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GLASGOW MOLECULAR PATHOLOGY NODE

EPSRC Engineering and Physical Sciences Research Council

NHS Greater Glasgow and Clyde

MRC Medical Research Council

Advanced Epidemiology: Methods designed to accommodate unobserved confounding

Janet Bouttell, February 2020

Health Economics and Health Technology Assessment (HEHTA)

Intended learning outcomes:

- To understand that there are methods which attempt to deal with unmeasured confounding
- To be familiar with the names and general approaches of some of these methods
- To have an appreciation of the strengths and limitations of these methods

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- **What is confounding? – (**variable) that influences both the dependent variable and independent variable causing a spurious association
- **What is observed confounding?**
- **What is unmeasured confounding?**
- **What is unmeasured time-varying confounding?**

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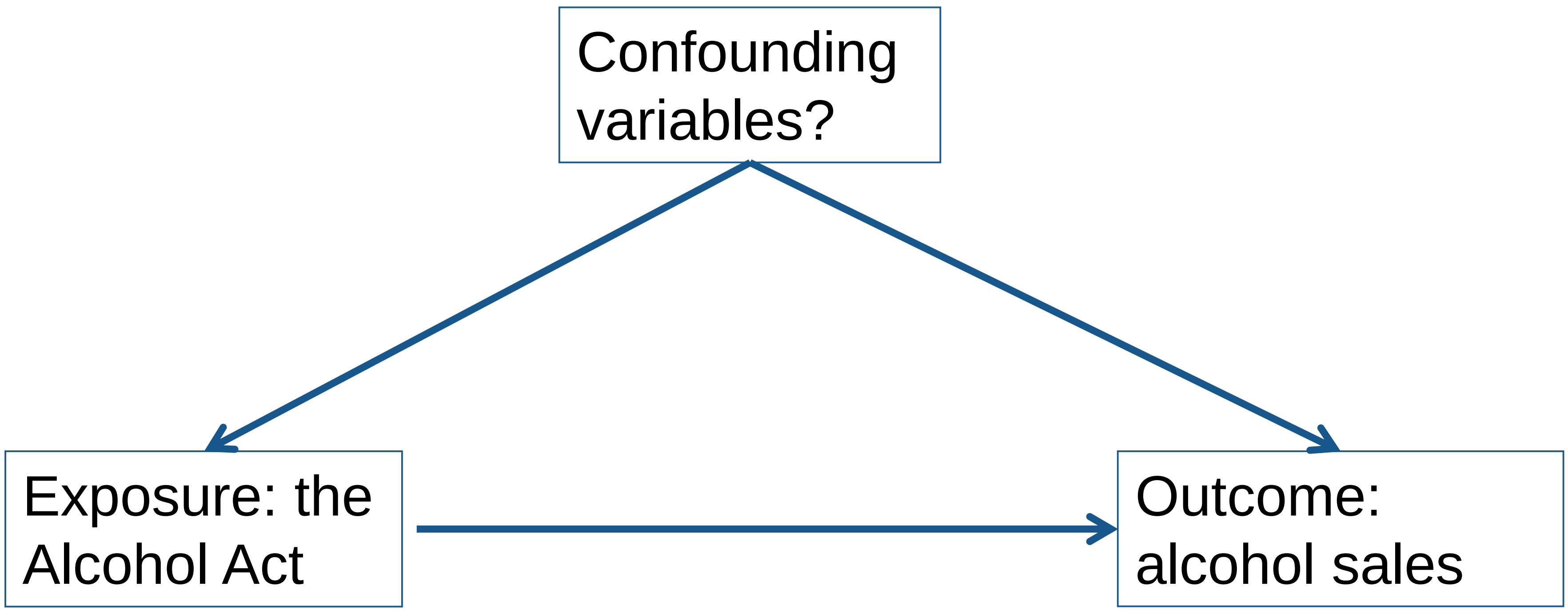
Confounding - what's the problem?

Hypothesis – the Alcohol Act (2011) reduced alcohol consumption in Scotland



Robinson et al (2014)

Confounding - what's the problem?

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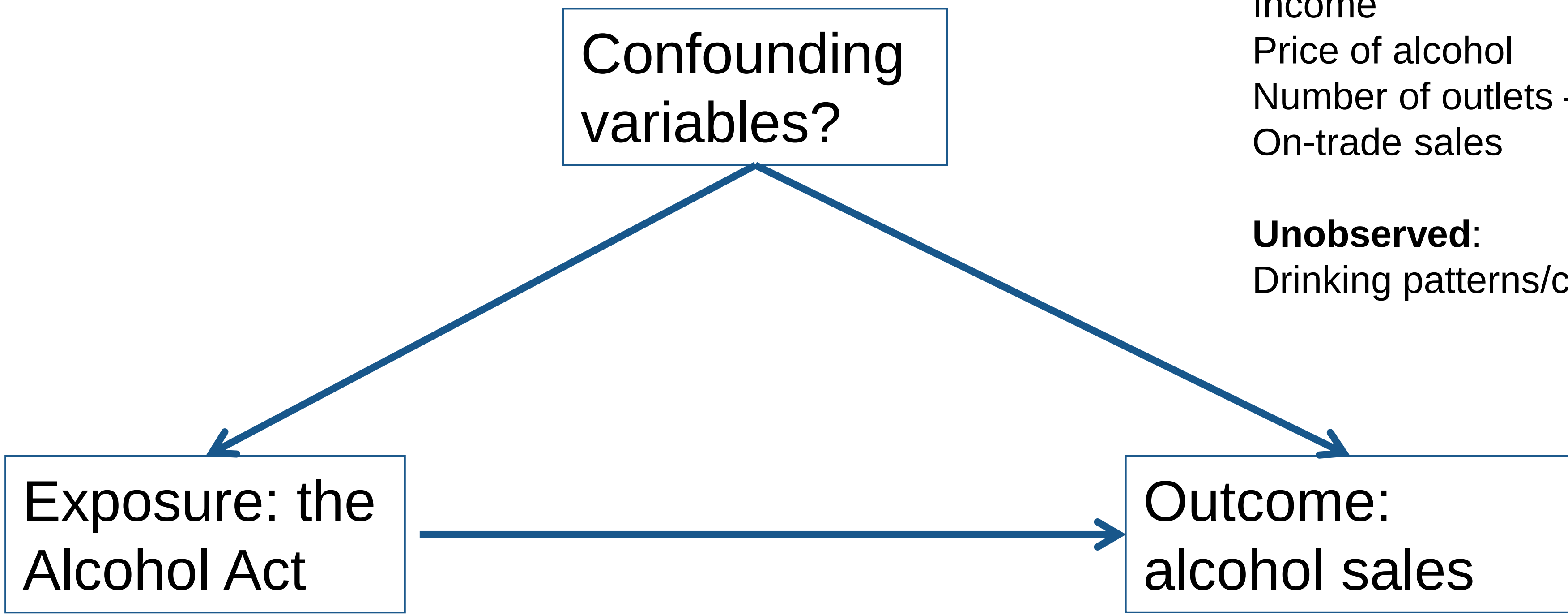

Observed:
Income
Price of alcohol
Number of outlets – on and off
On-trade sales

Unobserved:
Drinking patterns/culture?

