Regression discontinuity & Interrupted time series

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Regression Discontinuity Design (RDD)

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RCT: random assignment to treatment and control

- Groups are balanced in expectation on all variables, including unobserved ones

$\Rightarrow$ RCT gold standard for estimating causal effects of treatments

- Observational studies: often hard to justify that treatment groups are comparable, including on unobservables. Examples:

- Effect of vaccination: those who choose to get vaccinated are different from those who don't in ways that are hard to adjust for

- Effect of C-section vs natural delivery on children's health: hard to find comparable groups

Regression discontinuity design

- Method for estimating (causal?) treatment effects in observational studies
- Treatment/exposure assignment based on some arbitrary cut-off value of a continuous variable (called forcing variable)

- Prescriptions based on some clinical measure:

     CD4+ count for HIV treatment

     Risk score for statins

- Cancer screening for certain age groups

- Vaccination programme by birth date

- Neonatal treatment based on birth weight
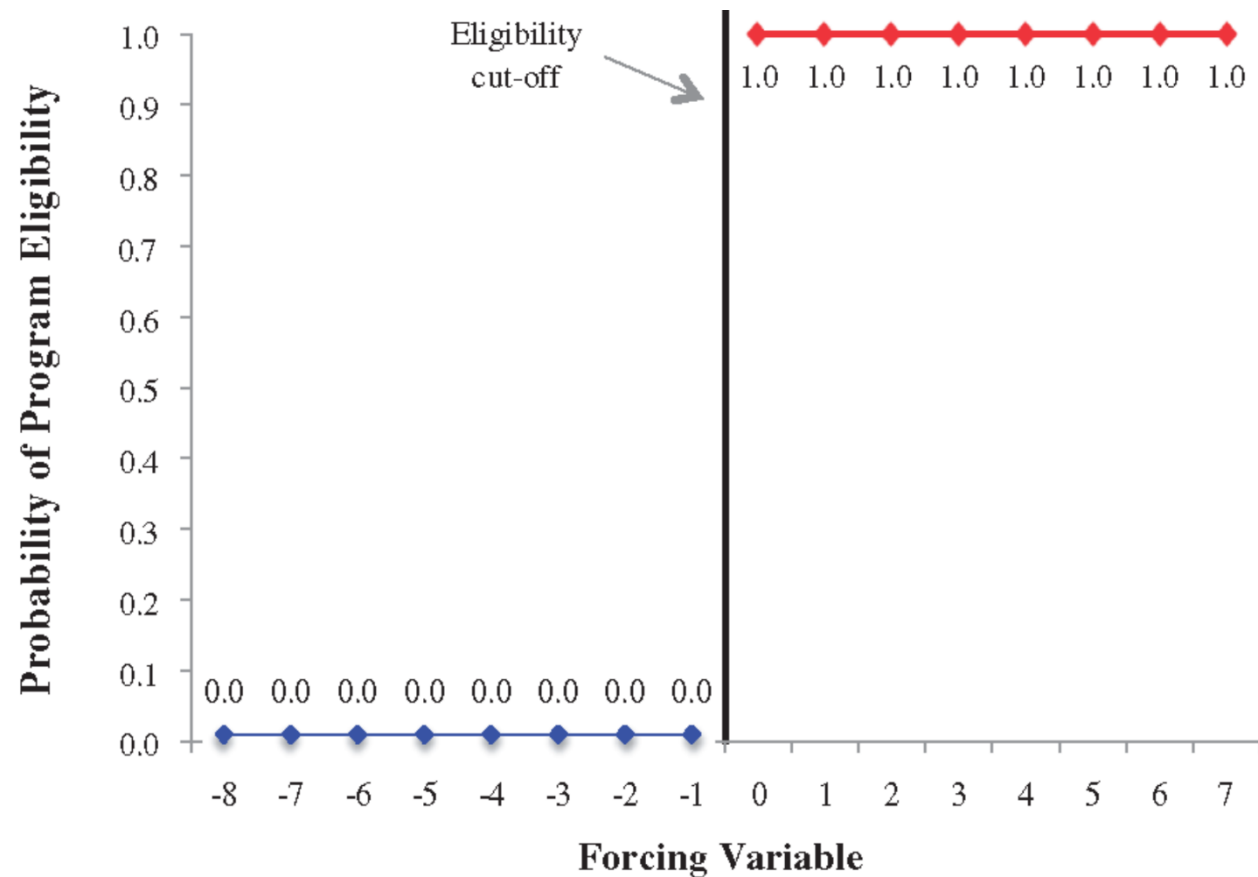
- Time since policy change

Sharp or fuzzy?

