

Stepped Wedge Design

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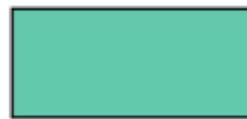


Stepped Wedge Design

Clusters	Time					
	1	2	3	4	5	6
1	Unexposed	Exposed	Exposed	Exposed	Exposed	Exposed
2	Unexposed	Unexposed	Exposed	Exposed	Exposed	Exposed
3	Unexposed	Unexposed	Unexposed	Exposed	Exposed	Exposed
4	Unexposed	Unexposed	Unexposed	Unexposed	Exposed	Exposed
5	Unexposed	Unexposed	Unexposed	Unexposed	Unexposed	Exposed

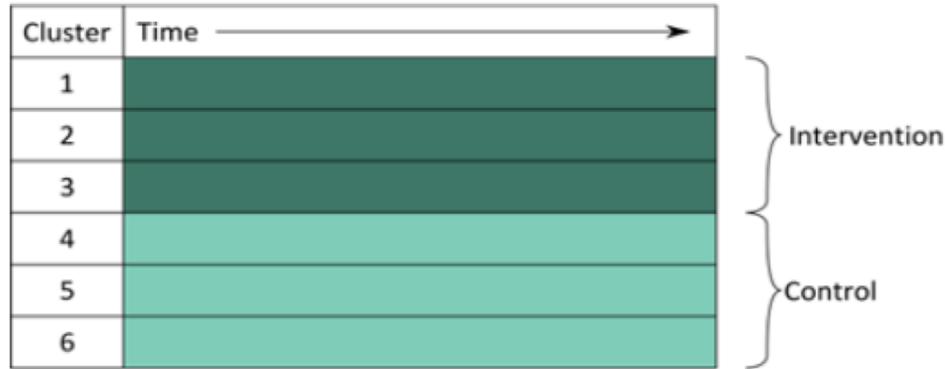


Exposed to intervention

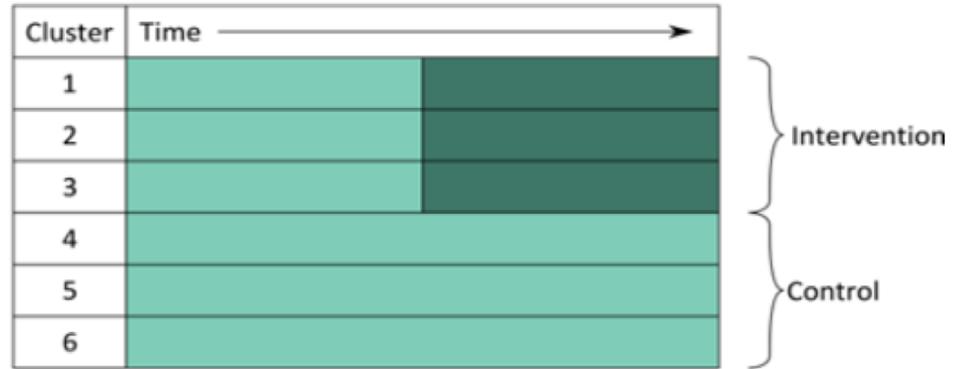


Unexposed to intervention

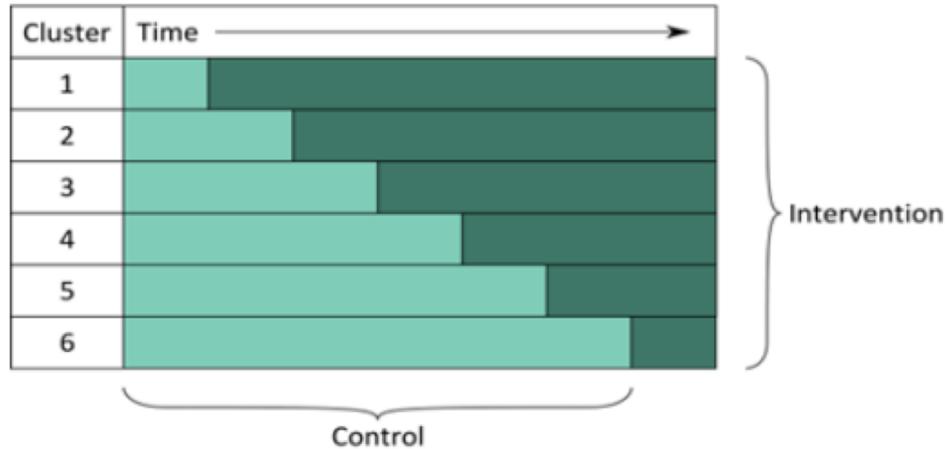
(a) Parallel Cluster Study



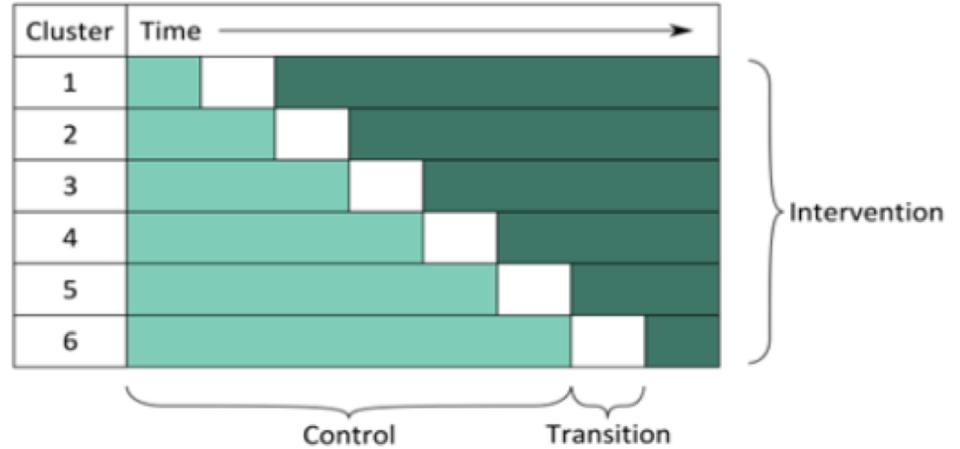
(b) Parallel Cluster Study with a Baseline Period



