Data Monitoring Committees (DMC)

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Overview

- Why monitor data?
- When a DMC is needed?
- Statistical issues
- DMC composition
- DMC meetings
- Study team responsibilities
The Name Game

- Data Monitoring Committee (DMC)
- Independent Data Monitoring Committee (IDMC)
- Data & Safety Monitoring Boards (DSMB)
- Etc.
The Need for Oversight

- Ethical responsibility to study participants
- Responsible parties:
  - Investigators
  - Study Team
  - Sponsors
  - Institutions
  - IRBs
  - DMCs
Why monitor data?

- ICH E9 on Statistical Principles describes two types of data monitoring:
  - Monitoring quality of the study
  - Monitoring treatment group comparisons of outcome data (interim analysis):
    - Safety
    - Efficacy
When is a DMC needed?

- All clinical trials should be monitored for safety
- Level of oversight will depend on study size, study population, and intervention
- A DMC is needed if there is a:
  - Need for independence
  - Need to maintain blinding
  - Need for expertise
When is a DMC needed?

- Ellenberg’s\(^1\) criteria (at least two):
  - Definite information on Safety or Efficacy of a medical intervention is expected
  - Potential of unacceptable toxicity
  - Mortality or other major endpoint
  - Early stopping for efficacy is ethically important

- Additional criterion: Practicality

\(^1\) Ellenberg, SS, Fleming, TR, DeMets, DL. Data Monitoring Committees in Clinical Trials. Wiley
**DMC vs. IRB**

- One DMC for a study even if multicenter
- Study focused
- Review of unblinded data
- Review of study progress, safety and efficacy data
- Membership based on more heavily on technical expertise

- A study may need oversight from multiple IRBs
- Institutional/local focused
- Does not review of unblinded data (or very rare)
- Review of study progress, safety, but not normally efficacy data
- Membership based on a mix of technical and non-technical members
Statistical Issues in Interim Review

- Repeated testing of outcome data increases the chance of a type I error
Who should be in a DMC?

- DMC should be multidisciplinary:
  - Clinician(s)
  - Statistician(s)
  - Clinical trial experts
  - Bioethicist?

- Different trials might require the inclusion of different disciplines on a DMC
DMC meetings

- Initial meeting before study initiation
- Interim review meetings throughout the course of the study
Initial meeting (Organizational meeting/Study preview)

- DMC charter:
  - Role and responsibilities
  - The structure of the meeting: Open, closed and executive sessions
  - Discussion and voting procedures
  - Reports to/from the DMC
- Protocol (IRB approved?)
- Informed Consent Forms
- CRFs and DM plans
Initial meeting cont-d

Data and Safety Monitoring Plan:

- Adverse Event system
- Content of interim reports (key efficacy and safety outcomes of interest)
- Procedures to manage access to reports
  - Use of an Independent Statistician
- Frequency of interim reports
- Statistical methods and stopping rules
Interim review meetings:

Open session

Trial performance:
- Accrual
- Follow-up
- Protocol violations
- Summary of GCP site monitoring reports
- Baseline characteristics
- Safety and efficacy outcomes, all treatment groups combined
Subsequent meetings: Closed sessions

- Review interim analyses (Safety and Efficacy):
  - continue as originally designed,
  - be modified, or
  - be terminated (Safety, Efficacy, Futility)

- No single statistical test should be used as a strict rule for decision-making
DMC recommendations

- After each meeting, the DMC should provide the study leadership with written information concerning findings and recommendations.
- The DMC should carefully not to provide any unblinding information.
Study Team Responsibilities

- Primarily responsible for safety oversight
- Provide necessary documents for study preview including DSM monitoring plan
- Provide interim reports as planned (alert DMC of upcoming reviews)
- Participate in DMC meetings
- Transmit summary of DMC findings and recommendations to the appropriate IRBs
- Respond to all DMC recommendations
Information Flow for interim reviews

Study Team

PI
Statistical Center

IRB

DMC

Sponsor
Key points

- All clinical studies need a DSM plan
- Some need a DMC
- Implications of Interim Analysis:
  - Access, confidentiality, blinding issues
  - Statistical Issues
- Plan, plan, plan
Resources

- FDA Guidance on the Establishment and Operation of DMCs
  http://www.fda.gov/cber/gdlns/clintrialdmc.htm