What is the target of certainty of evidence rating?

GRADE guidance

On behalf of the “ Certainty in evidence” Project Group

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Background & Aim

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GRADE UPDATE OF PAPERS

The GRADE Working Group clarifies the construct of certainty of evidence

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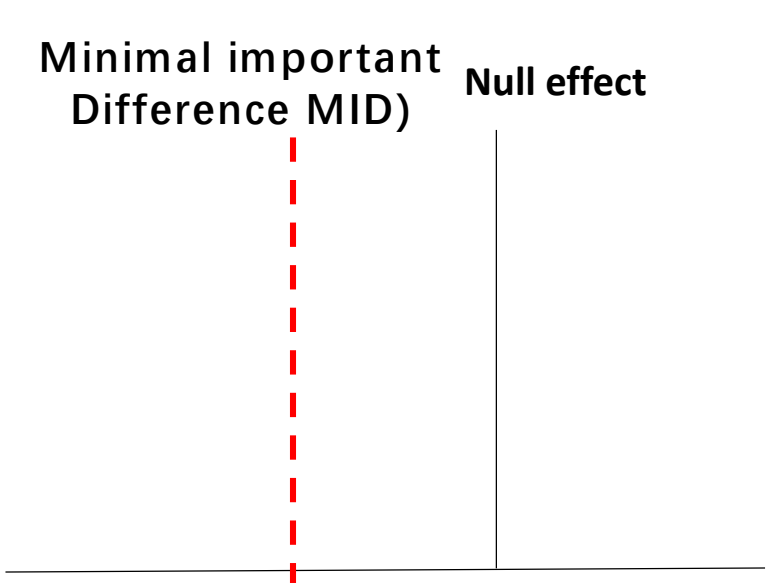
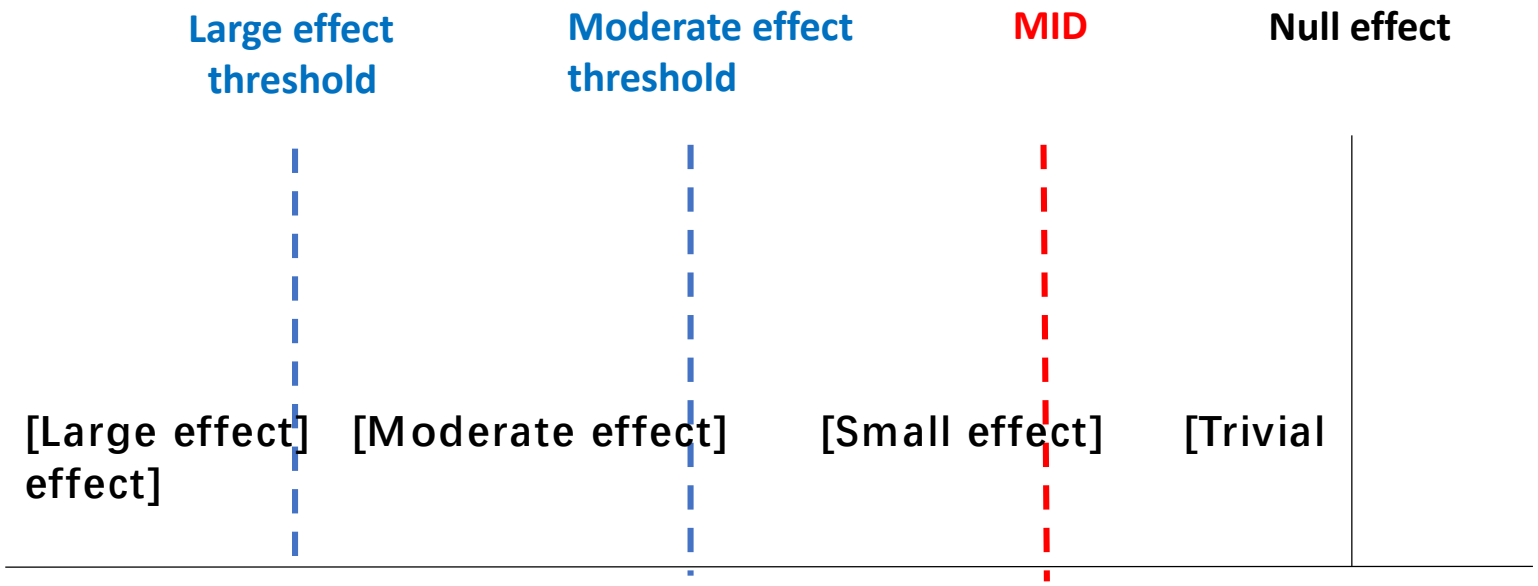
We are NOT assessing our confidence in point estimates of effects, but rather our confidence in where effects lie relative to particular threshold(s).



