Introduction to Comparative Effectiveness Research Using Observational Data

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Educational Objective

- Understand study design, data enhancement, and statistical methods to conduct quasi-experimental CER using observational data, especially administrative data
  - Quasi-Experimental Study Designs
  - Sample Selection
  - Covariates/risk adjustment
  - Statistical Adjustment

CER: Definition

- Comparative effectiveness research is the conduct and synthesis of research comparing the benefits and harms of different interventions and strategies to prevent, diagnose, treat and monitor health conditions in “real world” settings
  - Sox & Greenfield, 2009 Ann Int Med

Treatments Considered in CER

- CER uses an expansive definition of “treatment”
  - Compares the results of one approach for managing a disease to the results of other approaches.
  - Interventions compared may include medications, procedures, medical and assistive devices and technologies, diagnostic testing, behavioral change, and delivery system strategies.
  - Study designs and data are needed for conducting a wide variety of studies
    - E.g., both Drug A vs Drug B studies, and Patient Centered Medical Home vs. usual primary care studies.

Outcomes Assessment in CER

- CER uses expansive definition of outcomes
- Administrative data can be a source of many outcomes
  - Outcomes from administrative data
    - Utilization based outcomes (e.g., hospitalization for stroke/MI)
    - Death
  - Outcomes from ancillary data, e.g.,
    - Functional outcomes from Medicare Current Beneficiary Survey
    - Patient satisfaction from CAHPS
    - Health status, cognitive status for nursing home residents in the minimum data set (MDS)
- Costs are not the focus of CER
Why do CER on observational data?

- What need or niche does observational CER on observational data serve?
  - We can never do all the RCTs we need
  - RCTs will always enroll a select group of patients
    Results may not generalize to the total population of patients
  - RCTs will never enroll enough people
    Sub group analyses are needed
    You don’t want to know what the average effect of Drug A vs Drug B is, you want to know the effect of the drug A vs Drug B on you.
  - Technology changes too fast for RCTs

Challenges for CER on observational data

- Heterogeneity of treatment effects
  - Heterogeneity of risks and benefits across individuals
  - Changes in response to treatment as patient ages, develops new conditions
- Need to evaluate treatment effects on universal health outcomes, not just disease-specific outcomes
- Treatments that are beneficial for one disease may exacerbate another.
  - This risk increases with the number of other health conditions
- e.g., effect of antihypertensive meds on health person versus 75 year old with dementia, osteoporosis, depression and 10 other meds.

Challenges for CER for ptsns with multiple chronic conditions (Tinetti & Studenski, 2011)

- Larger N’s with heterogeneous populations
- Longer follow-up periods
- New methods for health transitions over time
- New measures of health outcomes
- Expand use of MCBS, MDS and other longitudinal surveys that have general health outcome information
- Conduct research on common disease pairs

Opportunities for CER using CMS data

- Coke vs Pepsi studies
  Patient/clinician self-selection on unobserved confounders is less acute if treatments are similar
- Observational studies conducted along side a clinical trial
  You know if you’ve solved the unobserved confounding problem if your CER reproduces the results of an RCT
- Use those same data/methods to address issues left unexplored by the RCT (e.g., different patients, different settings, slightly different treatments, etc.)
- CER studies that mimic an RCT that would never be conducted (e.g., studies involving pregnant women, the oldest old, etc.)
- Simulation studies
- What else?

Basic Elements of a CER Study

Basic elements of CER:

- Rigorous study design
- Appropriately chosen treatment group
- Appropriately chosen control group
- A “treatment”
- 1 or more outcomes
- Patient demographics
- Measures of patient comorbidity and severity of illness
- Methods for dealing with unobserved confounding & selection bias
Illustration of a CER Study

- The comparative effectiveness of Centrally Active (CA) versus non Centrally Active ACEIs on preventing dementia

- Angiotensin Converting Enzyme Inhibitors (ACEIs) are widely prescribed for hypertension and heart failure.
- Coke vs Pepsi. There are many ACEIs (lisinopril, ramipril, benazepril, captopril, etc.) and not much differentiation.
- Some cross the blood brain barrier (CA)
- Some think this may forestall the incidence of dementia/Alzheimer’s
- Work in Progress

Summary

- CER covers an expansive definition of treatments and outcomes
- Not just Drug A vs Drug B
- Opportunities for CER using observational data to fill in the gaps left by RCTs
- Major challenge is unobserved confounding

Outline for the week

Monday
- Introduction
- Causality
- Study design
- Issues regarding treatment

Tuesday
- Review of Does X cause Y?
- Risk adjustment
- Propensity scores

Wednesday
- Finish propensity scores
- Review Graham paper
- Difference in Difference estimation
- Introduction to instrumental variables

Thursday
- Instrumental Variables
- Review of Brooks paper

Friday
- Missing data
- Putting it all together with example
- Wrap-up discussion

References & Resources