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Thinking Outside the Box of RCT's: What Additional Rigorous Options are There?

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The Way Forward for ACF Research with American Indians and Alaska Natives

April 18, 2014

Acknowledgements

Center for Alaska Native Health Research (CANHR)

- Jerry Mohatt (d.)
- Jim Allen
- Carlotta Fok
- Stacy Rasmus
- Bill Charles
- People Awakening Team
- "Small Sample Conference"

Families and Communities Research Group

- Patrick Tolan
- Deborah Gorman-Smith
- Michael Schoeny

Chicago Center for Youth Violence Prevention

Rush University College of Nursing

Does banging pans cause elephants to flee?

- Charley has an effect, but no *counterfactual.*
- He does not know what would have happened if he had not banged the pans.
- The *counterfactual* is the same people, place and time but without Charley banging pans.
- Research methods exist to provide estimates of the *counterfactual*.
- The *counterfactual* is essential for determining whether our interventions have caused the effects we observe.

Cause and Effect: Other Views

- The law of causality, I believe, like much that passes muster among philosophers, is a relic of a bygone age, surviving, like the monarchy, only because it is erroneously supposed to do no harm. (Russell, 1913, p. 1).
- A “causal line,” as I wish to define the term, is a temporal series of events so related that, given some of them, something can be inferred about the others whatever may be happening elsewhere. (Russell, 1948, p. 459).

Cause and Effect

- Neyman-Rubin Causal Model
  - Let Y(0) be an outcome in the absence of treatment
  - Let Y(1) be the same outcome with treatment
  - Effect of the treatment = Y(1) – Y (0)
- The problem of estimating cause and effect is a problem of missing information.
  - Y(0) is missing for those who receive treatment
  - Y(1) is missing for those who do not receive treatment

Counterfactual

- The factual is a situation with certain actors at a certain time with intervention present.
- The counterfactual is exactly the same situation and actors at the same time absent the intervention.
- All research methods approximate the counterfactual
- All research methods have strengths and weaknesses for approximating the counterfactual.

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Threats to Internal Validity:

Why a study may fail to approximate the counterfactual

(Campbell & Stanley, 1967; Shadish, Cook and Campbell, 2002)

1. Ambiguous temporal precedence
2. Selection
3. History
4. Maturation
5. Regression
6. Attrition
7. Testing
8. Instrumentation
9. Interactive Effects

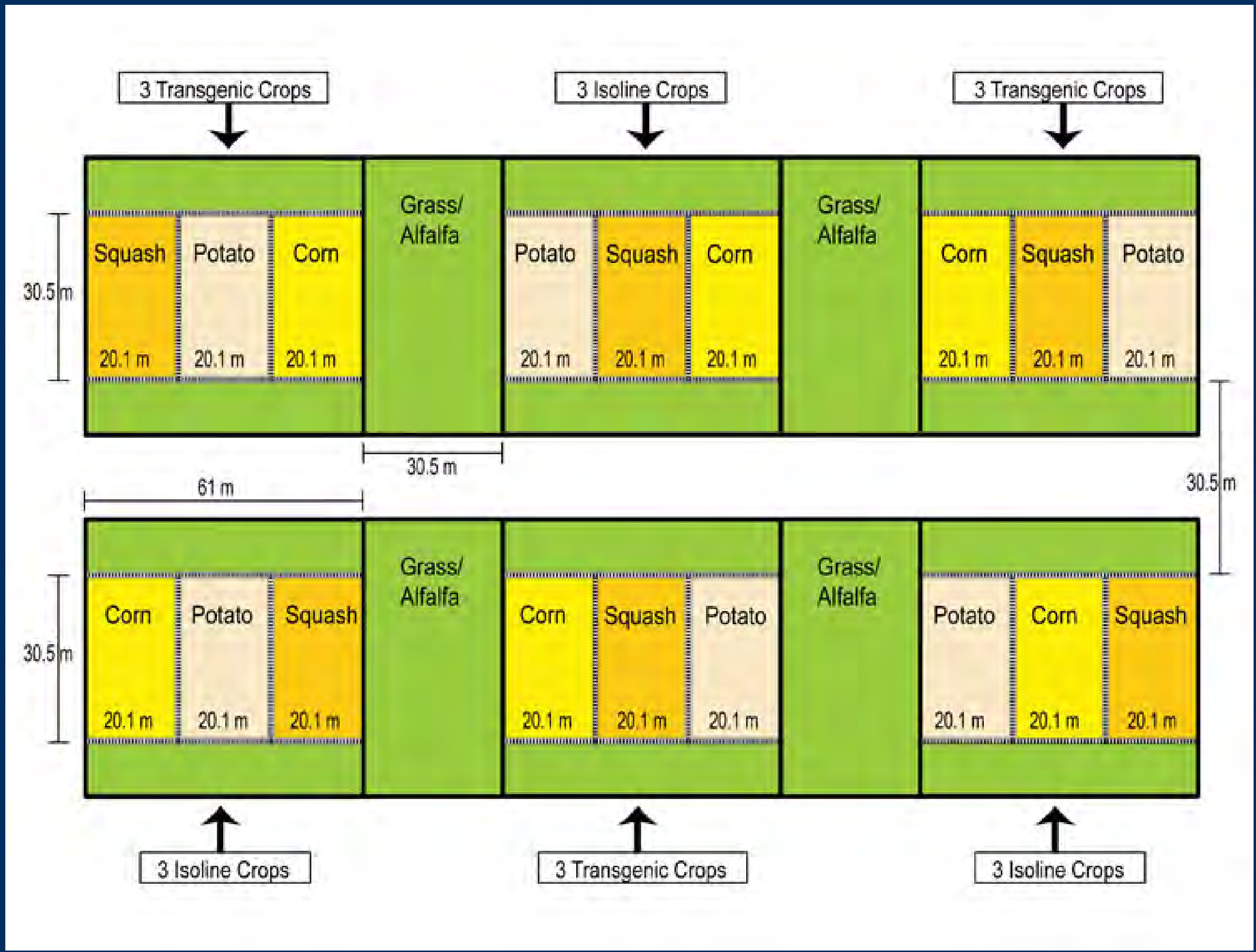
Examining the Box:

How RCT approximates the counterfactual

- Sampling representative of a defined population
- Random assignment
- Control conditions
- Blinding of participants and investigators.