There are two kinds of RDD

1) **Sharp**: all individuals on one side of the cut-off are given the treatment and none on the other side gets treated

    - Typical examples are inclusion in screening and vaccination programs

2) **Fuzzy**: the probability of getting treated increases at the cut-off

    - Some at each side of the cut-off are treated

    - Assignment based also on other considerations (e.g. doctor's judgements)

Sharp RDD (Canadian study on early effects of HPV vaccine programme)
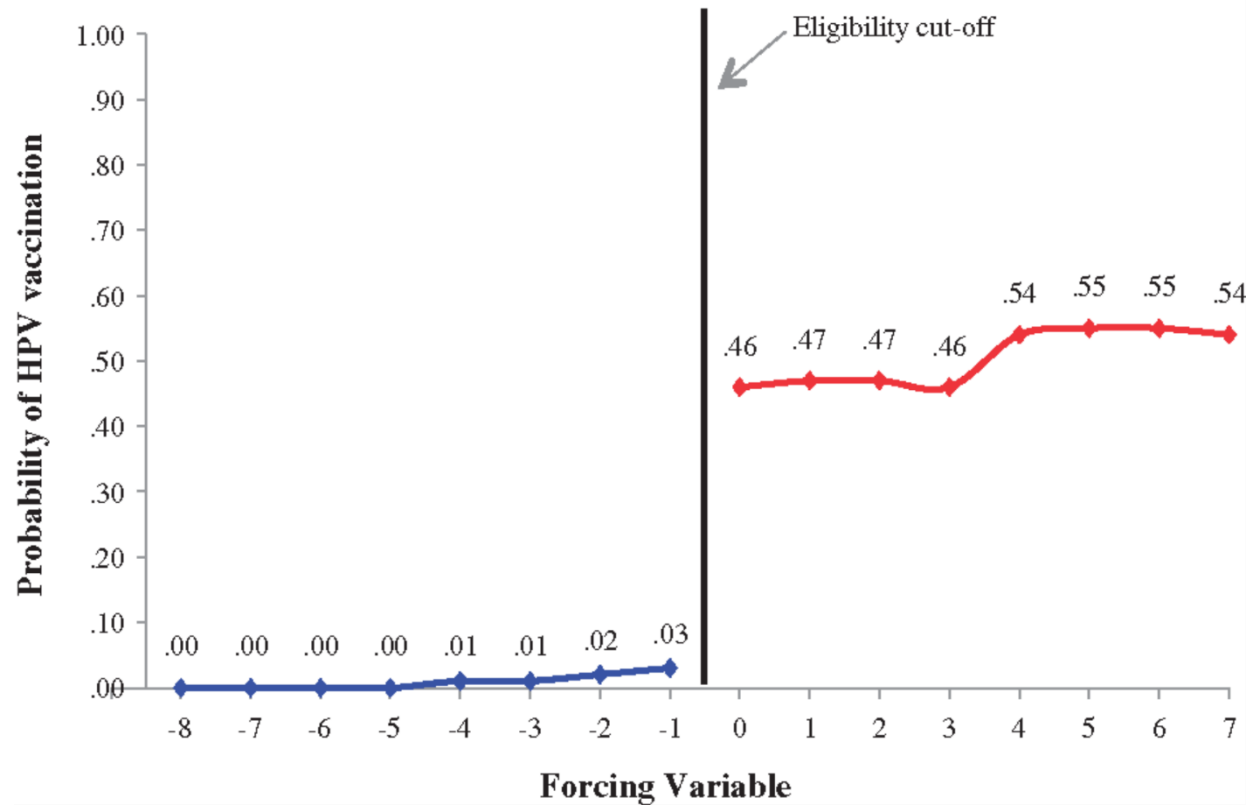## - all girls born after a certain date are *eligible* for vaccine

Fuzzy RDD:

