Society for Medical Decision Making

Short Course on

Propensity Methods

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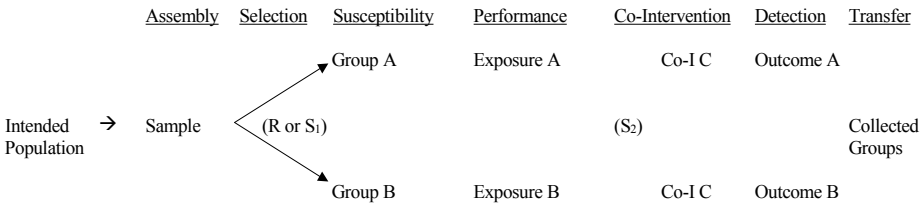
Goals:

- need for risk adjustment
- dimensions of risk
- adjusting for selection bias
- adjusting for selection bias can be helpful in risk adjustment strategies
- sensitivity analysis can help inform results from observational studies

Objectives:

- seven key aspects of research architecture
- simple (direct) adjustments for single variables
- five dimensions of risk
- contribution of selection bias to the likelihood of susceptibility bias in observational studies
- use of a propensity score in the evaluation of an exposure in an observational study
- use of sensitivity analysis in an observational study

Seven Key Aspects of Research Architecture*



*Adapted from Feinstein

Goal: Comparability of the groups who did and did not receive the exposure of interest (except for the actual receipt of the exposure)

- **Bias**
  - **Overt** – perform adjustment techniques using **measured covariates**
  - **Hidden** – assess the potential for affecting results with sensitivity analysis
    - Create a false exposure effect (FP)
    - Masking a true exposure effect (FN)
    - Right direction – misestimation of effect

Feinstein's intellectual model
for the evaluation of the scientific quality of
cause-effect research

Distorted assembly

- defines the subjects who will subsequently be compared
- the **sample** assembled should **reflect the population** to which results will be generalized
- if this is not true then distorted assembly has occurred
- subjects considered eligible for the study and
- application of specific inclusion/exclusion criteria will determine the pool of baseline characteristics of the sample

Selection bias

- process determining **who receives** the **exposure** being compared
  - can occur when subjects are selected to receive a given exposure (or co-intervention)
  - exposure is based on their baseline characteristics (covariates) and
  - covariates are related to different likelihoods of outcome
- **unmeasured covariates** may or may not be associated with the measured baseline characteristics
- contrasted with patients who receive a given exposure by a **random process**
  - expectation that exposed and unexposed groups will have approximately equal distributions of covariates (measured and unmeasured)

Susceptibility bias

- comparibility of baseline characteristics of Group A and Group B
- occurs when persons receiving the exposures being compared have importantly different expectations, at baseline, of the outcome of interest
- differences in expectations of outcomes are a function of importantly different baseline characteristics

Performance bias

- comparison of Exposure A with Exposure B
- occurs if the exposures being compared are not applied with the same proficiency
- relates to differences in dosage schedules, compliance rates, etc.

Co-Interventions

- additional medical interventions (beyond the exposure of interest) that may influence the likelihood of achieving the outcome of interest

Outcome bias

- comparison of Outcomes in A with Outcomes in B
- occurs if the process for determining the status of the outcome of interest in each Group is applied unequally
- arises from differential surveillance, diagnostic testing, or diagnostic interpretation

Transfer bias

- comparison of members of 'original' cohorts of subjects in Groups A and B
- occurs when members of the complete cohorts of Groups A and B are lost
  - dropouts
  - intra-study exclusions
  - crossovers
  - during statistical manipulations
    (e.g., because of missing values of measured covariates in some types of regression)

II. Simple adjustment/standardization

Adjustments of raw rates

- made with the intention of removing or reducing the effects of unfair comparisons
- 'leveling the playing field', by accounting for factors that patients bring to an encounter
- essential for drawing meaningful inferences about observed healthcare related outcomes
  - effectiveness of treatment,
  - performance of providers,
  - quality of care, etc.

Headline in today's **COMPETING HOSPITAL NEWS**:

"Local Teaching Hospital losing colon cancer treatment race to Community General"....

Data from the hospital association, 2000

- 63% of Community General's patients achieved remissions after colon cancer treatment.
- 44% remission rate at Local Teaching Hospital for treatments of colon cancer

The reporter from COMPETING HOSPITAL NEWS calls you (the well known health outcomes / statistics expert) for your opinion about why Local Teaching Hospital may be doing so poorly. She says she has more data from the hospital association.

What do you want to know?

Table 1

Proportion of Cases by Stage of Cancer

Cancer Stage	Community General	Local Teaching Hospital	Total
I	98 (49%)	49 (10%)	147 (21%)
II	48 (24%)	151 (30%)	199 (28%)
III	52 (26%)	302 (60%)	354 (51%)
Total	198 (100%)	502 (100%)	700 (100%)

Table 2

Remission Rates by Cancer Stage

Cancer Stage	Community General		Local Teaching Hospital		Total	
I	80/98	(82%)	40/49	(82%)	120/147	(82%)
II	28/48	(58%)	88/151	(58%)	116/199	(58%)
III	16/52	(31%)	94/302	(31%)	110/354	(31%)
Total	124/198	(63%)	222/502	(44%)	346/700	(49%)

III. Dimensions of Risk

- First step, delineate the **goals of risk adjustment**
- Risk
  - For whom
  - Over what time period
  - For what outcome