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Methods designed to accommodate unobserved confounding

1. Difference-in-difference
2. Interrupted time series
3. Synthetic controls
4. Regression discontinuity
5. Instrumental Variables

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Difference in difference

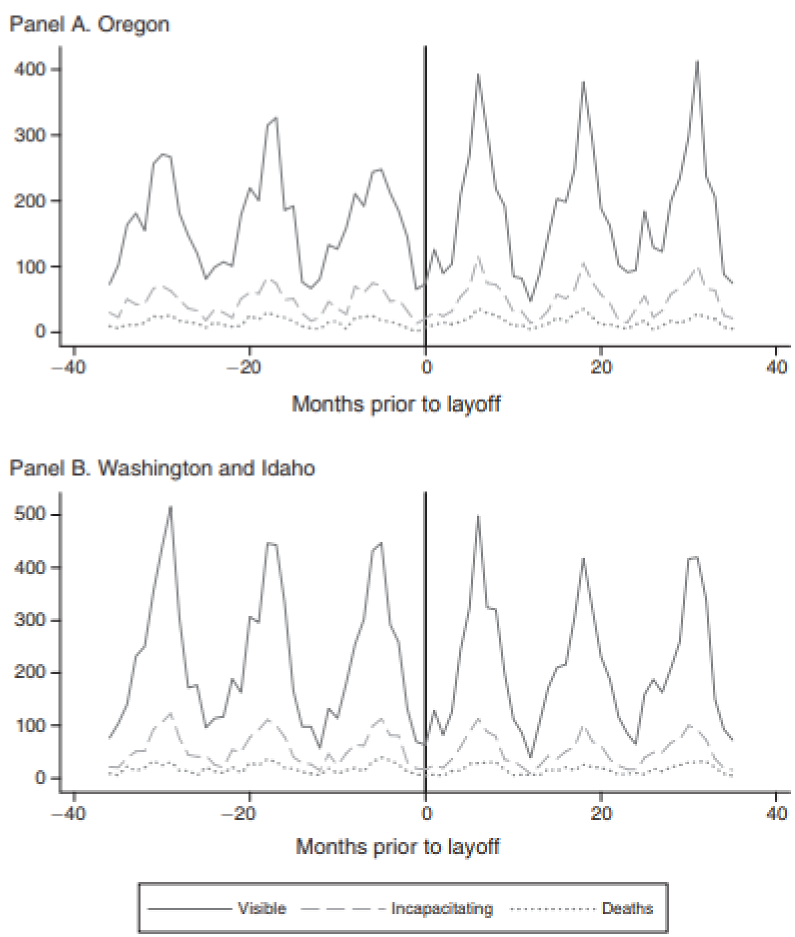

FIGURE 4. INJURIES ON HIGHWAYS IN OREGON, WASHINGTON, AND IDAHO OUTSIDE CITY LIMITS—DRY WEATHER CONDITIONS

- Change in outcome variable in intervention/control areas before and after the intervention
- Difference between those two differences
- E.g +50 Oregon -10 Washington and Idaho – DiD = 60 injuries
- Sometimes uses just one time point before and after
- How does it account for unobserved confounding?
- Limitations – parallel trends (similarity of control area)

DeAngelo and Hansen: Police enforcement and traffic fatalities (2014)

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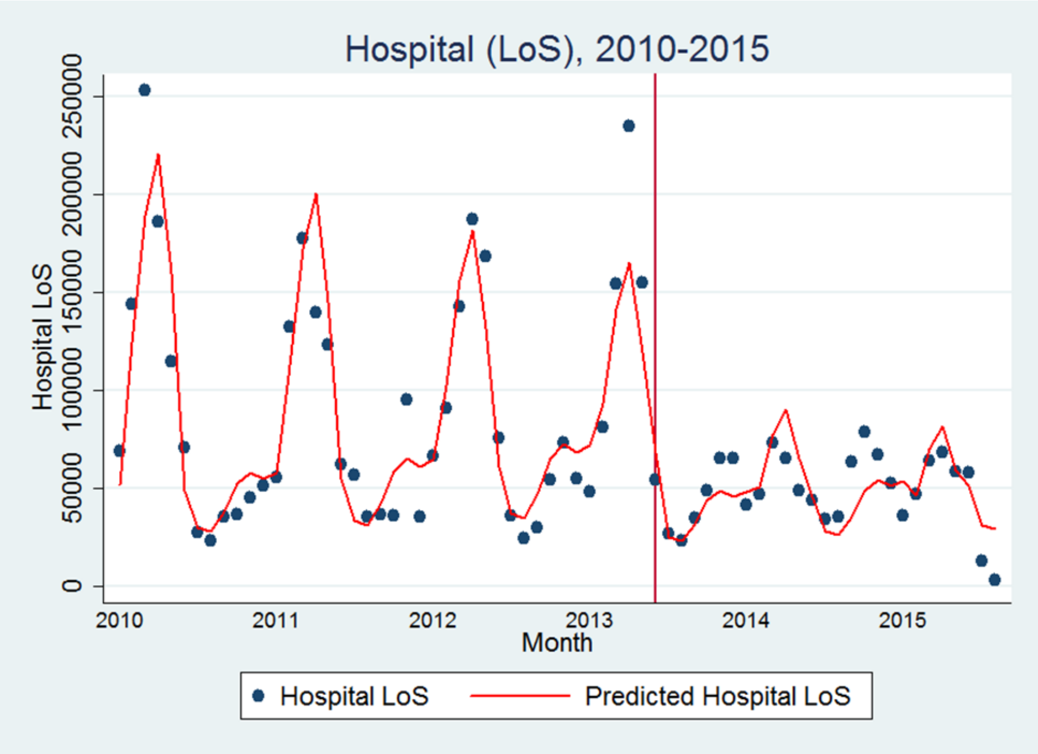
Interrupted time series



- Trend in outcome compared pre and post intervention
- What is the control/counterfactual here?
- Model accounts for auto-correlation, seasonality and underlying trend
- Can also add in a control – overlap with DiD
- Limitations – power/data, similarity of control area (if used)

Heggie et al, Hospital costs and rotavirus innoculation (2018)