- probability of *actually getting* the HPV-vaccine by birth date

Two more fuzzy examples

Probability of HIV treatment in South Africa based on CD4+ count

Probability of C-section for breech babies in Denmark by time since Lancet study
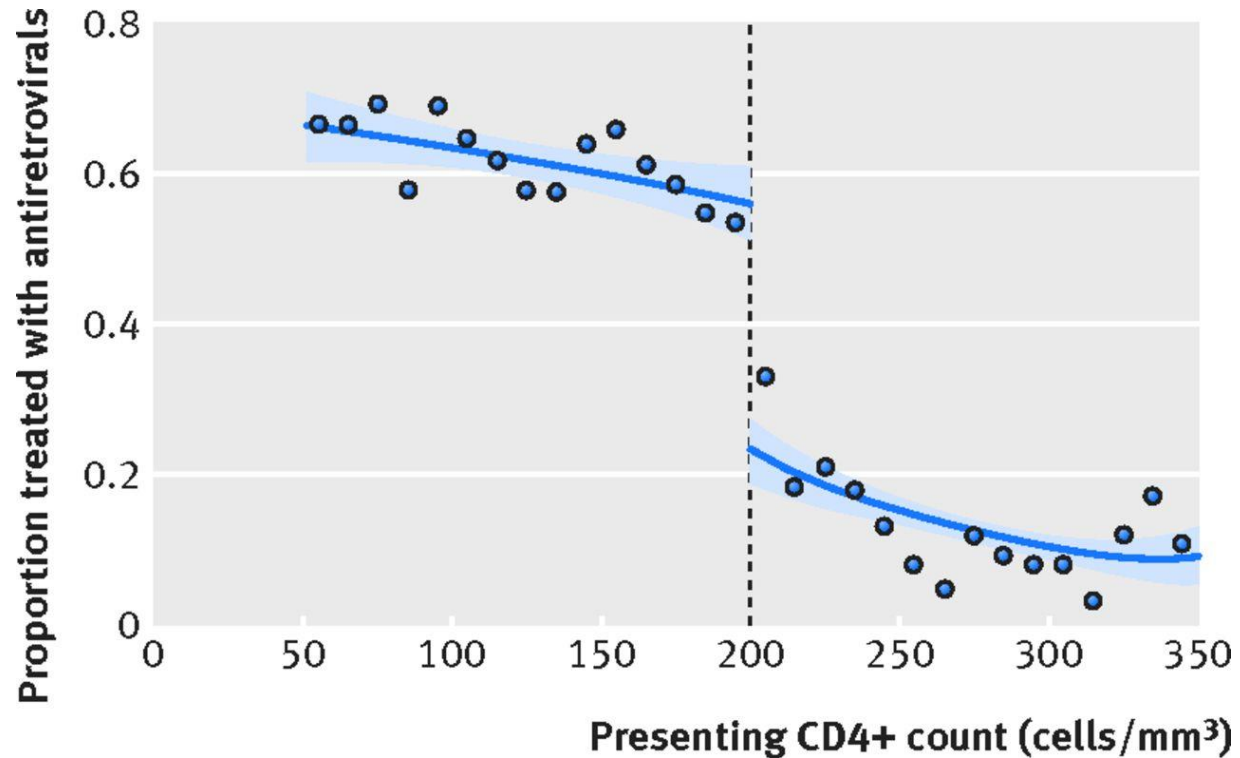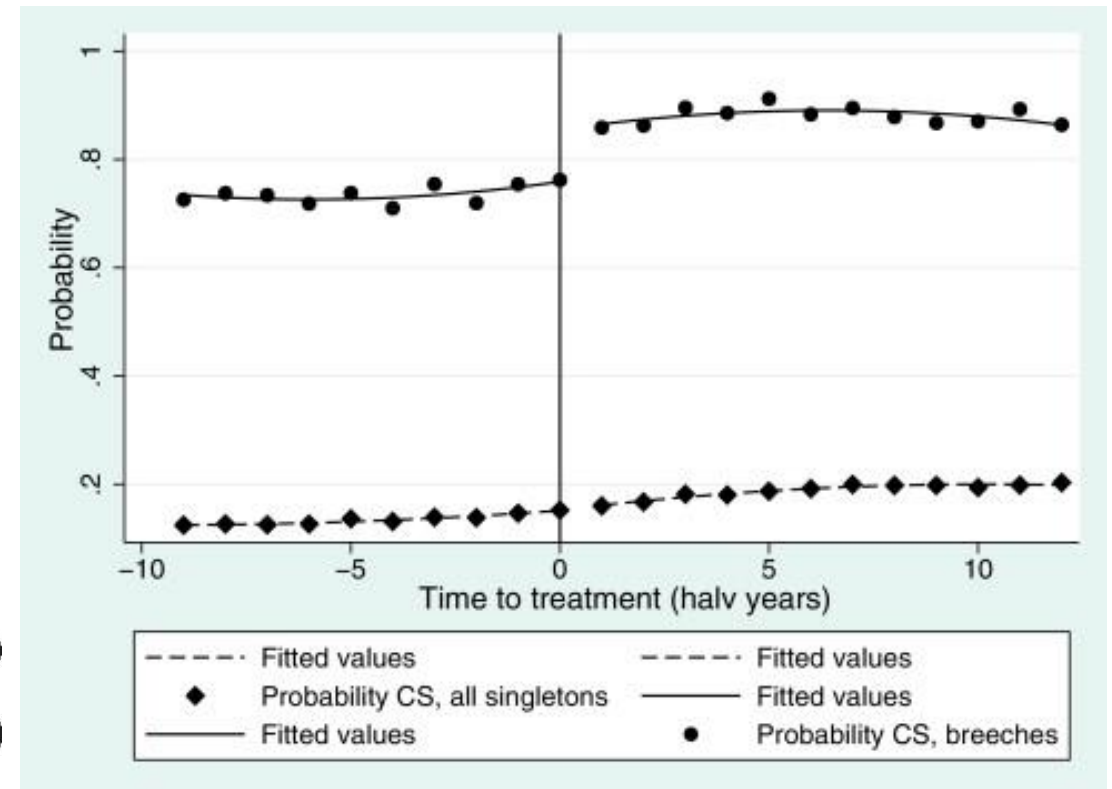
Atheendar S Venkataramani et al. BMJ 2016;352:bmj.i1216