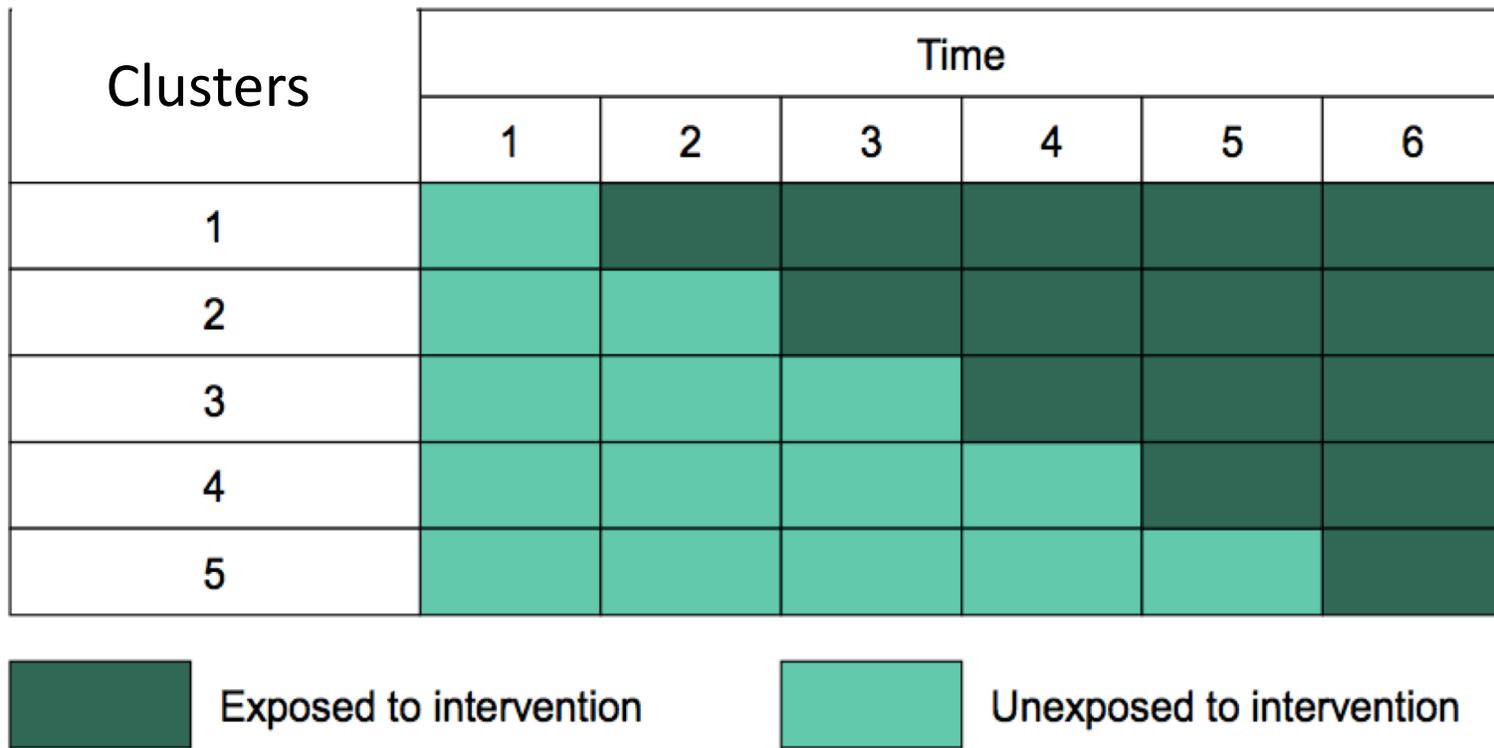
(c) Conventional Stepped Wedge Study



(d) Stepped Wedge Study including Transition Period



An alternative to traditional parallel cluster studies, in which the intervention is delivered in only half the clusters with the remaining clusters functioning as controls.



