### **Examples of Instrumental Variable Analyses**

Maria Glymour Department of Society, Human Development and Health Harvard School of Public Health

mglymour@hsph.harvard.edu

SPER Conference June 25, 2012

## Outline

- Finding an instrumental variable
- IVs in randomized trials: Moving To Opportunity
- Answering a parallel question with a natural experiment (lottery)
- IVs from natural experiments: compulsory schooling law changes
- IVs from genes: FTO as an IV for maternal obesity
- Goals:
  - 1. Recognize contexts in which IV analyses might be feasible and useful
  - 2. Recognize the limitations and assumptions of the IV analysis

## How do you find an Instrumental Variable?

- 1. Randomize
- 2. Some other possible sources of exogenous variation:
  - a. Geography of city
  - b. Policy variations
  - c. Institutional features (banking policies, loan guarantees)
  - d. Timing of newly available resources
  - e. Wait lists or lotteries for subsidies
  - f. Genetic polymorphisms

Randomizing is generally preferable, because the IV assumptions are more plausible and the 1<sup>st</sup> stage effects are often larger.

## Example 1, Moving To Opportunity Trial

- Families with children in urban public housing developments invited and randomized to:
  - Control
  - section 8, or
  - "low poverty" section 8 (must move to neighborhood with <10% poverty)
- Once randomized:
  - 60% of section 8 group moved
  - 47% of low poverty group moved.
- This may sound bad, but compare to a drug-based trials:
  - Women's Health Initiative: "At the time the trial was stopped, 54.0% of study participants assigned to receive CEE and 53.5% of those assigned to receive placebo had discontinued use of their study medication." –Hsia 2006
  - TODAY: "Adherence to the medication regimen before the primary outcome was reached or the study was completed ranged from 84% at month 8 to 57% at month 60" -TODAY study group, NEJM 2012

## Example 1, Moving To Opportunity

Multiple causal questions one might try to address with data from the Moving To Opportunity (MTO) trial:

- Does moving from very high poverty public housing developments benefit the health of mothers or their children?
- 2. Does living in a low poverty neighborhood benefit the health of mothers or their children?



## Example 1, Moving To Opportunity

Multiple causal questions one might try to address with data from the Moving To Opportunity (MTO) trial:

- Does moving from very high poverty public housing developments benefit the health of mothers or their children?
- 2. Does living in a low poverty neighborhood benefit the health of mothers or their children?



## Design

- Families with children in urban public housing developments invited and randomized to:
  - Control
  - section 8, or
  - "low poverty" section 8
- Once randomized:
  - 60% of section 8 group moved
  - 47% of low poverty group moved.

This is the "first stage" estimate if you think of moving from the development as the endogenous variable.

# Did the trial affect neighborhood environment?

Poverty Rate	Control	ITT (Low Poverty)	
	Mean	Difference	P-value
Baseline	53.1%	-0.4	0.41
At 1 Year	50.0%	-17.1	<.001
At 5 Years	39.9%	-9.9	<.001
At 10 Years	33.0%	-4.9	<.0001

This is the "first stage" estimate if you think of neighborhood poverty as the endogenous variable.

From ludwig 2011

## IV analyses in MTO

- Standard 2-stage least squares
- In most IV analyses, we think the "treated" group includes some "always treated" people and some "compliers".
- The IV estimate refers to effect in the "complier" subgroup who received treatment because of the value of the IV.
- However, primary analyses of MTO define the endogenous variable as moving from the development *with the voucher given by the trial*.
- In this definition of the treatment, it is impossible to be treated if you are not randomized to receive a voucher.
- Therefore, everyone who is "treated" is a "complier" and the
  IV effect estimate = effect of treatment on the treated (TOT)



Response if assigned to receive a voucher:

Don't Move

Response if assigned to not receive a voucher:

Don't Move	Never- Takers	Compliers
Move	Contrarians/ Defiers	Always Takers

Move



Response if assigned to receive a voucher:

Don't Move

Response if assigned to not receive a voucher:

•		
	Never- Takers	Compliers
MUVC	Contrarians/ Defiers	Always Takers

Move

### Early Results for Behavioral Problems, Boston 2 Year Low Poverty Group vs Controls

	Control Mean	ITT Difference (SE)	TOT/IV Difference (SE)
Boys	.326	090	184
		(.041)	(.088)
Girls	.193	023	046
		(.030)	(.056)

From Katz QJE 2001

## Mid-Term (5-7 year) Results for Children's Mental Health (K6)

	Control Mean	ITT Difference (SE)	TOT/IV Difference (SE)
Boys	162	.069	.167
		(.091)	(.223)
Girls	.268	246	508
		(.091)	(.060)

## **Trial challenges**

- Mixed effects, attributable to
  - Small samples?
  - Heterogeneous effects?
- Uncertainty about the salient component of the treatment
  - Social disruption associated with moving?
  - Changes in residential environment?
  - Changes in schooling?
- Who are the compliers?

