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Natural experiments in epidemiology and public health Strengths and limitations

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Overview

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Annu. Rev. Public Health 2017. 38:351–70 The Annua Review of Public Health is online at publicalth.annualreviews.org https://doi.org/10.1146/annurev-publicalth- 031816-044208	Keywords difference-in-differences, propensity score, synthetic controls, regression discontinuity, instrumental variables, near-far matching Abstract	⁸ Department of Medicine, University of Ottawa, Ottawa, Canada Accepted 6 February 2017; Published online 8 July 2017				
heory and methods Using health Counc	natural experiments to evalu interventions: new Medical il guidance	ate population Research	Natural Experiments: An Overview of Methods, Approaches, and Contributions to Public Health Intervention Research			

Peter Craig,¹ Cyrus Cooper,² David Gunnell,³ Sally Haw,⁴ Kenny Lawson,⁵ Sally Macintyre,⁶ David Ogilvie,⁷ Mark Petticrew,⁸ Barney Reeves,⁹ Matt Sutton,¹⁰ Simon Thompson¹¹

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ABSTRACT

Natural experimental studies are often recommended as a way of understanding the health impact of policies and other large scale interventions. Although they have

The Medical Research Council (MRC) has recently published guidance to help researchers The Annual Review of Public Health is online at and users, funders and publishers of research evidence make the best use of natural experi-۲ 1

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Keywords

population health interventions, evaluation methods, causal inference

Abstract

Population health interventions are essential to reduce health inequalities and tackle other public health priorities, but they are not always amenable to experimental manipulation. Natural experiment (NE) approaches are at-

A working definition

Natural experimental studies exploit some event or process that occurs independently of the researcher and divides a population into exposed and unexposed groups

A good natural experimental study depends on some combination of

- A clear understanding of the process(es) determining exposure
- An appropriate 'identification strategy'
- Careful testing of assumptions (e.g. covariate balance tests)
- Exclusion of alternative explanations (e.g. placebo or falsification tests)

Confidence strengthened by

Replication in other study designs, settings, populations, datasets, etc.

Trials, natural experiments and observational studies

- Randomisation offers a very general solution to the problem of selective exposure to treatment ('endogeneity')
 - Allows causal inference with very weak assumptions
 - Not always politically acceptable, ethical, affordable or practically possible
- Selective exposure to treatment is the central problem for observational studies, rarely perfectly solved
- What makes natural experiments special?
 - 'as if randomisation'
 - Adjustment for 'unobserved confounders'

Other definitions

1. 'As-if' randomisation

'[I]n a valid natural experiment, we should find that potential confounders are balanced across the treatment and control group, just as they would be in expectation in a true experiment ... because the process of treatment assignment itself mimics a random process.' (Dunning T. 2012. *Natural experiments in the social sciences. A design based approach*. Cambridge, CUP)

2. Control for unobserved confounders, by

- 'Real life randomisation'
- Instrumental variables
- Regression discontinuity
- Difference in differences
- Fixed effects
- Interrupted time series

Advantages of natural experiments

- Can (sometimes) be implemented when trials are
 - Impractical (e.g. national policy changes, legislation, etc.)
 - Politically unacceptable (e.g. as above)
 - Unethical (e.g. to assess wider outcomes of health interventions, health outcomes of social interventions, or long term outcomes)
- May (sometimes) have higher internal or external validity
 - Avoid artificiality (e.g. in selection of study sites, delivery of intervention, scale/coverage of the intervention)
 - Avoid threats to validity specific to randomised trials (e.g. confounding of intervention by trial procedures to maximise compliance and/or follow-up)
- May (sometimes) be quicker and cheaper
 - Can be conducted retrospectively
 - Often use routinely collected data

Trials and natural experiments – an example



Suicide rates in Sri Lanka 1880-2005

Prevention of suicide with regulations aimed at restricting access to highly hazardous pesticides: a systematic review of the international evidence

David Gunnell*, Duleeka Knipe*, Shu-Sen Chang, Melissa Pearson, Flemming Konradsen, Won Jin Lee, Michael Eddleston

Summary

Background Pesticide self-poisoning accounts for 14-20% of suicides worldwide. Regulation aimed at restricting Lancet Glob Health 2017 access to pesticides or banning highly hazardous pesticides is one approach to reducing these deaths. We systematically 5:e1026-37 reviewed the evidence of the effectiveness of pesticide regulation in reducing the incidence of pesticide suicides and Published Online August 11, 2017 overall suicides.

http://dx.doi.org/10.1016/

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Effectiveness of household lockable pesticide storage to $\mathcal{M} \in \mathbb{C}$ reduce pesticide self-poisoning in rural Asia: a community-based, cluster-randomised controlled trial

Melissa Pearson, Chris Metcalfe, Shaluka Jayamanne, David Gunnell, Manjula Weerasinghe, Ravi Pieris, Chamil Priyadarshana, Duleeka W Knipe, oa Keith Hawton, Andrew H Dawson, Palitha Bandara, Dhammika deSilva, Indika Gawarammana, Michael Eddleston, Flemming Konradsen

Summary

Background Agricultural pesticide self-poisoning is a major public health problem in rural Asia. The use of safer Lancet 2017; 390:1863-72 household pesticide storage has been promoted to prevent deaths, but there is no evidence of effectiveness. We aimed Published Online to test the effectiveness of lockable household containers for prevention of pesticide self-poisoning. August 11, 2017

- Small pilot studies were promising
- Lockable storage for pesticides widely promoted by industry and international agencies
- Large well-designed trial with long follow-up showed no effect on incidence of self poisoning

