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| **TableA .The Cochrane Collaboration’s tool for assessing risk of bias** |
| **Random sequence generation** |
| **Low risk of bias** | The investigators describe a random component in the sequence generation process such as: referring to a random number table; using a computer random number generator. |
| **High risk of bias** | The investigators describe a nonrandom component in the sequence generation process. Usually, the description would involve some systematic, nonrandom approach, for example, sequence generated by odd or even date of birth; sequence generated by some rule based on date (or day)of admission.  |
| **Unclear risk of bias** | Insuﬃcient information about the sequence generation process to permit judgement of“Low risk”or“High risk.”  |
| **Allocation concealment** |
| **Low risk of bias** | Participants and investigators enrolling participants could not foresee assignment because one of the following, or an equivalent method, was used to conceal allocation: central allocation (including telephone, web-based and pharmacy-controlled randomization); sequentially numbered drug containers of identical appearance. |
| **High risk of bias** | Participants or investigators enrolling participants could possibly foresee assignments and thus introduce selection bias, such as allocation based on using an open random allocation schedule(e.g., a list of random numbers); assignment envelopes were used without appropriate safe guards(e.g., if envelopes were unsealed or nonopaque or not sequentially numbered).  |
| **Blinding of participants and personnel** |
| **Low risk of bias** | Any one of the following: no blinding or incomplete blinding, but the review authors judge that the outcome is not likely to be influenced by lack of blinding; blinding of participants and key study personnel ensured, and unlikely that the blinding could have been broken. |
| **High risk of bias** | no blinding or incomplete blinding, and the outcome is likely to be influenced by lack of blinding; blinding of key study participants and personnel attempted, but likely that the blinding could have been broken, and the outcome is likely to be influenced by lack of blinding.  |
| **Unclear risk of bias** | Any one of the following: insuﬃcient information to permit judgement of“Low risk”or“High risk”; the study did not address this outcome.  |
| **Blinding of outcome assessment** |
| **Low risk of bias** | Anyone of the following: no blinding of outcome assessment, but the review authors judge that the outcome measurement is not likely to be influenced by lack of blinding; blinding of outcome assessment ensured, and unlikely that the blinding could have been broken. |
| **High risk of bias** | Anyone of the following: no blinding of outcome assessment, and the outcome measurement is likely to be influenced by lack of blinding; blinding of outcome assessment, but likely that the blinding could have been broken, and the outcome measurement is likely to be influenced by lack of blinding.  |
| **Unclear risk of bias** | Any one of the following: insuﬃcient information to permit judgement of “Low risk” or “High risk”; the study did not address this outcome.  |
| **Incomplete outcome data** |
| **Low risk of bias** |  Anyone of the following: no missing outcome data; reasons for missing outcome data unlikely to be related to true outcome (for survival data, censoring unlikely to be introducing bias). |
| **High risk of bias** | Anyone of the following: reason for missing outcome data likely to be related to true outcome, with either imbalance in numbers or reasons for missing data across intervention groups; for dichotomous outcome data, the proportion of missing outcomes compared with observed event risk enough to induce clinically relevant bias in intervention eﬀect estimate. |
| **Unclear risk of bias** | Any one of the following: insuﬃcient information to permit judgement of “Low risk” or “High risk” (e.g., number randomized not stated, no reasons for missing data provided); the study did not address this outcome.  |
| **Selective reporting** |
| **Low risk of bias** | Any of the following: the study protocol is available and all of the study's pre-specified (primary and secondary) outcomes that are of interest in the review have been reported in the prespecified way; the study protocol is not available but it is clear that the published reports include all expected outcomes, including those that were pre-specified (convincing text of this nature may be uncommon). |
| **High risk of bias** | Anyone of the following: not all of the study's prespecified primary outcomes have been reported; one or more primary outcomes is reported using measurements, analysis methods, or subsets of the data(e.g., subscales) that were not prespecified.  |
| **Unclear risk of bias** | Insuﬃcient information to permit judgement of “Low risk” or “High risk”, it is likely that the majority of studies will fall into this category. |
| **Other bias** |
| **Low risk of bias** | The study appears to be free of other sources of bias |
| **High risk of bias** | There is at least one important risk of bias. For example, the study had a potential source of bias related to the specific study design used, or has been claimed to have been fraudulent; or had some other problem. |
| **Unclear risk of bias** | There may be a risk of bias, but there is either insuﬃcient information to assess whether an important risk of bias exists or insuﬃcient rationale or evidence that an identified problem will introduce bias. |