Most of these issues arise whether you use IV or ITT to analyze the data

## Example 1a:

• Causal question:

Does moving from very high poverty public housing developments benefit the health of mothers or their children? We did a trial, but do you believe the results? Can we get more evidence? Voucher lottery

- We match mortality data to information on every child in public housing that applied for a housing voucher in Chicago in 1997(N=11,848).
- Families were randomly assigned to the voucher wait list, and only some families were offered vouchers.
- Families randomized to the voucher moved to census tracts with an average of 7 points lower poverty.

- Match mortality data to information on every child in public housing that applied for a housing voucher in Chicago in 1997(N=11,848).
- Families were randomly assigned to the voucher wait list, and only some families were offered vouchers.

- Match mortality data to information on every child in public housing that applied for a housing voucher in Chicago in 1997(N=11,848).
- Families were randomly assigned to the voucher wait list, and only some families were offered vouchers.
- Families randomized to the voucher moved to census tracts with an average of 7 points lower poverty.

- Treatment group= children whose families were assigned a waitlist number from 1 to 18,110, and so were offered a voucher by May 2003
- Control group = everyone assigned a higher lottery number.
- OLS with a person-quarter panel dataset for 1997:Q3 through 2005:Q4
- $y_{it}$  measures child *i*'s outcome in quarter *t*, *PostOffer*<sub>it</sub> =1 if child *i*'s family was offered a voucher prior to *t*, else *PostOffer*<sub>it</sub> = 0
- X = control variables (whether the family is offered a voucher some time *after* quarter *t*, gender, splines for baseline age (kinks at 1, 2, 5, 8 and 15) and calendar time (kinks every 6 calendar quarters). Clustered standard errors.

Session 2.2 Findings Instruments

## Jacob & Ludwig 2011 • ITT: $y_{it} = \alpha + \beta_1 (PostOffer_{it}) + \mathbf{X}\Gamma + \varepsilon_{it}$



Leased<sub>it</sub> = 
$$\alpha + \theta_1 PostOffer_{it} + \mathbf{X}\Gamma + \gamma_t + \varepsilon_{it}$$

$$y_{it} = \alpha + \pi_1 Leased_{it} + \mathbf{X}\Gamma + \gamma_t + \varepsilon_{it},$$

#### IV analyses of a housing voucher lottery ITT IV Boys Only Death All Causes 100.32 60.44 203.88 (-51.52, 172.4) (-175.12, 582.92) Girls Only Death All Causes -130.2038.16 -40.88 (-65.28, -16.52) (-207.6, -50.4)

Same analytic approach to natural experiment generated by a lottery and randomized experiment. Similar message re gender effect modification. Note large CIs.

# Example 2, natural experiment based on policy change

• Causal question:

Does completing additional years of education improve memory in old age?

## Substantive Question

Multiple studies show that years of education predicts old age cognitive function, cognitive change, and dementia.

Causality questionable.



## Natural Experiments for Education



## Natural Experiments: UK Education Reform Effect on Education



Fig. 1. Effect of 1947 Reform on Fraction Leaving Full-time Education at or Before Age 14

From Banks and Mazzona, 2012

Natural Experiments: UK Education Reform Effect on Education Reform had a powerful and immediate effect on about half the population of 14 years olds.



Fig. 1. Effect of 1947 Reform on Fraction Leaving Full-time Education at or Before Age 14

## Natural Experiments: IV Estimates for Education effect on EF



Fig. 9. Effect of 1947 Reform on Executive Functioning (Conditional on Leaving Before 16)

From Banks and Mazzona, 2012

## Natural Experiments: IV Estimates for Education Effect on EF

#### Note sensitivity to model for temporal trends.



Fig. 9. Effect of 1947 Reform on Executive Functioning (Conditional on Leaving Before 16)

From Banks and Mazzona, 2012

## Estimating the IV effect

• Banks & Mazzona call this a "fuzzy regression discontinuity design" and estimate with 2SLS.

	Males		Females		
	Year band=1	Year band=3	Year band=1	Year band=3	
Memory	.60 (.35)	.43 (.19)	.51 (.34)	.35 (.19)	
Exec Fx	.64 (.36)	.37 (.19)	10 (.39)	.09 (.21)	

## IV Estimates Using US Policy Changes

- Banks and Mazzona replicated earlier findings in the US
- Advantage of the US context:
  - Education is decentralized, so there were more places that changed policies
  - Allows for better control of secular trends: you can rule out a sudden change in 1947.
- Disadvantage of the US context:
  - Effect of the laws was very small
  - Generally not well enforced, most people would have attended more school than required anyway
  - Complier group is small.



## IV Analyses

- State schooling policies
  - Compulsory school to drop out (CSL) or receive a work-permit (CSL-W)
  - Based on policy in state of birth when school-age
  - 2-Sample least squares analysis
- Exposure (endogenous) variable:
  - Years of education (self-report)

## Data Set: 1<sup>st</sup> Stage

- IPUMS (Census) 5% 1980 sample,
- Birth years 1900-1947
- Years of education linked to CSLs and CSL-Ws based on state of birth
- Link predictions from 1<sup>st</sup> stage regression model to individual data in the 2<sup>nd</sup> stage based on state of birth and all covariates.