Randomness and the Counterfactual

- Randomness in selection and assignment assumes interchangeable units.
  - Exclusion criteria
- Randomness in selection and assignment assumes stable units.
  - ITT
- Randomness in selection and assignment assumes consistent environments
  - Split plot, HLM



- **Figure 1.** Split-plot experimental design consisting of 3 replicates of two genotypes: transgenic and isoline. Main plots were split among 3 crops consisting of sweet corn, potatoes, and winter squash. Transgenic cultivars targeted Lepidoptera in corn, Coleoptera in potato and aphid-transmitted viruses in squash.

Blinding and the Counterfactual

- If research participants do not know what treatment they are receiving, there is less likelihood of biased reports and ratings.
- If assessors do not know what condition they are assessing, there is lower likelihood of "halo" effects.

RCT is a good design in some circumstances.

- Best when
  - Condition can be hidden from subjects
  - Condition can be hidden from assessors
  - Condition can be hidden from investigators
  - Individuals can be randomly selected from a pure population
  - Assignment procedures are truly random
- Has problems if
  - Conditions cannot be hidden
  - People move
  - People may not cooperate with treatment
  - Naïve hypotheses can affect measures
  - Focal issue does not occur in isolation

Randomized Controlled Trial

Threat to internal validity	Performance
Ambiguous temporal precedence	+ Intervention precedes outcome change
Selection	? Recruits may opt out when assigned
History	+ affects I and C equally
Maturation	+ affects I and C equally
Regression	+ affects I and C equally
Attrition	? Differential attrition of I and C
Testing	+ affects I and C equally
Instrumentation	+ does not change between I and C
Interactive Effects	? cooperation with treatment

Thinking Outside the Box: Three Alternative Designs

1. Roll-out Designs (DWLD and SWD)
2. Interrupted Time Series Design (ITSD)
3. Regression Point Displacement Design (RPDD)

1. Roll-out Designs

- Logistics may prohibit starting all communities, schools, settings at the same time.
- Power can be increased by randomizing start times as well as settings (Brown et al., 2006, 2007).

Time frame		Standard wait-listed design		Full dynamic wait-listed design	
Period	Time block	Trained	Not trained	Trained	Not trained
1	1	16	16	4	28
	2			8	24
	3			12	20
	4			16	16
2	1	32	0	20	12
	2			24	8
	3			28	4
	4			32	0

Dynamic Waitlisted Design

- Works well for time-limited interventions where maintenance of effects is a concern.
- Power is increased because every community serves as its own control group.
- Analysis: Mixed effects regression model with random effect for community and fixed effects for time, period (observation, intervention, followup) and interactions.

Dynamic Waitlisted Design

		Time					
	Community	0	1	2	3	4	5
Randomize	1	O					
	2	O					
	3	O					
	4	O					
	5	O					

X=intervention, O=observation

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Dynamic Waitlisted Design

		Time					
	Community	0	1	2	3	4	5
Randomize	1	O	O				
	2	O	X				
	3	O	O				
	4	O	O				
	5	O	O				

X=intervention + observation, O=observation only

Dynamic Waitlisted Design

		Time					
	Community	0	1	2	3	4	5
Randomize	1	O	O	O			
	2	O	X	O			
	3	O	O	O			
	4	O	O	X			
	5	O	O	O			

X=intervention + observation, O=observation only

Dynamic Waitlisted Design

		Time					
	Community	0	1	2	3	4	5
Randomize	1	O	O	O	X		
	2	O	X	O	O		
	3	O	O	O	O		
	4	O	O	X	O		
	5	O	O	O	O		

X=intervention + observation, O=observation only

Dynamic Waitlisted Design

		Time					
	Community	0	1	2	3	4	5
Randomize	1	O	O	O	X	O	
	2	O	X	O	O	O	
	3	O	O	O	O	O	
	4	O	O	X	O	O	
	5	O	O	O	O	X	

X=intervention + observation, O=observation only

Dynamic Waitlisted Design

		Time					
	Community	0	1	2	3	4	5
Randomize	1	O	O	O	X	O	O
	2	O	X	O	O	O	O
	3	O	O	O	O	O	X
	4	O	O	X	O	O	O
	5	O	O	O	O	X	O

X=intervention + observation, O=observation only

Dynamic Waitlisted Design

Example: QPR Study

- Brown et al., 2006; Wyman et al., 2008
- Gatekeeper training
- 32 north Georgia schools selected
- Standard waitlist design used in the first year
- Training inefficiency led to switch to DWLD
- Poisson mixed effects regression used to detect change in rate of referral for suicidality

Stepped Wedge Design

		Time					
	Community	0	1	2	3	4	5
Randomize	1	O					
	2	O					
	3	O					
	4	O					
	5	O					

X=intervention + observation, O=observation

Stepped Wedge Design

		Time					
	Community	0	1	2	3	4	5
Randomize	1	O	X				
	2	O	O				
	3	O	O				
	4	O	O				
	5	O	O				

X=intervention + observation, O=observation

Stepped Wedge Design

		Time					
	Community	0	1	2	3	4	5
Randomize	1	O	X	X			
	2	O	O	X			
	3	O	O	O			
	4	O	O	O			
	5	O	O	O			

X=intervention + observation, O=observation

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Stepped Wedge Design

		Time					
	Community	0	1	2	3	4	5
Randomize	1	O	X	X	X		
	2	O	O	X	X		
	3	O	O	O	X		
	4	O	O	O	O		
	5	O	O	O	O		

X=intervention + observation, O=observation

Stepped Wedge Design

		Time					
	Community	0	1	2	3	4	5
Randomize	1	O	X	X	X	X	
	2	O	O	X	X	X	
	3	O	O	O	X	X	
	4	O	O	O	O	X	
	5	O	O	O	O	O	

X=intervention + observation, O=observation

Stepped Wedge Design

		Time					
	Community	0	1	2	3	4	5
Randomize	1	O	X	X	X	X	X
	2	O	O	X	X	X	X
	3	O	O	O	X	X	X
	4	O	O	O	O	X	X
	5	O	O	O	O	O	X

X=intervention + observation, O=observation

Stepped Wedge Design

- Works well for interventions with anticipated dose effects.
- Like the dynamic waitlisted design, power is increased because every community serves as its own control group.
- Analysis: Mixed effects regression model with random effect for community and fixed effects for time, intervention condition and the interaction.