Minimally contextualized approach



Partially contextualized approach

Step 1: Choose the degree of contextualization

minimally/partially contextualized approach

Step 2: Choose and set the threshold(s)

Step 3: Determine the target of certainty rating

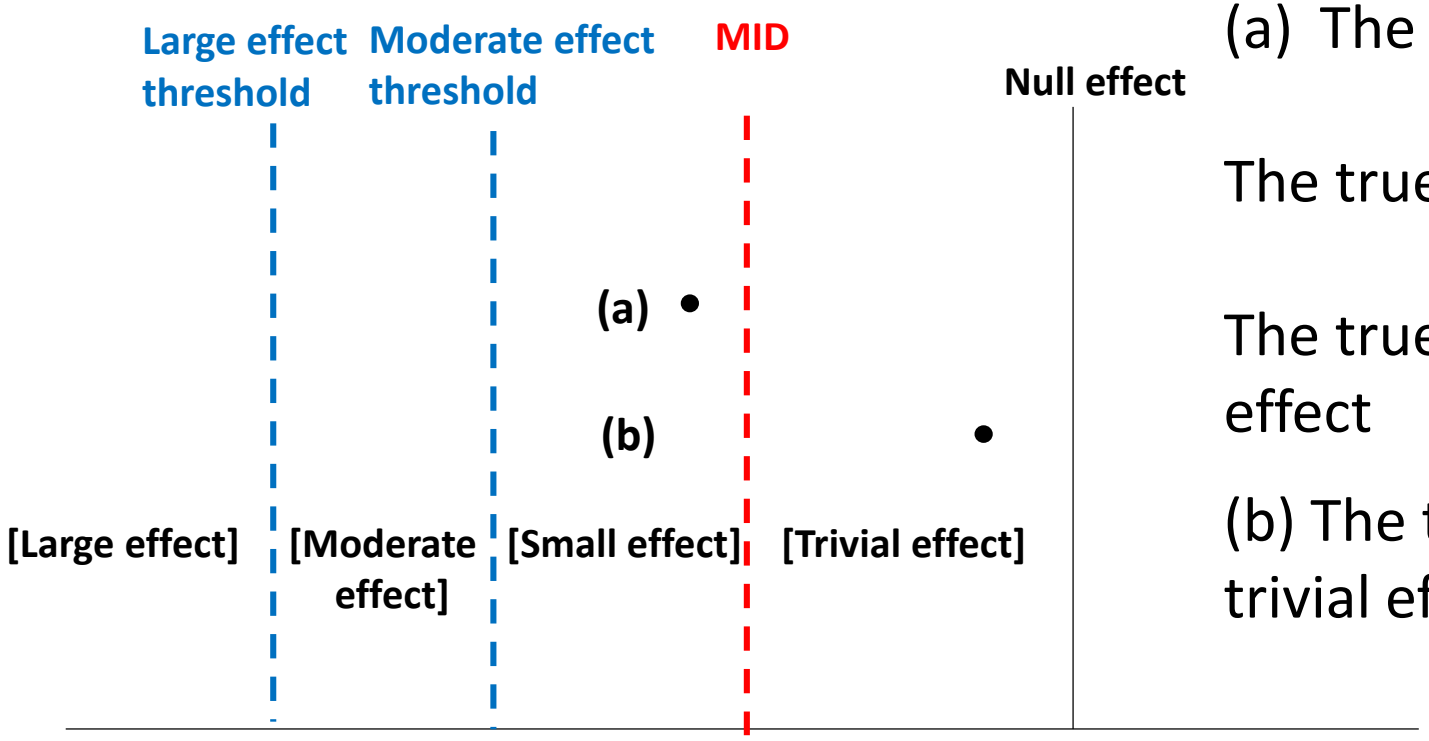
the position of point estimate in relation to the chosen threshold(s)

Step 4: Confidence interval crosses no threshold don’t rate down imprecision

Confidence interval crosses a threshold rate down for imprecision

The target of certainty rating will depend on

the point estimate in relation to the chosen threshold(s)