## Data Set: 2<sup>nd</sup> stage

- Health & Retirement Study, 1992-2000: panel enrollment by birth cohort (whites only due to evidence on enforcement)
- Cognitive assessments and state of birth on 21,041 individuals born 1900-1947
- CSLs and CSL-Ws

## **Two-Sample Least Squares**



## Covariates

- Unadjusted
- Sex
- Birthyear (indicators for every year)
- State of birth indicators

• State characteristics: age 6 % black, % urban, and % foreign born; age 14 manufacturing jobs per capita and wages per manufacturing job

4

1

2

### Do the Instruments Predict Education?

#### First stage regression results (from IPUMS 5% sample)

	1. Unadjusted Model	2. Birthyear and sex	3. Model 2 + state of birth	4. Model 3 + state condns
CSLs	0.238	0.110	0.062	0.037
	(0.236, 0.240)	(0.108, 0.112)	(0.059, 0.064)	(0.034, 0.040)
CSL-Ws	0.143	-0.032	0.063	0.044
	(0.146, 0.141)	(-0.034, -0.029)	(0.060, 0.066)	(0.040, 0.048)
CSL-Ws UNR	-1.397	-0.282	-0.204	0.034
	(-1.429, -1.365)	(-0.315, -0.249)	(-0.238, -0.17)	(0.000, 0.069)

## How Strong is the 1<sup>st</sup> Stage?

		1. U	nadjusted Model	2. B a	irthyear <sup>*</sup> nd sex.	3. M state	lodel 2 + e of birth licators	4. N	Aodel 3 + state
		β	95% CI	β	95% CI	β	95% CI	β	95% CI
Model r <sup>2</sup> wit instrumental	hout variables	С	0.0000	0	.1080	0.	.1599	0	.1626
Model r <sup>2</sup> inc instrumental	luding variables	С	0.0465	0	.1127	0.	.1613	0	.1631
Variance exp instrumental	plained by variables	C	).0465	0	.0047	0.	.0014	0	.0005

Not technically "weak" instruments, but clear that a small violation of the IV assumptions could introduce a large amount of bias.

## IV Estimates for Education: CSLs

Estimated effect of 1 year ed'n on cogniti	(	Cognition			
Model covariates	$\beta_{IV}$	95% CI <sup>^</sup>	$\beta_{IV}$	95% CI <sup>^</sup>	
1. Unadjusted	0.33	(0.27, 0.39)	0.19	(0.12, 0.26)	
2. Birthyear, and sex	0.30	(0.14, 0.46)	0.34	(0.05, 0.63)	
3. Model 2 + birth state	0.18	(0.02, 0.33)	0.03	(-0.22, 0.27)	
4. Model 3 + state condns	0.34	(0.11, 0.57)	-0.06	(-0.37, 0.26)	
5. OLS estimates 0.09	9 (0.08	8, 0.10)	).15 (0.	14, 0.16)	

## **Evaluating Instruments**

- Is the dependent variable independent of the instrument conditional on the endogenous variable?
- Over-identification tests, if you have multiple instruments
- Inequality constraints (for categorical endogenous variables)
- Evaluate the association between the instrument and the outcome across environments that modify the 1<sup>st</sup> stage association

## Sensitivity Analyses

- Including education >13 years
  - $\beta_{IV}$  (memory, model 3): 0.15 (-0.01, 0.31)
- Restricting to education > 13 years
  - Instruments do not predict education or memory for individuals with >13 years of school
  - $\beta_{IV}$  (memory, model 3): -1.04 (-3.70, 1.62)
- Inverse probability weighted for missing Memory (parental SES, self-report chronic condns at baseline)
  - $\beta_{IV}$  (memory, model 3): 0.19 (0.03, 0.36)

# Example 3: Maternal FTO as an IV for effect of mom's BMI on child's BMI

Goal was to test developmental overnutrition hypothesis: exposure during gestation affects child BMI



## IV effect estimates for Maternal BMI on Offspring total fat mass

	OLS	IV	P-value for test of difference OLS vs IV
Total Fat Mass	0.26 (0.23, 0.29	-0.08 (-0.56, 0.41)	.17

#### From Lawlor PLoS Medicine 2008



## **Doubting Instruments**

- Do they have other pathways to the outcome?
  - Quarter of birth
- Is there a common cause of the instrument and the outcome?
  - State of birth
- Do they actually affect anyone's exposure?
  - Tax policies

## Thinking of Instruments, Creating Instruments

- Often ecological
- Policy changes
- Policy discontinuities
- Differences in "expert" opinion
- Encouragement designs: randomize the incentive
- Ask:What is the process that determines exposure? Is any part of this process arbitrary/random?
- Content matter experts are very valuable team members

## Conclusions

- Many important questions not convincingly answered with observational evidence
- Abandon the difficult questions? Or learn what we can from fraught methods?
- IV adds:
  - A way forward with observational data
  - Sometimes a parameter estimate of special interest
  - Pushes us to identify interventions that change exposures
- Not a replacement for evidence from observational research or RCTs, but a useful supplement

## end

48

06-19-2012