during the systematic review course	Eva	Bezawit
Bezawit	Traditional healers contribution to disease control in a pastoralist community: systematic review.	Eva	Martina
Martina Reiten	Which instruments are used for measuring pain after stroke in the literature?	Eva	Melf

Name	Tentative research question	Tutor	Opponent
Soheir	The Prevalence of Non-communicable Disease Risk Factors in East Africa Adults	Geir	Erik
Erik Oftedahl	metaanalyse eller review om assosiasjonen mellom sivilstatus og selvmord	Geir	Thandile
Thandile	Iron supplementation in children with severe acute malnutrition	Geir	Ingrid Kristine
Ingrid Kristine	To assess the effect of the Prosigna Breast Cancer Prognostic Gene Signature Assay (Prosigna test) for predicting disease recurrence in breast cancer patients.	Geir	Soheir

Name	Tentative research question	Tutor	Opponent
Binyam	Does behavior change communication applied in developing text message intervention in maternal and child health?	Hilde	Berit
Josien	What are essential clinical decision making skills for Caesarean section in Low and Middle income countries	Hilde	Binyam
Berit	Is Postpartum depression a determinant when evaluating models of maternal care in developing countries?	Hilde	Josien