

Goals of RCT Design

- Minimize bias in estimate of treatment effect
- Maintain type I error
- Sufficient statistical power
- Feasible and Applicable
- Leon et al., *Biological Psychiatry*, 2006; 59:1001-1005.

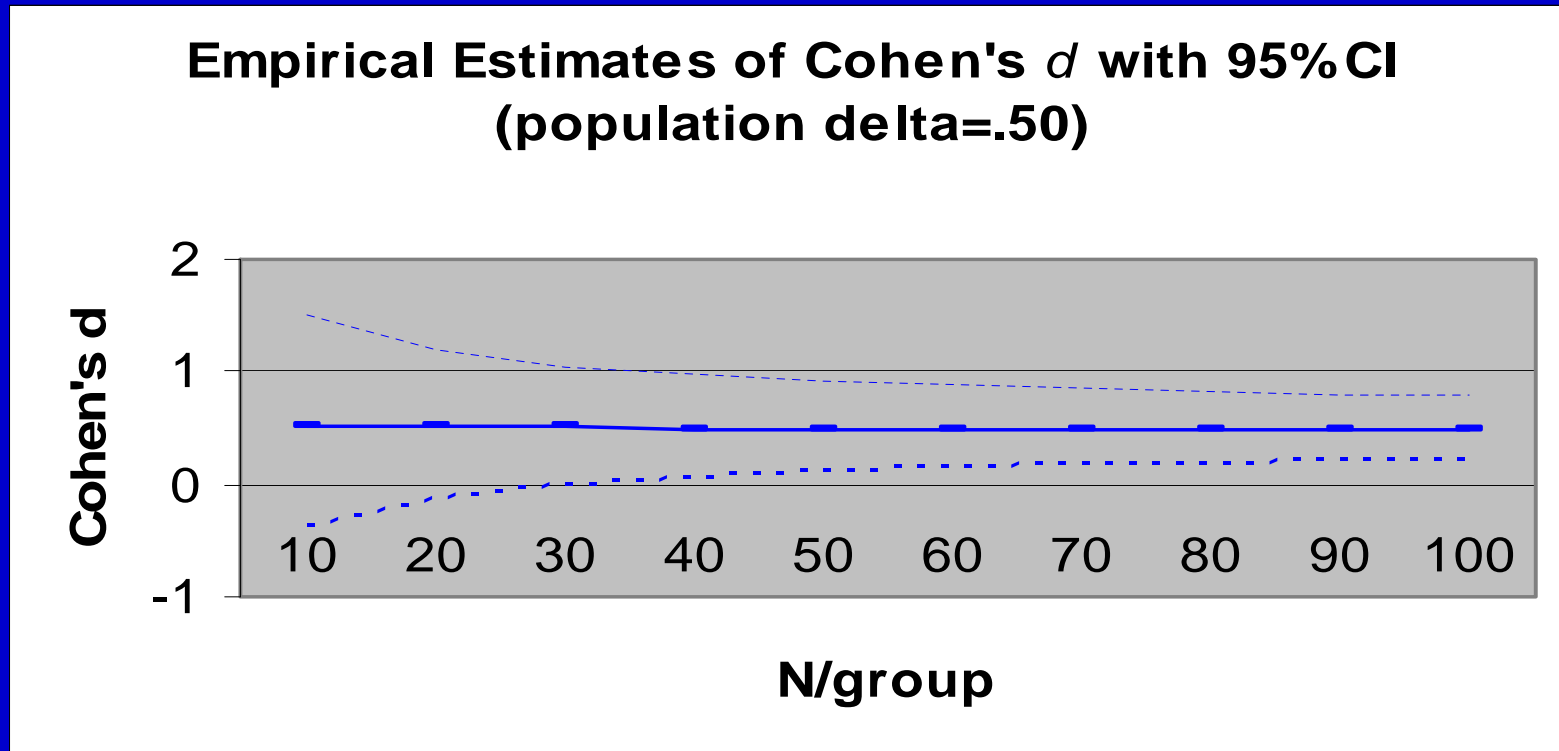
RCT Design

- Randomized group assignment
- Double-blinded assessments
- Control or comparison groups

Attrition Interferes with RCT Goals

- Introduces bias in estimate of the treatment effect
- Smaller N reduces statistical power
- Limits feasibility and generalizability

RCT Design Stage: Pilot Data to Estimate the Effect Size?



