Supplement 1. Criteria for risk of bias analysis

Randomisation:
Low risk of bias – Randomisation was undertaken. The methods used were adequate (e.g. computer-generated random numbers, table of random numbers) and allocation concealment (e.g. central allocation) was used.
Unclear risk of bias – There was insufficient information to determine whether the method used for randomisation was likely to introduce confounding. If randomisation was undertaken, there was insufficient information about the method of allocation concealment.
High risk of bias – Randomisation was not undertaken. Observational methods were used to allocate participants to interventions in a non-randomised way. If randomisation was undertaken, the method of allocation concealment was either unsatisfactory (e.g. open random allocation schedule or not completed).

Enrolled population:
Low risk of bias – The enrolled population were selected using well defined clinical criteria and clinician judgement. The selection of subjects is representative of the exposure-outcome distribution.
Unclear risk of bias – The methods used to enrol participants nor the selection criteria for enrolment were clearly specified.
High risk of bias – Enrolment involved patient judgement. The methods used did not account for an intentionally skewed selection of subjects (disproportionality large selection of diseased individuals receiving an intervention).

Sampling
Low risk of bias – The study population was clearly specified and was representative of the population being studied. Appropriate inclusion and exclusion criteria were applied uniformly. The sample was sufficiently large to provide confidence in obtained effect estimates ($\beta \leq 20\%$).
Unclear risk of bias – Information was insufficient to allow assessment of whether bias was attributable to sampling.
High risk of bias – The sample was not representative of the studied population and the sampling methods applied were inadequate. Sample size analysis was performed but the acquired sample did not reflect those results.
Blinding of participants

**Low risk of bias** – Blinding was performed adequately. A dummy design was implemented to ensure successful blinding. No blinding was performed but the outcome measurement was unlikely to be influenced by a lack of blinding.

**Unclear risk of bias** – Information was insufficient to allow assessment of whether the type of blinding used was likely to induce bias on the estimate of effect. Blinding was performed but lacked a dummy design.

**High risk of bias** – No blinding or incomplete blinding was applied. Outcome measurement likely influenced by lack of blinding.

Blinding of assessors

**Low risk of bias** – Blinding was performed adequately. A dummy design was implemented to ensure successful blinding. No blinding was performed but the outcome measurement was unlikely to be influenced by a lack of blinding.

**Unclear risk of bias** – Information was insufficient to allow assessment of whether the type of blinding used was likely to induce bias on the estimate of effect. Blinding was performed but lacked a dummy design.

**High risk of bias** – No blinding or incomplete blinding was applied. Outcome measurement likely influenced by lack of blinding.

Incomplete outcome data

**Low risk of bias** – The underlying reasons for attrition were unlikely to influence the conclusions made. Appropriate methods were employed to handle missing data.

**Unclear risk of bias** – Information was insufficient to allow an assessment of whether reason for attrition of the method to handle missing data was likely to introduce bias.

**High risk of bias** – Conclusions made are clearly biased due to the underlying reasons for attrition. The methods used to handle missing data were unsatisfactory.

Selective reporting of results

**Low risk of bias** – The prespecified trial protocol was available with all prespecified outcomes of interest being reported on. If no prespecified protocol, the study provides a balanced dialogue of obtained results in the context of the primary and secondary endpoints of the study.

**Unclear risk of bias** – Information was insufficient to allow assessment of whether the magnitude and the direction of the observed effect were related to selective outcome reporting.
**High risk of bias** – There are obvious issues with reporting. Primary outcomes are not fully reported or *ad hoc* endpoints are created and discussed. Statistical reporting lacks robustness.

**Measurement**

**Low risk of bias** – The study uses a validated tool (e.g. patient reported outcome measure) or well defined clinical criteria to assess changes in clinical condition between baseline and follow up. The tools and clinical criteria are adequately described in text. If the tool was not validated, the new tool was piloted in an appropriate manner prior to use. Where applicable, methods adequately limit recall bias (e.g. crossover design).

**Unclear risk of bias** – Insufficient information provided to consider the impact of the measurement technique on effect estimates.

**High risk of bias** – Effect estimates are likely biased due to inappropriate or inadequate measurement techniques. The study methods do not account for additional biases as a consequence of inappropriate or inadequate measurement techniques (e.g. recall bias).

**Source of funding**

**Low risk of bias** – The study was funded by a sponsor who had no vested interest in the results or funding disclosure suggests that no funding was received for this study (e.g. small single centre observational study). No conflicts of interest to be declared by authors.

**Unclear risk of bias** – Information was insufficient to allow assessment of whether the magnitude and the direction of the observed effect were related to the source of funding. Declared conflicts of interest have potential to introduce bias.

**High risk of bias** – The trial was funded by a sponsor who had vested interest in the results of the trial (e.g. drug manufacturing company) or funding disclosure suggests that no funding was received for the study (e.g. large multicentre randomised control trial).