Stepped Wedge Design

Example:

- Intervention to address outbreak of antibiotic resistant bacteria in long-term care (LTC)
- Four LTC hospitals randomly assigned to starting times over a 6 month rollout period
- 42 months of assessment per facility
- 18-20 months of baseline before intervention*

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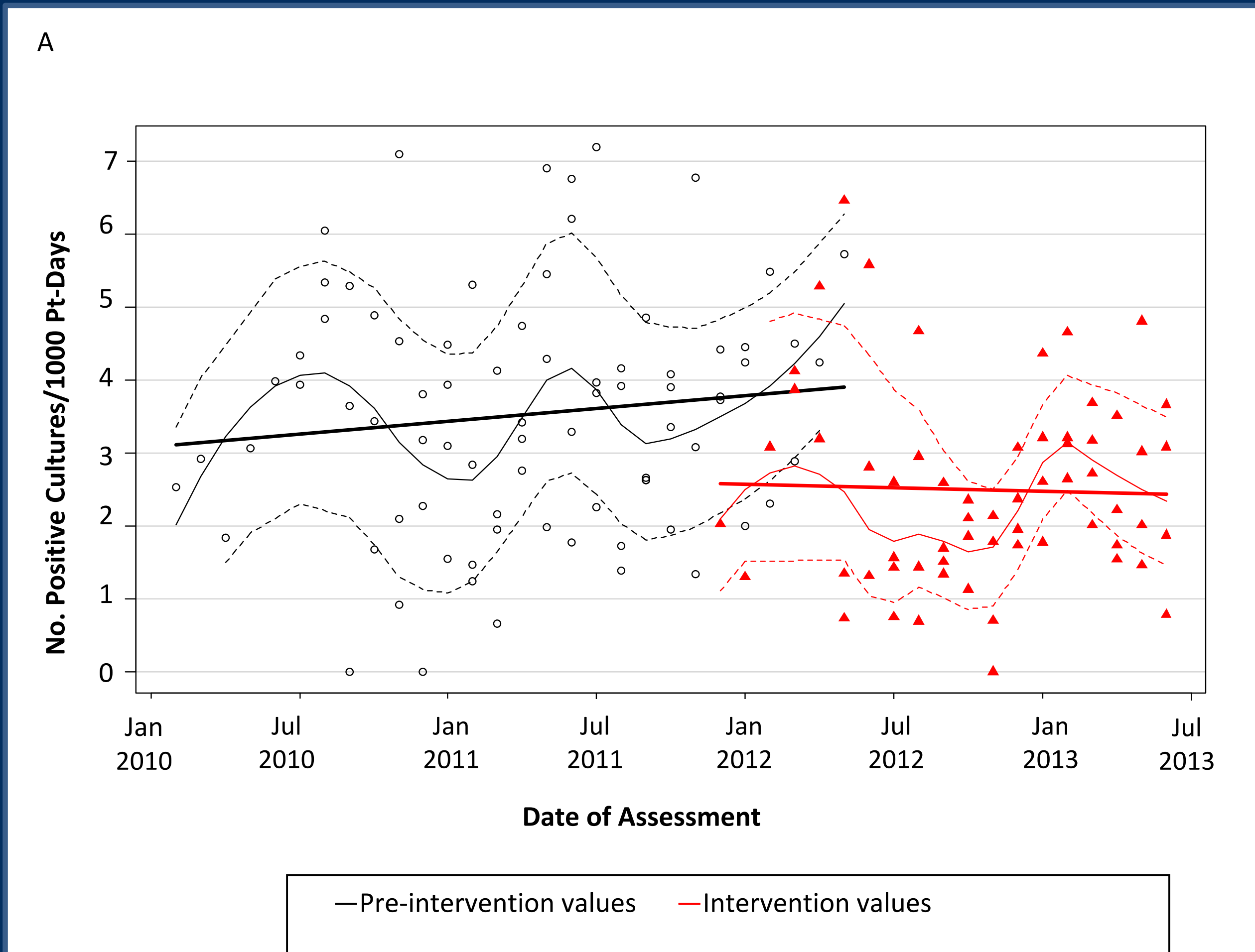
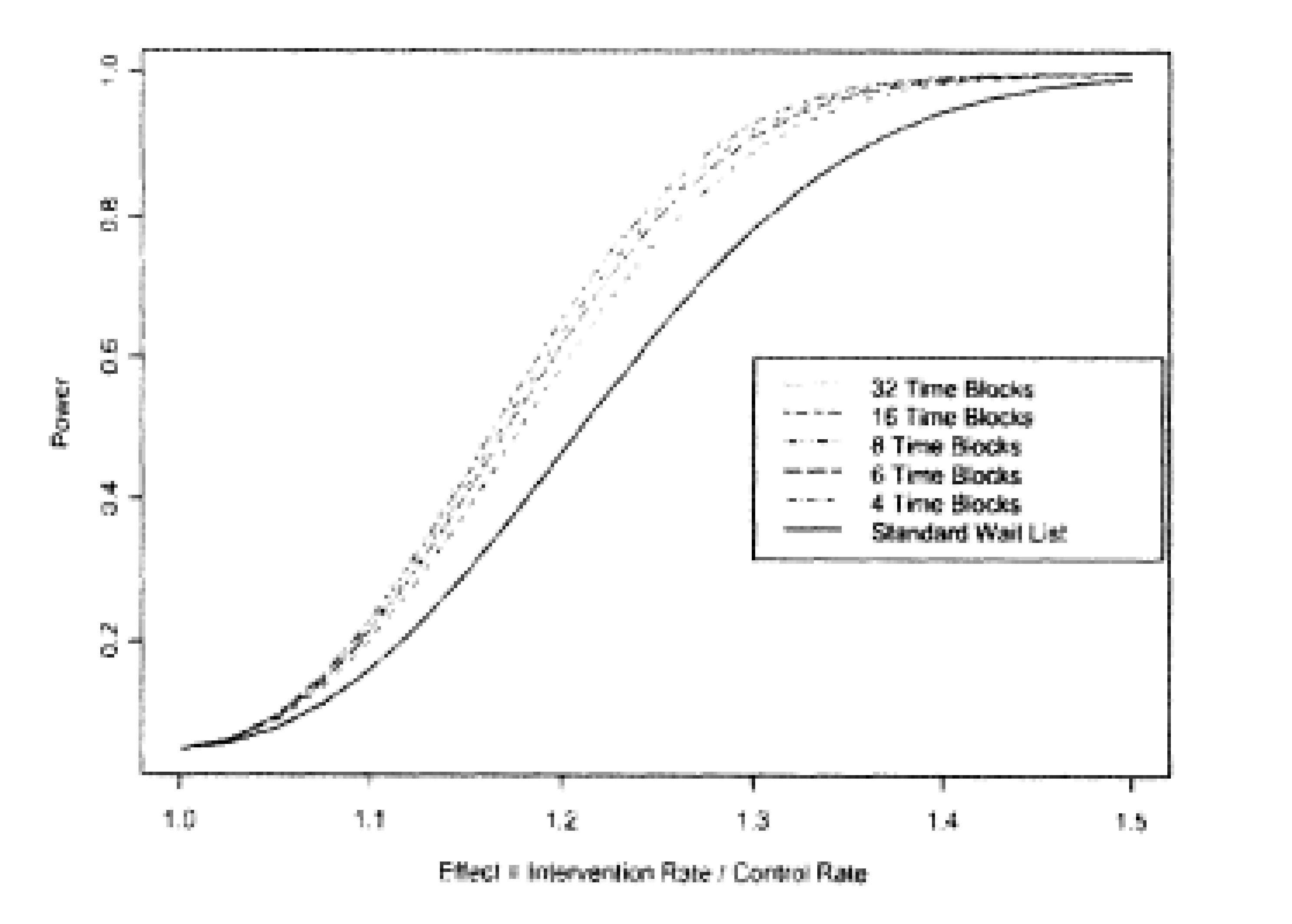
Stepped Wedge Design: Results