The design includes an initial period in which no clusters are exposed to the intervention. Subsequently, at regular time intervals (the “steps”) one cluster (or a group of clusters) crosses from the control to the intervention.

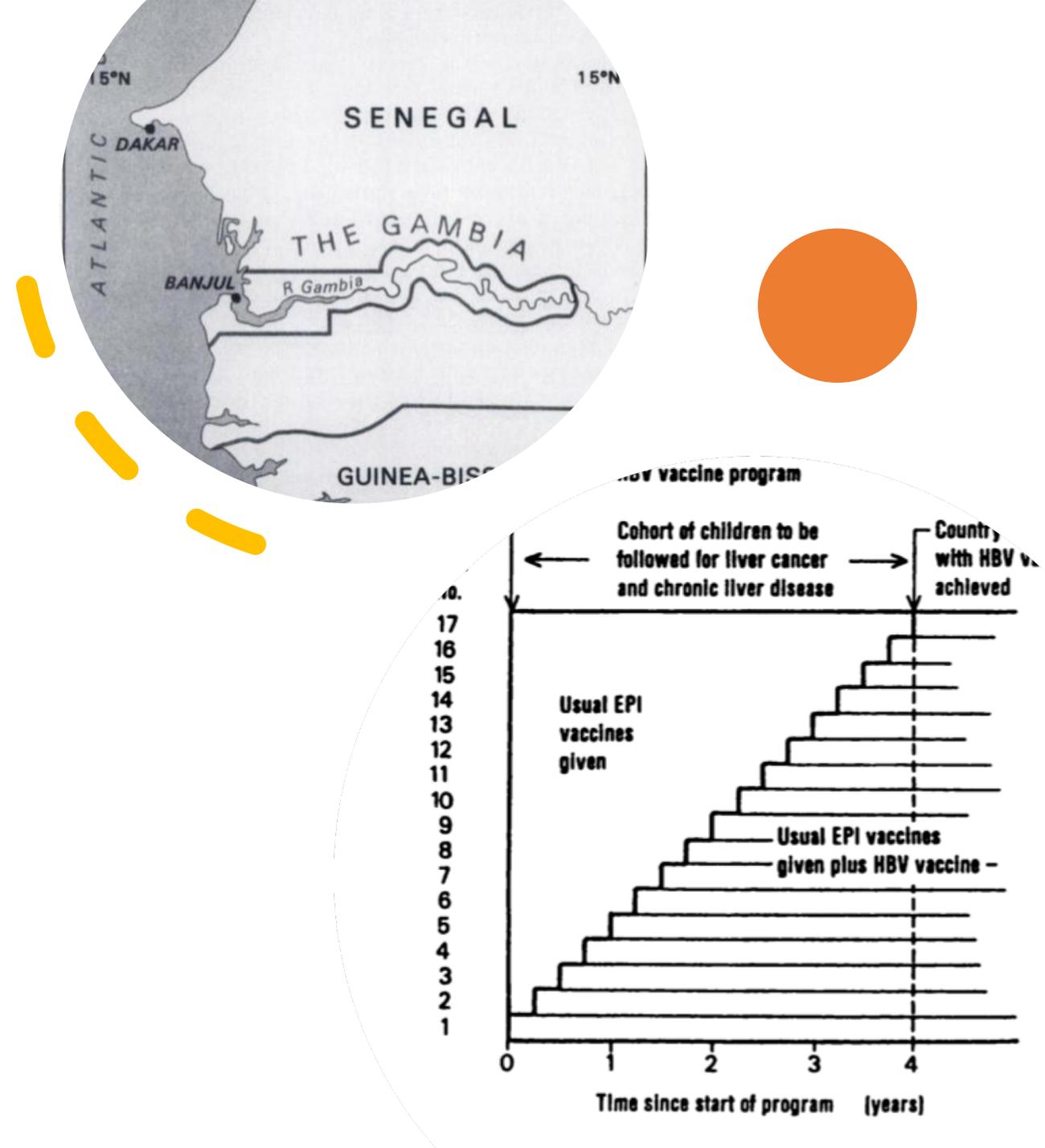
Data collection continues throughout the study, so that each cluster contributes observations under both control and intervention observation periods.

