The Role of BIOSTATISTICS in Clinical Research

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How Many Biostatisticians do you need for your Study?

• No Biostatisticians are needed
• One Biostatistician
• Two Biostatisticians
• A Biostatistical center
Lead Study Biostatistician (LSB) defends choices to questions raised by stat reviewers (protocol or paper)

Responsibility = Credit/Blame
Biostatistician Role

- Protocol Development
- Data Management
- Study Implementation
- Study Monitoring
- Data Analysis
- Report/Manuscript Writing
Protocol Development

- Objectives
- Definition of Endpoints
- Study Design
- Sample size
- Analysis Plan
Objectives

• Based on the objectives of the study:
  – Clear specification of the hypotheses to be tested (or parameters to be estimated)
  – Selection and definition of endpoints
Study Design

• Is the study design appropriate to provide the data needed to answer the objectives?

• Selection/recruitment of Participants:
  – Define procedures for minimizing selection bias
  – If an RCT, define randomization procedures (sequence generation, and allocation concealment), blinding

• Length of follow up and frequency of contacts
Sample Size

• Justification in terms of power or precision for the primary endpoint

• Method used to calculate the sample size
  – Should be consistent with the primary method for data analysis, and appropriate for the study design

• Historical data to support the assumptions

• Justification in terms of feasibility
Analysis Plan Summary

• Provides the statistical methodology for the assessment of the primary objective(s):
  – Statistical Hypotheses and testing procedures
  – Primary Analysis Population

• Discusses statistical methods to be used in planned interim analyses. (Role of a DSMB)
Analysis Plan Summary

• Purposes:
  – Assuring objectives can be achieved
  – Justifying design and data collection
Protocol Review

• It is highly recommended that the LSB reviews the full protocol prior to final review/sign-off:
  – Clarity
  – Completeness
  – Consistency
  – Data quality issues
  – Feasibility
Protocol writing

- Objectives (input)
- Endpoints (input)
- Study Design (input)
- Randomization procedures (writes)
- Allocation concealment (input)
- Sample size (writes)
- Analysis plan (writes)
Data Management

- CRF Development:
  - Content
  - Design

- Dataset specification:
  - Annotation of CRFs
  - Record Layout

- Validation:
  - Error checking specification
  - Test data
Study Implementation

• Sampling Selection
• Implementation of Randomization procedures
  – Typically performed by an independent biostatistician with the instructions provided by the LSB
Study Monitoring

• Monitoring for Quality

• Monitoring for Safety/Efficacy:
  – Use of an Independent Biostatistician
  – LSB still responsible for the content, analysis methodology, and data transfer coordination
Data Analysis

• Write a detailed analysis plan:
  – All hypothesis to be tested and testing procedures (or parameters to estimate)
  – Analysis populations
  – Interim analysis and adjustments to type I error
  – Hierarchy of analysis
Data Analysis

• Should be written prior to un-blinded review of the data or even prior to data collection:
  – Helps you prepare for report and manuscript writing
  – Helps in the validity and credibility of the results
Data Analysis

- Fishing Expedition
- Data Mining
- Data Dredging
- Data Torturing
- Data Driven Analysis
- Shotgun Approach
- Exploratory Analysis
Report/Manuscript Writing

• Method Section:
  – Description of the data (design, endpoints)
  – Statistical Methodology

• Result Section:
  – Data presentation (tables, graphs, etc.)

• Discussion Section:
  – Appropriate interpretation of results.

• Usually the third author in papers
How many biostatisticians does it take to change a light bulb?

a) Only one, they're accustomed to menial work.

b) Two, you have to plan for subject dropout in any clinical trial.

c) Three, the probability of a biostatistician boring someone else to sleep is 2/3.

d) None, having the biostatistician's name appear on the protocol for changing the bulb will be enough.

e) 1.5, the average of (a) to (d).

f) It depends on the purpose for changing it and the design of the bulb.
How many Biostatisticians do you need for a Study?

• Lead Study Biostatistician
• Assistant Biostatistician
• Consultant Biostatistician
• Independent Biostatistician
• Verifying Biostatistician
• Supervising Biostatistician
Final Remarks

• The LSB should be involved in most aspects of a study
  – Plays a major role in protocol development, DM review, interim reporting, and data analysis

• The LSB ensures that ICH E9 guidelines on Statistical Principles are followed to:
  – Minimize Bias and Maximize Precision

• The LSB cares about data because s/he does the analysis, so s/he should be involved in any aspect/decision related to the data