Statistical Power for Roll-out Designs



1. Roll-out Designs

Ambiguous temporal precedence	+ Intervention precedes outcome change
Selection	+ Random assignment of start times
History	+ Affects I and C equally
Maturation	+ Affects I and C equally
Regression	+ Affects I and C equally
Attrition	? I or C may not want to wait
Testing	+ Affects I and C equally
Instrumentation	+ Does not change between I and C
Interactive Effects	+ Should affect I and C equally

2. Interrupted Time Series Design

- Sequence of observations interrupted by intervention.
- Observations before intervention establish baseline levels.
- Observations during the intervention measure immediate effects.
- Observations after the intervention ends measure maintenance of effects.

2. Interrupted Time Series Design

0 0 0 0 0 0 0 0 0 0 0

X → → X

Best for interventions with a defined term where maintenance of effects is a concern.

Also works well with no control and only one intervention unit.

Historical events threaten internal validity.

2. Interrupted Time Series Design

Example 1: Impact of Chicago Center for Youth Violence Prevention (CCYVP) on violence in one targeted Chicago community

Outcome: Number of violent crimes per month per police beat

Predictors: Time, period, time*period interaction

Analysis: Poisson linear mixed model with comparison to other communities

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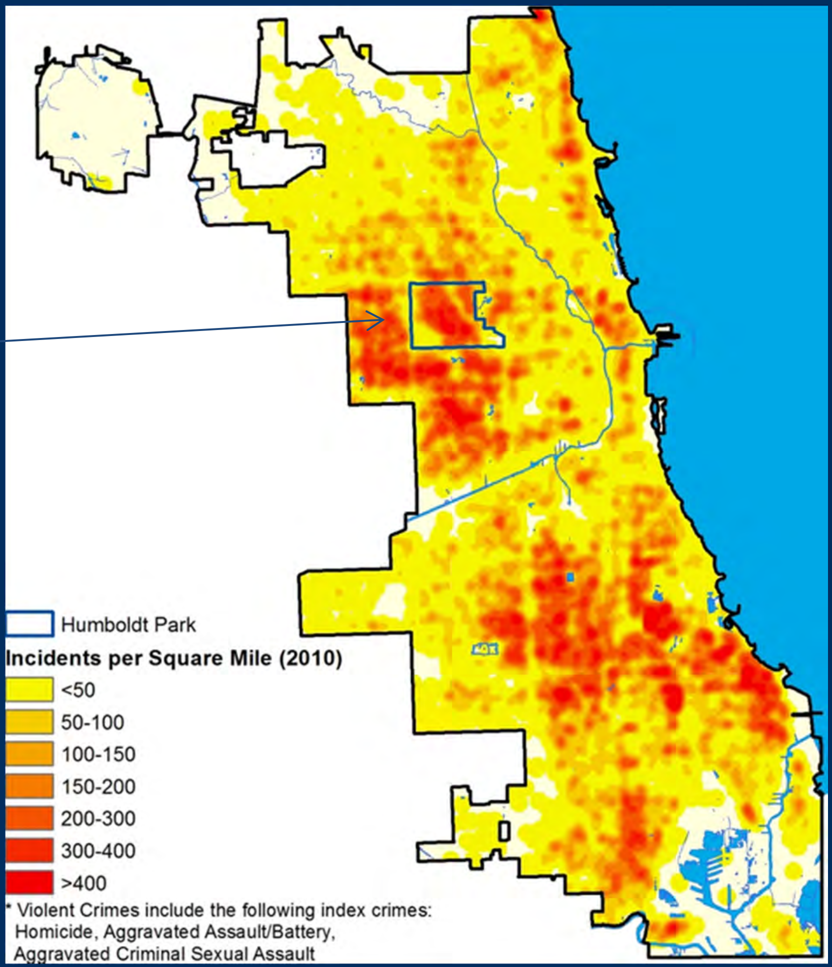
Violent Crime in Chicago 2010