Assess the impact of proposition 99

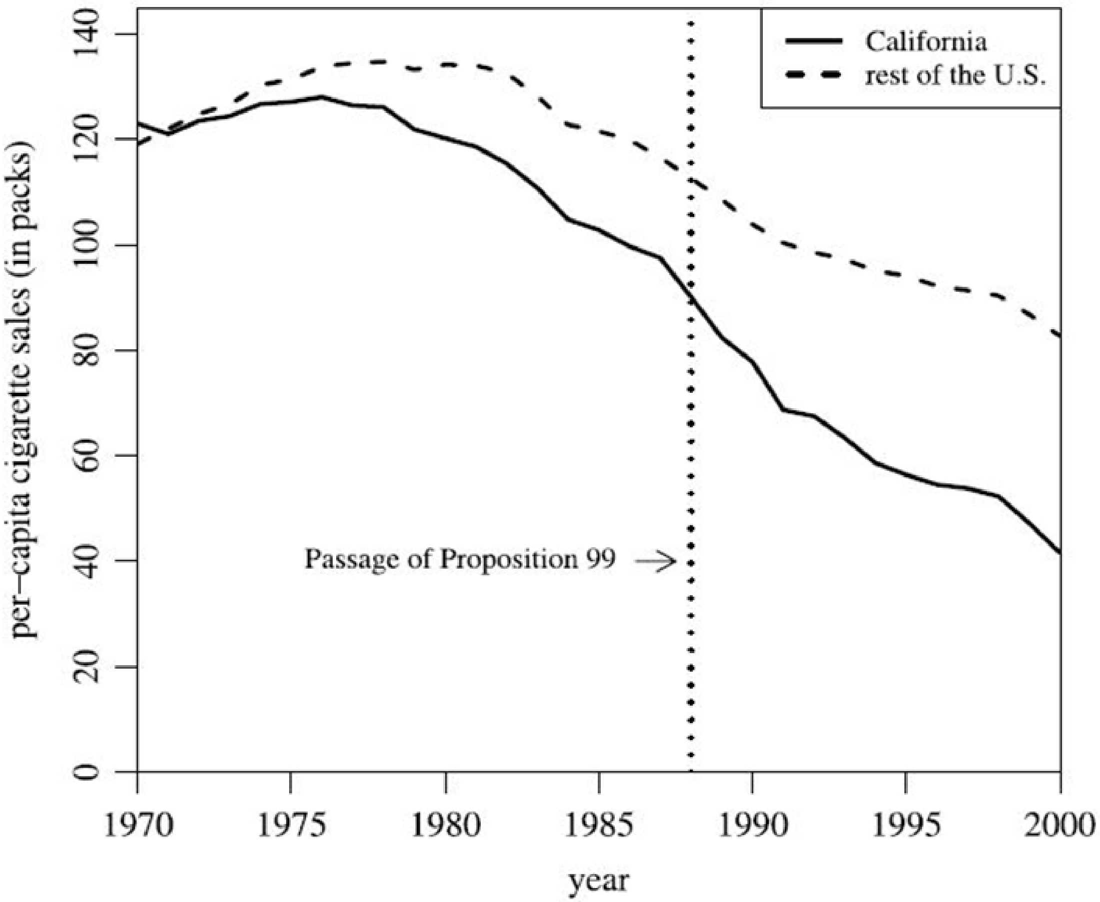


Figure 1. Trends in per-capita cigarette sales: California vs. the rest of the United States.

- How would you assess the impact of Proposition 99?
- Could you use an interrupted time series or a difference in difference approach?
- What would be the limitations of that?
- Could you overcome the problem?

Abadie et al (2010)

Synthetic controls

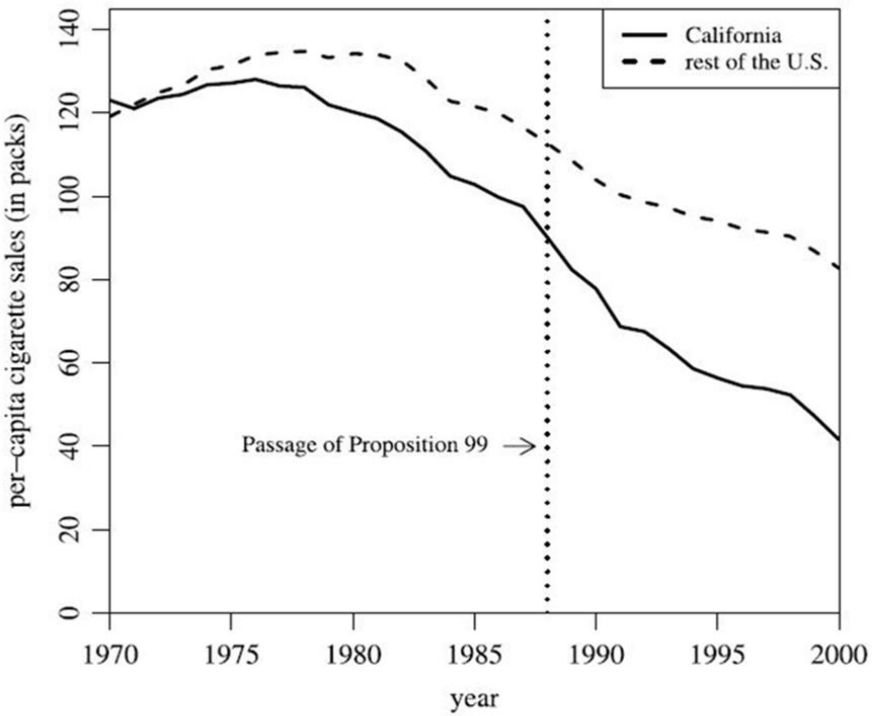


Figure 1. Trends in per-capita cigarette sales: California vs. the rest of the United States.

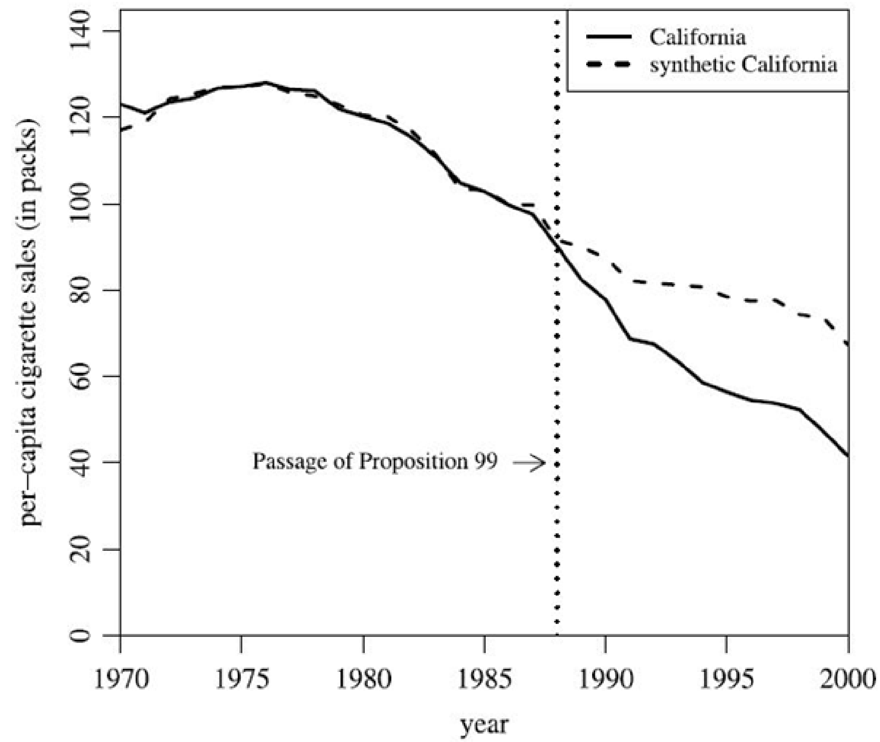


Figure 2. Trends in per-capita cigarette sales: California vs. synthetic California.

