Open House, 2014

CAUSAL INference WORKING GROUP
Department of Biostatistics
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Estimating population treatment effects

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Big picture: Two main research areas

Both relate to estimating population treatment effects

Broad interests in making better use of large administrative datasets to estimate causal effects (including in randomized and non-randomized designs)
Propensity score methods for non-experimental studies

- **Methods question:**
  - What are the best approaches to use when you can’t randomize and just have a treatment and comparison group to compare?
  - How do we know when the methods “worked”?

- **Substantive questions:**
  - Is a suicide prevention program in Denmark effective?
  - Does adolescent marijuana use lead to lower employment in adulthood?
  - Does breastfeeding promote weight loss after childbirth?
  - Does a suicide prevention program in Denmark prevent future suicides?
  - Did Connecticut’s gun control law reduce homicides?
Generalizing randomized trial results to target populations

- **Methods questions:**
  - Can we assess and enhance the ability of randomized trials to predict what would happen in some target population?

- **Substantive questions:**
  - Should the state of Maryland implement PBIS?
  - How many lives would be saved if HAART was given to all newly infected people with HIV?
Other students and post-docs working with me

- Hwanhee Hong (Post-doc)
  - Network meta-analysis, Bayesian methods for covariate measurement error
- Trang Nguyen (Post-doc)
  - Mediation with multiple ordinal mediators
- Yenny Webb-Vargas (PhD student)
- David Lenis (PhD student)
  - Propensity scores in case control studies, Implications of and solutions for covariate measurement error in non-experimental studies
- Vivek Khatri (MHS student)
  - Missing data and propensity score methods, Consequences of measurement error on multiple covariates
- Kate Freeland (ScM student)
  - Performance of an alternative to propensity score matching
- Cyrus Ebnesajjad: Helps with everything!
• Typically, we statisticians rely on the assumption that observations are i.i.d.

• This is often false, especially when observations come from people who interact with one another.
I’m working on methods for causal and statistical inference using data sampled from members of social network.
research questions

Methodological questions:

- When and how can we identify causal effects when subjects interact with one another in complicated ways?
- How can we design randomized trials for networks? (With Michael Rosenblum and Matt Satriano)
- How can we perform valid statistical inference when network structure makes observations dependent?

Substantive questions:

- Do the effects of a microenterprise intervention in rural Uganda spill over to affect friends and relatives of the subjects assigned to the intervention?
- What is the effect of consolidation of care on the incidence of HIV in at-risk populations in India?
other projects

- Assessing the effects of environmental exposures on health outcomes using Geisinger medical records.
- Using electronic medical records, combined with external information, to predict individual treatment responses and improve individualized treatment decisions. (With Scott Zeger, Jon Ellen, and a future postdoc)
Research Areas

- Sensitivity Analysis (Aidan McDermott, Chenguang Wang, Ivan Diaz)
- Outcome-dependent two-phase sampling (Yi Lu)
- Inferences with Multiple Data Sources (Parichoy Pal Choudhury, Ivan Diaz, Kevin Psoter)
- Inference in the Presence of Death (Chenguang Wang, Elizabeth Colantouni)
Background knowledge

- Estimators can be constructed from efficient influence function (EIF)
- Such estimators usually have desired properties: consistent, locally efficient, etc.
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- Estimators can be constructed from efficient influence function (EIF)
- Such estimators usually have desired properties: consistent, locally efficient, etc.

What is the question?

- How to get these “good” estimators automatically?

Why it matters?

- Theoretical derivation of EIF is difficult
- FINITE life vs INFINITELY many underived EIFs?
- A unified algorithm for a large class of questions.
What did we do?

- Use property of EIF (related to estimating equation), to convert it into a zero-finding problem
- An algorithm to get the estimator, without the knowledge of EIF
- Implement the algorithm in R
  - Mean treatment effect
  - Median treatment effect
  - General purpose code
Computerizable estimator
Constantine, Tianchen, Zhenke and Iván

▶ What did we do?
  ▶ Use property of EIF (related to estimating equation), to convert it into a zero-finding problem
  ▶ An algorithm to get the estimator, without the knowledge of EIF
  ▶ Implement the algorithm in R
    ▶ Mean treatment effect
    ▶ Median treatment effect
    ▶ General purpose code

▶ What did I learn?
  ▶ Influence function, functional derivative
  ▶ Robust estimation
Example: Guided Care study

Background: specially trained nurses to help deliver patient-centered care

Study website: http://www.guidedcare.org/


Online course and certificate for specially trained nurses
Matched-pair cluster randomized (MPCR) design

One pair

Assign one to intervention and the other to control

Scenario 1

Scenario 2

Assigned control
Assigned intervention
MPCR design

Goal

Observed

If all are assigned control

if all are assigned intervention

Zhenke Wu (zhwu@jhu.edu)
Michael Rosenblum
Research
Research focus: Improved design and analysis of randomized trials
PCORI and FDA grants to:
1. Develop new adaptive designs
2. Demonstrate in stroke, Alzheimer’s disease, HIV prevention, and cardiac resynchronization devices;
3. Build open-source software tool enabling investigators to tailor new adaptive enrichment designs to their specific research goals and constraints.
Research

Problems involve: semiparametric methods, realistic simulation, intensive computation/optimization, software development.

Ivan Diaz, Elizabeth Colantuoni: Leveraging prognostic baseline variables to improve power

Emily Huang: Estimating proportion who benefit

Tianchen Qian: Increasing power in adaptive designs with delayed outcomes

Yu Du: Bounds on bias in standard and adaptive designs

Claire Ruberman: Minimum dose required to provide high level of HIV protection from PrEP
Adaptive Clinical Trial Designs

FDA is Interested:

“A large effort has been under way at FDA during the past several years to encourage the development and use of new trial designs, including enrichment designs.”
Adaptive Clinical Trial Designs

• Pharmaceutical Companies are Interested:

“An adaptive clinical trial conducted by Merck saved the company $70.8 million compared with what a hypothetical traditionally designed study would have cost, according to a company...”
Trial Design with Improved Precision - Tianchen
Joint work with Michael and Huitong

► What is the question?
  ▶ Improve precision in group sequential tests

► Why it matters?
  ▶ Clinical trials are EXPENSIVE!
  ▶ Improved precision ⇒ Larger power ⇒ Save sample size ⇒ $$$
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▶ What is our result?
  ▶ Make use of information that people usually don’t use in randomized trial: baseline variables, short-term outcomes
  ▶ Make use of data structure
  ▶ Save sample size by over 30%! That’s millions of $!
Trial Design with Improved Precision - Tianchen
Joint work with Michael and Huitong

- What did I do?
  - Coding, coding, coding...
    Simulation based on real data to show improved precision
  - Oops! Theory!
    How much precision gain can we get?
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▶ What did I do?
▶ Coding, coding, coding...
  Simulation based on real data to show improved precision
▶ Oops! Theory!
  How much precision gain can we get?

▶ What did I learn?
▶ Knowledge and experience: group sequential tests
▶ Parallel computing and job control on cluster
▶ TMLE, a powerful tool that is recently developed
Low heat

High heat
Low heat
High heat
REGION A

V.S.
What part of the heat shock effect is being mediated by brain region A?

What assumptions are needed to claim it as a causal effect?