Title	**Issues in Data Monitoring and Interim Analysis of Trials**
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Aim

To address issues about Data Monitoring Committees (DMCs) in randomized controlled trials (RCTs), ie, why and when DMCs are needed, roles and responsibilities, structure and organisation, information needs and ownership, decision making, and reporting arrangements.

Conclusions and results

Suggested criteria for determining when RCTs do not need an independent DMC include: a DMC would not make a contribution; observed differences would not prompt a protocol change (eg, early stopping); and a DMC's decisions would not likely differ from those after internal monitoring.

Roles, responsibilities, and procedures of DMCs should be agreed in advance. A template for a charter is suggested. The central role is to monitor accumulating evidence related to benefit and toxicity. DMCs for regulatory-related trials should be aware of special requirements and regulatory consequences.

Advantages were identified for larger- and smaller-sized DMCs. A DMC should be independent and multidisciplinary (at least 1 statistician and 1 clinician). Consumer and ethicist membership is controversial. The Chair is influential and likely to be most effective if experienced, understands statistical and clinical issues, and is facilitating and impartial. No evidence is available to judge approaches to training. Costs should be covered, but other rewards must be minimal and not affect decisions.

A minimum frequency of DMC meetings is usual, with the committee able to meet at shorter notice. Face-to-face meetings are preferable, but teleconferencing can be used in some situations. Both open sessions (eg, general issues such as recruitment) and closed sessions (eg, for confidential information such as interim analyses) are common.

A DMC should cover benefits and risks, and be balanced, accessible, and current. Disadvantages of 'blinded' analyses seem to outweigh advantages. Information about comparable studies should be included.

Various statistical approaches can be used. However, DMCs usually reach decisions by consensus. The general view is that DMCs should be advisory rather than executive since the trial organizers are ultimately responsible for the trial.

Recommendations

Data monitoring should be considered for all RCTs. An early DMC meeting is helpful to agree on roles, responsibilities, and operations. The proposed charter provides a structure for this. DMC membership (often 3 to 8) is chosen to optimize performance. A minimum frequency of meetings, preferably face-to-face, is usual. A DMC's primary purpose is to ensure that continuing a trial is ethical and considers both individual and collective ethics. Errors are less likely if a DMC takes a systematic approach and knows the range of recommendations open. The recommended standard name is Data Monitoring Committee (DMC).

Methods

Systematic literature reviews of DMCs and small group processes in decision making; sample surveys of reports on RCTs, recently completed and ongoing RCTs, and policies of major organizations involved in RCTs; case studies of 4 DMCs; interviews with experienced DMC members. All focused on 23 pre-stated questions.

Further research/reviews required

Areas that warrant further research include: widening DMC membership beyond clinicians, trialists, and statisticians (eg, include consumers or ethicists); initiatives to train DMC members; methods of DMC decision making, eg, voting and formal decision-making tools; *open* data monitoring; DMCs covering a portfolio of trials rather than single trials; DMC size and membership, incorporating issues of group dynamics; empirical study of the workings of DMCs and their decision making; and which trials should or should not have a DMC.

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