

# GRADE – factors affecting the quality of the evidence

## Factors that can lower the quality of evidence

1. Confidence decreases in the estimates of an intervention's effect if studies have major limitations that could bias their estimates of effect. In randomised trials these limitations include, for example, a lack of allocation concealment; a lack of blinding (particularly if the outcomes are subjective and their assessment highly susceptible to bias); a large loss to follow-up; failure to adhere to an intention-to-treat analysis; or a failure to report outcomes (typically those outcomes for which little or no effect was observed).
2. Widely differing estimates of effects across studies, for which there are no compelling explanations, reduce confidence in knowing what the true effect is. Variability may occur due to differences between populations (e.g. interventions may have smaller relative effects in disadvantaged populations); differences in interventions (e.g. smaller effects with smaller financial incentives); or outcomes (e.g. subtle differences in the assessment or definition of an outcome). If investigators fail to identify a plausible explanation when variability occurs, the quality of the evidence decreases.
3. Decision makers must also be aware that the quality of evidence may be lowered by three types of indirectness. The first occurs when one of two interventions (A and B) are being considered. While randomised comparisons of A and B may be unavailable, randomised trials may exist which compare A to no intervention and B to no intervention. These may allow indirect comparisons to be made of the magnitude of the effect of A and B. However, such evidence will be of a lower quality than that provided by a head-to-head comparison of A and B. The second type of indirectness occurs when surrogate outcomes are used, such as a process measure that may (or may not) accurately reflect what can be expected in terms of an important outcome, such as mortality or morbidity. The third type of indirectness relates to differences between the population, intervention or comparator, and those included in the other relevant studies. The degree to which the results can be transferred to other contexts is commonly referred to as 'applicability' (or generalisability). Criteria for assessing the extent to which the results of a review of health systems arrangements are likely to be applicable to your setting are described in [Table 4.1](#).

4. When studies include relatively few people and few events and therefore have wide confidence intervals (or large p-values), less confidence can be placed in an estimate.
5. The quality of evidence will be reduced if there is a high likelihood that some studies have not been reported (typically those that have shown no effect). The risk of such publication bias is greater when published evidence is limited to a small number of trials, all of which are sponsored by people with vested interests in the results.

### **Factors that can raise the quality of evidence**

1. Even good observational studies will generally only yield low-quality evidence, because of the many potential confounders that are either not known or are not measured. However, occasionally these studies may provide evidence of moderate or even high quality. The larger the magnitude of effect, the less likely it is that this could be explained by confounders. The evidence will be stronger in such instances.
2. The presence of a dose-response gradient can increase our confidence in estimates of effects if, for example, larger effects are associated with more intensive variations of an intervention, as might be expected.
3. When an effect is found, if all plausible confounding would decrease the magnitude of effect, the quality of the evidence is higher since we can be more confident that an effect is at least as large as the estimate and may be even larger. Conversely, particularly for questions related to safety, if little or no effect is found and all plausible biases would lead us towards overestimating an effect, we can be more confident that there is unlikely to be an important effect.