Jensen VM, Wüst M. Can Caesarean section improve child and maternal health? The case of breech babies. J Health Econ 2015;39:289-302

Identification strategy

- Except for treatment, individuals on each side (but close to) the cut-off are otherwise similar (treatment assignment ignorable?)
- Whether someone is just below or just above the cut-off is essentially random (especially if the forcing variable is measured with error)
- «Quasi-random» assignment close to the cut-off
- Essential to check for balance on observables close to the cut-off

   (Similar to balance checking of baseline characteristics in a RCT)
- Notice: only local similarity is assumed

So what?

- Main question: Does discontinuity in treatment probability at the cut-off give discontinuity in the outcome?
- The only reasonable explanation for an discontinuity in outcome is discontinuity in treatment(??)
- Early studies too ambitious: tried to estimate global treatment effects

  - Individuals are really only assumed similar around the cut-off

- Treatment effect evaluated at the cut-off => local treatment effect
- Is this interesting? External validity issues.
- Sometimes what we want (evaluate if treatment regime is appropriate)

HIV treatment in South Africa

Local treatment effect: patients presenting just below the threshold had a 35% lower hazard of death than those presenting just above the threshold.

C-section for breech babies in Denmark
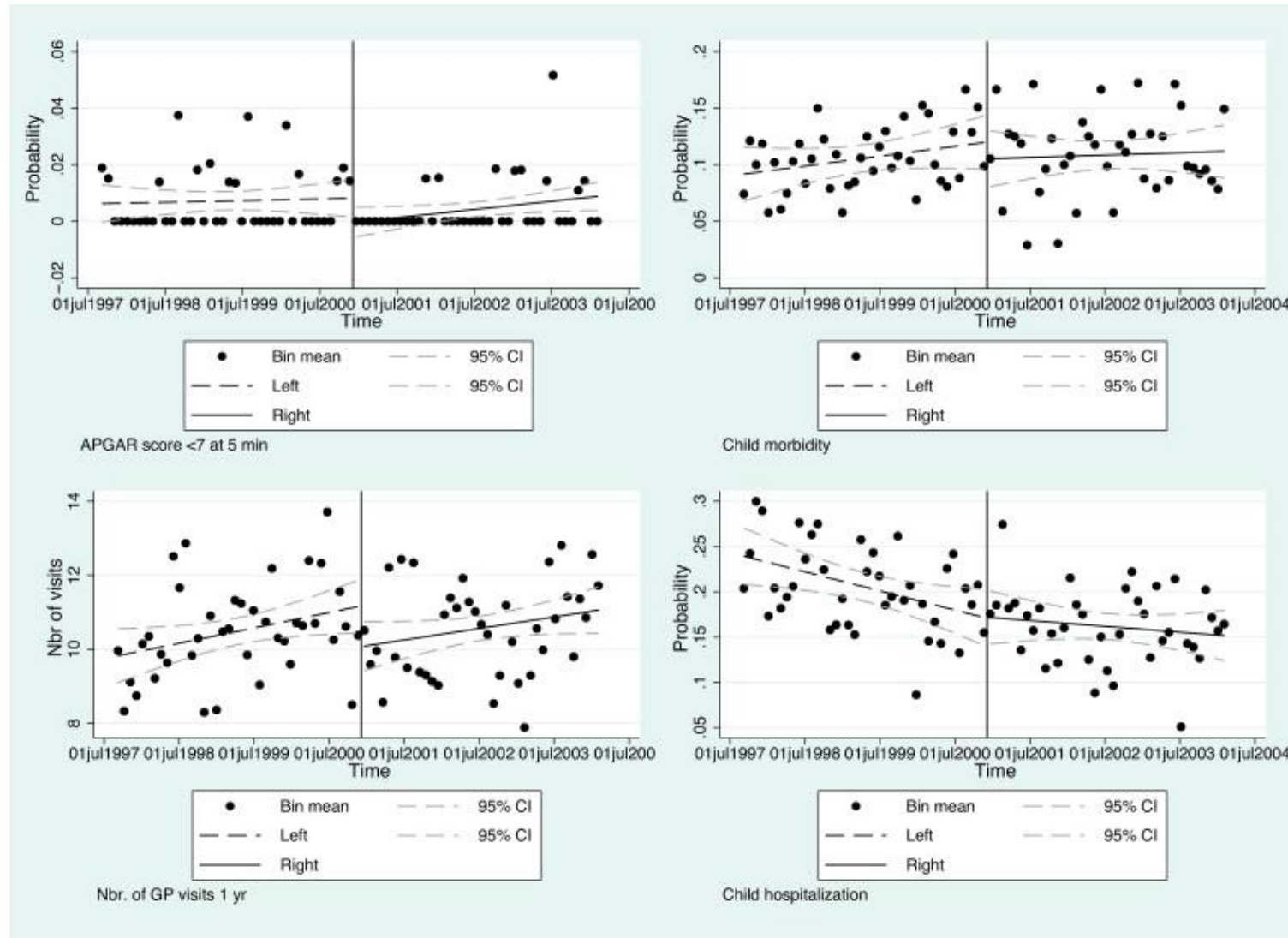
We find that CS decreases the child's probability of having a low APGAR score and the number of family doctor visits in the first year of life. We find no significant effects for severe neonatal morbidity or hospitalizations.

