



Perinatal Trials Toolkit

Statistical approaches to data monitoring

Stopping rules

The data monitoring committee (DMC) monitors data on hazards and benefits to determine if they are sufficiently persuasive to warrant either closing recruitment to a trial or changing the protocol (terminating one or more subgroups).

Statistical criteria (stopping rules) are now regarded as providing guidelines rather than rules which should be considered alongside other information which demand an element of judgement from DMCs

- includes external evidence from other trials
- assessment of whether interim results would be persuasive enough to change clinical practice
- broader issues such as ensuring ethical standards, quality assurance in trial conduct

Interim analyses

An interim analysis is an analysis comparing intervention groups at any time before the formal completion of the trial, usually before recruitment is complete (CONSORT Statement). Interim analyses are required to inform the deliberations of the DMC.

Things to think about when planning interim analyses

- | | |
|--------------------------------------|---------------------------------|
| Frequency of meetings? | What information is required? |
| Timing of meetings related to trial? | Who produces it? |
| Who decides on dates of meetings? | What is produced? |
| Means of communication? | Who sees the data and when? |
| Who can suggest unplanned analyses? | Who owns the data and analyses? |
- What reports are required?
- Cover benefits and risks in a balanced way
 - Accessible style
 - Avoid excessive detail
 - Current as possible
 - Blinded or not?

Summary of statistical approaches

This is a brief summary of Appendix 1 of the HTA Report: *Issues in data monitoring and interim analysis of trials (Grant 2005)*
For more information please consult that document.

Frequentist

Fixed type I error rate
Limited number of interim analyses at preset times

Pocock model – commonly used – common boundary for Type I error
O'Brien and Fleming model (USA) – much more conservative at the beginning of a trial

Likelihood approach

Informal continuous monitoring scheme

Haybittle-Peto Rule

Trial should be stopped on efficacy grounds if there is both:

- proof beyond reasonable doubt* that for all or some types of patients one particular treatment is clearly indicated
- evidence that might reasonably be expected to influence patient management of many clinicians who are already aware of the results of other main studies

*Proof beyond reasonable doubt – more than 3 results with $p < 0.001$

Other approaches

Other statistical approaches include Bayesian and decision-theoretic. For more information see Grant 2005.

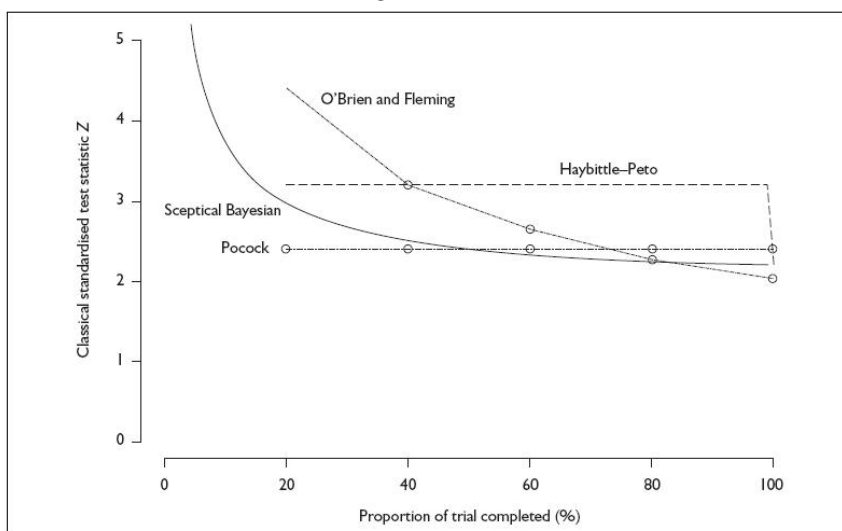


FIGURE 7 Haybittle-Peto, O'Brien and Fleming, Pocock and sceptical Bayesian stopping boundaries for five interim analyses from Grant 2005 *Issues in data monitoring and interim analysis of trials* HTA 2005;9(7)



[See related toolkit - Establishing a data monitoring committee](#)

This toolkit was prepared by Caroline Crowther and Rebecca Tooher.

References:

Grant A, Altman D, Babiker A, Campbell M, Clemens F, Darbyshire J, Elbourne D, McLeer S, Parmar M, Pocock S, Spiegelhalter D, Sydes M, Walker A, Wallace S, and the DAMOCLES Study Group. *Issues in data monitoring and interim analysis of trials*. HTA 2005;9:7.

Edwards S, Lilford R, Braunholtz D, Jackson J, Hewison J, Thornton J. *Ethical issues in the design and conduct of randomised trials*. HTA 1998;2(15).

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