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Synthetic controls

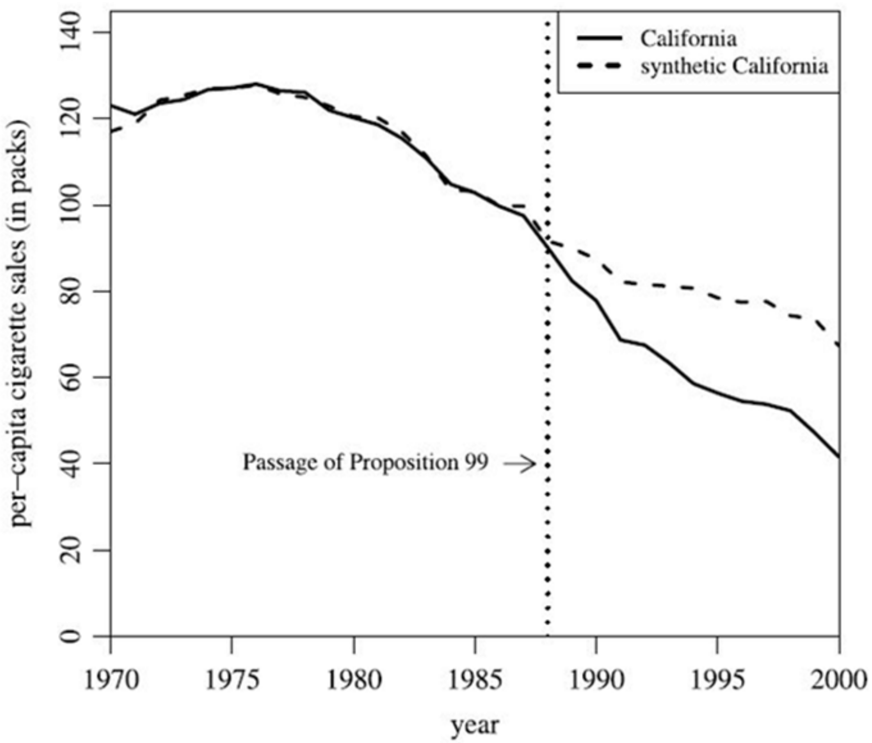
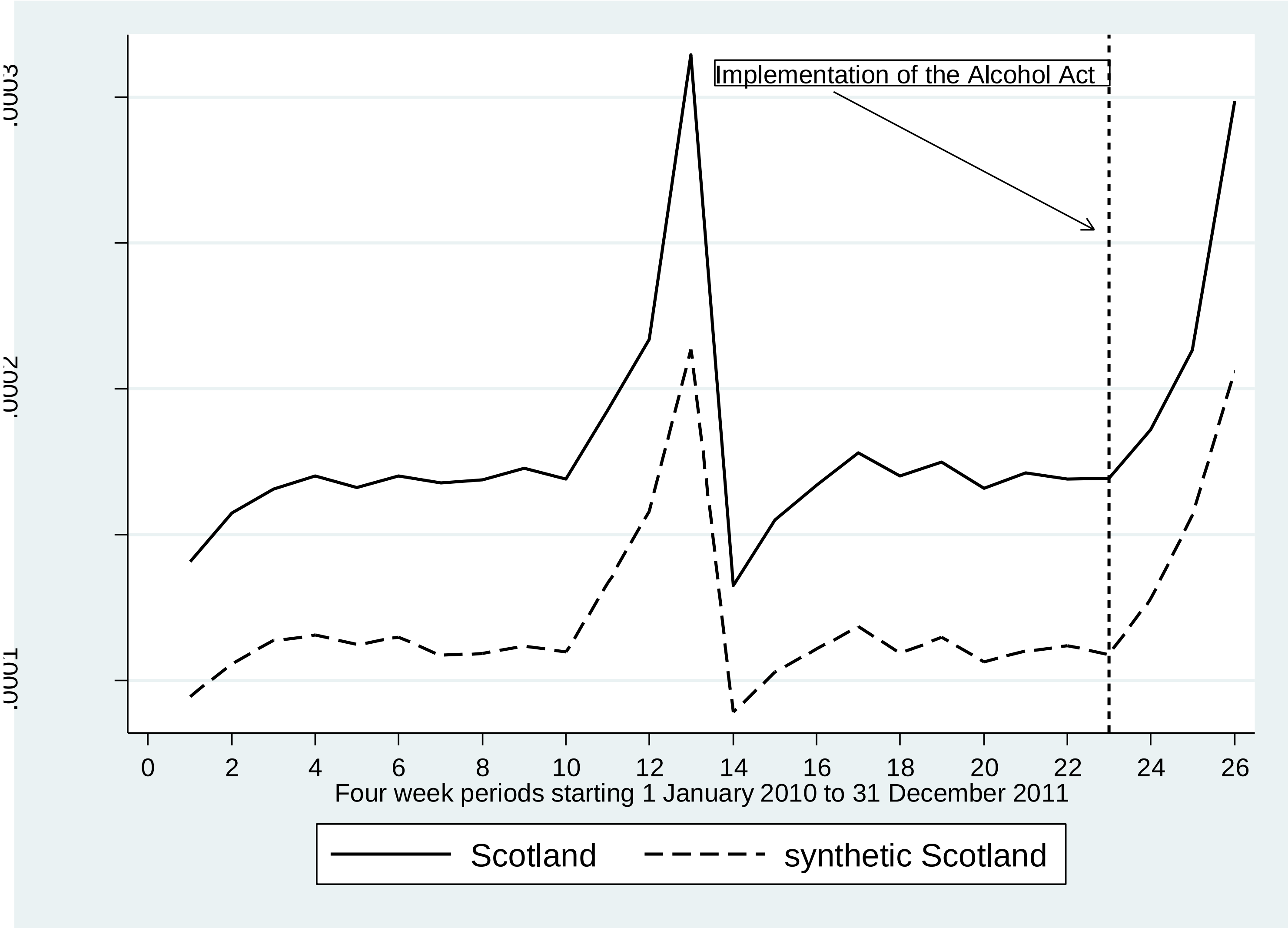


Figure 2. Trends in per-capita cigarette sales: California vs. synthetic California.

