

ISCTM 2012 Autumn Conference
October 2, 2012
Marina del Rey, California

Combining Medications to Enhance Depression Outcomes (CO-MED):

A Clinical Trial that Combined Explanatory and Pragmatic Elements

Joanne B. Severe, M.S.

DISCLOSURES

- **None**
- **At the time CO-MED was funded and conducted, I was a federal employee at the National Institute of Mental Health responsible for operations oversight on this trial**



**Combining Medications to Enhance
Depression Outcomes (CO-MED):**

**A Clinical Trial that Combined
Explanatory and Pragmatic Elements**

Goals of Presentation

- Features of the CO-MED Trial and Where They Rank on the PRECIS Wheel
- Impact of CO-MED Trial features on the Results and the Generalizability of those Results
- Lessons Learned

OUTCOMES

- Real-world frontline clinician questions
- Does STARTING treatment for MDD with 2 different anti-depressant medications instead of one result in **higher rates** of remission at 12 weeks, **faster** remission, and **sustained** remission (at 28 weeks)
- Results could change treatment practice guidelines for MDD
- Real-world outcome measure = Remission (not just symptom decrease)
- Remission defined using Participant Self-Report measure (QIDS-SR-16)
- Rigorous definition, requiring two consecutive Remission-qualifying ratings, not just “one good week”

FLEXIBILITY OF THE INTERVENTIONS

Experimental and Control Conditions

Components of the Study Design

- Randomized participants
- Three cells: 2 Experimental condition vs 1 Control condition
- Medication choices fixed
- Single-blind treatment delivery (including use of placebo)
- Guided dosing regime
- No depression-specific psychosocial treatment allowed

PARTICIPANT ELIGIBILITY CRITERIA

- Number of Sites (15)
- Types of Sites
- Geographic and Ethnic Diversity
- Large Sample Size
- No advertising.....patients seeking care
- Broad Inclusion Criteria Tempered by 22 Exclusion Criteria

PRACTITIONERS

Experimental and Control Conditions

EXPERTISE

- Sites chosen partially on basis of performance of clinicians
- Training
- Supervision
- Performance Feedback and Improvement Efforts

ADHERENCE

- Manuals
- Monitored

PARTICIPANT COMPLIANCE

- Time spent to develop alliances, provide education
- Reminder calls for treatment visits
- Follow up calls for missed visits
- Self-Reported Adherence Questionnaires, real-time entry, and Feedback to practitioners
- Protocol medications provided at no cost
- Patients received payment for their time