Jensen VM, Wüst M. Can Caesarean section improve child and maternal health? The case of breech babies.
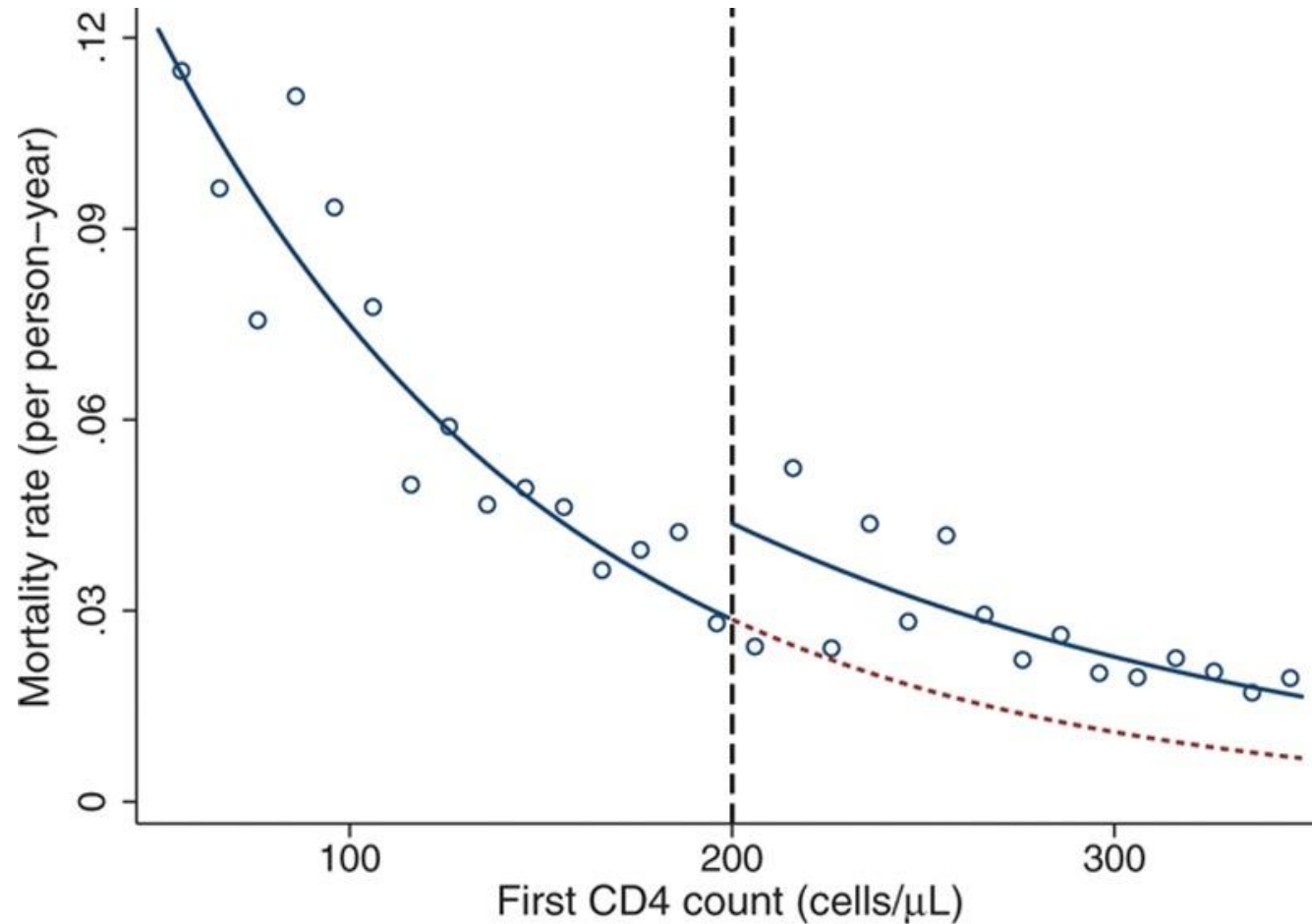J Health Econ 2015;39:289-302