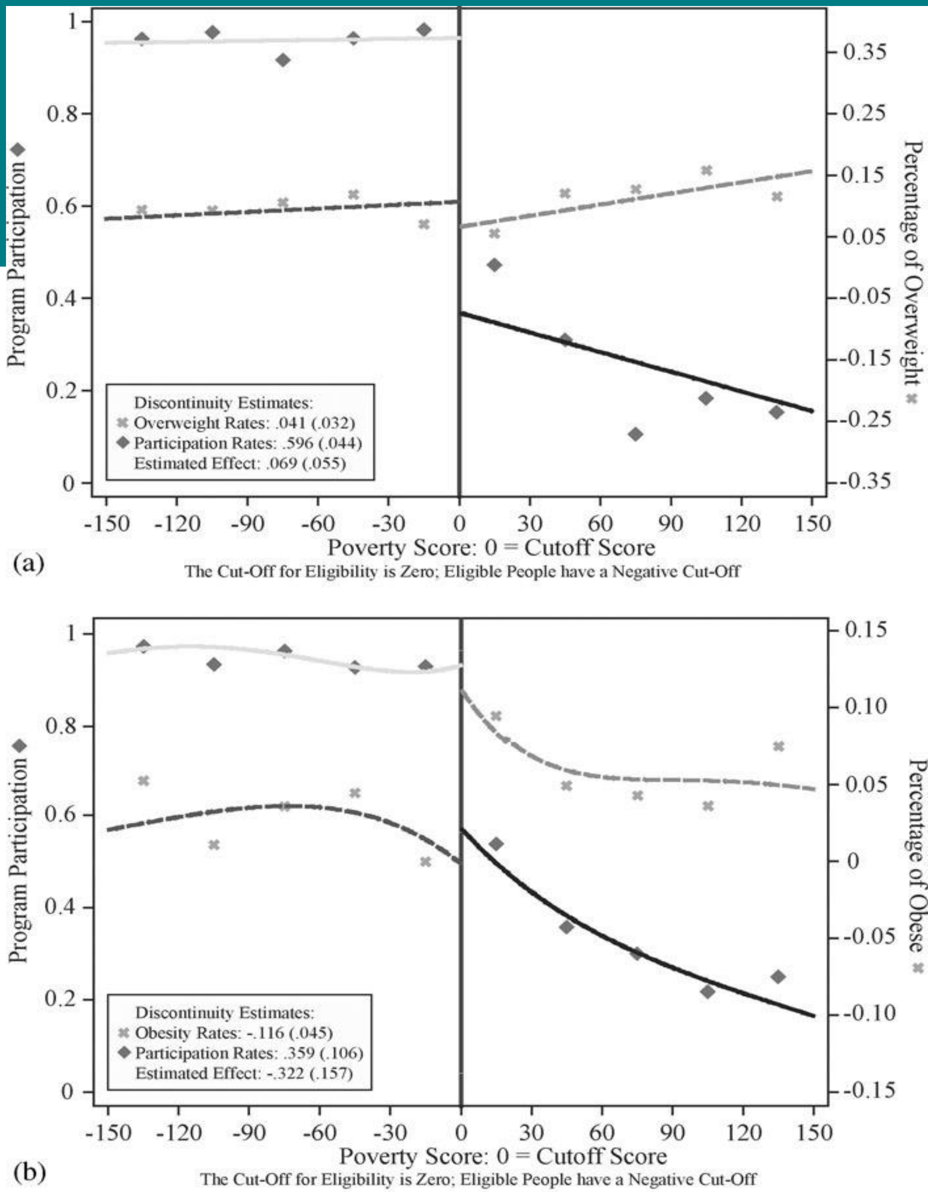
- Trend in the outcome in intervention compared to synthetic control area
- Synthetic control is weighted average from pool of potential controls
- How does it overcome unmeasured confounding?
- Why can this method cope with time-varying unmeasured confounding where DiD and ITS can’t?
- Limitations – data and outliers

Synthetic controls – outlier problem – sales of spirits in Scotland



Oportunidades to reduce overweight and obesity in Mexico?

Regression discontinuity



Average program participation (marked with ◆) and overweight/obesity rates (marked with ✖) are plotted as a function of five categories of the povery score on each side of the eligibility cut-off. The lines are conditional expectations of specification as in equations (3) and (4) in the text. They are estimated using the whole range of data with poverty scores of +/- 500. Based on Schwarz (1978), the preferred specifications for men include first order polynomial terms on both sides of the cut-off and fifth order for women.

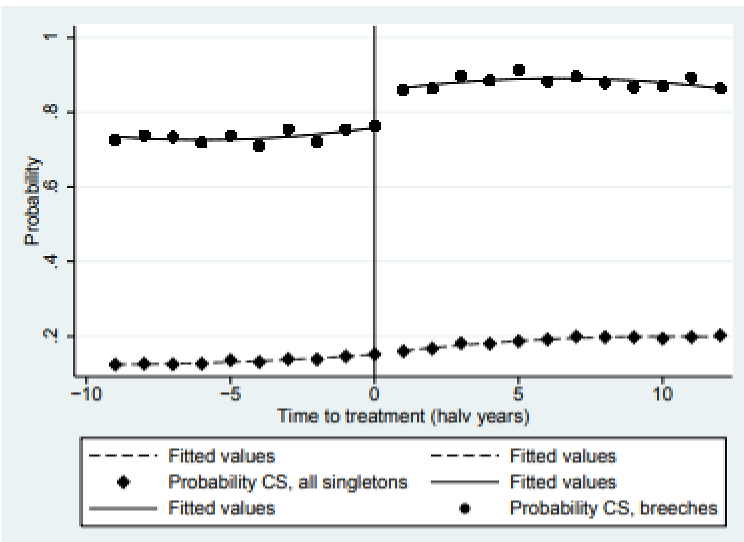
- Outcomes compared in units defined by scores above and below a cut-off in a continuous variable that determines exposure
- Units either side of the cut-off should be similar
- Trade-off between power (want numbers) and minimising confounding
- Limitations – only appropriate where you have a cut-off for entitlement

Andalon (2011)

Health Economics, Volume: 20, Issue: S1, Pages: 1-18, First published: 01 August 2011, DOI: (10.1002/hec.1773)