(a) The true effect is greater than the null

OR

The true effect is greater than the MID

OR

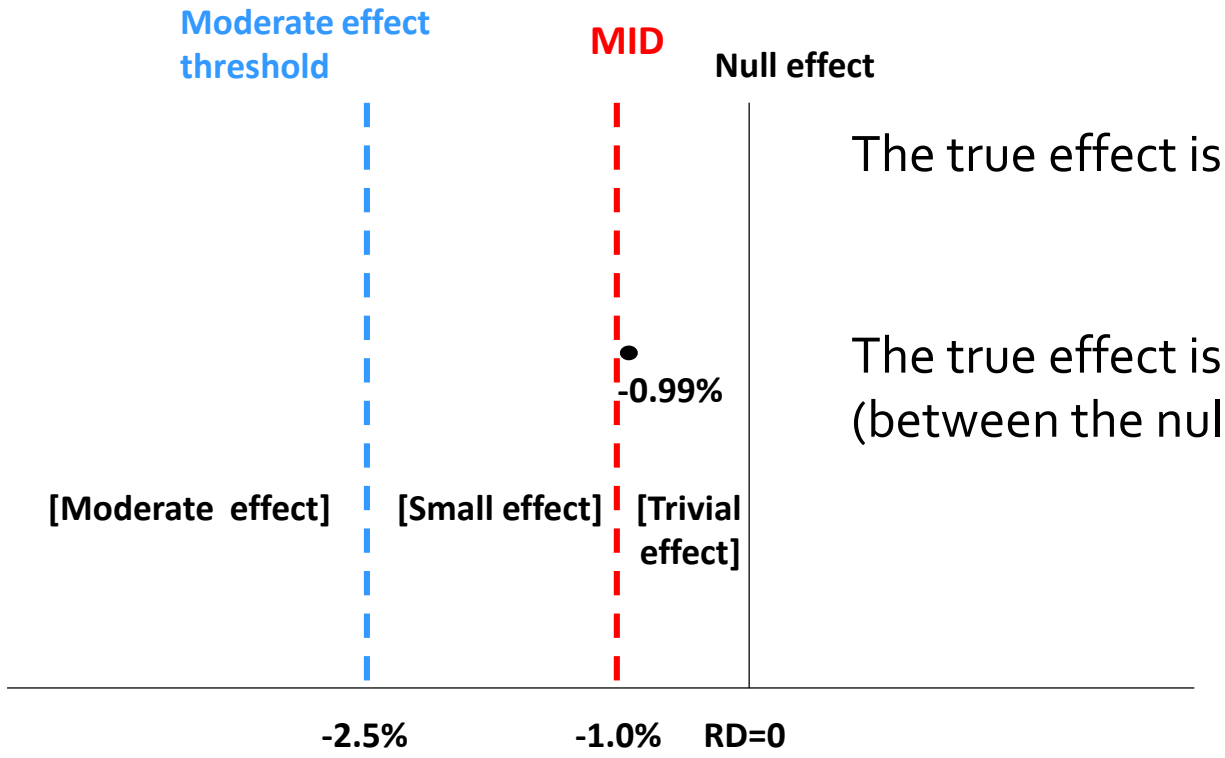
The true effect represents small important effect

(b) The true effect falls within the range of trivial effect (a trivial effect is present)

When the point estimate is very close to the threshold

Approach 1: We still rate our certainty in relation to a single threshold.

Approach 2: We rate certainty in relation to adjacent threshold(s).



The true effect is trivial (between null and MID)

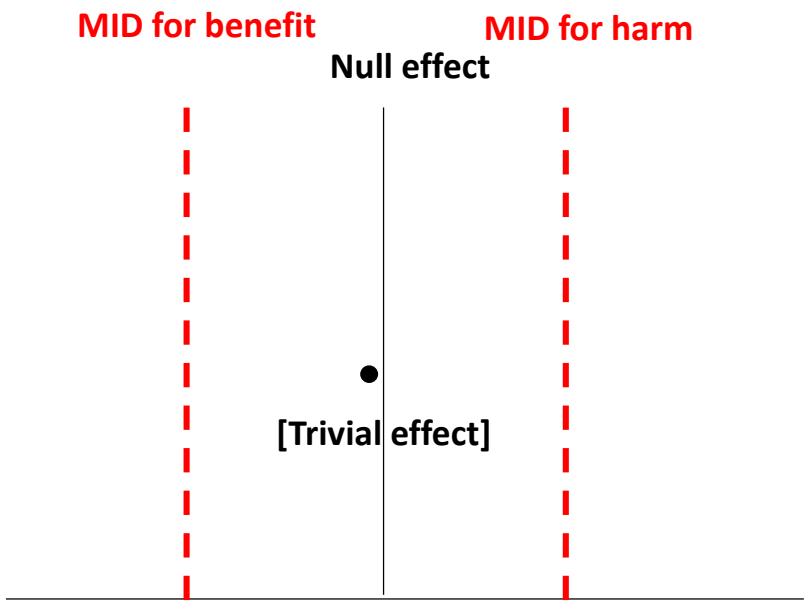
OR

The true effect is trival or small but important (between the null and moderate effect threshold