The Gambia Hepatitis Intervention Study

The Gambia Hepatitis Intervention Study was a large-scale vaccination project in The Gambia.

It was initiated in July 1986

Consisted in the introduction of national hepatitis B (HBV) vaccination of young infants progressively over a 4-year period, with the purpose of preventing chronic liver disease and hepatocellular carcinoma (HCC).



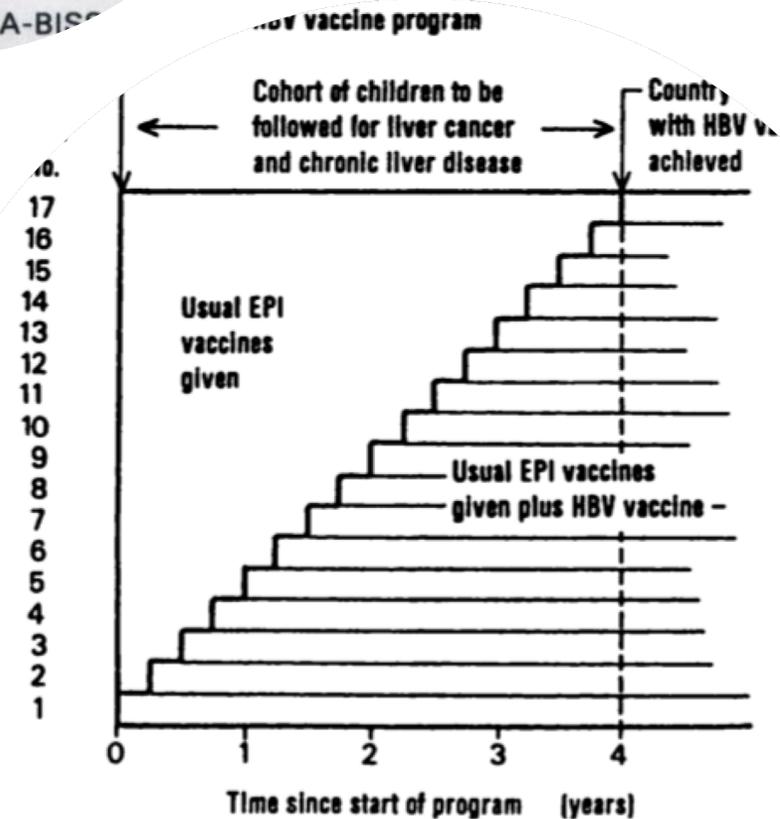
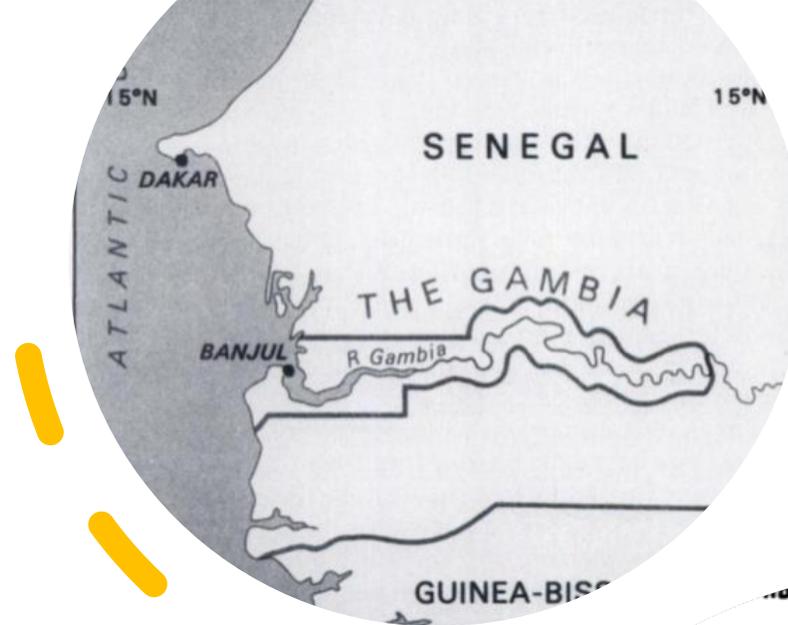
The Gambia Hepatitis Intervention Study

