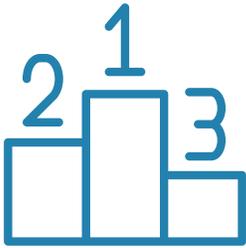


GRADE Framework in Systematic Reviews

What is GRADE?

GRADE (Grading of Recommendations, Assessment, Development and Evaluations) is a transparent framework for developing and presenting summaries of evidence and provides a systematic approach for making clinical practice recommendations. It is the most widely adopted tool for grading the quality of evidence and for making recommendations with over 100 organizations worldwide officially endorsing GRADE. AAPD currently uses the GRADE approach for evaluating evidence.



Why is GRADE Important?

Systematic reviews are used by decision makers to make recommendations for clinical actions, best practice, or practice guidelines. Systematic reviews “provide essential, but not sufficient information for making well informed decisions.” People who use reviews draw conclusions about the quality of evidence provided by the authors. In systematic reviews, “the quality of evidence reflects the extent of confidence that an estimate of effect is correct.” GRADE provides “a systematic and transparent approach for rating the certainty of evidence in systematic reviews.”

GRADE and Recommendations

In GRADE, recommendations can be strong or weak, in favor or against intervention.

- Strong recommendations suggest that all or almost all persons would choose that intervention.
- Weak recommendations imply that there is likely to be an important variation in the decision that informed persons are likely to make.
- The strength of recommendations are actionable: a weak recommendation indicates that engaging in a shared decision-making process is essential, while a strong recommendation suggests that it is not usually necessary to present both options.

Recommendations are more likely to be weak rather than strong when the certainty in evidence is low when there is a close balance between desirable and undesirable consequences, when there is substantial variation or uncertainty in patient values and preferences, and when interventions require considerable resources.

GRADE Criteria

In the GRADE system, the evidence is therefore initially set to either high (if included studies are randomized studies) or low (if they are observational studies). There are then 5 criteria that can be used to downgrade one, two, or in the case of indirectness, sometimes three steps. These are:

1. Risk of bias in individual studies – e.g. methodological issues in included studies such as inadequate blinding (participants knew they were in control/treatment group)
2. Inconsistency of results between studies
3. Indirectness of evidence – e.g. participants were children although the systematic review was about adults
4. Imprecision – results were not statistically significant, or the effect was clinically important once the studies were meta-analyzed
5. Publication bias – result was biased due to a file-drawer effect, as studies not showing a statistically significant effect are less likely to be published.

Additionally, observational studies starting at low can be upgraded based on 3 criteria: large effect, dose-response effect and “Effect of all plausible confounding factors would be to reduce the effect (where an effect is observed) or suggest a spurious effect (when no effect is observed)”. An example of the ‘dose-response effect’ refers to a finding that a larger dose of medicine leads to better treatment outcomes. The last criteria is complex but refers to situations where there is a bias (e.g. all doctors are told about a potential side effect) among clinicians to over-diagnose certain side effects but nevertheless no increased number of side effects is found in the studies.

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GRADE Scale

The tables below from the GRADE handbook provides a very useful summary of the 5 downgrading and 3 upgrading criteria:

Quality of Evidence Scales

| Grade | Definition |
|----------|--|
| High | We are very confident that the true effect lies close to that of the estimate of 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 is substantially different. |
| Low | Our confidence in the effect estimate is limited: The true effect maybe substantially different from the estimate of effect. |
| Very Low | We have very little confidence in the estimate effect: The true effect is likely to be substantially different from the estimate of effect. |

Factors that REDUCE the quality of evidence

| Factor | Consequence |
|--|-----------------|
| <u>Limitations in study design or execution (aka risk of bias)</u> | ↓ 1 or 2 levels |
| <u>Inconsistency of Results</u> | ↓ 1 or 2 levels |
| <u>Indirectness of Evidence</u> | ↓ 1 or 2 levels |
| <u>Imprecision</u> | ↓ 1 or 2 levels |
| <u>Publication Bias</u> | ↓ 1 or 2 levels |

Factors that INCREASE the quality of evidence

| Factor | Consequence |
|--|-----------------|
| <u>Large magnitude of effect</u> | ↑ 1 or 2 levels |
| <u>All plausible confounding would reduce the demonstrated effect or increase the effect if no effect was observed</u> | ↑ 1 level |
| <u>Dose-response gradient</u> | ↑ 1 level |