Limitations of natural experiments

- Difficulty in finding suitable instruments, controls, cutoffs, etc.
- Quality, coverage and accessibility of routinely collected data may be problematic
- Effects (especially 'by products' such as health effects of social interventions) may be relatively small
- Thorough testing of assumptions, exclusion of alternative explanations, etc., complicates analysis and presentation of findings

An example: welfare reform and lone mothers' mental health in the UK

- Age of youngest child at which lone parents are expected to seek work as a condition of receiving income-related benefits has been reduced in steps from 16 to 5
- Policy is expected to improve health by increasing employment and incomes among lone parents
- Data drawn from Understanding Society, a large scale longitudinal survey of UK households, interviewed at yearly intervals
- Primary outcome measure: mental health subscale of SF12 (physical health subscale and general health also assessed)
- Changes in health among lone parents newly exposed to conditionality compared with changes among lone parents who remain unexposed, or who were continuously exposed

Effect of change in age cut-off from 7 to 5



Analysis

 Difference-in-difference analysis (linear regression) with clustering of observations

$$Y_{it} = \alpha + \beta_1 Int_i + \beta_2 follow_i + \beta_3 Age_i + \beta_4 Kids_i + \beta_5 Education_i + \beta_6 follow_i^*Int_i + \varepsilon_{it}$$

- Inverse probability weights to address attrition
- Multiple imputation with chained equations (20 rounds) to address missing covariates

Age cut-off reduced from 7 to 5 years

	Model 1	95% CI	Ρ	Model 2	95% CI	Р
Mental health						
Compared to CG1	-1.41	-4.10, 1.28	0.303	-1.39	-4.08, 1.29	0.307
Compared to CG2	-2.30	-4.58, -0.02	0.048	-2.29	-4.57, 0.00	0.050
Physical health						
Compared to CG1	-0.03	-2.17, 2.12	0.980	-0.04	-2.19, 2.10	0.970
Compared to CG2	0.31	-1.46, 2.09	0.729	0.24	-1.55, 2.04	0.790
Self-rated health						
Compared to CG1	0.05	-0.17, 0.27	0.658	0.05	-0.17, 0.27	0.667
Compared to CG2	0.11	-0.08, 0.29	0.258	0.11	-0.07, 0.30	0.223

CG1: Remained unexposed Model 1: Unadjusted CG2: Already exposed

Model 2: Adjusted for maternal age, education and no of kids

Age cut-off reduced from 10 to 7 years

	Model 1	95% CI	Ρ	Model 2	95% CI	Р
Mental health						
Compared to CG1	-2.47	-5.49, 0.55	0.108	-2.45	-5.48, 0.57	0.111
Compared to CG2	-1.10	-3.83, 1.62	0.425	-1.28	-4.00, 1.45	0.357
Physical health						
Compared to CG1	0.63	-1.79, 3.04	0.609	0.65	-1.76, 3.05	0.594
Compared to CG2	-0.48	-2.49, 1.53	0.638	-0.48	-2.50, 1.54	0.642
Self-rated health						
Compared to CG1	0.03	-0.19, 0.25	0.798	0.03	-0.19, 0.25	0.792
Compared to CG2	0.10	-0.10, 0.31	0.338	0.11	-0.10, 0.32	0.297

CG1: Remained unexposed Model 1: Unadjusted CG2: Already exposed

Model 2: Adjusted for maternal age, education and no of kids

Pooled results for both changes in age cut-off

	Model 1	95% CI	Р	Model 2	95% CI	Р
Mental health						
Compared to CG1	-2.13	-4.17, -0.09	0.040	-2.13	-4.17, -0.10	0.040
Compared to CG2	-2.12	-3.96, -0.28	0.024	-2.21	-4.13, -0.30	0.024
Physical health						
Compared to CG1	0.41	-1.25, 2.07	0.628	0.42	-1.23, 2.07	0.614
Compared to CG2	-0.03	-1.44, 1.38	0.971	-0.17	-1.65, 1.32	0.825
Self-rated health						
Compared to CG1	0.04	-0.11, 0.20	0.579	0.04	-0.11, 0.20	0.578
Compared to CG2	0.10	-0.04	0.169	0.13	-0.01, 0.27	0.071

CG1: Remained unexposed Model 1: Unadjusted CG2: Already exposed

Model 2: Adjusted for maternal age, education and no of kids

Robustness checks

Common trends



- Alternative model specifications, e.g.
 - Included lone fathers
 - Excluded mothers with child aged <1
 - Narrowed age range of controls
 - Modelled covariates as outcomes
 - Etc., etc.

Conclusions

- Exposure to the new job seeking requirements may lead to poorer mental health for lone mothers, though the effects are small at an individual level, and further work is needed to determine whether they are real, and whether they persist
- Conclusion is strengthened by
 - Clearcut change in exposure, easy to model in survey data
 - Consistency of effects for both changes in age cutoff and both sets of comparisons
 - Specificity of effects (no effect on physical or self-assessed health)
 - Robustness checks
- Could be strengthened further by
 - Longer follow-up
 - Replication in other (preferably larger) datasets

Reflections

- The value of natural experimental approaches lies in widening the range of interventions that can usefully be evaluated
- The only distinguishing feature of such approaches is the use of some assignment rule (a process or event) that divides a population into exposed and unexposed units
- Rules such as 'as-if randomisation' or control for unobserved confounders do not distinguish consistently between weak and strong designs
- Strong natural experimental studies have a range of strengths rather than a single defining characteristic; minimising bias is not the only goal of study design
- We should try to avoid the temptation of defending one method by downgrading others

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