The first team were randomly selected to start the vaccination in July 1986;

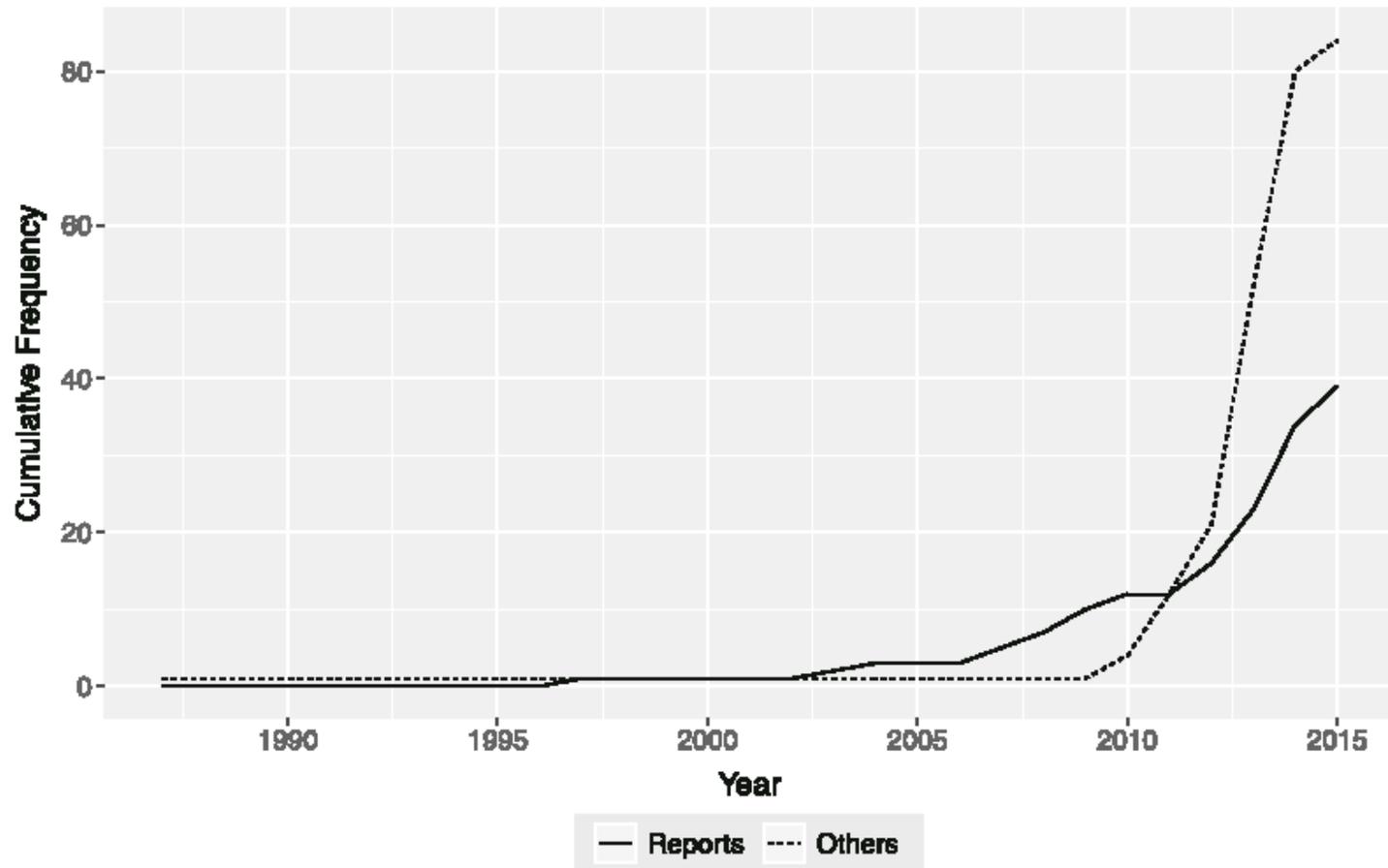
Every three months another team was randomly selected;

