Data and Safety Monitoring Board (DSMB)

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Overview

- Why monitor data?
- Why a DSMB?
- Statistical issues
- DSMB composition
- DSMB meetings
- Study team responsibilities
The Name Game

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

- Ethical responsibility to study participants
- Responsible parties:
  - Investigators
  - Protocol Team
  - Sponsors
  - Institutions
  - IRBs
  - DSMBs
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
Why a DSMB?

- Need for independence
- Need to maintain blinding
- Need for expertise

NIH/NIADD’s policy:
- All clinical trials should be monitored for safety
- Level of oversight will depend on study size, study population, and intervention
**DSMB vs. IRB**

- One DSMB 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.
Interim analysis

Test for difference in proportions failing in two groups without adjustment for multiple testing

**Decision Rule:** \( \text{Reject null if } |Z| \geq 1.96 \)

**Overall Type I Error Rate**

- Single test at end of study: \( \text{-----} > 0.05 \)
- Two tests, equally spaced: \( \text{-----} > 0.08 \)
- Five tests, equally spaced: \( \text{-----} > 0.14 \)

*(Friedman, Furberg and DeMets, 1996)*
Who should be in a DSMB?

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

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

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

- Operational Plan (DSMB charter):
  - Role and responsibilities
  - The structure of the meeting: Open, closed and executive sessions
  - Discussion and voting procedures
  - Reports to/from the DSMB
- 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
Subsequent 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

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

- After each meeting, the DSMB should provide the study leadership with written information concerning findings and recommendations (through the Executive Secretary, and corresponding NIH program officer).

- The DSMB 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 DSMB of upcoming reviews)
- Participate in DSMB meetings
- Transmit summary of DSMB findings and recommendations to the appropriate IRBs
- Respond to all DSMB recommendations
Information Flow for interim reviews

Study Team

PI
Statistical Center

IRB

DSMB

NIAID
Key points

- All clinical studies need a DSM plan
- Some need a DSMB
- Implications of Interim Analysis:
  - Access, confidentiality, blinding issues
  - Statistical Issues
- Plan, plan, plan
- ICSSC, OCRA and PPD can help
**Resources**

- DATA AND SAFETY MONITORING BOARD (DSMB) GUIDELINES
  

- DSMB Report Templates
  
  http://www.icsssc.org/templates_resources.htm