INTENSITY OF FOLLOW UP

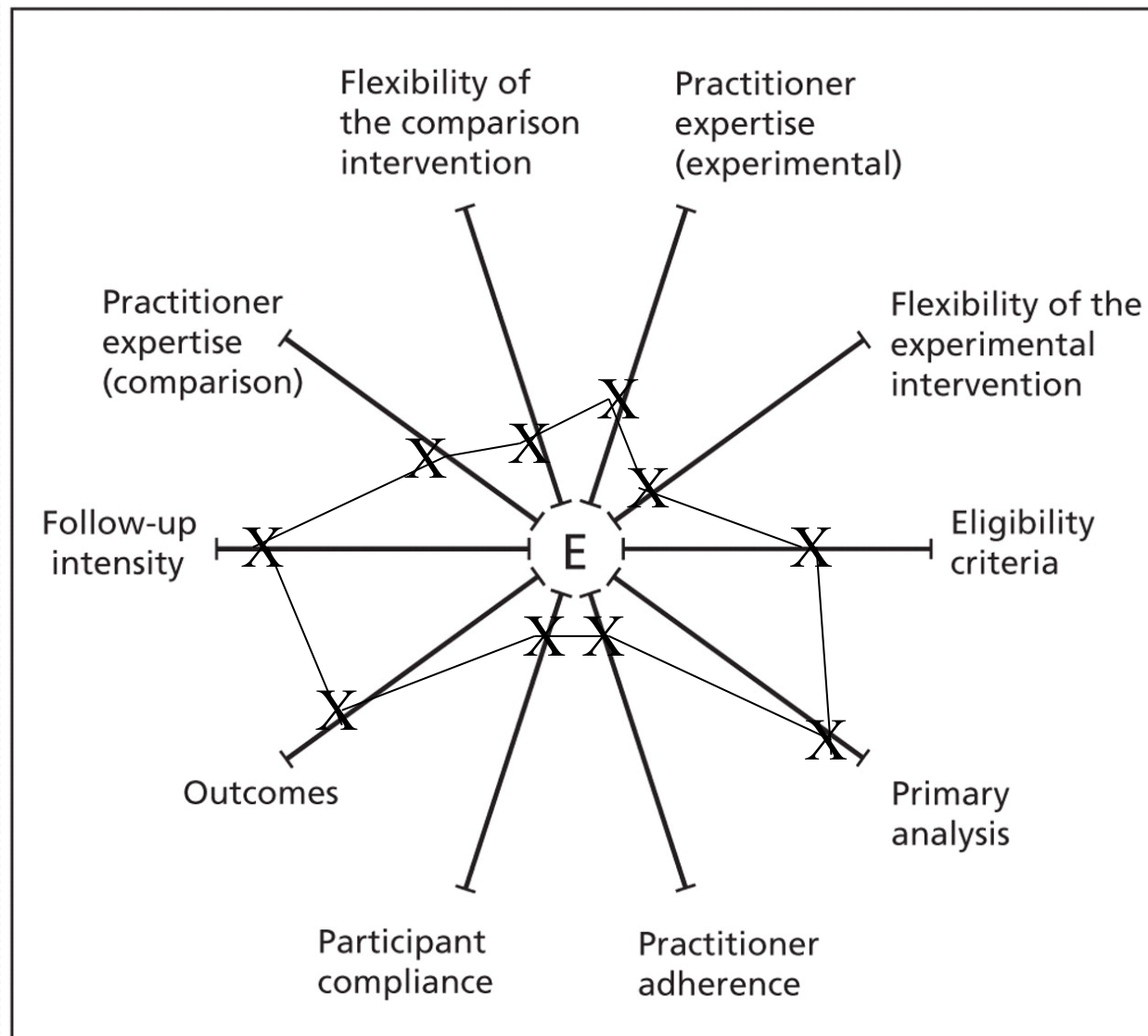
Visit Schedule

- Every other week for 3 months
- Once per month for 4 months

PRIMARY ANALYSIS

- All participants included -- ITT analysis
- 76% of participants did not exit prior to 12 weeks
- Used last two consecutive scores to determine remission
- Guarded against fleeting “good week”
- Carried last observations forward, but required at least 2 post-baseline scores
- Classified those with fewer than 2 post-baseline scores as Non-Remitters
- Analysis was Each Combination Treatment vs Monotherapy

Using the PRECIS “wheel” of the pragmatic–explanatory continuum indicator summary.
“E” represents the “explanatory” end of the pragmatic–explanatory continuum.



Thorpe K E et al. CMAJ 2009;180:E47-E57

CONCLUSIONS

CO-MED was a Hybrid Clinical Trial

Explanatory:

Methods – Study Design, Experience

Operations – Training, Monitoring

Well-delivered Treatments – Adherence, Compliance

Pragmatic:

Broad Public Health Questions

Settings

Sample

CONCLUSIONS

What Does the Ranking Mean for the Results?

- Generalizable to broad population of those with MDD who get well-delivered care
- This is slightly different than the question of “Does it work in usual care?”
- But what are the standards for usual care when administering treatment like this?
- So, how pragmatic is the overall study question?

KEY LESSON LEARNED

- It is extremely important to consider the balance between explanatory and pragmatic decisions in each domain for their individual and collective effects on how this alters the major outcome question and to whom the results will apply.