Simulation Study: 10,000 simulated data sets for each combination of d and N
(Leon, Schz Bull, 2008)

95% CI: $d \pm [t * 2 / \sqrt{N}]$

(Kraemer, AGP 2006 63:484-9)

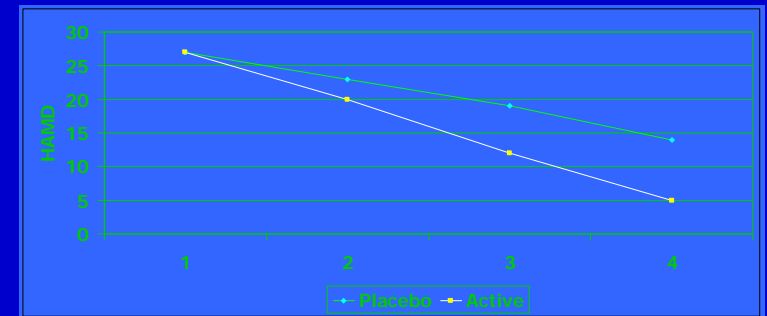
Choosing Statistical Strategy for RCTs

- What is the form of the dependent variable?
- What is sample size?
- How many assessment times per subject?
- * * Use an approach that includes subjects with incomplete data.

Mixed-Effects Models: Illness Severity over Course of RCT

- Unit of analysis: weekly or monthly assessments
- Do not exclude Ss with some missing data
- Can quantify group differences as rate of change over time

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- With ignorable dropout, mixed-effects models can be used for valid inference.
 - Attrition explained by covariates or earlier measures of outcome



See: Laird & Ware, 1982; Hedeker and Gibbons, 2006

Non-ignorable Dropout

Dropout depends on unobserved outcome data

- Dropout due to unobserved symptom severity or adverse events

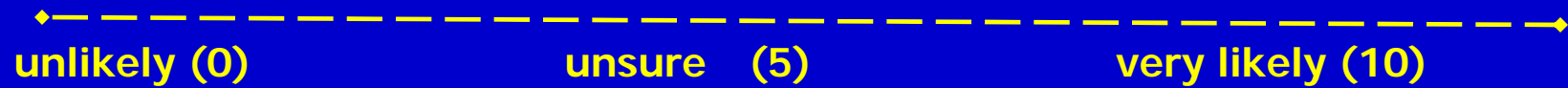
Predictors of dropout are not known or unavailable

Pattern-mixture model: dropout pattern

Selection model: demographic and clinical predictors of dropout

Predict Dropout: *Intent to Attend*

Baseline: "How likely is it that you will complete the study?"



Weekly: "How likely is it that you will attend next assessment session?"



These data could change non-ignorable dropout to ignorable.

Intent to Attend

- Simple assessment and adds minimal burden.
- Identify those at risk of attrition.
 - Accommodate S's needs with *blinded* follow-up questions.
- As a predictor of attrition, *Intent to Attend* is consistent with the Theory of Reasoned Action, which asserts:
 - An individual's actions are based on his or her intentions to perform those actions. (Ajzen and Fishbein, 1980)

Intent to Attend

- Incorporate in sensitivity analyses.
- Included in ongoing RCTs for schizophrenia, depression, ptsd, bipolar disorder, substance abuse and panic disorder.
- Value of *Intent to Attend* will depend on degree of bias reduction.
 - Association of *Intent* with Attrition, Outcome, and Group.
- Simulation study examined bias with and without *Intent to Attend*.