SOP: Blinding of the primary outcome assessment

Version	Author(s)	Date	Changes	Approved by
1.0	Caroline Barkholt Kamp	09.05.24	Initial version	Steering Committee
1.1	Johanne Juul Petersen Mathias Lühr Hansen Caroline Kamp	10.11.24	Updated layout Updated method to align with 'SOP: Assessment of the primary outcome'	Janus Christian Jakobsen
1.2	Johanne Juul	17.09.25	Updated with information about acknowledgement of blinded assessors	Caroline Kamp

Content

Why blind the primary outcome assessment?

Several observational studies have shown that inadequate blinding of participants, personnel, and outcome assessors in randomised clinical trials tends to introduce bias by overestimating the beneficial treatment effects of an intervention for all outcome types [1-4]. Due to the nature of the experimental intervention of the SafeBoosC-IIIv trial, it is difficult to blind the clinical staff and the parents. In order to minimise bias in the assessment of the primary outcome, the assessment must be performed by a person who is blinded to treatment allocation. This Standard Operating Procedure describes a suggested methods on how blinding may be obtained.

Suggested methods for blinding

The primary outcome of the SafeBoosC-IIIv trial is hospital-free days within 90 days of randomisation. The assessment of the primary outcome is based on a review of clinical records and contact with the parents. Data will be registered in the primary outcome log and transferred to the electronic Case Report Form (eCRF) in OpenClinica (see 'SOP: Assessment of the primary outcome'). We suggest the following method for a blinded primary outcome assessment:

- **Review of clinical records**: At 90 days from randomisation, a colleague, unaware of group allocation (blinded assessor), will review the available clinical records, to determine the number of hospital-free days from randomisation and until discharge. If the clinical records include definite up-to-date information about survival status (e.g. through a centralised registry), the blinded assessor will also determine survival status from the clinical records. Prior to the assessment, the principal investigator will identify any records that could reveal group allocation and ensure this information is not available to the blinded assessor, during the review of the clinical records. Alternatively, the principal investigator could print the clinical records, identify and exclude notes that include information on group allocation, and let the blinded assessor review the remaining records in print.
- **Contact with parents**: After reviewing the clinical records, the blinded assessor must contact the infant's parents (e.g. by phone or email) and ask if the child has been to a hospital at other times than days in hospital registered in the clinical records. If the parents report that the infant has been to a hospital at other times, the blinded assessor must note the additional hospital days in the primary outcome log. If the clinical records do not include

definite up-to-date information about survival status (e.g. through a centralised registry), the blinded assessor will also ask the parents about survival status.

Based on the described assessments above, the blinded colleague will complete the primary outcome log (see 'SOP: Assessment of the primary outcome' for additional details). The principal investigator may transfer the data registered in the primary outcome log to the eCRF.

Reporting of blinding method

The investigator may choose another method for blinded assessment of the primary outcome. However, the method must be approved by the trial manager on behalf of the Steering Committee. The investigator must report and describe the chosen method to the trial manager at caroline.kamp@ctu.dk before enrolment of participants.

Acknowledgement of blinded assessors

Blinded assessors will be recognised for their work as 'non-author collaborators' in the publication of the primary outcome results.

A non-author collaborator may be defined as: 'Another type of contributor who is a nonauthor member of a formal group and who contributes significantly to the work but does not qualify for authorship. These individuals may be listed as collaborators in an Acknowledgement or Article Information section.' [5].

Thus, a non-author collaborator will be mentioned in the publication under 'Collaborators', and the publication will also appear in a PubMed search of the non-author collaborator's name. Similar principles will apply as for co-authors: a total of 10 infants must be assessed by the blinded assessors to obtain collaboratorship (co-authors will have to randomise and complete data entry for 10 infants to obtain co-authorship).

References

[1] Savovic J, Turner RM, Mawdsley D, Jones HE, Beynon R, Higgins JPT, et al. Association Between Risk-of-Bias Assessments and Results of Randomized Trials in Cochrane Reviews: The ROBES Meta-Epidemiologic Study. Am J Epidemiol. 2018;187(5):1113-22.

[2] Hrobjartsson A, Emanuelsson F, Skou Thomsen AS, Hilden J, Brorson S. Bias due to lack of patient blinding in clinical trials. A systematic review of trials randomizing patients to blind and nonblind sub-studies. Int J Epidemiol. 2014;43(4):1272-83.

[3] Hrobjartsson A, Skou Thomsen AS, Emanuelsson F, Tendal B, Hilden J, Boutron I, et al. Observer bias in randomized clinical trials with measurement scale outcomes: a systematic review of trials with both blinded and nonblinded assessors. CMAJ. 2013;185(4).

[4] Hrobjartsson A, Thomsen AS, Emanuelsson F, Tendal B, Rasmussen JV, Hilden J, et al. Observer bias in randomized clinical trials with time-to-event outcomes: systematic review of trials with both blinded and non-blinded outcome assessors. Int J Epidemiol. 2014;43(3):937-48.

[5] Fontanarosa P, Bauchner H, Flanagin A. Authorship and Team Science. JAMA. 2017;318(24):2433-7.