



Dissecting a cohort study

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Part 1



Exercise #1

Graham *et al.* (2015) Circulation

“Cardiovascular, bleeding and mortality risks in elderly Medicare patients treated with dabigatran or warfarin for nonvalvular atrial fibrillation”

- Team up into groups of 4
- Identify
 - Target
 - Comparator
 - Outcome
 - Time at risk
 - Model



T and C cohorts

- Elderly (≥ 65) Medicare beneficiaries (A, B and D) with nonvalvular atrial fibrillation who initiated therapy with dabigatran (T) or warfarin (C)

Is this correct?



Inclusion criteria

All patients who:

- Have any inpatient or outpatient AF or atrial flutter ICD9 codes
- Filled at least 1 prescription for either drug between Oct 19, 2010 - Dec 31, 2012

Index date: first prescription date



Exclusion criteria

All patients who:

- Have < 6 months of Medicare enrollment before index date
- Were < 65
- Received prior treatment (when?) with NOAC or warfarin
- Were in a skilled nursing facility on index date (why?)
- Were in hospice on index date (why?)
- Had a hospitalization “that extended beyond the index dispensing date”
- Undergoing dialysis (when?)
- Were kidney transplant recipients
- Had diagnoses of valvular disease, DVT, PE, joint replacement during baseline 6 months



Outcomes

- Stroke
- Major gastrointestinal and intracranial bleeding
- Acute myocardial infarction
- Mortality



Time at risk

- Follow-up starts on index date + 1 and censored at:
 - Medicare disenrollment
 - > 3 day gap in anticoagulant supply
RX fill for a different anticoagulant
 - Start of hospice
 - Initiation of dialysis or kidney transplant
 - Admission to nursing facility
 - End of study



Part 2



Exercise #2

Go back to Graham's paper

Discuss:

- What threats are there to the validity of the study results?
- How do Graham *et al.* address these threads?



Confounding

- Using propensity score model: Logistic regression with “initiated dabigatran” as outcome and predictors:
 - Sociodemographics
 - Prescriber characteristics
 - Baseline comorbidities
 - “Other potentially relevant variables”
- 1:1 ratio, greedy matching
- Balance assessment via:
 - Standardized mean difference (target: ≤ 0.1)



Measurement error

- Sensitivity and specificity of the outcome measures?

Study Outcomes

The primary outcomes were ischemic stroke, major bleeding with specific focus on intracranial and gastrointestinal bleeding, and AMI. Secondary outcomes were all hospitalized bleeding events and mortality. The *International Classification of Diseases, Ninth Revision, Clinical Modification* codes used to define these outcomes are listed in Table II in the online-only Data Supplement. The codes defining ischemic stroke have a **positive predictive value (PPV) of 88% to 95%.**¹⁸⁻²⁰ Major bleeding was defined as



Overall systematic error

- Negative controls could show amount of residual bias

