Background

The use of statistical analysis plans (SAPs), drawn up in advance of unblinded analysis, is an accepted means of reducing bias in RCTs by minimising selective analysis. However, while health economics analysis plans (HEAPs) to guide trialists in conducting economic evaluations alongside RCTs are becoming more widespread, they lag behind SAPs in terms of acceptance and standardisation, and there is a fundamental question over the value they add to trials.

A statistical analysis plan (SAP) is a…

“…document that contains a more technical and detailed elaboration of the principal features of the analysis described in the protocol, and includes detailed procedures for executing the statistical analysis of the primary and secondary variables and other data”

ICH Topic E 9 Statistical Principles for Clinical Trials. NOTE FOR GUIDANCE ON STATISTICAL PRINCIPLES FOR CLINICAL TRIALS.

Objectives

➢ To map current practice and beliefs about the appropriate implementation (or otherwise) of HEAPs, with a view to determining content and drawing up good practice guidelines in future work.
➢ To provide a forum in which health economists and other interested parties engaged in economic evaluations could open a dialogue on the need for HEAPs and methods of standardisation.

Current status

Pre-specified analysis plans have been used in other areas of economics. However, guidance on preparing HEAPs for RCTs, and their appropriate content, is currently extremely sparse. HEAPs are commonly unpublished, but may be published as standalone appendices or as part of a SAP. To date, HEAPs include variable content, and may or may not be scrutinised by trial steering committees.

Workshop

On 10 October 2015, a workshop was held in Bristol, United Kingdom, to discuss issues associated with HEAPs. 50 participants, who were mainly academic health economists, heard presentations from speakers before breaking into smaller groups for discussion sessions.

Presented sessions included accounts of practical experiences of using HEAPs in RCTs, alongside perspectives from SAP guidelines, NICE and wider economics. In the discussion sessions, participants debated topics including the appropriate content of HEAPs. Other discussions covered issues such as:

1. Until what point should a HEAP be a ‘live’ document?
2. How should post hoc analyses be handled?
3. What subheadings should a HEAP include?
4. When might a HEAP be unnecessary?
5. Who should approve a HEAP?
6. When should a HEAP be approved?
7. Would a combined SAP/HEAP be preferable?
8. Are deviations from the plan acceptable?
9. Should the plan be followed if the intervention is not effective?
10. Should HEAPs be published/peer-reviewed?

Workshop participants raised a number of potential advantages and disadvantages of preparing a HEAP.

Advantages | Disadvantages
---|---
Reduction of reporting bias | Impossible to predict all data issues
Reduces impact of staff turnover | Loss of potentially useful post hoc analyses
Defining variables can secure better quality data | Potential loss of useful new methodology
Can anticipate problems before analysis pressure is on | Added complexity – oversight is necessary
Robust rebuttal to reviewer requests | Time consuming to prepare...
Protects junior staff from overzealous research partners | …bureaucratic burden on a small workforce
Can facilitate communication and good habits | Methods section already written

Discussion

Feedback from the workshop suggested that health economists consider that constructing a HEAP would have some merits in trial-based economic evaluations. However, there was agreement that HEAPs should not necessarily be followed slavishly. The majority of health economists present were in favour of a combined SAP and HEAP, rather than a standalone HEAP.

HEAPs differ from SAPs in a number of ways that mean guidance for writing a SAP does not necessarily apply to a HEAP. Fundamentally, economic evaluation is carried out in a different evaluative framework with the needs of decision makers considered. This often leads to the need for extrapolation beyond the follow-up of the trial (drawing on external evidence). An economic evaluation may use a different primary outcome, and blinding economic analyses only are rapidly being developed.

HEAPs are currently characterised by inconsistency but there is an appetite for additional guidance. As it seems likely that the use of HEAPs will continue to increase in the future (and, potentially, be required by funding bodies or regulators), clarity on the appropriate usage and content would be advantageous. We plan to conduct a Delphi survey of practising health economists to determine suitable content for a HEAP.

Acknowledgments

We thank the workshop participants for their contributions; the summary views presented here are the authors’. This work was undertaken with the support of the MRC ConDuCT-I Hub (Collaboration and innovation for Difficult and Complex randomised controlled Trials In Invasive procedures - MR/K025643/1) and the MRC Network of Hubs for Trials Methodology Research (MR/L004933/1-N65).

Olken, B. J. Econ. Perspectives 29(3) p62

“I am opposed to the laying down of rules or conditions to be observed in the construction of bridges lest the progress of improvement tomorrow might be endangered or shackled by recording or registering as law the prejudices or errors of today.”

Isambard Kingdom Brunel (1806-1859)

School of Social and Community Medicine
http://www.bristol.ac.uk/social-community-medicine/centres/healtheccon/