

Biostatistics in Rehabilitation Research

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“Statistical Considerations” section

- Reviewers expect specifics as to design and analysis considerations
 - What will you measure?
 - How will you measure it?
 - What will you do with the data once you collect it?
- Best to find a statistician to write these sections
- What should these section(s) include?
 - Depends on type of study



Proposal should

- Specifically state hypotheses that the research will test
- Tie hypotheses to the specific aims
- Operationally define the concepts
 - Higher scores on SF-36 rather than better quality of life
- Delineate primary and secondary outcomes



Proposal should

- Delineate primary and secondary outcomes
- Primary outcome:
 - Be prepared to defend
 - Study will rise or fall depending on what happens with this outcome
- Secondary outcomes
 - Important enough to collect



General guidelines

- Each specific aim should involve one or more outcomes
 - Analysis plan for each specific aim
- Power calculation/sample size section
 - usually based on primary aim/outcome
- Some debate about power calculations for secondary outcomes



Power calculations

- Only as good as the preliminary data that go into it.
- Forces proposal to be specific about hypotheses to be tested



Other sections specific to type of study: Observational study

- Non-intervention study describing population characteristics
- Sampling plan crucial.
 - What's the population of interest?
 - How will subjects from this population be recruited?
 - How will you ensure adherence to the sampling plan (i.e., high response rate)
 - Particularly important for defining population means, percentages



Cohort study

- Comparing interventions that are not assigned by experimenter
- Example:
 - Surgical vs. drug therapy.
 - Follow subjects over time after intervention
- Need section describing how you will adjust for potential differences between the groups.



Matched Case Control Study

- Normal vs Diseased Control Group
- How will you do the matching?
- Can you ensure that matches are likely to be found?
- Specific statistical techniques used in matched studies



Clinical Trials

- Gold standard for assessing interventions
- Carries with it increased demands for rigor in the proposal
 - inclusion/exclusion
 - dose/treatment modifications
 - adverse event reporting procedures
 - manual of operations



Clinical Trials

- Increased demands for rigor in the statistical section
 - masking of treatments
 - randomization
 - data safety monitoring plan (DSMP)
 - interim analysis plan
 - plan for data management



Masking of Observers

- Particularly important because of difficulty of double masking of interventions
- Proposal needs to describe in detail how masking will be done



Randomization

- Must have formal plan
- Needs to be auditable
- There are specific ways of doing the randomization:
 - Blocked randomization
 - Adaptive randomization
 - Minimization



Data & Safety Monitoring Plan

- Required on all NIH-supported clinical studies
- Need to have contemporaneous data entry
- What information about the study does the PI know and what effect might that have on the study?
- Data and Safety Monitoring Board needed whenever PI is blinded or for high risk studies



Interim Analyses

- Analyses conducted while trial is on-going
- Address issues of
 - study conduct
 - assess evidence collected so far
- Control of overall significance level
- Formal Methods need to be described
- Interaction with data and safety monitoring plan



Data Management

- Particularly for clinical studies, how the data is entered is important
- Necessary for data and safety monitoring
- Quality control



Statistical Software

- Describe the statistical software that will be used for analyses
- Helps to clarify the planned statistical approach



Pilot studies

- Can be any of the types of studies previously mentioned (observational/ cohort/case-control/clinical trial)
 - Reduced prominence of sample size calculations
 - Often done in terms of precision
- How will data collected inform you about a future (non-pilot) study?



Statistical Methods

- Statistics is a dynamic field
- Statistics taught in an introductory course many years ago may not be adequate in today's environment
- Consult with knowledgeable statistician
 - Give enough time for statistician to understand the proposal and integrate statistics section with entire proposal



Consulting with a statistician

- Be prepared to explain research area and rationale for proposal *in detail*
 - Can be useful exercise in itself
- Bring background papers, including those with statistical methods described
 - But don't insist! These methods may not be appropriate for your study



Consulting with a statistician

- Allow some free rein on planned analyses (allow/support innovative statistical analyses)
 - May address scientific questions more directly than existing methods
 - Statistician often more invested in the research
 - Often viewed highly favorably by reviewers
 - But: should be over and above more standard methods of analysis, with explanation of why more sophisticated methods are needed.