Regression discontinuity

Figure 1: CS rate for all non-breech and breech pregnancies, 1996-2006

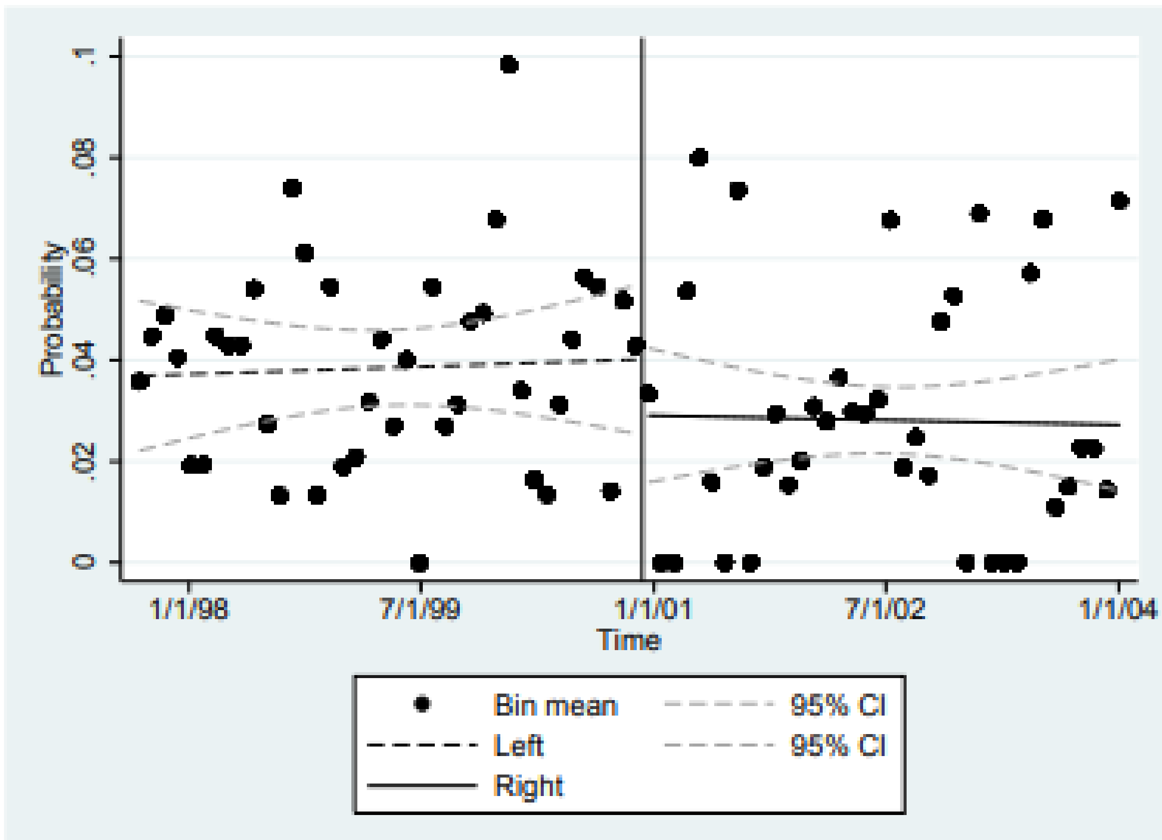


Notes: The plot shows the average probability of a CS per half-year. The vertical line is the date for the Danish dissemination of the TBT results. The sample includes all singleton births irrespective of parity.

- Second example – Jensen and Wust (2015)
- RCT in 2000 suggested that caesarean section safer for mothers and babies when baby breech.
- Major change in practice – very quickly
- Time discontinuity allowed study of women and babies on the margin

Regression discontinuity

Figure 8.7: Probability of APGAR score<=7 at 1 min for breech babies at term with parity>1



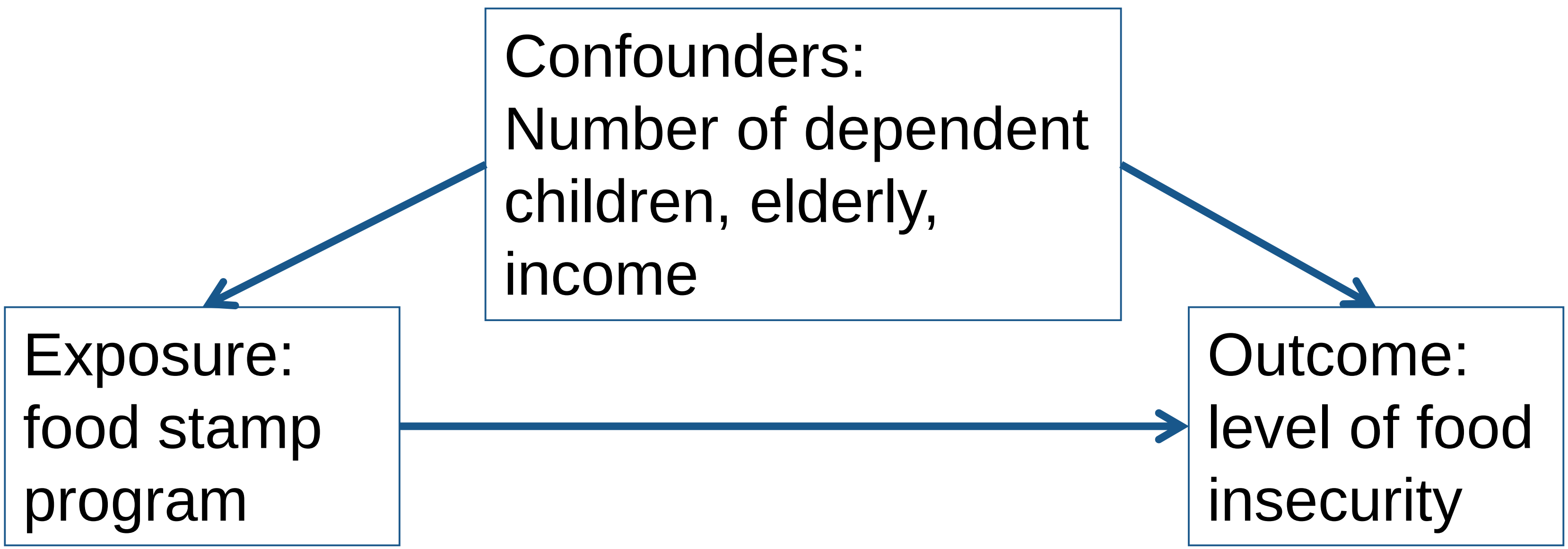
Hypothesis – food stamp program participation reduces food insecurity

Exposure: food stamp program $\longrightarrow$ Outcome: level of food insecurity

(Yen et al, 2008)

Instrumental Variables

Hypothesis – food stamp program participation reduces food insecurity



(Yen et al, 2008)

