

**OBSERVATIONAL
MEDICAL
OUTCOMES
PARTNERSHIP**

OMOP Methods:
Application to Comparative Effectiveness

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Motivation

“Information is like fish:
it’s better when it’s fresh.”

Comparative Effectiveness

- “Comparative effectiveness research (CER) is the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care. The purpose of CER is to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health care at both the individual and population levels.”
(Initial National Priorities for CER 2009)

Why Most Databases Were Created

- Payers track expenditures for multiple purposes
 - Managed care / Insurance companies
 - Employers
 - Governments (e.g., Provinces in Canada)
- Clinicians track patients to manage care
 - GPRD, other Electronic Medical Records

NOTE: REMEMBER that the data reflect the underlying healthcare delivery system (and its idiosyncrasies) and, in most cases, were not designed to address specific research questions

Secondary Data: Challenges

- Missing data/ confounders: smoking, OTC, ETOH
- Loss to follow-up (turnover in health care plans – an issue in the US)
- Inexact measures (measurement error, e.g., BP, or subjective measures with little standardization)
- Data quality issues (e.g., mis-coding)

An Example of a Challenge

- Consider a 30 year old woman diagnosed with asthma
- Prescribed an inhaled beta-agonist
- Claims data show she is “compliant” (defined by regular refills of Rx at the appropriate time interval)
- Yet she experiences an acute exacerbation after 8 months of use
- Does this event reflect lack of efficacy?



The News and Observer Sunday, December 8, 1991

"An inhaler prescribed by her doctor helps Gail Pouncey's smoke-scarred lungs- like many survivors, she suffered respiratory injuries in the Imperial fire."

Secondary Data: Information Asymmetry

- Many benefits (e.g., improvement in BP, Daily Activities) are not clinical diagnoses, so they are not captured (although the proportion of people who benefit will often “outweigh” the proportion harmed)
 - Limited capture of utilization-based measures (switching drugs, ER visit, hospitalization, etc.) or reduction in clinical events (e.g., MI)
- Most ‘risks’ **are** clinical and would be captured in clinical encounter
 - But we do not always know how impactful they are nor what the perception is by patients and providers

More asymmetry

- General lack of systematic ‘surveillance’ and capture of benefit (in addition to how it is/is not captured in these databases)
 - “When something bad happens to me, my condition worsens so I may go to the doctor/hospital. But if I’m taking a drug and getting better, then I’m LESS likely to go back to the doctor/hospital. So, the benefit we're trying to measure has a strong (inverse) relationship with health service utilization, and the databases only reflect secondary data based on health service utilization.” (P. Ryan, 2010)
- Need to define which benefits can be reliably measured in these data sources
 - Could an OMOP-type experiment inform CER methodological research?
 - Empirically evaluate the validity of different methods against a host of potential benefit endpoints, to determine which ones can and can't be trusted.

Where is the Innovation That Will Inform Change in Health Care?

- Can we design studies *into* the database?
 - Special data collection forms, e.g., screens that pop up for patients matching a specific set of criteria
- Can we *tailor* additional aspects of data collection (as we would in a primary data collection effort) within the context of an existing data collection system?
 - Use of large simple studies (naturalistic), with “randomization into the database”
 - Other “adaptive” designs?
 - Cluster randomization (e.g., randomize practices? communities?)
- This is being done, but not widely (?)

How Can we Encourage Innovation?

- The *same* clinical data capture can be used as data capture for randomized (or observational) studies.
- This will require:
 - Infrastructure to produce new data collection tools and integrate those into existing systems (*with minimal interference with routine practice*)
 - Training for clinicians on use
 - Training for clinicians in clinical epidemiology?
- Software to do this already exists or is in development (e.g., GPRD)

MESSAGES TO TAKE HOME

- We should expect to see variation in results from different observational studies (or from different databases within a distributed network)
- We don't want variation in results to come from sources over which we CAN have control (e.g., definitions of conditions or exposure)
- Effect sizes, when comparing benefits of active therapies, are likely to be small
 - Confounding and other biases are CRUCIAL to understand and address!
 - (If you thought studying risks was hard, just wait ...)

BACKUP SLIDES

Large Simple Randomized Study: Advantages & Disadvantages

- Biases are reduced through randomization
- Strong weight of evidence
- Active allocation-not dependent on market uptake
- Closer to actual practice (“naturalistic”) and closer to effectiveness than efficacy
- Cost more than database study
- Change in treatment practices may affect results in subjects enrolled later into the study
- Assesses treatment “strategy,” not necessarily long-term exposure

ZODIAC Design

- Unblinded Ziprasidone versus olanzipine (1:1)
- No further study interventions after randomization
 - Free to change regimens and dosing, consistent with patient's clinical response
- 1-year follow-up
- Primary endpoint: non-suicide mortality
 - Secondary included discontinuation of study medication
- February 2002 – February 2006

ZODIAC Inference

- With changes in medications after randomization, what inferential question is being addressed?
- *Initial choice* of medication?
- QUESTION: Could ZODIAC have been conducted, given the simple design, within the context of an existing database?