Birth weight and intensive care in Norway

Probability of getting intensive care by birth weight. 1500g = "Very low birth weight"
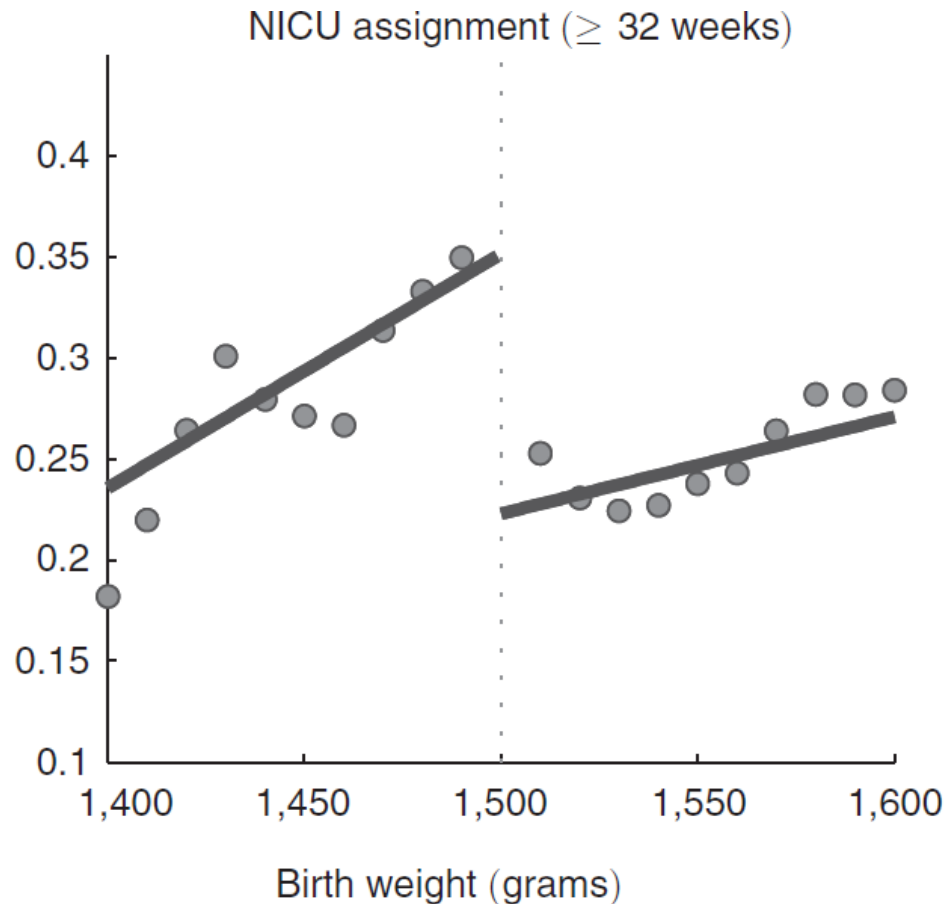
Infant mortality by birth weight
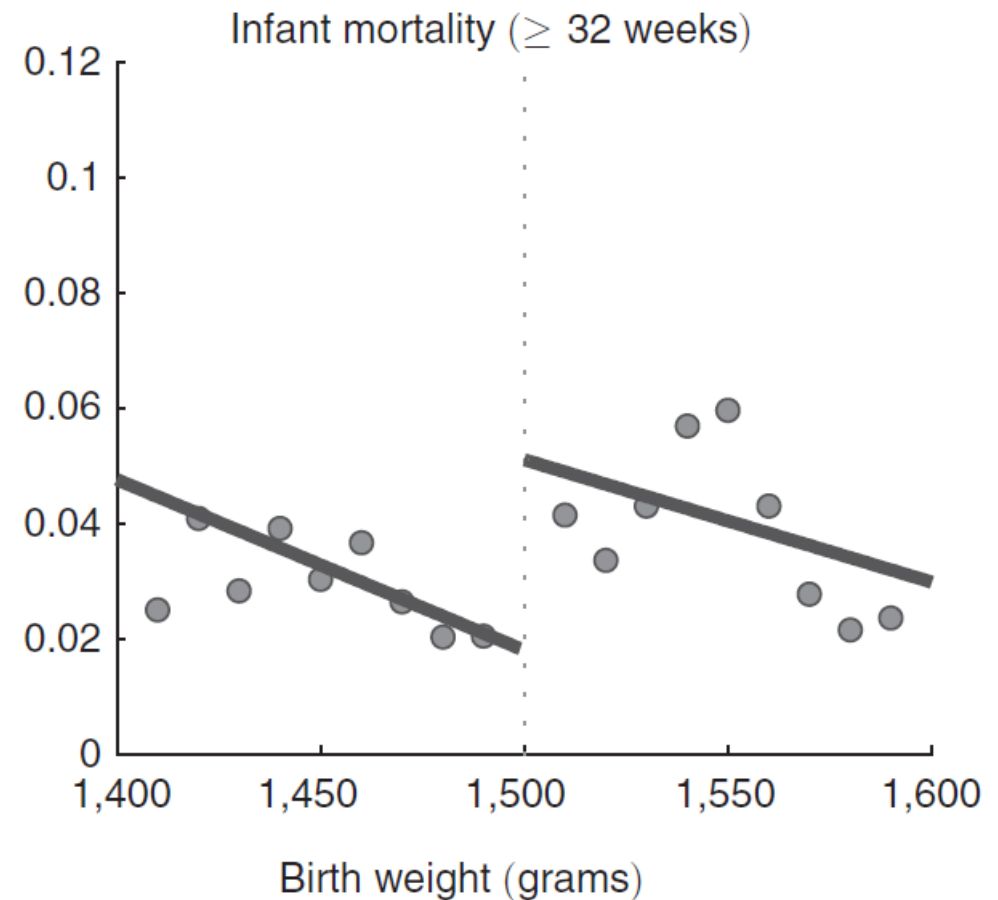
Bias-precision trade-off

