Causal Inference Case Studies

(adopted from Irene Chen, MIT)
Case studies

1. Post surgical opioid abuse
2. Diabetes treatment management
Drug overdose deaths in America

*Some deaths on this chart may overlap if they involve multiple drugs.
Share of organ donors who died of drug overdoses

Source: Organ Procurement and Transplantation Network
Research

Postsurgical prescriptions for opioid naive patients and association with overdose and misuse: retrospective cohort study

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Do postsurgical opioids cause opioid abuse?

- T: dosage, refills
- Y: opioid abuse
- X: other diagnoses

Diagram:
- T → X → Y
- Y → X → T
- X → T → Y

Questions:
- How do postsurgical opioids lead to opioid abuse?
- What role does dosage and refills play in this process?
Aetna Insurance claims

Pros

• Complete patient record
• Hospital and pharmacy care
• Surgical claims from CPT, outcomes from ICD-9 codes

Cons

• Lacking granular information about hospital stays (e.g. lab values)
• CPT and ICD-9 codes can be incorrect or manipulated for billing purposes
Data source

Include

• Patients with “complete” medical and pharmacy insurance records
• Underwent first surgery
• Opioid naïve: little/no previous opioid use

Final cohort

• Large dataset (37 million)
• Longitudinal (2008-2016)
• After inclusion criteria, 1 million opioid naïve patients undergoing surgery
Do postsurgical opioids cause opioid abuse?

Dosage, refills

Other diagnoses

Opoid abuse
How do we define T, Y, and X?

What is treatment T?
• Refill
• Total dosage
• Duration of use

What is outcome Y?
• ICD-9 code for opioid dependence, abuse, and overdose
• Only include diagnosis codes related to prescription opioids

What are confounders X?
• Demographics (age, sex)
• US state of residence
• surgery type group
• surgery year
• presurgical diagnoses
Statistical analysis

• Weighted linear regression for log transformed weekly rates of misuse
  • Each week weighted according to sample size
  • Create outcome of adjusted analysis of time until misuse event using Cox proportional hazards (survival analysis!)
  • Results report multiplicative percentage increases in rate

• Sensitivity analysis to rule out structural confounders
  • Interaction term between duration and year indicator
  • Interaction between duration and state of residence indicator
  • Build in an unobserved confounder with a Bernoulli random variable
Recap: Postsurgical opioid use to misuse

• “Duration more than dosage use may cause opioid misuse”
• Use covariate adjustment to estimate multiplicative effects
• Interaction terms
Case studies

1. Post surgical opioid abuse
2. Diabetes treatment management
Personalized Diabetes Management Using Electronic Medical Records

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Abstract

OBJECTIVE Current clinical guidelines for managing type 2 diabetes do not differentiate based on patient-specific factors. We present a data-driven algorithm for personalized diabetes management that improves health outcomes relative to the standard of care.
Type 2 Diabetes Treatment Still a Mystery
What do we include in this analysis?

Inclusion criteria
• Patients in hospital EMR for >1 year
• Prescription for at least one blood glucose regulation agent
• At least three recorded laboratory results for HbA1C
• No recorded diagnosis of type 1 diabetes (from ICD-9 code 250.x1 or 250.x3)

Final cohort
• 10k patients, 48k patient visits
• Access to demographic information
• Analyze all associated EMR data
What makes two patients similar or different?

Features

- Differentiate 13 lines of therapy
- Patient visit every 100 day and average HbA1C after visit (75-200 days after)
- Collect what standard of care was actually administered

[Slide 17 of lecture 15]
Which treatment will lead to lower HbA1C?

Which treatment will lead to lower HbA1C?

- **T** (line of therapy)
- **X** (demographics)
- **Y** (Subsequent HbA1C)
Model

- For each patient visit, find kNN regression to predict HbA1C under every possible treatment
- Algorithm prescribes regimen with best predicted outcome if predictive improvement exceeds threshold
- Evaluation compared actual treatment and outcome with recommended therapy and outcome
- Sensitivity analysis by drawing new training and testing splits
[Figure 1 of Bertsimas et al, 2017]
**A** Recommendation: Switch from insulin monotherapy to metformin monotherapy

**B** Outcomes for similar patients who were prescribed...

**C** Predicted HbA1c (%): 8.3

- PATIENT ID: 12XXXXX
- AGE (Years): 61.9
- SEX: F
- RACE/ETHNICITY: Black
- CURRENT HbA1c (%): 10.1
- CURRENT REGIMEN: Insulin

**D** Patient Treatment & HbA1c History

[Figure 2 of Bertsimas et al, 2017]
Recap: Diabetes treatment management

• “kNN over patients can recommend diabetes treatments”
• Use matching to estimate different treatment effects
• Evaluate by comparing predicted and actual treatment and HbA1C values
• Sensitivity analysis through repeated sampling of training and test data