Humboldt Park

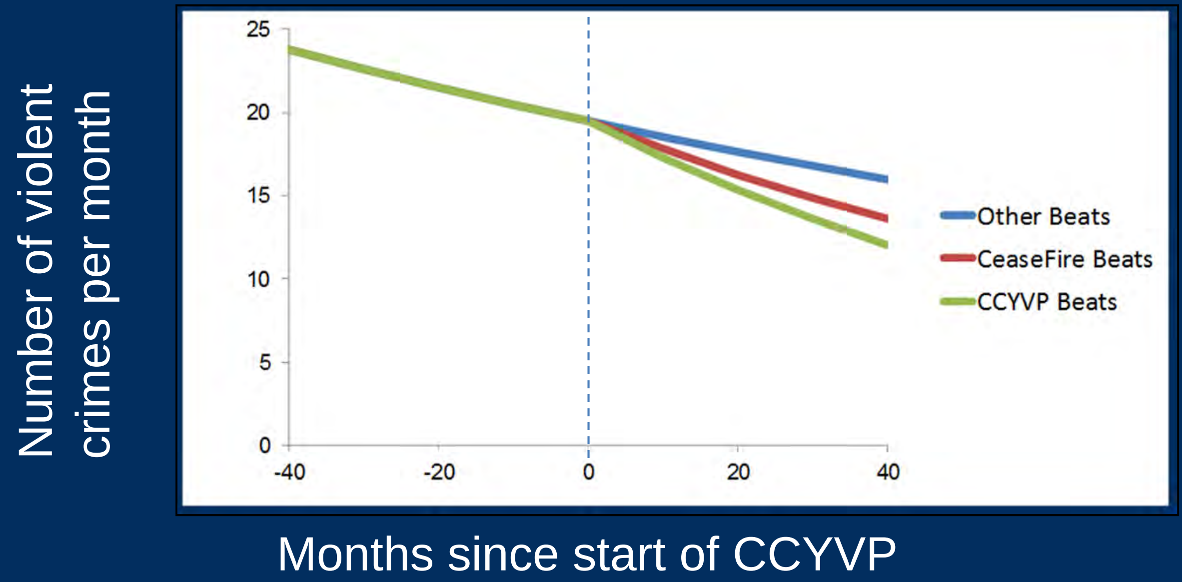


2. Interrupted Time Series Design

3 Years of Intervention

Significant reductions in violent crime

Compared with all other police beats in Chicago, and other police beats where CeaseFire is present



Chicago Police Department
CCYVP: Chicago Center for Youth Violence Prevention

2. Interrupted Time Series Design

Example 2: Impact of a culturally-focused CBPR intervention on 54 Yup'ik Youth from a single community

Outcomes: Reasons for Life and Reflective Processes

Predictors: Time, period, time*period interaction

Analysis: 3 ways of thinking about time

- Intervention dose at each wave
- Chronological time centered when individual began intervention
- Cohort with which the individual began

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2. Interrupted Time Series Design

Example 2: Results

	Estimate	*SE*	*df*	*t*	95% CI Lower	95% CI Upper	*p*	Effect size (*d*)
Reflective Processes								
Dose	0.015	0.008	119	1.96	0.0005	0.030	.05	.35
Dose X Protective	0.001	0.009	119	0.11	-0.017	0.019	.91	.02
Reasons for Life								
Dose	0.012	0.007	120	1.76	-0.001	0.026	.08	.32
Dose X Protective	0.011	0.009	120	1.25	-0.006	0.028	.21	.23

Interrupted Time Series Design

Threat to internal validity	Performance
Ambiguous temporal precedence	+ Baseline precedes intervention
Selection	+ Units are their own controls
History	? Problem if no comparison
Maturation	? Problem if no comparison
Regression	+ Affects baseline and I phases equally
Attrition	+ Units are their own controls
Testing	+ Affects baseline and I phases equally
Instrumentation	+ Does not change between baseline and I
Interactive Effects	? Interaction of testing and intervention

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3. Regression Point Displacement Design

- How to evaluate a CBPR intervention conducted in a single community?

Figure 2. The Yukon-Kuskokwim (Y-K) Delta with YKHC medical facilities marked.

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Use population data to estimate expected values.

