

# Methodological considerations and treatment of non-randomized controlled trial (RCT) data

Jennifer Weuve, MPH, ScD

Associate Professor of Epidemiology



# Why RCTs can be useful

1. Participants in treatment groups are **“exchangeable,”** on average.  
*i.e.,*

Risks of outcome prior to treatment assignment are distributed evenly across groups.

No confounding.

# Why RCTs can be useful

## 2. **Treatments** (and non-treatment) are **well-defined** (consistency).

*E.g.*, In-home music therapy twice per week for 12 weeks with designated therapist and protocol vs. wait list ...

... as opposed to ...

...any music therapy vs. no therapy over 12-week period.

# But RCTs are not a panacea for all questions about effective strategies of care

1. Impracticalities of **duration**
2. Can **evaluate only few treatments** at a time. Limited capacity for comparing effectiveness

E.g., different frequencies of cognitive rehabilitation

E.g., PWD caregiver social support + cognitive rehabilitation for PWD vs one of these vs neither.

3. RCT **participants may not reflect population(s)** to which we would like to apply findings.

# Potential for non-RCT research to inform care interventions for PWD and their caregivers

Numerous past and ongoing large cohort studies with prospective data collection, representing wide variety in ...

- Interventions represented (types, durations, patterns)
- Settings
- Caregiver and PWD characteristics

# Harnessing the potential of non-RCT research

## 1. Design and analyze as if they were RCTs, i.e., “**target trial emulation**”

Hernán MA, Robins JM. Using big data to emulate a target trial when a randomized trial is not available. *Am J Epidemiol*. 2016 Apr 15;183(8):758-64. frequencies of cognitive rehabilitation

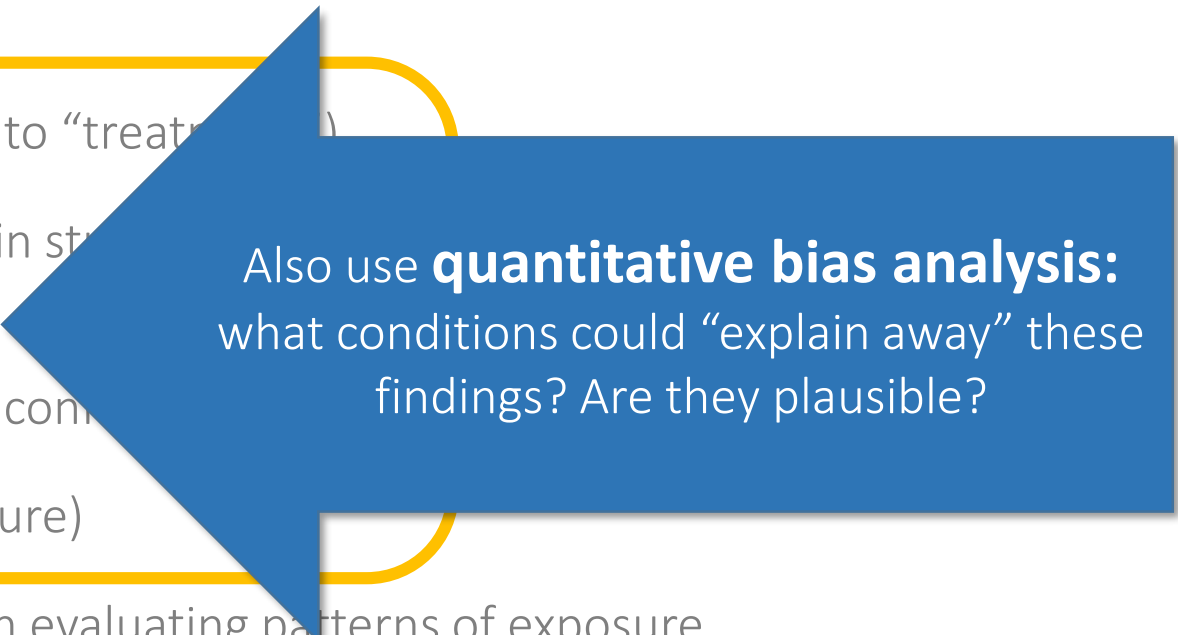
### **Match design and analysis choices to fit protocol of RCT you would have conducted**

- Eligibility criteria, treatment strategies, assignment procedures, definition of “time zero” and follow-up period, outcome of interest, causal contract of interest, analysis plan
- Substitute analytic strategies where protocol impossible to match (e.g., adjustments instead of random assignment)

# Harnessing the potential of non-RCT research

## 2. Use of strategies to address plausible non-causal explanations for findings

- **Confounding** (different risks for outcome prior to “treatment”)
- **Selection bias** (participation and continuation in study and risk of outcome; in RCTs, too)
- **Mismeasurement** (of key exposure, outcome, confounder)
- **Reverse causation** (outcome influences exposure)
- **Treatment-confounder feedback bias** (when evaluating patterns of exposure over time, and earlier exposure affects a factor that influences both later exposure and the outcome)



Also use **quantitative bias analysis**:  
what conditions could “explain away” these findings? Are they plausible?

# Harnessing the potential of non-RCT research

## 3. **How well do results transport** to other settings and populations?

- Suppose the results of a RCT non-RCT have been determined to be valid *within the study population*.
- What would the **impact be in a different target population?**
- The **science of transportability**.
  - Can we identify the transportability of an intervention?
  - Can we satisfy assumptions needed to estimate the effect in another population?
  - What is the impact in another population?



# Methodological considerations and treatment of non-randomized controlled trial (RCT) data

Jennifer Weuve, MPH, ScD

Associate Professor of Epidemiology

