Methodological Challenges in Randomized Effectiveness Trials in Psychiatry

- **Phil Wang** – NIMH Perspective
- **Susan Murphy** – Sequential Treatments; issues in design and analysis
- **Don Hedeker** – Longitudinal data analysis; data analytic strategies for incomplete data
- **Amy Grogg** – Applying results to Policy decisions

Why Do We Do Effectiveness Trials?

- Clinical development program focus on meeting regulatory objectives
  - quality, safety, efficacy
- Usually limited exposure
  - ST, small numbers
- Homogenous samples
  - not the usual clinic population

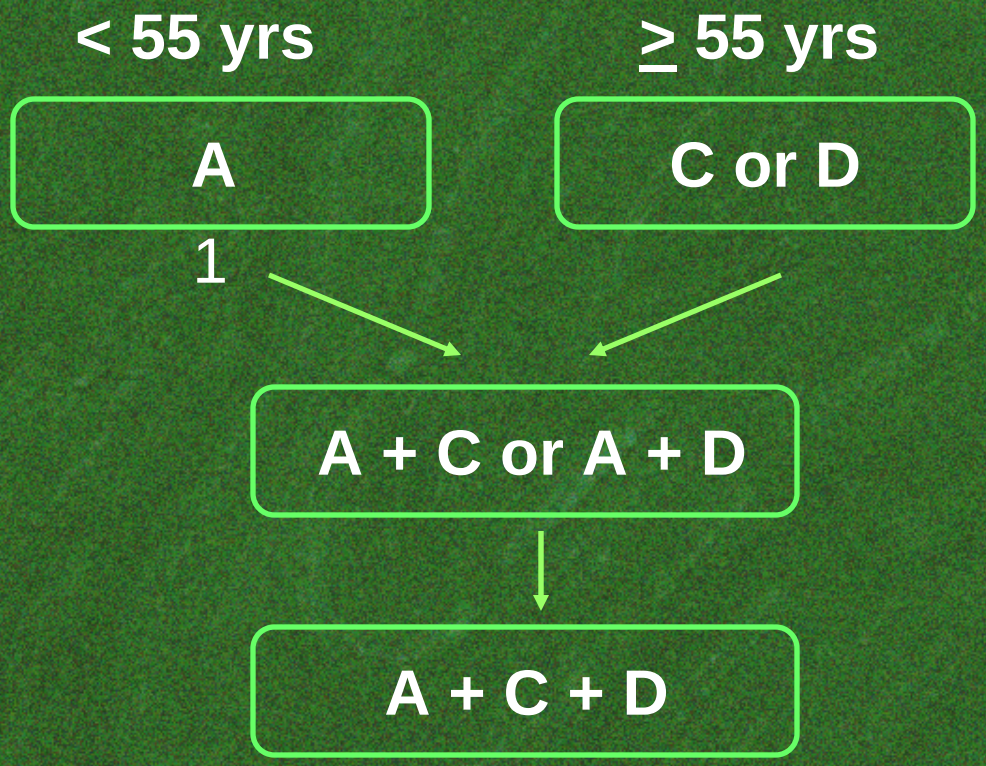
Why Do We Do Effectiveness Trials?

- Heterogeneity of response
  - no single treatment is usually effective
- High risk of relapse in chronic conditions
  - Difficulty in achieving full and prolonged remission
- Evaluation of impact of side-effects
  - Emergence of new safety/tolerability issues
- Translation of clinical trial results into “real world” outcomes

The Future Prospects

- Impact of Pharmacogenomics
  - Efficacy, safety, tolerability
- Assume a chronic disease model and not "one size fits all"
  - NOT one drug; one dose
  - Step; combination therapies

Chronic Disease Models - Hypertension



A = ACE Inhibitor
C = Ca Channel Blocker
D = Thiazide diuretic

- Plus : statin, aspirin

Chronic Disease Model Schizophrenia

- Positive Symptoms
- Negative Symptoms
- Cognition

} Pharmaco and Psychological therapies

Chronic Disease Model Schizophrenia

- Preventative measures
  - cardiovascular disease
  - metabolic syndrome
  - suicidality
  - tardive dyskanesia
- Supportive measures – social care, rehabilitation

Effectiveness Trials

- What we have learnt :
  - design
  - analysis
  - limitation of current methodologies
- Where do we go from here?

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