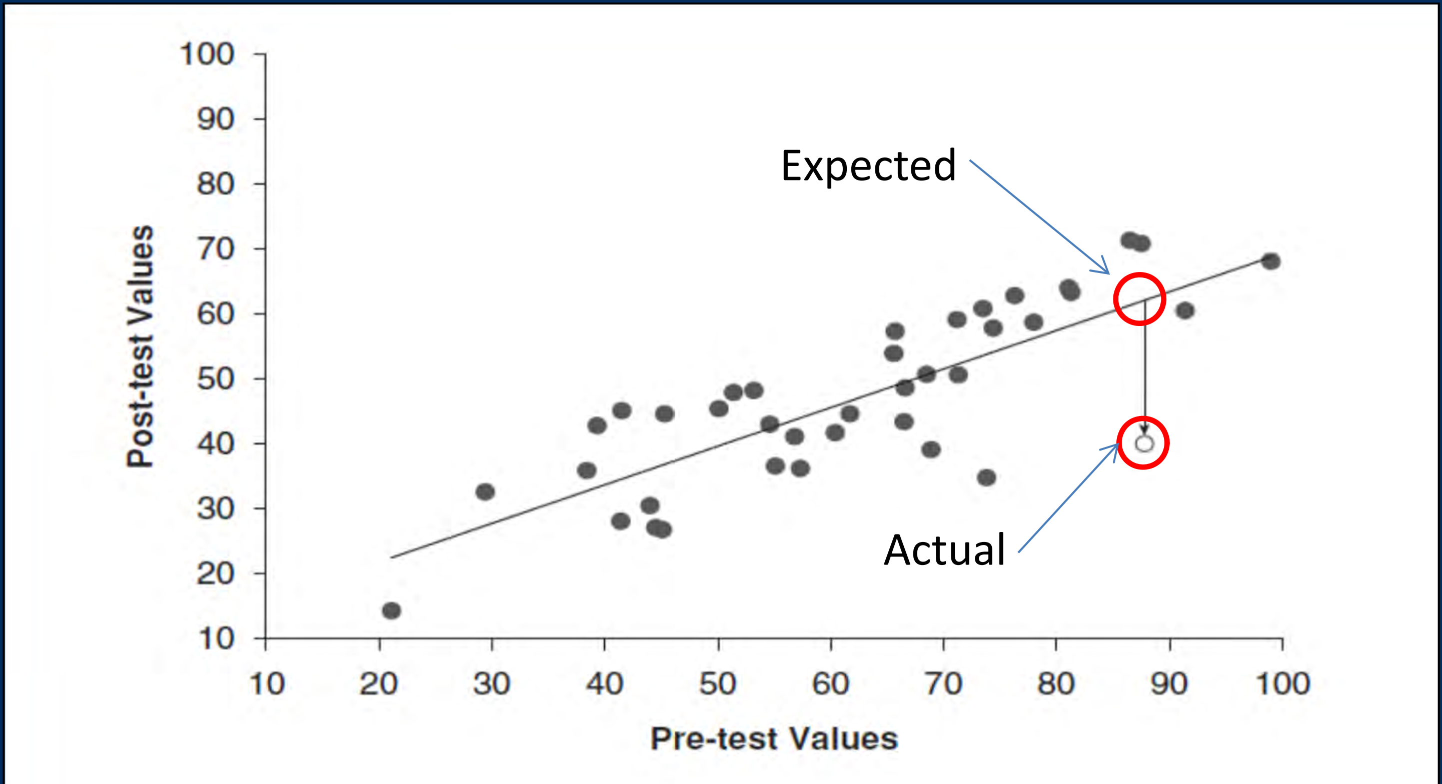

Figure 3. Illustration of the regression point displacement research design (Linden et al., 2006).

3. Regression Point Displacement Design (RPDD)

- Variant of the Regression Discontinuity Design
- Helpful when there is only one community or a few communities receiving intervention.
- Uses archival data on the population from which the intervention communities was drawn.
- Helpful if intervention communities were randomly drawn, but not necessary.
- Propensity scores can be used as covariates adjust for non-randomness of selection.

3. Regression Point Displacement Design (RPDD)

- Requirements
  - Archival measures on population prior to and after intervention period
  - Outcome measure that is stable over time: Correlation > .9 preferred.
  - Outcome measure need not be identical at pretest and posttest
  - Random selection of intervention unit, or
  - Information to predict selection for intervention

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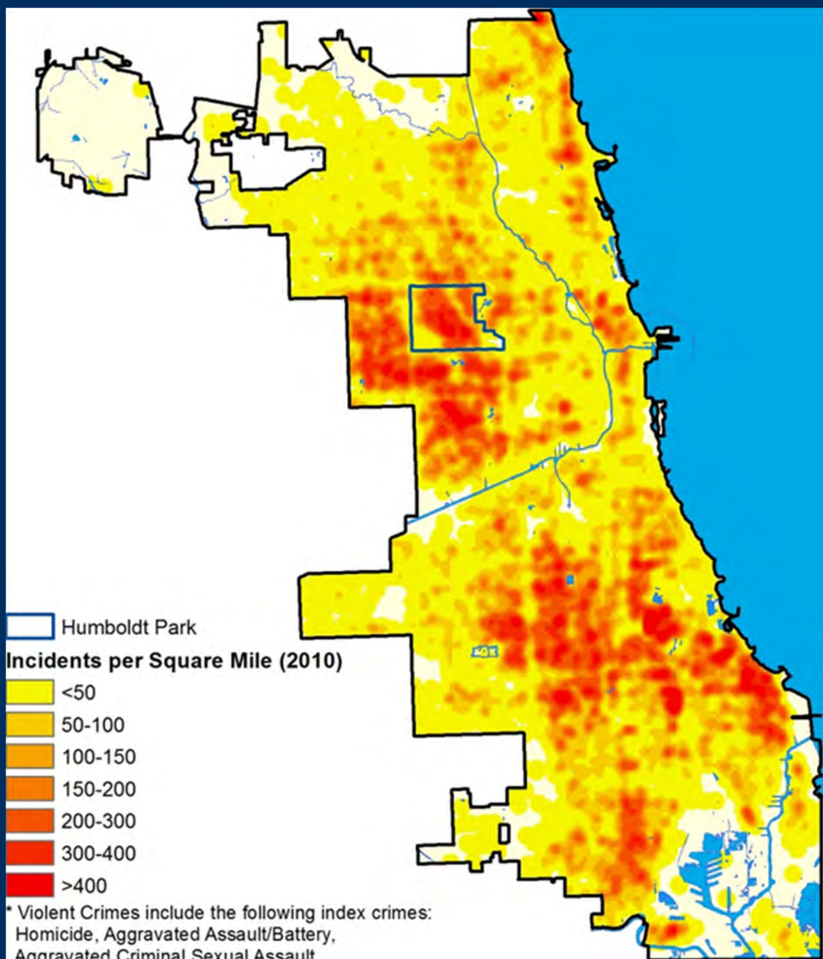
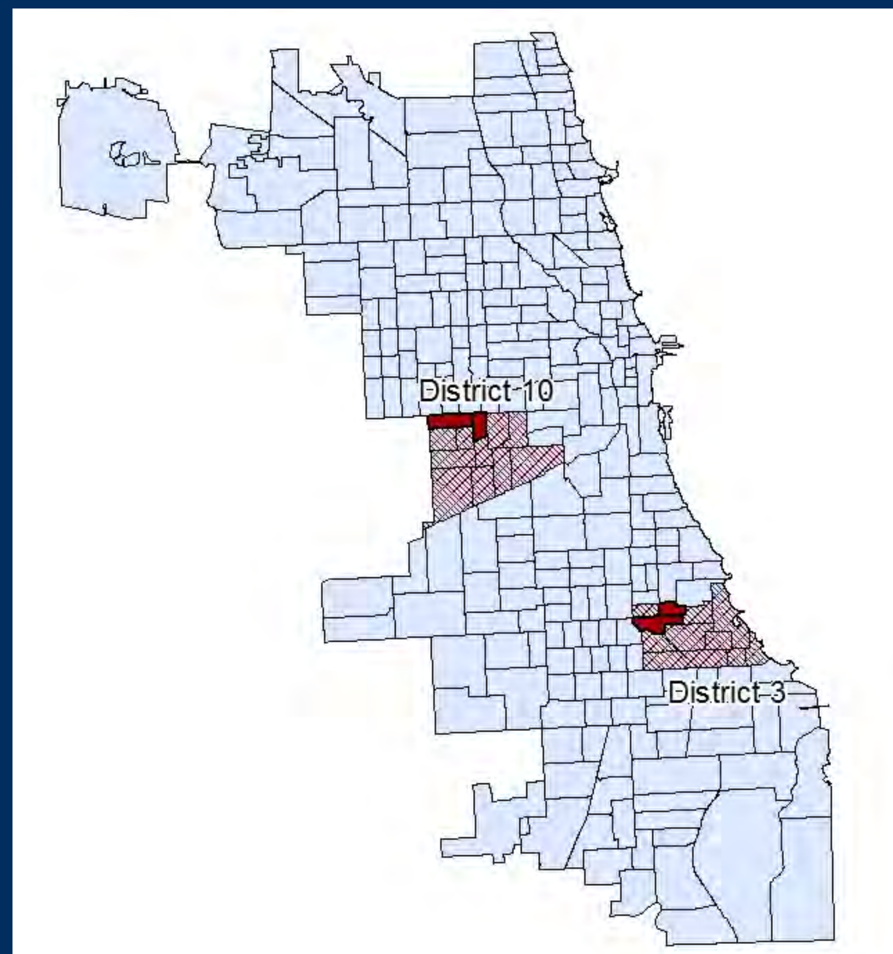
Example: Evaluation of CeaseFire