Reasons for choosing this design:

- limited availability of the vaccine
- the desirability of having comparison groups available from the same time period;
- the severe logistic difficulties that would have been encountered with randomization at the individual level;
- the hope that HBV vaccine would be widely available at the end of the study when all teams would have delivered the vaccine.



Stepped Wedge Designs have been increasingly used in the evaluation of service delivery type interventions.



*others: protocols, trial registration, conference presentations

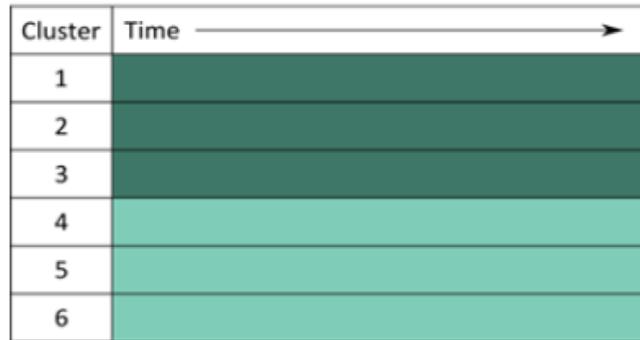
Grayling, Wason & Mander, 2017

Why?

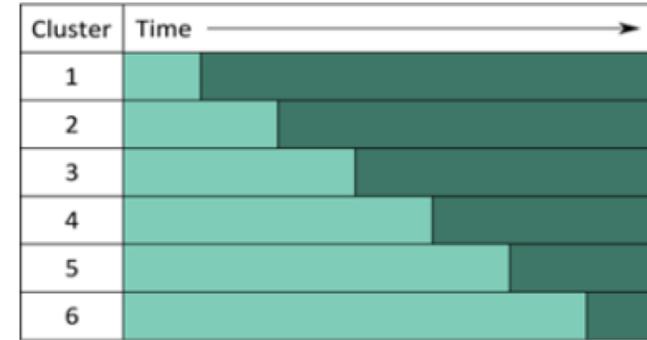
Advantages...

- ... Accounts for underlying differences between communities
- ... Outcomes are still measured at individual level
- ... Cluster flexibility; Clusters can be large (e.g. cities, school etc.) or small (families, classrooms)
- ... Offers an alternative when individual randomization is not feasible or the effect is expected at the community level
- ... May overcome logistical issues
- ... May overcome ethical issues

Disadvantages?



OR



Compared with a parallel cluster design, it is at greater risk of ...

Time bias. Time is considered one of the main confounders since underlying secular trends need to be carefully accounted for.

Contamination. The transition between control period and intervention may not be so smooth.

Furthermore, outcomes in the intervention condition may be obtained from participants who are yet to be exposed to the intervention.

