KCE questions for applicants regarding sample size justification for RCT proposal

How to determine the sample size of your study? Questions to help applicants applying for funding for a Randomised Controlled Trial to the KCE Trials

This set of questions related to the underlying justification of the sample size used in a randomised controlled trial grant proposal. Relevant guidance for researcher and funders on choosing the target differences and justifying the sample size calculation has recently been published[1] as has an extensive review of methods for choosing the target difference.[2, 3] Please check if you used a conventional sample size calculation as defined below.

Conventional sample size calculation for randomised controlled trials
The conventional or traditional approach to a sample size calculation is one where the number of participants required to achieve a pre-set level of statistical power given the assumptions made (such as the statistical significance level and target difference which is specified according to the outcome type and specific calculation used). It has been described also been described a "statistical hypothesis testing" or "Newman Pearson approach". This methodology is based upon a frequentist or classical statistics framework as opposed for example to one based upon a Bayesian approach to statistics. It is by far the most common way for which the sample size required for a randomised controlled trial is determined. Usually, the sample size chosen is one which is sufficient in this regard only for a single primary outcome though sometimes more than one primary outcome, or even a key secondary outcome is someone done.

Please see Cook et al[2] and Spiegelhalter et al[4] for further discussion and references to the wider literature on statistical methods for sample size determination for randomised controlled trials.

Q1 Please clarify the basis of the choice of the sample size*

Conventional sample size calculation	☐
Bayesian	☐
Another statistical basis (e.g. precision)	☐
It was not based upon statistical considerations	☐

If your answer to Q1 was "conventional sample size" above please complete Q2-5 only below, if "Bayesian" or "Another statistical basis" then answer only Q6, and "It was not based upon statistical considerations then please complete only Q7 and Q8.

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If a conventional approach was used as per Q1

Q2 Please confirm which outcome(s) the sample size calculation is based upon

Outcome	*Name*	*Description (include point in time, method of assessment)*
1		
(2)		

Q3 For each of the outcomes stated above in Q2 please clarify whether the target difference would be important or not in terms of the key stakeholder groups (e.g. patients, clinician, and healthcare funder).

Outcome	*Response*
1	
(2)	

Q4 For each of the outcomes stated above in Q2 please clarify whether the assumed target difference is realistic in terms of existing evidence relevant to the trial intervention

Outcome	*Response*
1	
(2)	

Q5 Please detail the calculation of the sample size in sufficient detail and the tool used such that it can easily be reproduced by a statistician.

Outcome	*Response*
1	
(2)	

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If a Bayesian or an alternative statistical approach was used as per Q1

Q6 Please state the approach used and provide references to the relevant literature. Please also explain the choice of this approach, and how it achieves the aim of a sample size calculation in terms of i) reassuring about the additional value of the new study, and ii), guide clinical practice in a meaningful way and influence key stakeholders.

If the choice of the sample size was not based upon statistical consideration as per Q1

Q7 Please justify the use of this approach with reference to the aim of the study and its design

Q8 Please details the considerations which led to the stated sample size being choosen

References

1. Cook JA, Julious SA, Sones W, Hampson LV, Hewitt C, Berlin JA et al. DELTA(2) guidance on choosing the target difference and undertaking and reporting the sample size calculation for a randomised controlled trial. The BMJ. 2018;363:k3750. doi:10.1136/bmj.k3750.
2. Cook JA, Hislop J, Adewuyi TE, Harrild K, Altman DG, Ramsay CR et al. Assessing methods to specify the target difference for a randomised controlled trial: DELTA (Difference ELicitation in TriAls) review. Health Technol Assess. 2014;18(28):v-vi, 1-175. doi:10.3310/hta18280.
3. Hislop J, Adewuyi TE, Vale LD, Harrild K, Fraser C, Gurung T et al. Methods for specifying the target difference in a randomised controlled trial: the Difference ELicitation in TriAls (DELTA) systematic review. PLoS medicine. 2014;11(5)(e1001645). doi:10.1371/journal.pmed.1001645.
4. Spiegelhalter DJ, Abrams KR, Myles JP. Bayesian Approaches to Clinical Trials and Health-Care Evaluation. 1st ed. Statistics in Practice. Chicester: John Wiley & Sons; 2004.