Example: Evaluation of CeaseFire

- Outreach workers and violence interrupters
- Organized by police districts and beats
- Evaluation of 1 year of CeaseFire in two districts
- 2 of 25 police districts received intervention
- Pre-post correlation for homicide = .91 ($p<.01$)
- Predictors of selection: Crime, poverty, political influence

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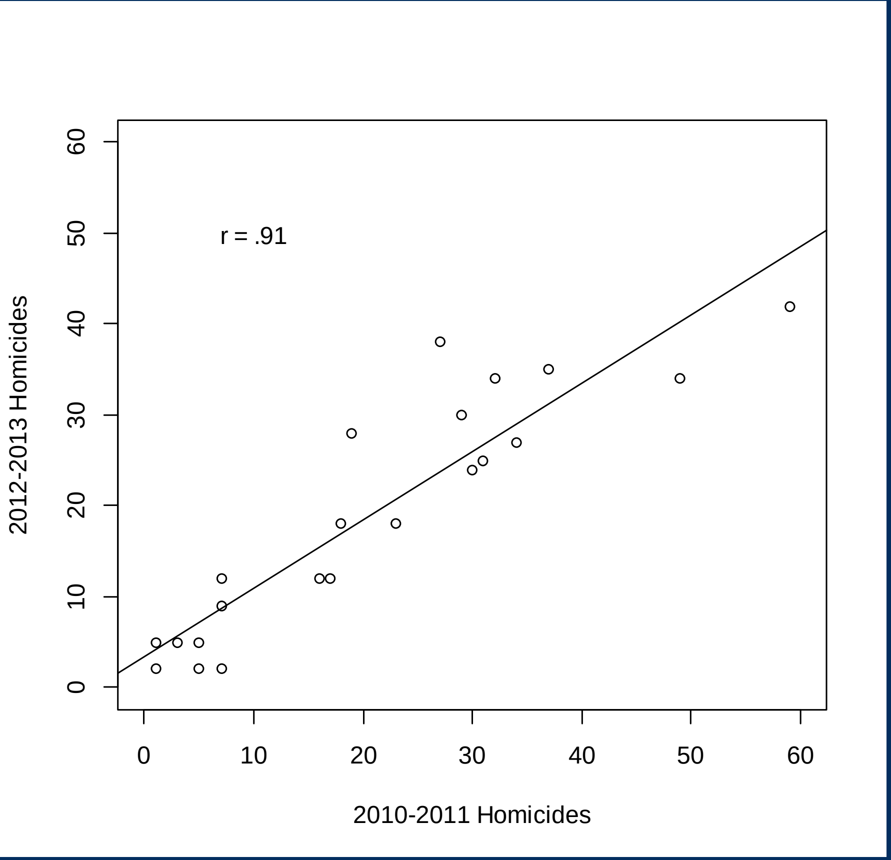
Homicides in Chicago Police Districts



Example: Evaluation of CeaseFire

- Analysis
  1. Logistic regression to predict selection of any police beat for CeaseFire
  2. Regression
     - Outcome: 2012-2013 homicides
     - Predictors
       – 2010-2011 homicides
       – Codes for Districts that received intervention
       – Propensity score for selection from Step 1
       – Overall number of police reports*

Example: Evaluation of CeaseFire

- Results:
  - One city-funded CeaseFire district had significantly higher than expected homicides ($B = .54$, $p < .01$) and the other had significantly lower than expected homicides ($B = .54$, $p < .01$) .
  - There was a difference in CeaseFire tactics between the two districts.

