




Data Monitoring Committees and Stopping Rules

The Basics for Survival
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Purpose of DMCs


1. Ensure patient safety
2. Ensure trial stopped as soon as a reliable conclusion is possible
3. Ensure continued scientific validity and necessity
4. Stop if trial unlikely to answer original question (futility)
5. Enhance trial credibility



DMC Constitution

INDEPENDENT expertise in


- in clinical trials
- scientific basis of the treatment being tested
- clinical management of the disease
- biostatistics
- ethics



Ethical dilemma

Tension between


- the individual interests of patients about to be randomised and
- the collective ethics of making appropriate treatment policies for future patients by obtaining reliable trial data



Stopping trials early

DMCs make recommendations after considering complex issues including:

- Ethics
- Statistics
- Practicalities &
- Previous evidence and scientific underpinning



Interim analyses

- May be preplanned either by dates or by numbers enrolled (group sequential design)
- ↑ number of 'looks' at the data increases the risk of detecting a difference by chance (type I error)
- Tendency for 'regression to the truth' if trial continues or from future trials



Stopping rules/ guidelines

- Various systems proposed to set stringent nominal α values
 - O'Brien & Fleming – α increases
 - Peto-Haybitte – fixed low α value
 - Lan and DeMets – prespecify rate at which α value is used up
 - Stochastic curtailment: futility
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- Bayesian – place results in context of prior belief or evidence



Emerging positive trends

- Risk that new participants will receive an inferior treatment
BUT dangers of:
- Lack of credibility
 - Imprecision
 - Undue pressure on a qualified result
 - Mistakes



Emerging negative trends

- Ethically require weaker evidence if worse (asymmetry)
- May consider the minimum difference which would change clinical practice
- Or to stop if the chances are small of reaching statistical significance by the end of the trial