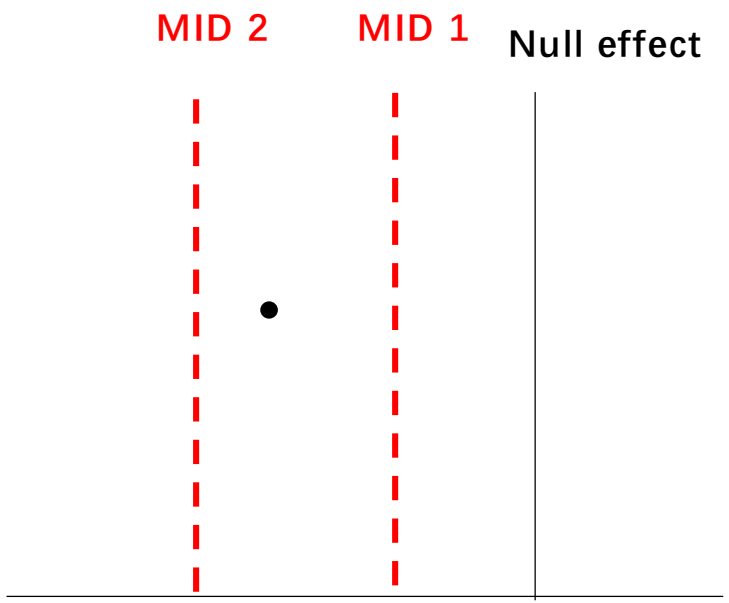
We can NEVER rate our certainty in point estimate alone (no effect)

So when estimate near null can’t rate certainty in non-null but in trivial effect

So need MIDs



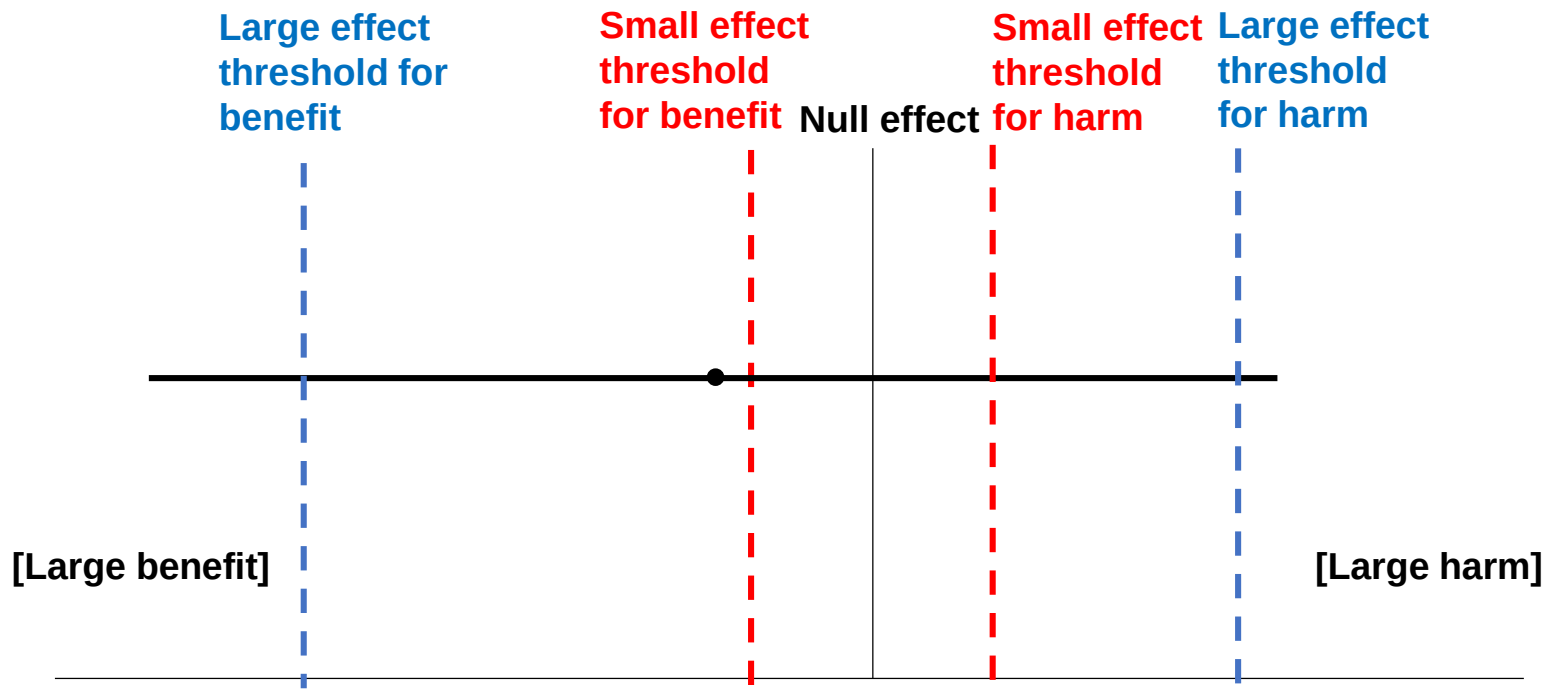
Using a particular degree of contextualization, where we set the threshold(s) will determine the target of certainty rating.



