Overview

- Terminology
- Advantages and Disadvantages
- Applications to Decision Making
- Opportunities & Challenges
Observational Studies: Terminology

Methods for studying patient outcomes

- Cross-Sectional Studies
- Cohort Studies
- Case-Control Studies
- Registries
- Interventional at Provider Level

Timing: prospective or retrospective
Advantages

- Studies reflective of real-world practice are useful for policy purposes.
- Studies possible in areas where experimental research is limited or impractical, e.g.,
  - Intentional exposure to potential harm
  - Compliance and adherence
  - Rare events
  - Long-term banking of tissue samples, etc.
Advantages and Disadvantages

- Testing hypotheses is more difficult
- Potential for bias needs to be understood and evaluated
- Sampling issues affect analysis and interpretation
Applications

- Biological
- Social
- Risk
Biological Effects of a Drug

Linkage of national clozapine registry with national death information

- **Purpose**: evaluate risk of pulmonary embolism
- **Data**: 67,072 current and former clozapine users
- **Analysis**: mortality rates on and off drug
- **Evidence used to**
  - Document rarity of SAE
  - Support labeling change for suicide prevention
FIGURE 1. Standardized rate differences for current and recent clozapine exposure, compared with past exposure (deaths per 100,000 person-years).
Physician Clinical Performance Assessments

“Quantitative assessment of physician performance based on rates at which their patients experience certain outcomes of care and/or rates at which physicians adhere to evidence-based processes of care.”

Health intervention programs

Intervene at provider level; observe patients
Health Intervention Program

- Web-based, point of care registry reinforces evidence based guidelines for CAD
- >100,000 patients have been discharged using the program in 500 hospitals
- Evidence clearly demonstrates impact on clinician behavior. E.g., in participating hospitals
  - Usage of statins increased >80%
  - Smoking cessation counseling doubled

Get with the Guidelines

Winner of Secretary of HHS 'Innovation in Prevention Award'
Quasi –Experimental (Cluster) Studies

- Sites are randomized to an intervention (or none)
- Patients at sites are observed for outcomes of interest
Controlled distribution programs

Goal: Promote safety through efforts to assure appropriate patients receive drug

Analyses evaluate

- Effectiveness of Risk Minimization
- Safety data for varied subgroups
- 2,000 sites; 15,000 patients; 2400 pharmacies
- Control distribution of medication to patients with potentially fatal adverse event
- Educate pharmacists and clinicians on prescribing guidelines, adverse events, and patient monitoring techniques
- Patients receive medication only after lab values verified
NRMI Background

Since its inception in 1990, over 1,600 hospitals have participated with NRMI in assessing their processes and outcomes in the care of patients with acute myocardial infarction (AMI). Among the areas NRMI examines are trends in treatment, length of hospital stay, mortality, and variations among specific patient populations.

To date, NRMI has collected data on more than 2.3 million AMI patients. NRMI tracks the highest-risk acute coronary syndrome (ACS) patients, including both ST-segment-elevation myocardial infarction (STEMI) patients and non-ST-elevation myocardial infarction (NSTEMI) patients. This broad view provides a more useful, real-world picture of trends in treatment of these conditions.

NRMI data have prompted more than 190 scientific publications and have been presented at scientific sessions of the American Heart Association, the American College of Cardiology, and other scientific forums. The five NRMI observational studies (NRMI 1, 2, 3, 4 and 5) examine how AMI patients have been treated in the past, how they are currently being treated, and how they may be treated in the future.
Strengths of Observational Research

REAL-WORLD DATA: Strong external validity

- Limited inclusion/exclusion criteria, so patients are more representative of usual practice
- Observed practice not dictated by protocol
- Comparative information comes from actual practices
- Estimates of impact of treatment are more realistic
Other Benefits of Observational Research

Participation can be more attractive
- No risk of placebo treatment for patients
- Physicians practice according to their best judgment

Unique opportunities for studying
- E.g., rare events, off-label product usage
Challenges to Conduct & Interpretation

- Provider recruitment
  Remuneration for services is low or non-existent due to concerns about the potential for influencing prescribing patterns
- Usually cannot require tests not ordinarily covered by traditional health insurance
- Source verification is rare
Challenges to Conduct & Interpretation

- Unmeasured factors can induce a bias of unknown magnitude
- Proper interpretation of results depends on the ability to estimate the likely magnitude and direction of threats to internal validity*

* Validity of inferences drawn as they pertain to members of the source population
Addressing Potential for Bias

e.g., Confounding by Indication
  - Do sicker patients get different treatments?
  - Address by measurement and analysis
    - Stratification
    - Propensity scoring
Challenges for Evaluation & Use

Growing need/reliance on observational data
  Health insurers, CMS/NQA, FDA, etc.

Electronic data: easier to collect & share
  - EDC tools help reduce cost of collection
  - More data are available for secondary analyses

Few tools available to grade evidence quality
  - Difficult to distinguish high quality efforts
  - Quality “grading” should account for purpose
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