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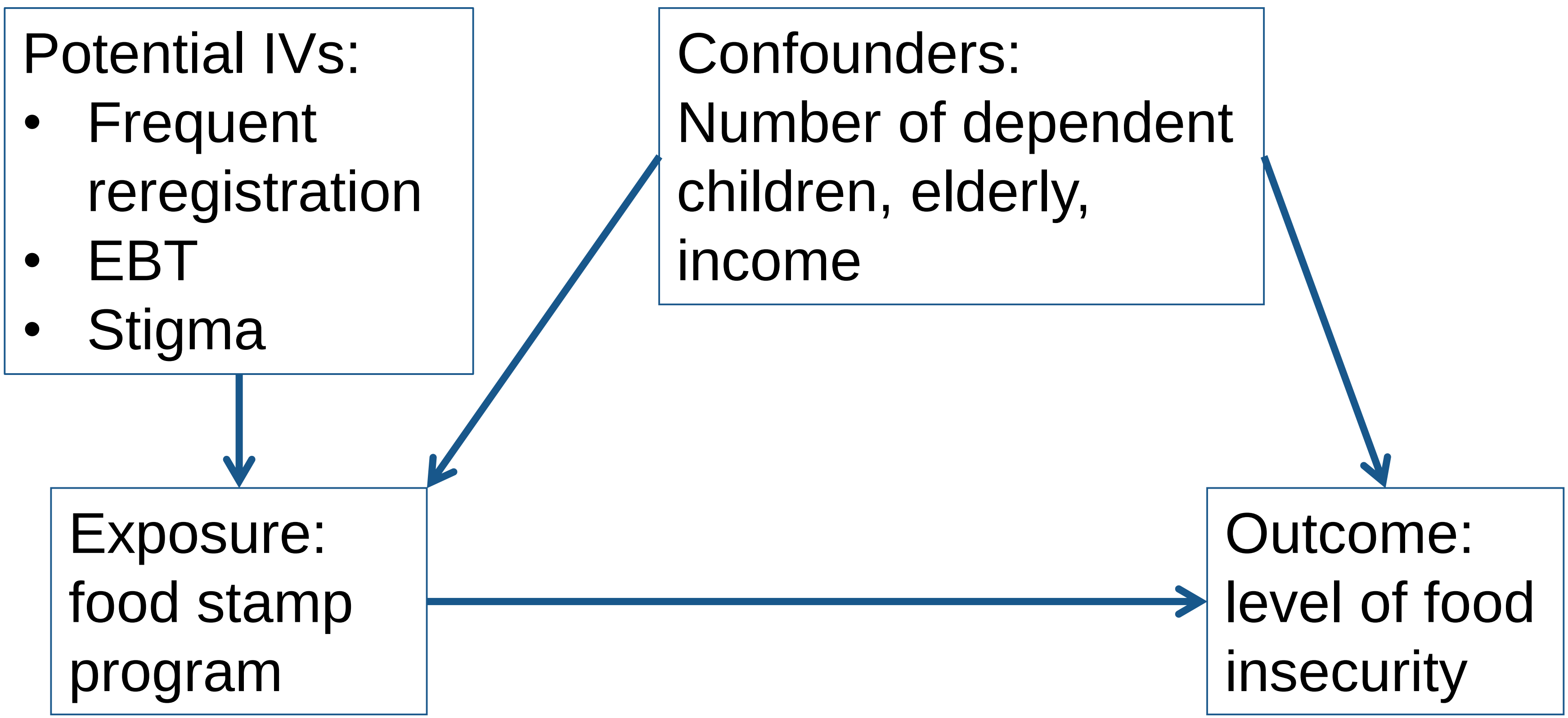
Instrumental Variables

Hypothesis – food stamp program participation reduces food insecurity (Yen et al, 2008)



Instrumental variables - summary

3 conditions

1. The IV must be correlated with the exposure – the stronger the better
2. The IV must not be associated with the outcome
3. The IV should not be associated with the confounding variable (which influences the outcome as well as the exposure)

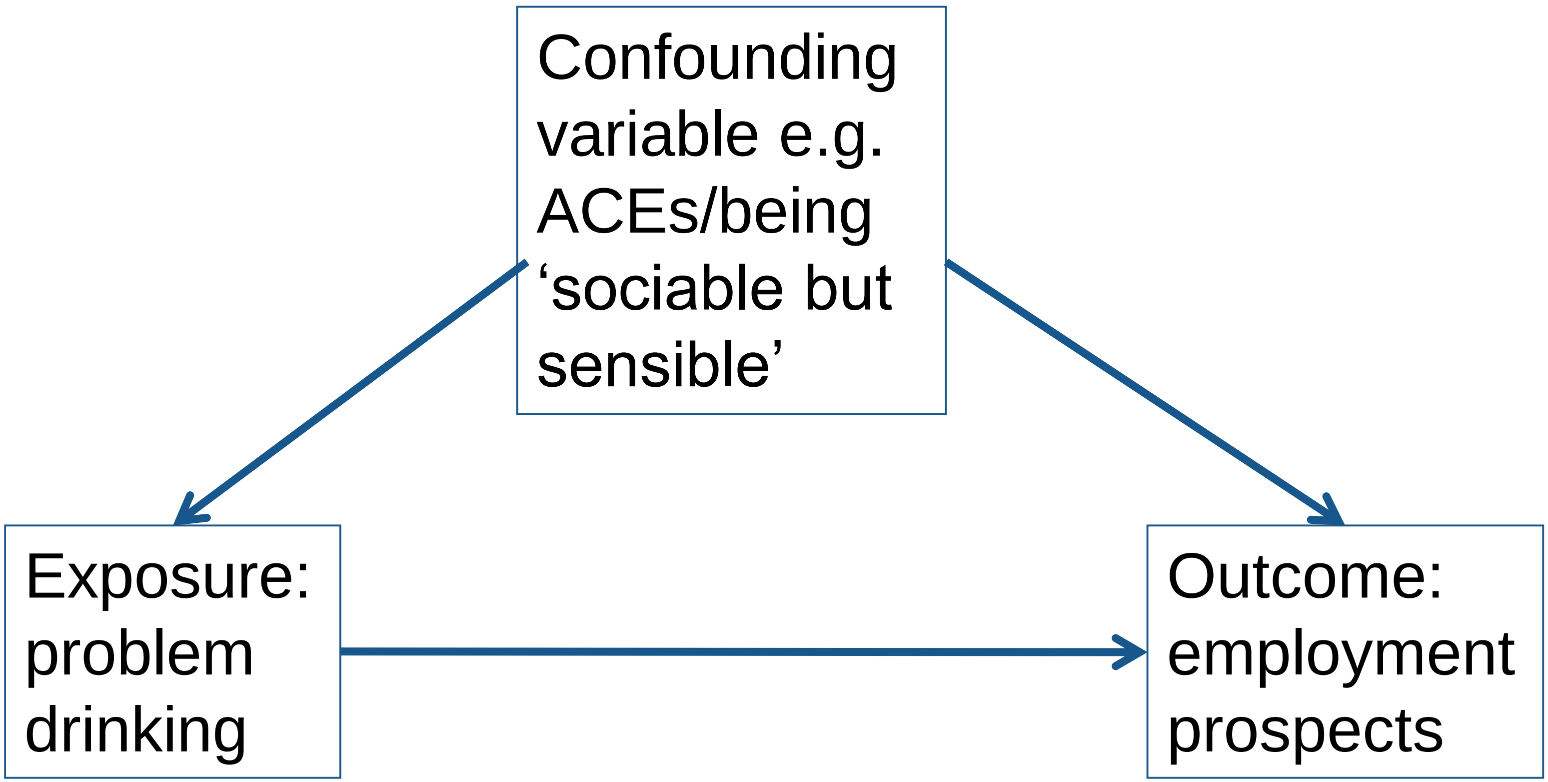
Limitations

1. Finding suitable instruments
2. Demonstrating that the assumptions are met

Hypothesis – problem drinking impacts employment prospects

Macdonald et al (2001)

