Hypothesis Specification

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- A good hypothesis is a fundamental building block of knowledge
- A good hypothesis is critical for scientific progress

- Good hypothesis is essential for getting research support (funded!)
- A good hypothesis is essential for a successful study

Characteristics of a Good Hypothesis

- simple & clear
- builds on existing knowledge
- testable question
- relevant question: outcome will affect clinical care and/or public policy

How to formulate a good hypothesis: where does one start?

- address a particular clinical challenge
- test a particular behavioral treatment
- target a particular risk factor

Primary & secondary aims

Distinction is important for:

- Writing of grant application
- Power analyses (sample size)
- Statistical analysis (inc. interim analyses)
- Operations & data collection

Primary hypotheses in (behavioral) clinical trials

- Main study question
- Applies to all participants
- Addresses primary outcome (preferably one that can be ascertained unambiguously)
- Usually only one (except for in studies testing > 1 interventions such as 3-arm design or factorial design)

Family Intervention in Stroke Trial (FIRST)

Test the effect of a psychosocial intervention compared to usual care on the primary endpoint of recovery of function at three and six months post-stroke.

Heart failure Adherence and Retention Trial (HART)

A self-management intervention, compared to attention control, will reduce the risk of adverse clinical outcome in patients with moderate heart failure.

Clinical outcome is defined as the combined endpoint of hospitalization for heart failure and all-cause mortality

Women's Health Initiative

A low-fat eating pattern is hypothesized to prevent breast cancer and colorectal cancer (and secondarily, CHD)

HRT is hypothesized to reduce risk for CHD and other cardiovascular conditions (and secondarily hip fracture)

Calcium and vitamin D supplementation is hypothesized to prevent hip fractures (and secondarily other fractures and colorectal cancer)

Physician's Health Study

Low dose aspirin is associated with a reduced risk of cardiovascular disease

Beta-carotene is associated with reduced cancer risk

Secondary Hypotheses

- Effect of intervention on secondary outcomes
  - Broader clinical goals/outcomes
  - Outcomes that are more difficult to ascertain with precision
  - Economic aims (costs and cost/benefit)

Secondary Aims

- Effect of intervention in subgroups
  - Age, gender & race
  - Socio-economic status
  - Place, region
  - Typically reduced power!!

Heart failure Adherence and Retention Trial (HART)

Primary hypothesis:

A self-management intervention, compared to attention control, will reduce the risk of adverse clinical outcome in patients with moderate heart failure.

Secondary hypotheses:

A self-management intervention, compared to attention control, will result in

a) slowed progression of heart failure
b) Improved quality of life
c) Reduced health care costs

"These" effects are consistent across gender, ethnicity, and socio-economic status

Mediating Hypotheses

- The “mechanisms”
  - changes in intervention group that may “explain” clinical benefit
  - usually target behaviors/emotions of behavioral intervention

Mediating Hypotheses - caveats

- Tempting, but challenging
  - desire to know why intervention works
  - participation in clinical trial may change many ‘things’, most of which are usually not measured
  - be ware of changes that occur in controls
  - temporal order between change in mechanisms and clinical benefit usually difficult to determine
  - may impose demands on design that can detract from primary aim(s)

ENRICHD study

- Test the effect of behavioral intervention (CBT), compared to usual control, on clinical outcomes in MI patients who are depressed or have low social support
- Mediating hypotheses:
  - Did intervention reduce depression?
  - Did intervention increase social support?
  - Did intervention reduce general distress, etc. etc.?

Aims and Study Design - I

- Primary Aims should determine
  - Basic trial design (e.g., parallel arms, factorial, cross-over)
  - Primary outcomes
  - Target population
  - Sample size
  - Duration of intervention
  - Duration of trial/follow-up

Aims and Study Design - II

- Secondary Aims may determine
  - Secondary outcomes
  - Specific composition of target population (& recruitment strategy)
  - Intensity/complexity of outcome data collection
  - Sample size?

Aims and Study Design - III

- Mediating Aims determine
  - Not the basic study design!
  - Additional data collection
  - Frequency and intensity of follow-up contact
  - Number of papers a trial will produce (or the amount of data that will never be analyzed….)