- Low bias only close to cut-off
- Inference based only on those very close to cut-off give imprecise estimates and low power (depending on data)
- Local regression better
- Expanding window (include individuals further away from cut-off) => increased power but higher risk of bias
- Try different window sizes and report all results
- Small discontinuity in treatment probability gives little power (the Danish study?)
- Adjusting for covariates can increase power (as in RCTs)
- Functional form assumptions

Concluding comments

- Many treatment decisions in medicine are based on more or less arbitrary cut-offs. Suggests that RDDs can be used more often.

- Studies comparing RDDs to RCTs show that they give comparable estimates of treatment effects, but that RDDs has lower power

van Leeuwen N et al. "Regression discontinuity was a valid design for dichotomous outcomes in three randomized trials." J Clin Epidemiol. 2018 Feb 24. pii: S0895-4356(17)30612-1. doi: 10.1016/j.jclinepi.2018.02.015. [Epub ahead of print]

- As opposed to RCTs, RDDs can be used to study how treatments/interventions work in real life, using observational data

- Alternative when RCTs are unethical or impractical

- Power issues might not be critical with registry data?

Reading materials

- Oldenburg CE, Moscoe E & Bärnighausen T, *Regression Discontinuity for Causal Effect Estimation in Epidemiology*, Curr Epidemiol Rep. 2016; 3: 233–241.

- Moscoe E, Bor J & Bärnighausen T, *Regression discontinuity designs are underutilized in medicine, epidemiology, and public health: a review of current and best practice*, J Clin Epidemiol. 2015 Feb;68(2):122-33.

Applied:

- Bharadwaj P, Løken KV & Neilson C, *Early Life Health Interventions and Academic Achievement*, American Economic Review vol. 103, no. 5, August 2013

Reading materials

- Bernal JL, Cummins S, Gasparrini A, *Interrupted time series regression for the evaluation of public health interventions: a tutorial*, Int J Epidemiol. 2017 Feb 1;46(1):348-355 (Data and code (R and Stata) are available online.)

- Cruz M, Gillen DL, Bender M, Ombao H, *Assessing health care interventions via an interrupted time series model: Study power and design considerations*, Stat Med. 2019 Jan 7. doi: 10.1002/sim.8067. [Epub ahead of print] (Resent paper that suggests some improvements to the standard design.)

Interrupted time series design (ITS)

Interrupted time series (ITS) design

- Close relative of RDD

- Forcing variable is calendar time

- Threshold is *known* date of intervention or policy change

- **Aggregated data** (as opposed to RDD when we observe individual responses)

- Examples

  - change of smoking regulations

  - changed speed limit

  - new advise on sleeping position of infants

Basic idea

Based on time series (evenly spaced sequential observations: continuous, count or binary)

- Trend interrupted by an intervention at a known date
- Hypothetical (counterfactual) scenario: unbroken trend => what we would expect without the intervention
- The effect of the intervention: compare observed and expected trend
- ITS works best when the outcome is expected to change quickly after the intervention

For example: effect of smoking on acute heart problems is OK

effect of smoking on lung cancer is problematic

Requirements

- Need a relatively long time series both before and after intervention
- Have to consider time varying confounders

    - seasonality

    - other changes happening at the same time?

- Sensitive to assumptions of how treatment affects outcome

    - gradual or sudden change?

    - change in level and/or slope of trend?