If set the small effect threshold at threshold 1
The true effect is larger than the threshold (an important effect)

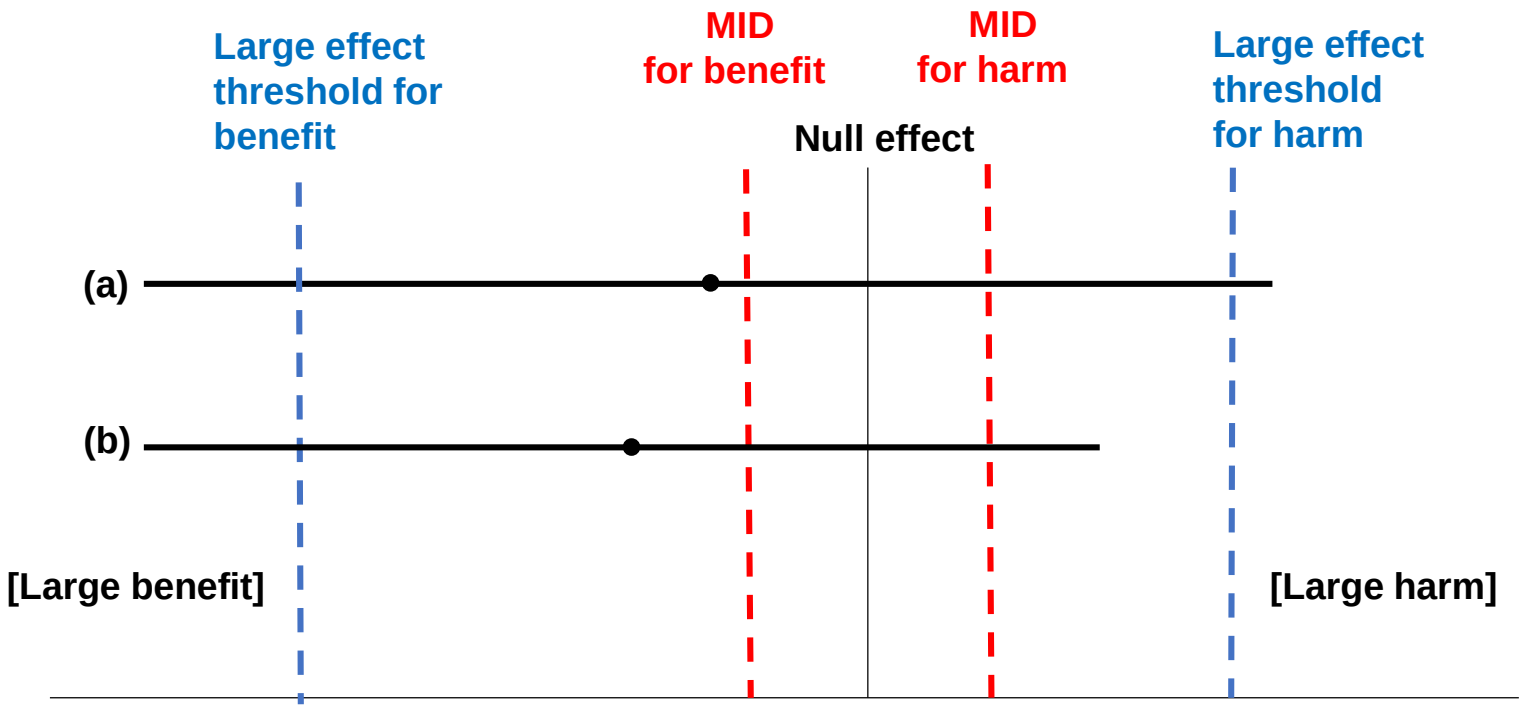
If set the small effect threshold at threshold 2
The true effect is smaller than the threshold (a trivial effect)

When the 95% confidence interval includes large benefit and large harm, it is not worthwhile to choose a particular threshold and hence not worthwhile to decide about the target of certainty rating.



