Unstable Control Groups in Pragmatic Trials

And Other

Problems that may be Beyond Rescue by Statistics

Agenda Description

- *Discussion on exploring techniques to anticipate changes in the control group. This is a major challenge for PCTs. Approaches such as stepped-wedge design, adaptive interventions/smart design, and adaptive designs are options. Small strategic ancillary studies may help investigators measure mediators without complicating PCT designs*

Disclaimer

- More complex designs are not necessarily the solution – adjustment is not a panacea
- Statistics can't always come to the rescue
- Anticipation and careful monitoring are critical

Outline

- Issues most relevant to control sites
- Other issues not restricted to control sites
  - Too general a topic to fully discuss
  - Important to mention
- Defense reminder for each topic
- Discussion encouraged

Contamination with elements of Intervention

- Some components of intervention may appear in usual care for some control sites
- One strategy is very complex intervention
  - Difficult to duplicate
  - BUT also difficult to generalize if successful
- Defense: Important to recognize and monitor intervention-like activities using same instruments and procedures

Evolving Adoption of Intervention

- Broad new Healthcare Initiatives focus on same problem
- Growing awareness drives local efforts (eg, overuse of pain killers)
- Defense: Again, important to monitor and document whenever possible.
- Statistics: look for differentially evolving trends in outcomes among controls that are adopters

Changes in Leadership

- Possible re-focusing of priorities
- Initial agreements no longer hold
- Can happen in both control and intervention sites; maybe differentially
- Defense: Important to have clearly specified MOUs to document what each side has agreed to do.
- Statistics: Sometimes possible to adjust or evaluate trends

Structural changes, eg Reorganization

- Sites close or merge
- Healthcare delivery model is revamped to address newer performance metrics
- Defense: Discussions of these possibilities should be addressed during recruitment

Fundamental Data Issues

- Developments that change meaning of the data
  - Changes in use of diagnostic codes (ICD9 to 10)
  - Newer technology changing eligibility or outcomes measurement
  - Could be differentially adopted
- Threats to definition of target population and comparison of outcomes
- Defense: Important to be able to monitor and to the extent possible to "try" to adjust

Trial or Site Imposed Data Differences

- Changing eligibility, eg to remedy low accrual rates
- Differences across clinics in ordering of checkbox codes, eg according to specialty
- Threats to definition of target population and also outcomes measurement
- Defense: Monitoring and Communicating to anticipate, record, and possibly adjust

Other Types of Study Modifications

- Enriching the population during the trial for higher baseline risk to increase event rate in controls
- Creates evolving target population
- Statistics:
  - Complicated trade-off between event rate and accrual rate
  - Involves potential interaction between intervention and estimated baseline risk?

Site Withdrawal due to Burden

- Some conditions of participation become onerous
- Proactive MOU should
  - Identify site responsibilities
  - Define eligible population
  - Specify activities to be conducted by research team
- Defense: Preliminary small pilot study can help

Balancing Act

Involves incredible cooperation and teamwork

Getting everyone on the same page