

Reasoning behind the recommendation

Open trials

Balance between desirable and undesirable

Increase in recruitment is large and desirable. However, blinding is a key component of internal validity and routine use of open trials is likely to undermine the integrity of at least some trials, especially those where outcomes are subjective, or participants and staff are able to alter the intervention delivery by knowing what treatment is being given. Many trials however are already open because it is impossible to blind them (e.g. many lifestyle change or educational trials, most surgical trials). Measures can be put in place to protect integrity, to a large degree at least, generally through blinded outcome assessment and/or objective outcomes. Recent evidence (<https://www.bmj.com/content/368/bmj.l6802.long>) found no average difference in estimated treatment effect between trials with and without blinded patients, healthcare providers, or outcome assessors. These results could reflect that blinding is less important than often believed, or weaknesses in this piece of work. Blinding was recommended where feasible.

So, where integrity is not threat, or blinding is anyway impossible, the balance seems to be in favour of an open trial. Where trial integrity is threatened, an open trial should not be used. This may change as more evidence on the impact of blinding becomes available.

Certainty of evidence

There are two studies (<https://www.ncbi.nlm.nih.gov/pubmed/16279289> and <https://www.ncbi.nlm.nih.gov/pubmed/15617949>). Both were well done randomised trial at low risk of bias. Both trials involved cheap, easily available drugs (the first involved vitamin D/ calcium, the second involved postmenopausal hormone therapy). The Cochrane systematic review of recruitment interventions (<https://doi.org/10.1002/14651858.MR000013.pub6>) considered the GRADE assessment to be High certainty of evidence.

We therefore judge the certainty of the evidence to be High for trials involving cheap, easily available drugs. We are less certain for other interventions because of Indirectness. For trials involving other interventions we suggest certainty in the evidence is currently Moderate.

Values and preferences

Randomisation to unknown treatments is widely cited (e.g. <https://doi.org/10.1002/14651858.MR000045>) as a barrier for participants to agree to taking part in trials. We concluded that this means that potential participants' preference is to know what treatment they are receiving. An open trial would do this so values and preferences are in line with the intervention.

Costs

The comparative cost of a open compared to a blinded trial design is uncertain. However, maintaining blinding adds complication, which is likely to add cost. Using blinded assessment in an open trial may also add cost, although it is likely that assessment would be be blinded in a blinded trial so the additional costs, if any, may be modest.

We concluded that the additional costs were uncertain but that, on balance, they were more likely reduced in an open design rather than a blinded design.

Our recommendation

Open trials can compromise integrity, e.g. by introducing differences in how outcomes are assessed. Where integrity is not compromised, we recommend trialists use open trials to increase recruitment.

Recommendation reached by:

- Shaun Treweek, University of Aberdeen, UK and Laura Clark, University of York, UK. With comments from Alison Avenell, University of Aberdeen and chief investigator of one of the two included studies (<https://www.ncbi.nlm.nih.gov/pubmed/16279289>).