

## **Appendix 2 (as supplied by the authors): Description of bias assessment**

Risk-of-bias components based on the Cochrane risk-of-bias tool classification

### **Sequence generation**

- Low risk of bias, if the allocation sequence is generated by a computer or random number table or similar
- Uncertain risk of bias, if the trial is described as randomized, but the method used for the allocation sequence generation was not described
- High risk of bias, if a system involving dates, names, or admittance numbers is used for the allocation of patients (quasi-randomized). Such studies were excluded.

### **Allocation concealment**

- Low risk of bias, if the allocation of patients involves a central independent unit, on-site locked computer, or consecutively numbered sealed envelopes
- Uncertain risk of bias, if the trial is described as randomized, but the method used to conceal the allocation is not described
- High risk of bias, if the allocation sequence is known to the investigators who assigned participants or if the study is quasi-randomized. Such studies were excluded.

### **Blinding**

- Low risk of bias, if the method of blinding is described
- Uncertain risk of bias, if the method of blinding is not described
- High risk of bias, if the participants or investigators are not blinded

### **Completeness of data outcomes**

- Low risk of bias, if it is clearly described if there are any post-randomization drop-outs or withdrawals and the reason for these drop-outs are described
- Uncertain risk of bias, if it is not clear whether there are any drop-outs or withdrawals or if the reasons for these drop-outs are not clear
- High risk of bias, if the reasons for missing data are likely to be related to true outcomes, “as-treated” analysis is performed, potentially inappropriate application of simple imputation, potential for patients with missing outcomes to induce clinically relevant bias in effect estimate or effect size

### **Selectivity of outcome reporting**

- Low risk of bias, if all the pre-defined (primary and secondary) outcomes are mentioned in the trial's protocol or in a design article have been reported in the pre-specified way
- Uncertain risk of bias, if there is insufficient information to assess whether the risk of selective outcome reporting is present
- High risk of bias, if not all the pre-specified outcomes are reported or if the primary outcomes are changed or if some of the important outcomes are incompletely reported

### **Academic bias**

- Low risk of bias, if the author of the trial has not conducted previous trials addressing the same interventions
- Uncertain risk of bias, if it is not clear if the author has conducted previous trials addressing the same interventions
- High risk of bias, if the author of the trial has conducted previous trials addressing the same interventions

### **Sponsor bias**

- Low risk of bias, if the trial is unfunded or is not funded by an instrument or equipment or drug manufacturer
- Uncertain risk of bias, if the source of funding is not clear
- High risk of bias, if the trial is funded by an instrument or equipment or drug manufacturer