APPLICATION OF INSTRUMENTAL VARIABLE METHODS IN HEALTH SERVICES RESEARCH

CHPS METHODS WORKSHOP
June 2, 2011
Organizers: Sue M. Marcus and Naihua Duan, Columbia University

INTRODUCTION
An instrumental variable (IV) manipulates treatment and affects an outcome only through its manipulation of the treatment (Imbens and Rosenbaum 2002). For example, within a randomized treatment trial, randomization to a drug treatment may impact the outcome only to the extent that the subject actually takes the drug (Rosenbaum 2010; Marcus and Gibbons 2002). IVs are useful for estimating treatment effects in observational studies when there is unobserved confounding, and also for examining causal mechanisms in randomized trials. Although IV methods have become increasingly popular during the last decade, the application and interpretation of instrumental variable estimates in health services research have been limited by overly restrictive assumptions that may not seem plausible in practice, weak instruments, and lack of IV methodology for longitudinal studies.

This workshop examines new approaches to applying and interpreting the results of IV methodology that provide practical strategies for addressing these limitations, including assessing sensitivity to violations of assumptions, strengthening weak instruments through various matching approaches, approaches for relaxing the assumption of homogeneous unit effects, and the application of IV methods for longitudinal data.

WORKSHOP SCHEDULE
9:15am-10am: Breakfast
10am-10:15am: Welcome: Carol Caton, Naihua Duan, Sue Marcus

10:15am-10:45am:
1. Sensitivity of instrumental variable estimates to violations of assumptions
Mary Beth Landrum*
Alisa Busch
Haiden Huskamp
James O'Malley
Harvard University, Department of Health Care Policy
** Presenting author at workshop*
Instrumental variable estimates are reliant on a set of assumptions that often cannot be tested empirically. Sensitivity analyses attempt to examine the robustness of estimates to plausible violations of these key assumptions. A variety of different methods to assess the robustness of estimates have been proposed and applied in the context of propensity score analyses. Recent work has also proposed the use of sensitivity analyses in IV analyses. These approaches include simple calculations of how estimates change under certain violations of assumptions and Bayesian approaches that make parameters governing key assumptions part of the model, thereby allowing uncertainty about violations of assumptions to be incorporated in statistical inferences. In this paper we compare the performance of various approaches in the context of an analysis of the comparative effectiveness of reformulated atypical anti-psychotics compare to their original formulations. We examine a variety of potential instruments including promotional spending on a reformulated therapy (relative to its original formulation) and characteristics of the treating physician, including specialty and prescribing preference (measured as the fraction of each physician's patients who use reformulated therapy vs. original formulation).

10:50am-11:20am:

2. Evaluating long term effects of a psychiatric treatment using instrumental variable and matching approaches

Bo Lu*
Ohio State University
Department of Biostatistics
blu@cph.osu.edu

Chih-Lin Li
Ohio State University
Department of Biostatistics

Sue M. Marcus
New York State Psychiatric Institute
Division of Biostatistics

**Presenting author at workshop*

Evaluating treatment effects in longitudinal studies is challenging due to the potential time-varying confounding and the potential unmeasured confounding. Propensity score based approaches, such as matching or weighting, are commonly used to handle observed confounding variables. The instrumental variable method is known to guard against unmeasured confounding in cross-sectional studies. We propose to combine both methods to estimate the long term treatment effect in a longitudinal psychiatric study. The NIMH collaborative multi-site treatment study of children with attention-deficit/hyperactivity disorder (ADHD) compared different treatment strategies for 579 children diagnosed with ADHD. The first 14 months was a randomized study and the participants were allowed to choose their desired treatment strategies afterwards. Follow-up measurements are taken at 24 and 36 months. The original randomization is a natural candidate as an instrumental variable, but its validity may weaken as the time progresses. Previous non-random treatment selection is considered to be highly associated with future treatment selection decision. Propensity score matching is used to create treatment groups with comparable covariate history, hence to construct a stronger instrument under certain assumptions.

11:20am-11:35am: Break

11:35am-12:05pm:

3. Application of instrumental variables methods to longitudinal analyses

James O'Malley
Harvard University
Department of Health Care Policy
omalley@hcp.med.harvard.edu

Instrumental variables (IVs) and longitudinal data are two mechanisms under which causally defendable results can be obtained from observational studies. It stands to reason that the application of IVs in a longitudinal context is preferable to a cross-section IV analysis and a pure longitudinal analysis. In this talk, two examples where IVs were used in a longitudinal analysis are reviewed. In the first example, comparison of the net cost of atypical and conventional antipsychotics, the instrument is a time varying variable (an external shock) defined on the unit of analysis. I show that the IV assumptions for cross-sectional data extend naturally to this type of longitudinal analysis. The second example involves peer effects; specifically, whether an individual's own health traits (e.g. BMI or obesity) are influenced by the health traits of other individuals (e.g. BMI). Because the "outcome" and "treatment" are from different individuals, the assumptions required of an IV for the estimation of peer effects have to be carefully scrutinized. For certain types of IVs, I argue that longitudinal data is a requisite for the IV assumptions to hold. In both examples, the candidacy of the prospective instrumental variables is evaluated and the substantive results of the IV analysis are discussed.