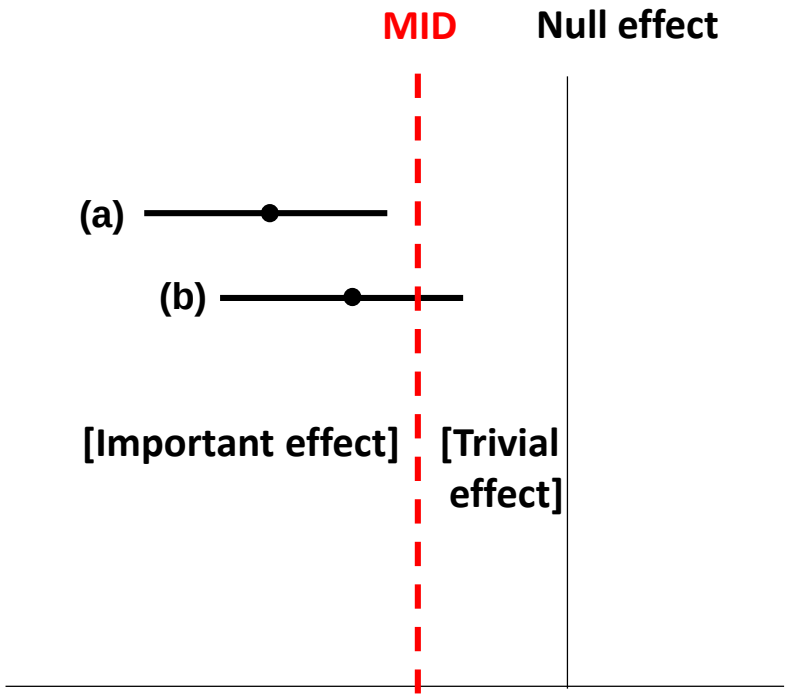
When 95% CI includes large benefit and large harm, not worthwhile to not worthwhile to decide about the target of certainty rating – very uncertain.

How wide 95% CI needs to be before we abandon being explicit about the target of certainty rating matter of judgement.



Confidence interval crosses no threshold don't rate down imprecision

Confidence interval crosses a threshold rate down for imprecision



(a) In relation to null or MID don't rate down

(b) In relate to null don't rate down
In relation to MID rate down

Real example

Using minimally contextualized approach

P: patients with sepsis (n=9,433 from 36 RCTs)

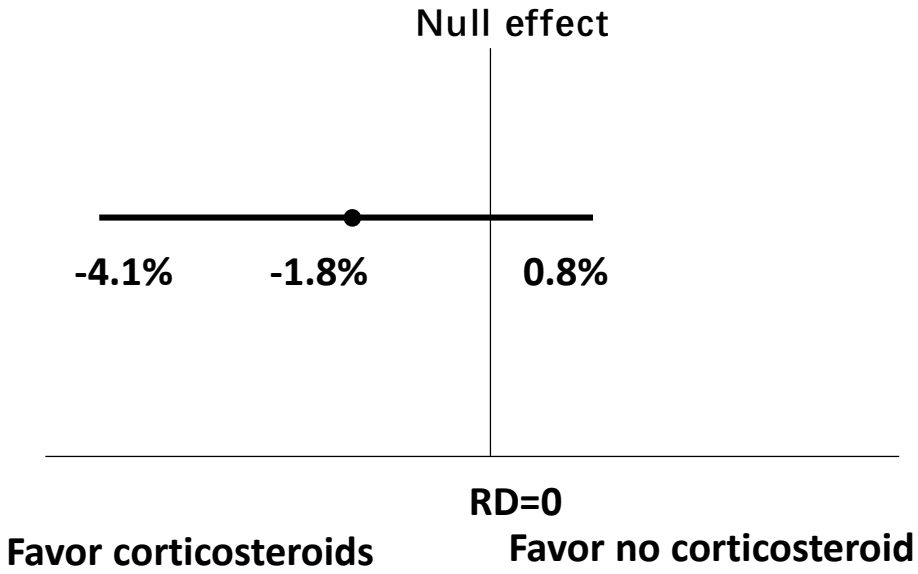
I: corticosteroids

C: no corticosteroids

O: short-term mortality (28-31 days)

