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# GRADE guidelines: 4. Rating the quality of evidence –study limitations (risk of bias)

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【日本語訳】

## GRADE ガイドライン: 4. エビデンスの質評価 – 研究の限界(バイアスのリスク [risk of bias])

抄録

GRADEアプローチにおいては、ランダム化試験はまず高い質のエビデンス、観察研究はまず低い質のエビデンスとみなされるが、関連するエビデンスの大半がバイアスのリスク(risk of bias)が高い研究から導かれたものならば、いずれも評価が下げられる場合がある。ランダム化試験によくみられる限界には、割り付けの隠蔽化や盲検化の欠如、フォローアップからの脱落、ITT(intention-to-treat <治療企図>)の原則に対する適切な考慮の欠如が含まれる。最近では、見かけ上の利益を理由とした早期中止や、結果に応じた選択的アウトカム報告の限界が確認されている。観察研究における主な限界には、不適切なコントロールの使用や、予後の不均衡に対する適切な補正の欠如が含まれる。バイアスのリスク(risk of bias)はアウトカムによって異なるが(例: QOLと比較し全死亡率ではフォローアップからの脱落が格段に少ないと考えられる)、多くのシステマティック・レビューではこれが全く検討されていない。ランダム化試験または観察研究について、バイアスのリスク(risk of bias)を理由に評価を下げるか否かを決断する場合、著者らは一連の研究を平均化するアプローチをすべきではない。むしろ、どのアウトカムについても、高リスクの研究と低リスクの研究が混在する場合にはバイアスのリスク(risk of bias)がより低い研究のみを組み入れることを検討すべきである。

Table 1
Study limitations in randomized trials

1. Lack of allocation concealment
   Those enrolling patients are aware of the group (or period in a crossover trial) to which the next enrolled patient will be allocated (major problem in "pseudo" or "quasi" randomized trials with allocation by day of week, birth date, chart number, etc)
2. Lack of blinding
   Patient, care givers, those recording outcomes, those adjudicating outcomes, or data analysts are aware of the arm to which patients are allocated (or the medication currently being received in a crossover trial)
3. Incomplete accounting of patients and outcome events
   Loss to follow-up and failure to adhere to the intention-to-treat principle in superiority trials; or in noninferiority trials, loss to follow-up, and failure to conduct both analyses considering only those who adhered to treatment, and all patients for whom outcome data are available
4. Selective outcome reporting bias
   Incomplete or absent reporting of some outcomes and not others on the basis of the results
5. Other limitations
   Stopping early for benefit
   Use of unvalidated outcome measures (e.g., patient-reported outcomes)
   Carryover effects in crossover trial
   Recruitment bias in cluster-randomized trials

Table 3
Summarizing study limitations for randomized trials

| Extent of risk of bias | Risk of bias within a study | Risk of bias across studies | Interpretation across studies[a] | Example of summary across studies |
|---|---|---|---|---|
| No serious limitations, do not downgrade | Low risk of bias for all key criteria (Table 1) | Most information is from studies at low risk of bias | High-quality evidence: the true effect lies close to that of the estimate of the effect | Beta-blockers reduce mortality in patients with heart failure [26] |
| Serious limitations, rate down one level (i.e., from high to moderate quality) | Crucial limitation for one criterion or some limitations for multiple criteria sufficient to lower ones confidence in the estimate of effect | Most information is from studies at moderate risk of bias | Quality of evidence reduced from high- to moderate-quality evidence: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different | Amodiaquine and SP together likely reduce treatment failures compared with SP alone in patients with malaria [27] |
| Very serious limitations rate down two levels (i.e., from high to low quality or moderate to very low) | Crucial limitation for one or more criteria sufficient to substantially lower ones confidence in the estimate of effect | Most information is from studies at high risk of bias | Quality of evidence reduced from high- to low-quality evidence: the true effect may be substantially different from the estimate of the effect | Open discectomy may reduce symptoms after 1 yr compared with conservative treatment of lumbar disc prolapse [28] |

*Abbreviation:* SP, sulfadoxine-pyrimethamine.
[a] This interpretation assumes no problems that necessitate rating down because of imprecision, inconsistency, indirectness, and publication bias.