SWAT 196: Implementation and maintenance of blinding of participants in the RAPSODI-UK surgical trial

Objective of this SWAT
To monitor and describe the strategies put in place to maintain blinding of trial participants in an orthopaedic surgical trial.

Study area: Blinding in surgical trials, Monitoring
Sample type: Participants
Estimated funding level needed: Very Low

Background
RAPSODI-UK (ISRCTN12216466) is a NIHR-funded surgical trial aiming to determine whether reverse shoulder replacement (rTSR) is superior to anatomic/conventional shoulder replacement (aTSR) for the treatment of painful osteoarthritis of the shoulder joint with an intact rotator cuff and suitable bone stock in patients aged 60 years and older, as measured by patient-reported pain and function using the Shoulder Pain and Disability Index (SPADI) at 24 months.

As far as possible, participants will be blinded to treatment allocation in order to reduce performance bias. During the consent process, participants will be asked to agree to being blinded to their allocated treatment for the entire 24-month follow-up period, with the reassurance that if there is ever a clinical need to know their allocation, they will be informed of this. Instances of unblinding will be recorded. In addition, outcome assessors (at the 24-month follow-up point only) will be blinded to treatment allocation in order to reduce detection bias.[1] Participant and assessor blinding can help mitigate the risk of over-estimating the treatment effect that has been found when comparing unblinded with blinded trials.[2] The surgeons, physiotherapists, nurses and other treating clinicians will not be blinded because this is not feasible.

Although initially it may be easy to blind participants who are having similar procedures under anaesthesia,[3] such as TSRs, there are numerous opportunities from the time of randomisation until completion of the 24-month follow-up where participants could be unblinded. This could occur when meeting with surgeons or physiotherapists for follow-up appointments and may depend on whether staff are too busy to ensure blinding is maintained. Follow-up appointments might take place at a different hospital to where the participant had their surgery and, for physiotherapy, some participants will be attending a different NHS Trust altogether. This increases the risk of unblinding to occur accidentally.

Furthermore, physiotherapists have stated that sometimes a patient can see the shape of their shoulder is different with a rTSR, which may unblind them to their allocation. There are also different physiotherapy rehabilitation protocols for each type of replacement, which has the potential to unblind participants, although the trial team have designed a standardised physiotherapy leaflet that can be used for either type of TSR. Another potential source for unblinding is whether participants who have been on the waiting list before being approached about the host trial may have had differences explained to them about, for example, the range of movement they could expect post-surgery, with likely improved elevation of the arm from rTSR than from aTSR.

There are reviews of blinding in preclinical, pharmaceutical and CTIMP trials [1,2] and of blinding in trials comparing surgery with sham surgery.[3] However, we could only find one paper [4] that gave some practical guidance on blinding measures that sites could implement and apply to a surgical trial. In this, Karanicolas et al.[5] suggested some “tips for blinding in surgical trials” but these are of limited application to the RAPSODI-UK trial.

To our knowledge, no studies have described practical strategies to maintain participant blinding in surgery trials. As such, this study within a trial (SWAT) aims to describe the strategies used to maintain participant blinding throughout the host trial using regular review of unblinding (starting with the end of the internal pilot and six monthly thereafter) and feedback and discussion with sites to optimise strategies.

Interventions and comparators
Intervention 1: blinding guidance, participant unblinding case report form, participant status log with blinding checklist per participant and blinding checklist.

Index Type:

Method for allocating to intervention or comparator
Not applicable, all sites receive intervention.

Outcome measures
Primary: Outcomes related to frequency and reasons for unblinding for each TSR group separately and overall: (1) proportion of participants who remain blinded throughout the follow-up period; (2) frequency of unblinding; (3) time point unblinding occurs (e.g. around the time of surgery, or during follow-up appointments etc); (4) location or healthcare setting where unblinding occurs (e.g. whether unblinding occurs in the anaesthetic room, theatre, ward, outpatient clinic etc); (5) how and why unblinding of the participant occurred; and (6) whether unblinding was intentional (e.g. clinical need) or accidental.
Secondary: We will also report (1) whether any strategies suggested to sites to maintain blinding are not done, the reasons for this, and whether this affects unblinding at sites; and (2) whether strategies are modified or new strategies are identified during the regular review of unblinding and feedback to sites and monitoring unblinding following this.

Analysis plans
Analyses will be descriptive. The number and proportion of participants who become unblinded, and the timing and other details of unblinding, will be reported by randomised group in the host trial and overall. We will also report the strategies used at each site and the level of unblinding by site.

Possible problems in implementing this SWAT
Timely reporting of unblinding occurrences may be an issue because sites may not be aware of unblinding at the precise time point it occurs, leading to potentially inaccurate data about when the unblinding occurred. However, we are providing sites with a bespoke case report form to complete whenever unblinding occurs and a tracking log to record when this has occurred.

Reassurances to sites will be given that accidental unblinding occurrences will not be viewed negatively, rather that these would provide useful information and insight into where the blinding procedures, paperwork and guidance may need improving. During Site Initiation Visits and any correspondence, we will communicate to sites about the importance of blinding, and of the trial team being notified of unblinding in case we need to adapt or alter our procedures.

References
1. Bespalov A, Wicke K, Castagne V (editors). Good Research Practice in Non-Clinicial Pharmacology and Biomedicine, Handbook of Experimental Pharmacology 257. (2019). Chapter: Blinding and Randomisation.
2. Boutron I, Estellat C, Guittet L, et al. Methods of Blinding in Reports of Randomized Controlled Trials Assessing Pharmacologic Treatments: A Systematic Review. PLoS Medicine 2006;3:e425.
3. Monaghan T, Agudelo C, Rahman S, et al. Blinding in clinical trials: Seeing the big picture. Medicina (Kaunas, Lithuania) 2021;57(7):647.
4. Sydes M, Wong W, Bakhai A, et al. Protecting blinded trials in electronic hospital systems. Clinical Trials 2022;19(2):231-3.
5. Karanicolas P, Farrokhyar F, Bhandari M. Blinding: Who, what, when, why, how? Canadian Journal of Surgery 2010;53(5):345-8.

Publications or presentations of this SWAT design

Examples of the implementation of this SWAT

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