Risk difference: -1.8%, 95% CI (-4.1%, 0.8%)

Degree of contextualization	Minimally contextualized approach
Threshold	Null effect
Target of certainty rating	Corticosteroids have an effect on mortality reduction.
Judgement for rating down	Rate down for imprecision



Real examples

Using minimally contextualized approach

P:patients with sepsis (n=9,433 from 36 RCTs)

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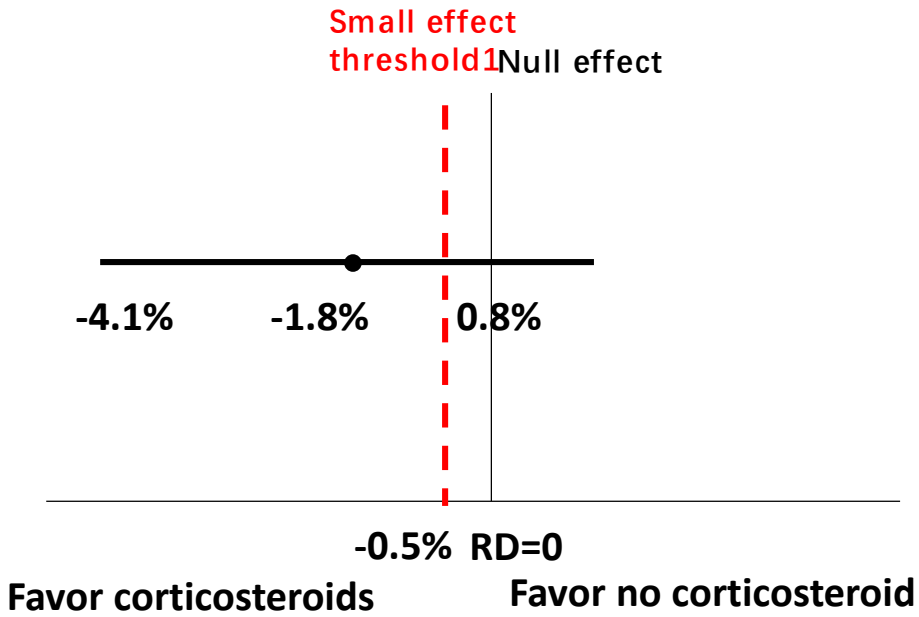

Degree of contextualization	Minimally contextualized approach	**Minimally contextualized approach**
Threshold	Null effect	**Small effect threshold (-0.5%)**
Target of certainty rating	Corticosteroids have an effect on mortality reduction.	**Corticosteroids have an important effect on mortality reduction.**
Judgement for rating down	Rate down for imprecision	**Rate down for imprecision**

Real example

Using minimally contextualized approach

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I: corticosteroids

C: no corticosteroids

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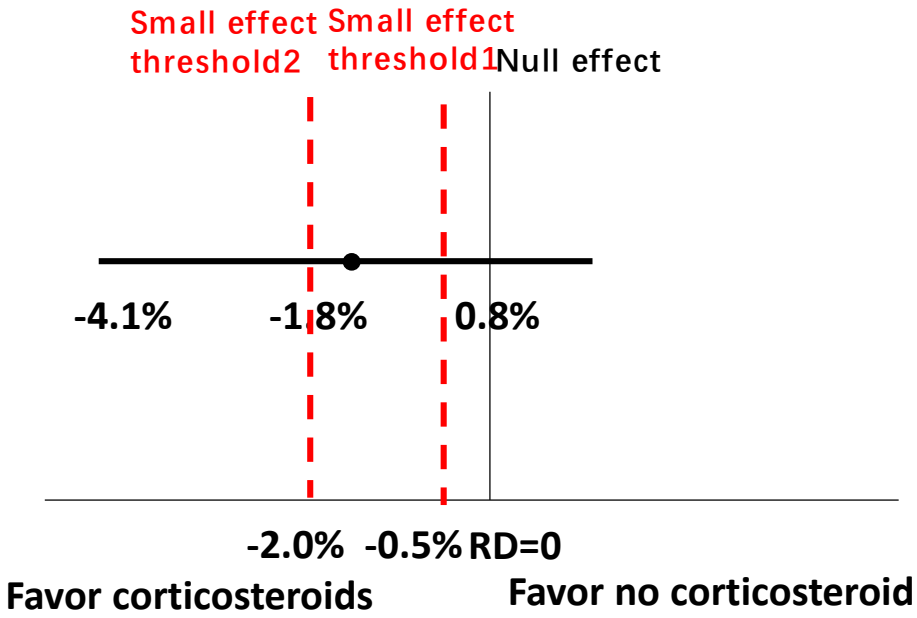
Risk difference: -1.8%, 95% CI (-4.1%, 0.8%)