12:05pm-1:05pm: Lunch

1:05pm-1:35pm:

4. Designing observational studies with stronger instruments

Mike Baiocchi*
Department of Statistics
The Wharton School of the University of Pennsylvania
mbaiocch@wharton.upenn.edu

Dylan Small
Department of Statistics
The Wharton School of the University of Pennsylvania

Peter Groeneveld
University of Pennsylvania School of Medicine

**Presenting author at workshop*

A common barrier to using instrumental variable (IV) techniques is having a "weak instrument." An analysis based on weak instruments suffers from several problems: large standard errors, or (if care is not taken) inappropriately small standard errors, as well as severe sensitivity to small violations of the assumptions of IV. It is a common belief that the strength of an instrument is fixed. This is false. In this talk we present a new matching-based IV technique, "near-far matching," which can be used to design studies which have stronger instruments. We will examine this method through a case study of carotid arterial stenting. We use Medicare data to estimate a complier average causal effect of drug alluding stents. The instrument we use is regional variation in utilization of drug alluding stents, at the health referral region (HRR) – as defined by the Dartmouth Atlas of Health Care. This instrument has been proposed in the literature but is commonly discarded because it appears to be a "weak instrument."

1:40pm-2:10pm:

5. Relaxing the instrumental variable assumption of homogeneous unit effects for identifying intervention components with improved outcomes in RCT

Sue M. Marcus*
New York State Psychiatric Institute
Division of Biostatistics
smarcus@pi.cpmc.columbia.edu
** Presenting author at workshop*

Pei Wang
Columbia University
Department of Biostatistics

Robert Rosenheck
Yale University

Often in practice, the IV assumption of homogeneous unit effects seems overly harsh and implausible. This paper will consider two instrumental variable approaches for relaxing the IV assumption of homogeneous unit effects, that given by Sobel (2008) and a non-parametric approach given by Rosenbaum (2010). These methods will be applied to data from a randomized trial (the HUD-VASH study) for homeless veterans with psychiatric and/or substance abuse disorders to identify whether and for whom utilizing an intervention component, special access to housing vouchers, is associated with improved homelessness outcomes. There are several critical barriers that impede valid causal inference for evaluating an intervention component such as voucher use. People with serious behavioral disorders may not be able to take advantage of priority access to housing vouchers even when it is offered. For example, almost one fourth of the veterans randomized to the case management plus voucher access condition did not actually utilize their vouchers, while 5.6% of those randomized to the case management-only group utilized vouchers. Using randomization as the instrument, we use an instrumental variable approach to estimate the effect of actually utilizing the voucher (e.g. Marcus and Gibbons 2002).

2:10pm-2:25pm: Break

2:25pm-2:55pm:

6. Does an oncologist's relationship to the for-profit pharmaceutical industry affect the treatment of elderly patients with cancer?

Rena Conti
University of Chicago
Department of Pediatrics
rconti@uchicago.edu

Objective: To determine the effect of treatment by oncologists with ties to the pharmaceutical industry relative to oncologists without industry ties on mortality of elderly patients with colorectal cancers, accounting for measured confounding using risk adjustment techniques and residual unmeasured confounding with instrumental variables methods.

Data Sources: Longitudinal administrative hospital records, stage of diagnosis, and death records were obtained for 200,000 patients aged >-65 admitted to non-federal acute care hospitals with a primary diagnosis of colorectal cancer from January 2008-January 2009 using Medicare-SEER data. Our principal measure of the existence of an oncologist's relationship to the for-profit pharmaceutical industry was whether the patient's primary oncologist was listed as a member of one of 9 companies' speaker's bureaus between 2008-2009 in a national report published by Propublica in 2010. We use supplemental data from IMS Health's IPS dataset to explore whether our analysis would differ substantially using alternative definitions of the existence and strength of physician-industry ties.

Study Design: This retrospective cohort study compares results using least squares multivariate regression with results from IV methods that account for additional unmeasured patient characteristics. Primary outcomes are 30-day and one year mortality,

secondary outcomes included treatment with medications manufactured by firms that provide MDs sponsorship.
Data collection/extraction methods: SEER-Medicare records are used to identify newly diagnosed colorectal, non small cell lung and pancreatic cancer patients. These records undergo comprehensive abstraction, including dates of (first) cancer diagnosis, primary treating oncologist, demographic characteristics, co-morbid conditions, stage of cancer diagnosis, severity of clinical presentation, diagnostic test results, and treatments after initial diagnosis and date and primary cause of death (if applicable). Treating oncologist's Medicare Provider ID found in Medicare-Seer data will be linked to the Propublica listing of pharmaceutical companies' speakers bureaus in 2008-2009 using the AMA master file. Area Resource Files are used to obtain MSA level rates of cancer incidence, prevalence and mortality, counts of oncologists practicing in the area and the availability of specialty hospital care.

3:00pm-3:45pm: Discussion

3:45pm-4:00pm: Wrap-up