Types of variables to consider

- Age
- Gender
- Race/ethnicity
- Socioeconomic status
- Culture
- Genetic characteristics

Types of variables to consider (cont'd)

- Acute clinical stability
- Principal diagnosis (case mix)
- Severity and chronicity of principal diagnosis
  - Clinical features: symptoms/signs
  - Pathological features: extent and location
- Extent, severity and type of comorbid disease

Types of variables to consider (cont'd)

- Function
  - Physical
  - Cognitive
  - Psychological
  - Psychosocial
- Health status
- Quality of life
- Attitudes and preferences

Propensity Score: P (exposure given baseline characteristics)

Definition: the conditional probability of receiving a particular exposure given a vector of measured covariates

- Represents the likelihood that a person with a given set of baseline characteristics (covariates) will receive the exposure of interest
- Reduces an entire set of baseline characteristics to a single composite characteristic adequately summarizes the collection of characteristics

Propensity Score

- Allows a straightforward evaluation of the degree of overlap of baseline characteristics between exposed and unexposed groups

  ---Is this degree of overlap sufficient for sensible comparisons between effects related to exposure and non-exposure?

- Can be used to produce strata (subclassification or stratification) with the same likelihood of exposure among those who actually did and did not receive the exposure of interest

  --- Subclassification does not depend on any particular functional form (such as linearity), whereas models do
  --- Generally 5 or more strata are sufficient to remove >= 90% of bias

Propensity Score

- Can be used for matching patients
- Can be used in a mutivariable adjustment model
- Multivariable logistic regression is often used (although other statistical models can be used)

Propensity Score

- Propensity score methods work better in larger samples (expected balance of covariates)
- Can develop and use more than one propensity score (e.g., one for primary treatment and one for a major co-intervention)
- **Outcome = propensity + susceptibility + exposure + noise**

Sensitivity Analysis for an Unmeasured Covariate

- Propensity scores can only adjust known (measured) covariates
- Apriori – include measures of all known important predictors of selection for exposure (covariates)
- Estimates are made of the effects that unmeasured covariates (with varying levels of association with selection and outcome) would have on study results
- Allows one to assess the likely stability of observational study results

10 Commandments of Propensity Model Development

THOU SHALT:

1. Be sure the number of predictors exceeds 10 times the number of outcomes modeled
2. Examine "predictor" variable for collinearity
3. Protect against over-modeling
4. Build a parsimonious model

THOU SHALT:

5. Perform regression diagnostics on residuals
6. Perform bootstrap analyses to assess shrinkage
7. Examine and compare Beta weights
8. Hold out a sub-sample for cross validation
9. Perform external validation on an un-modeled (new) sample

THOU SHALT:

10. IGNORE 1 THROUGH 9

Make sure the model adequately balances the covariates

Use of propensity scores in the investigation of medical problems – some examples

CWRU/MHMC

1. Effectiveness of right heart catheterization

- Connors AF, et al. The effectiveness of right heart catheterization in the initial care of critically ill patients. JAMA 1996;276;889-897.
- Connors AF, et al. The effectiveness of pulmonary artery catheterization in the initial care of non-operative critically ill patients: analysis of consecutive admissions to 147 intensive care units. (submitted)

2. Accuracy of physicians' prognostic estimates

- Dawson NV, et al. Survival estimates and accuracy of prognostic predictions for cancer patients vary by physician specialty. J Gen Intern Med 1998;13(Supplement): 18.

CWRU/MHMC (cont'd)

3. Outcomes of stroke and pneumonia

- Katzan IL, et al. Community-wide incidence and outcomes of pneumonia in patients hospitalized for acute stroke. J Gen Intern Med 2001;16(Supplement):190.
- Cebul, RD, et al. Increasing mortality for stroke patients hospitalized during an era of competing demands: implications for quality measurement. Ann Neurol 2001; (abst, in press)

4. Outcomes of rehabilitation services

- Murray PK, et al. Outcomes of rehabilitation services in nursing home residents. (submitted)

Other investigators

1. Medical vs. surgery for triple-vessel disease

- Myers WO, et al. Medical versus early surgical therapy in patients with triple-vessel disease and mild angina pectoris: a CASS registry study of survival. Ann Thorac Surg 1987;44:471-86.

2. Outcomes among patients with myocardial infarction

- Fiebach NH, et al. Outcomes in patients with myocardial infarction who are initially admitted to stepdown units: data from the Mutlicenter Chest Pain Study. Am J Med 1990;89:15-20.

3. Hospital mortality for Medicare patients

- Aiken LH, et al. Lower Medicare mortality among a set of hospitals known for good nursing care. Med Care 1994;32:771-87.

Other investigators (cont'd)

4. Hospitalized and ambulatory patients with community-acquired pneumonia

   - Stone RA, et al. Propensity score adjustment for pretreatment differences between hospitalized and ambulatory patients with community-acquired pneumonia. Med Care 1995;33:AS56-AS66.

5. Effectiveness of chemotherapy for advanced lung cancer

   - Earle CC, et al. Effectiveness of chemotherapy for advanced lung cancer in the elderly: instrumental and propensity analysis. J Clin Oncol 2001;19:1064-70.

6. Aspirin use for coronary artery disease and all-cause mortality

   - Gum PA, et al. Aspirin use and all-cause mortality among patients being evaluated for known or suspected coronary artery disease: a propensity analysis. JAMA 2001;286;1187-94.