Degree of contextualization	Minimally contextualized approach	Minimally contextualized approach	**Minimally contextualized approach**
Threshold	Null effect	Small effect threshold (-0.5%)	**Small effect threshold (-2.0%)**
Target of certainty rating	Corticosteroids have an effect on mortality reduction.	Corticosteroids have an important effect on mortality reduction.	**Corticosteroids have a trivial effect on mortality reduction.**
Judgement for rating down	Rate down for imprecision	Rate down for imprecision	**Rate down for imprecision**

Real example

Using partially contextualized approach

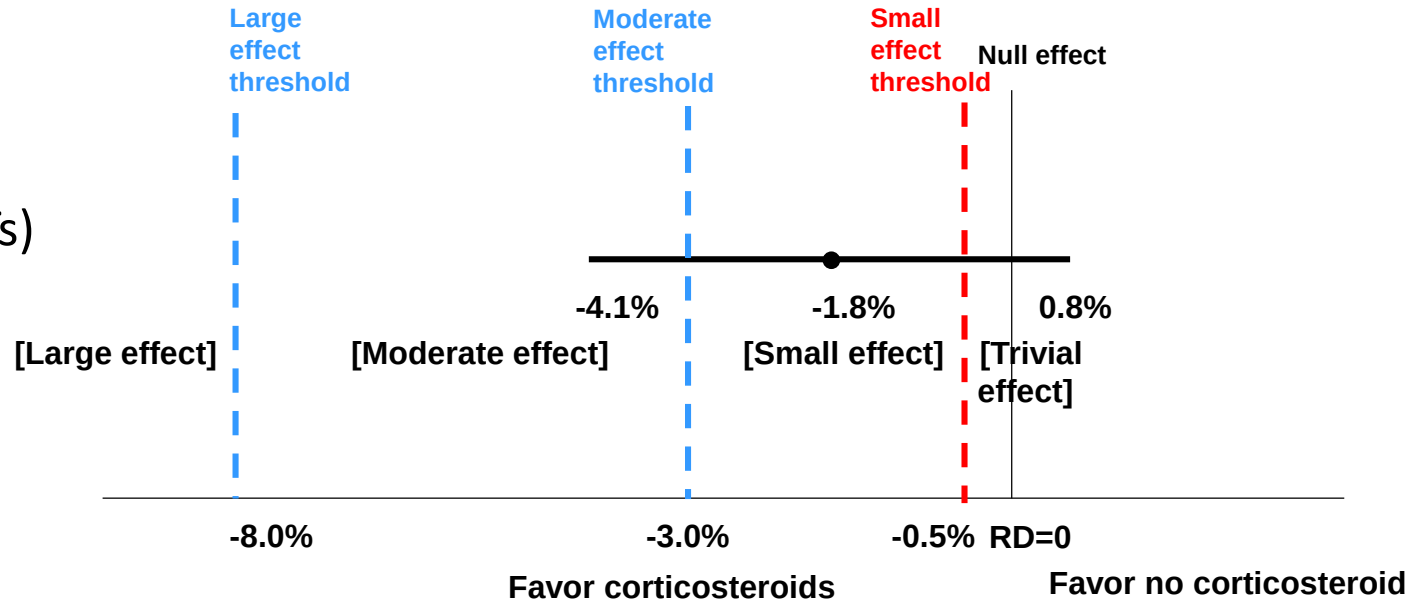
P:patients with sepsis (n=9,433 from 36 RCTs)

I: corticosteroids

C: no corticosteroids

O: short-term mortality (28-31 days)

Risk difference: -1.8%, 95% CI (-4.1%, 0.8%)



Degree of contextualization	Partially contextualized approach	Partially contextualized approach	Partially contextualized approach
Threshold	Small effect range	Moderate effect threshold	Large effect threshold
Target of certainty rating	Corticosteroids have a small but important effect on mortality reduction.	Corticosteroids have an effect that is smaller than a moderate effect.	Corticosteroids have an effect that is smaller than a large effect.
Judgement for rating down	Rate down for imprecision	Rate down for imprecision	Not rate down for imprecision

Conclusion

Principles based on prior GRADE guidance

- Never rate certainty in point estimate
- Rather in relation to threshold or range

More specific suggestions for target of certainty rating

Often very helpful in clarifying imprecision judgements