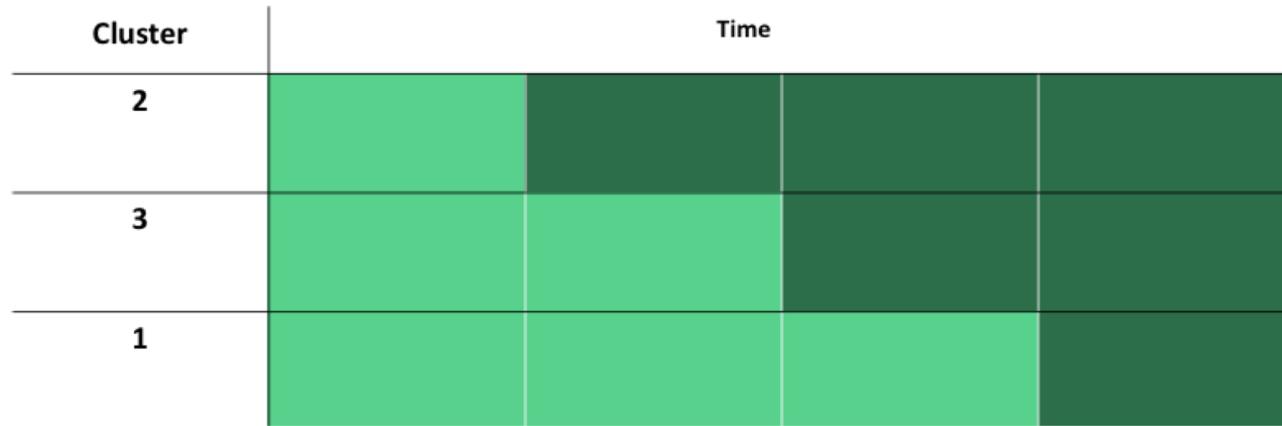
When choosing a stepped wedge design?

- Provides a means to conduct an evaluation which otherwise would not be possible;
- Facilitates cluster recruitment as it enhances the acceptability of an evaluation to stakeholders;
- Is the only feasible design due to pragmatic and logistical constraints (for example the roll-out of a scarce resource);
- Has increased statistical power over other study designs (which will include situations with a limited number of clusters).

“In situations when a conventional parallel-CRT is feasible, it is likely to be the preferred design.”

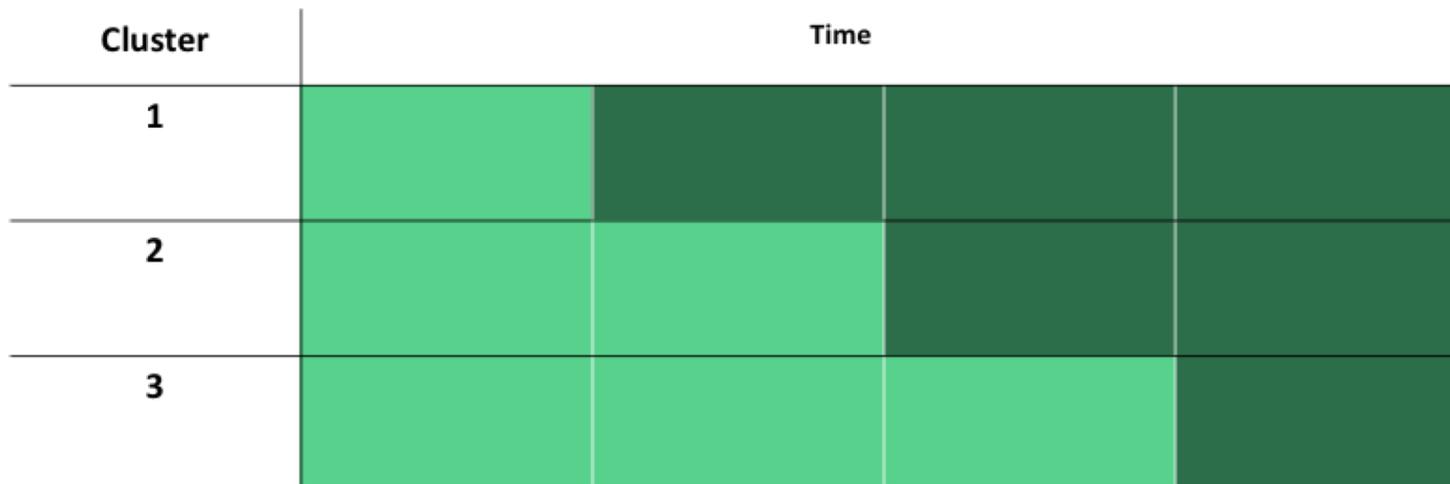
“Commonly cited reasons for choosing an SW-CRT are its perceived logistical, social, and ethical benefits.”