- Important to decide on this before you see the data (based on existing literature and background knowledge). Otherwise we might be misled by random fluctuations.

Example: smoking ban in Italy

- In January 2005 smoking was banned in all indoor public places
- Did it have an effect on the rate of hospital admissions for acute coronary events (ACEs) in Sicily?

ACE in Sicily, 2002-2006
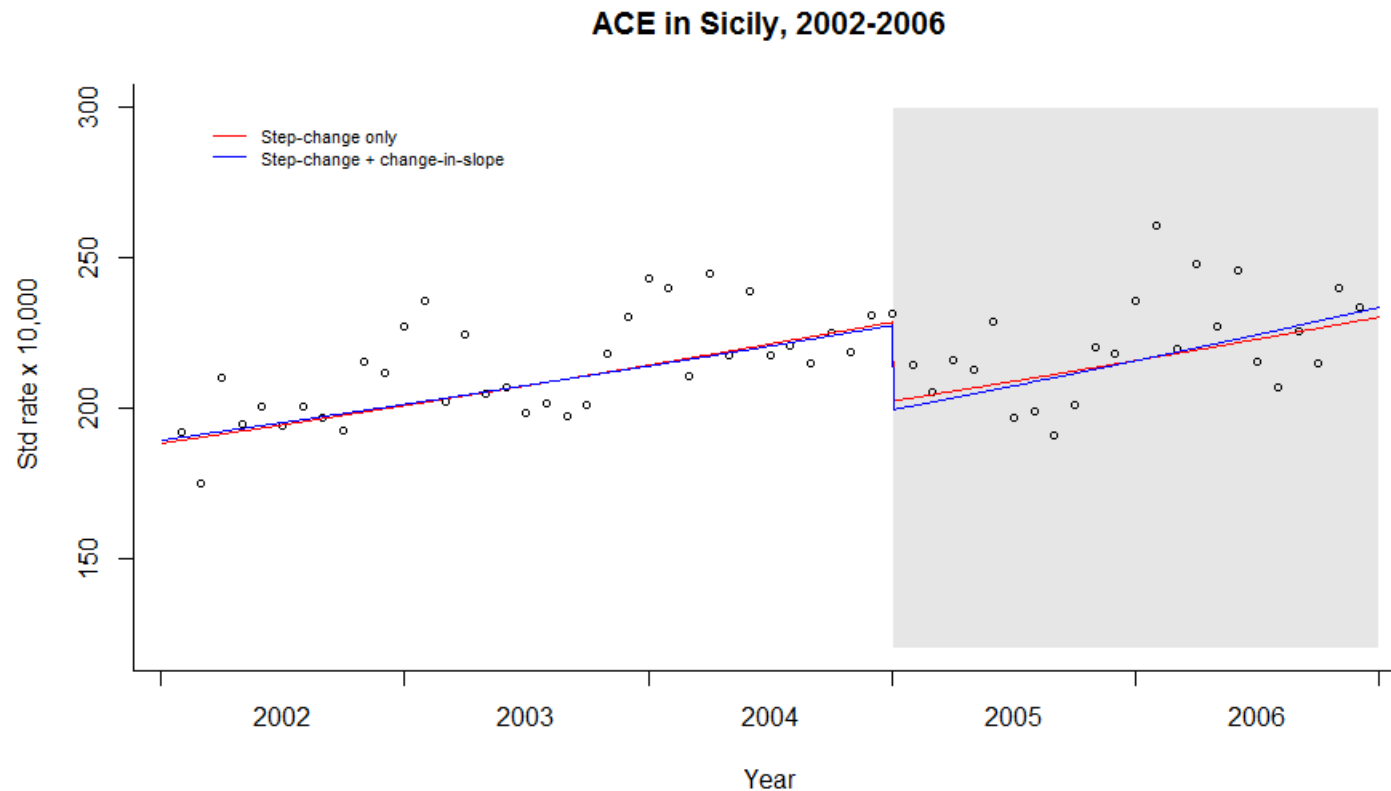
- Drop in level
- Slope unchanged

NB: slopes are adjusted for seasonality

ITS issues

- Key assumption: the only exposure that changes is the intervention
- Strength of ITS is that estimates are unaffected by stable confounders (like socio economic variables or age distribution) that change only slowly over time.
- Time varying confounders can be problematic
  - Seasonality is not that hard to deal with, but
  - often many things change at the same time (policy wise), and
  - people can anticipate changes (ex. welfare reform)
- Linear trend? Functional form assumption
- Autocorrelation (not hard to deal with)

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- Bernal JL, Cummins S, Gasparrini A, *Interrupted time series regression for the evaluation of public health interventions: a tutorial*, Int J Epidemiol. 2017 Feb 1;46(1):348-355 (Data and code (R and Stata) are available online.)

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