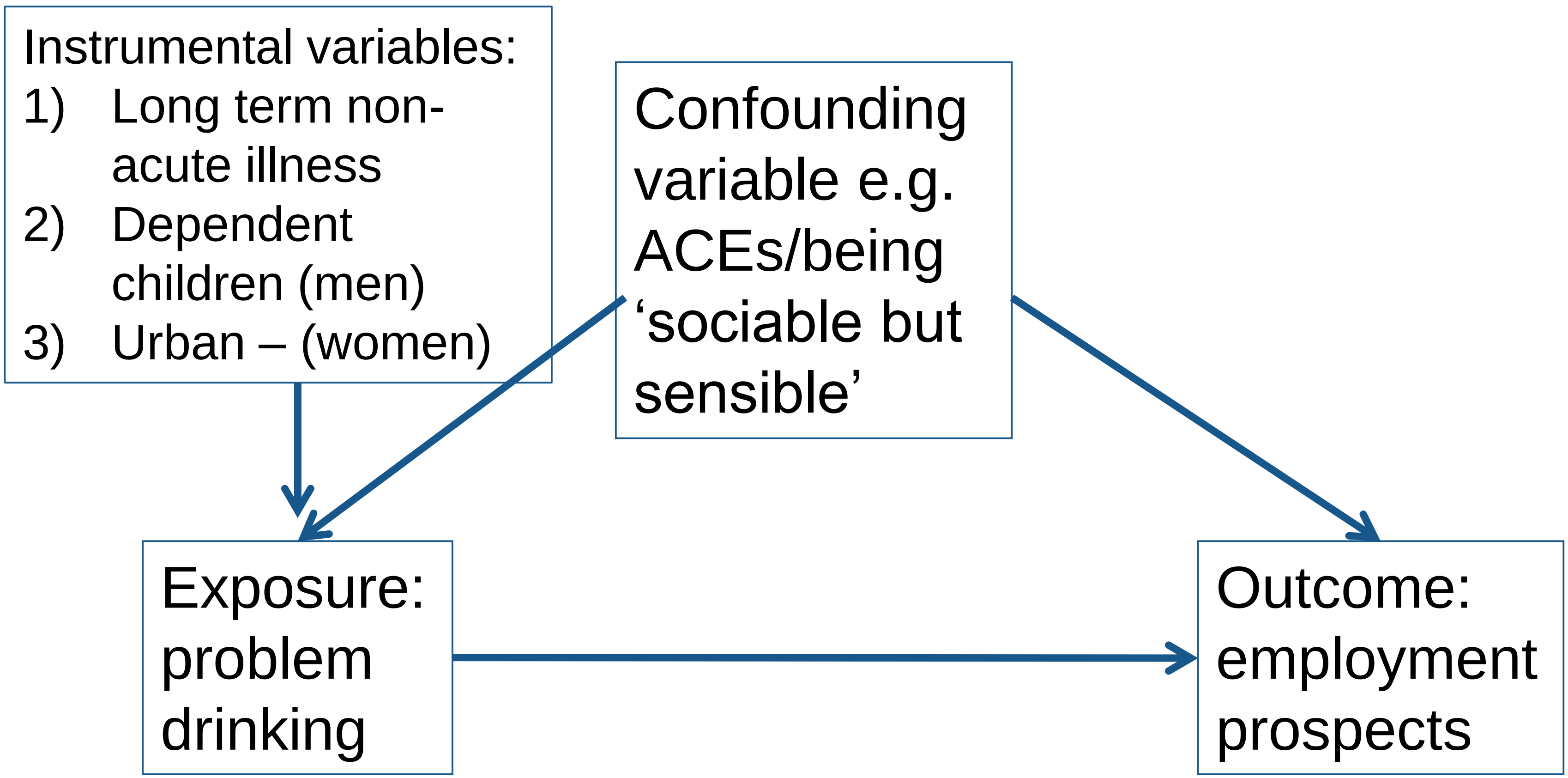
Hypothesis – problem drinking impacts employment prospects



Macdonald et al (2001)

Instrumental Variables

Hypothesis – problem drinking impacts employment prospects



Macdonald et al (2001)

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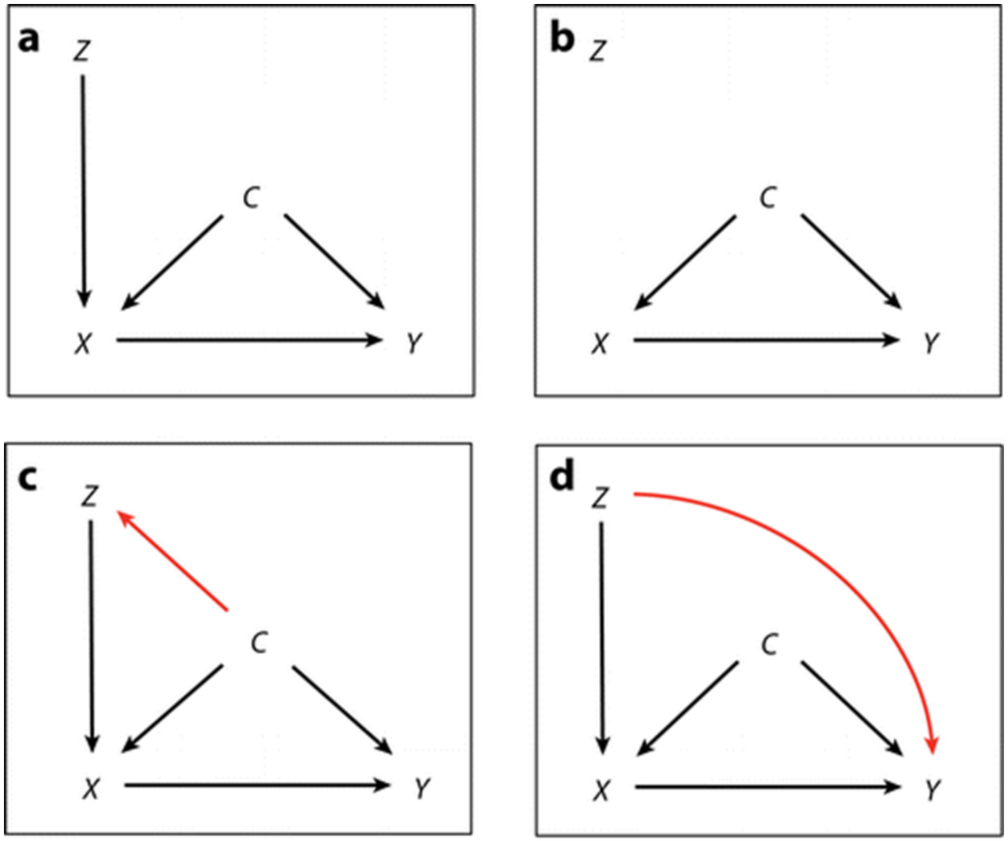
Instrumental variables - quiz



X = exposure of interest
Y = outcome of interest
C = confounder
Z = instrumental variable

In which of a-d would Z be an effective instrumental variable? Why?

Craig P, et al. 2017.
Annu. Rev. Public Health. 38:39–56

Practical exercise

1. **Three case studies – brief detail given (please make and note any assumptions you need)**
2. **Complete the outcome and interventions row and the confounders row**
3. **Decide which methods would be possible in each scenario - see description of the methods (Table 2 in Craig et al, 2017) overleaf**
4. **Select your preferred method then identify your counterfactual, data required and limitations**

Mendellian randomisation: a form of instrumental variable

https://www.youtube.com/watch?v=LoTgfGotaQ4

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Overview article

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