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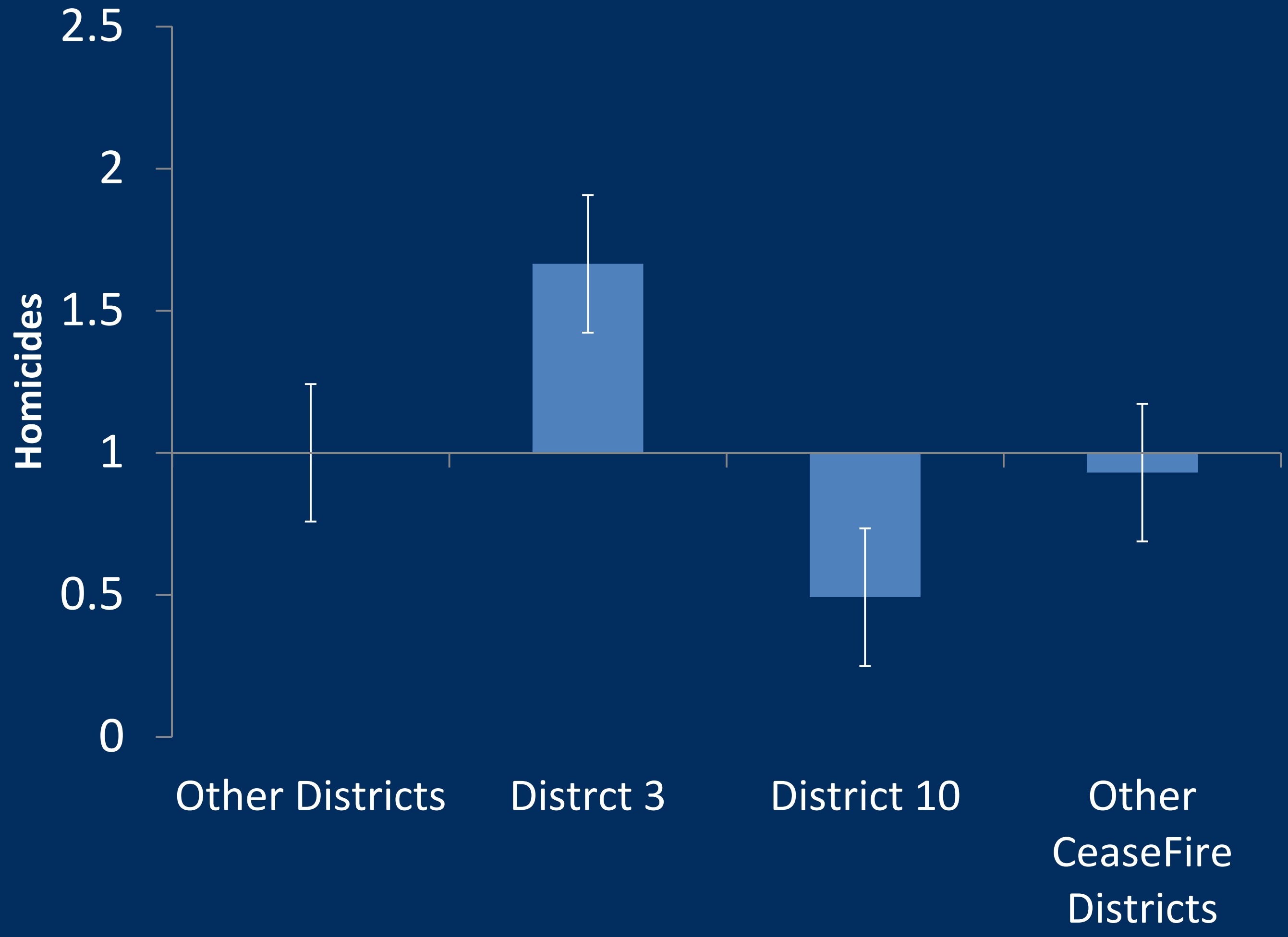
City-funded Districts (1-year of intervention)



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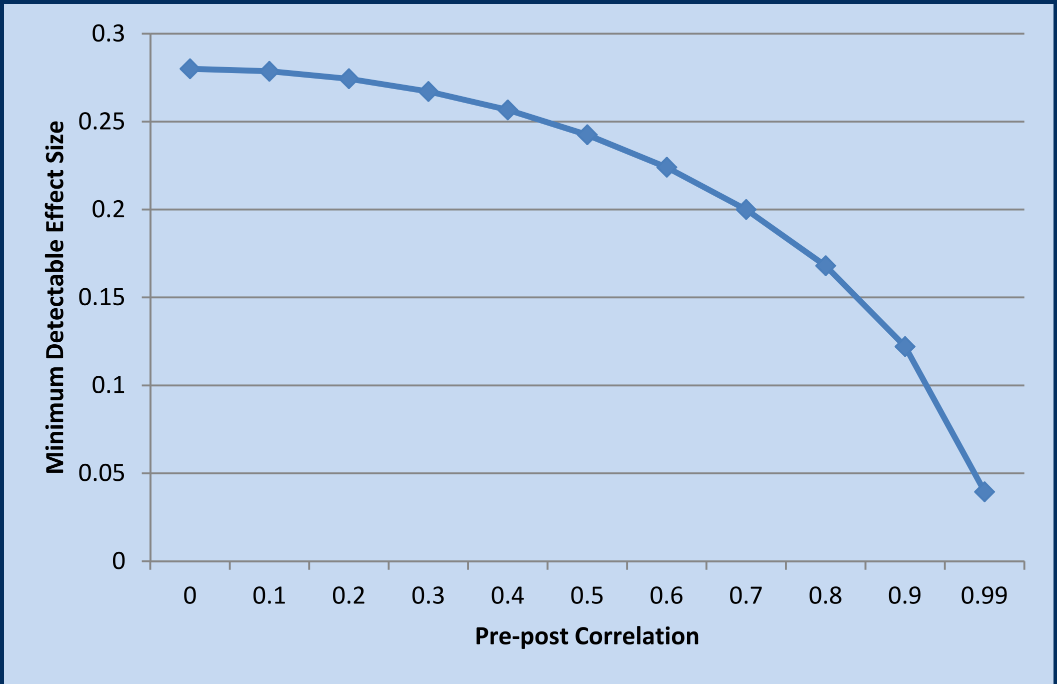
Power for the RPDD

As the pre-post correlation in the population increases, the minimum detectable effect size decreases.



3. Regression Point Displacement Design

Threat to internal validity	Performance
Ambiguous temporal precedence	? Depends on pre-post correlation
Selection	? Selection usually not random
History	+ Applies to entire population
Maturation	+ Applies to entire population
Regression	+ Expected in design
Attrition	? Attrition of Intervention units a problem
Testing	+ Archival records used
Instrumentation	+ Archival records used
Interactive Effects	+ Any that affect archival records

Summary: RCTs and Alternatives

	Ambiguous temporal precedence	Selection	History	Maturation	Regression	Attrition	Testing	Instrumentation	Interactive Effects
RCT	+	?	+	+	+	?	+	+	?
DWLD & SWD	+	+	+	+	+	?	+	+	+
ITSD	+	+	?	?	+	+	+	+	?
RPDD	?	?	+	+	+	?	+	+	+