

***Discussion:***

**Jim Neaton -**

**How to Construct an Optimal Interim Report:**

**What a DSMC Does and Doesn't Need to Know**

April 19, 2017

Judith D. Goldberg, Sc.D.

Professor of Biostatistics

# Personal Perspectives

View from:

	<b>DSMC Member</b>	<b>Study Statistician</b>
<b>Industry</b>	×	×
<b>Academia [NIH, other funded]</b>	×	×

# Does 'one size fit all?'

- Trial Design
  - Active vs Placebo Controlled
  - Superiority vs Noninferiority vs Equivalence
- Disease [severity]
- Risk to Trial Participants
- Seriousness of Outcome of Interest
- Trial Duration
- Potential for Impact on Trial Conduct
- Other considerations

# Interim Monitoring: How Often? Of What?

- Safety Monitoring
  - Frequency of monitoring [eg, every 6 months]
  - Unmasked (coded) treatment group assignment
  - Known, unknown adverse events
- Efficacy Monitoring
  - Success / Futility
  - Masked / Unmasked (coded) treatment group
  - Frequency of monitoring
    - At all DSMC meetings
    - At planned interim analysis times; how often
  - Interim analysis boundaries
    - Formal / informal

## *Example:* Placebo Controlled Masked RCT

- Non-life threatening
- Primary outcome: first recurrence by 12 months end of treatment period
- Accrual over 4 years, 18 months of followup
- Multi-center
- DSMC meetings 2x/year
  - Safety monitoring
  - Efficacy Monitoring

*Example:*

# Efficacy Monitoring

## DSMC / Investigator Views

### ■ DSMC

- Monitor unmasked efficacy at every meeting (approximately 8 times)
- Stopping boundaries at  $p$  very low
- One formal planned interim analysis: O'Brien Fleming boundaries for efficacy; no futility boundaries

### ■ Investigators

- One formal planned interim analysis: O'Brien Fleming boundaries for efficacy and futility
- No interim analyses

# Impacts on Study Conduct

## ■ **DSMC**

- Stated goal 'not to stop the study'
- Needs efficacy to evaluate safety

## ■ **Investigators**

- Would not like to stop study
- Efficacy would always be available to DSMC if any safety concerns at all
- Concerns re impact of repeated looks
  - On final p-value for efficacy
  - Influence on behavior

# Informal Survey

- Respondents confidentiality preserved
- Very small convenience sample
- Responses
  - Initial response:
    - DSMC needs to see everything
  - Thoughtful responses:
    - Depends on trial and implications



# *Acknowledgements*

- **Thank you to my statistical and clinical colleagues for thoughtful discussions of these issues**
- **Thank you to the speaker and panelists for a provocative discussion**