Randomised Stepped-Wedge Design



OR

Non-Randomised Stepped-Wedge Design



- The Randomised Stepped Wedge Design is preferable because it can decrease the likelihood of biased results.
- Non-randomised Stepped-Wedge Designs are a viable alternative when randomization is not possible and analysis accounts for time biases.

An example... “Hypos can strike twice intervention”

Assessing the effects of the intervention *Hypos can strike twice* consisting in giving an informative leaflet to patients seen by ambulance staff for a hypoglycaemic episode.

A non-randomised stepped wedge design.



An example... “Hypos can strike twice intervention”

The intervention was introduced in three clusters in the following order: Leicestershire and Northamptonshire, Nottinghamshire and Derbyshire, and Lincolnshire.

Main outcome represented by the number of unsuccessful hypoglycaemia calls.



An example... “Hypos can strike twice intervention”

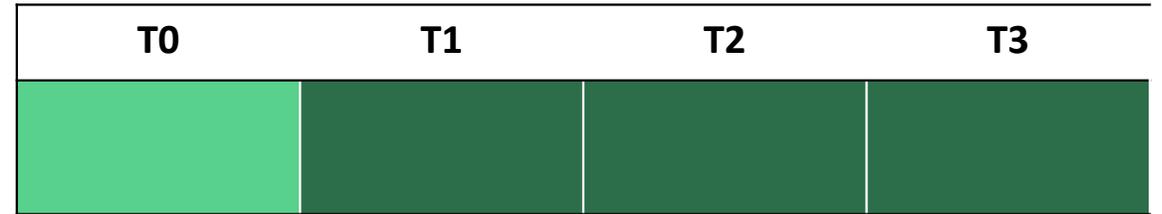
Cluster	Time			
	T0	T1	T2	T3
1 st Cluster L&N	Light Green	Dark Green	Dark Green	Dark Green
2 nd Cluster N&D	Light Green	Light Green	Dark Green	Dark Green
3 rd Cluster L	Light Green	Light Green	Light Green	Dark Green

Analysis Methods



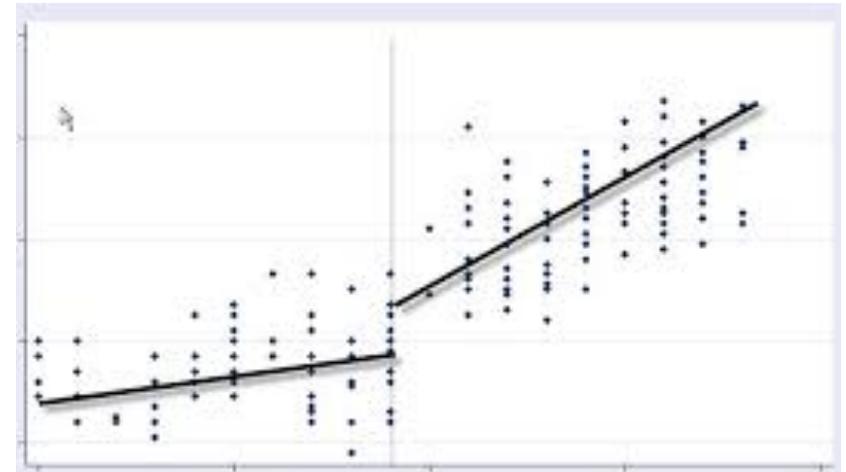
Paired t-test

- Analyse each cluster means
- Likely biased if there are time trends



Segmented regressions

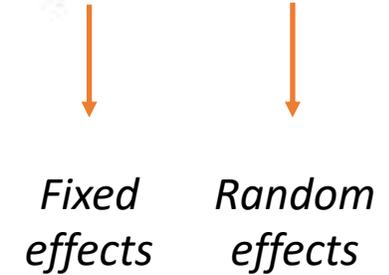
- Slope before and after the intervention
- Considers time trends biases



Linear Mixed Models (LMM)

- Within and between cluster analysis
- Continuous outcome variable
- Clusters must have equal sizes

$$\mathbf{y} = \mathbf{X}\boldsymbol{\beta} + \mathbf{Z}\mathbf{u} + \mathbf{e}$$

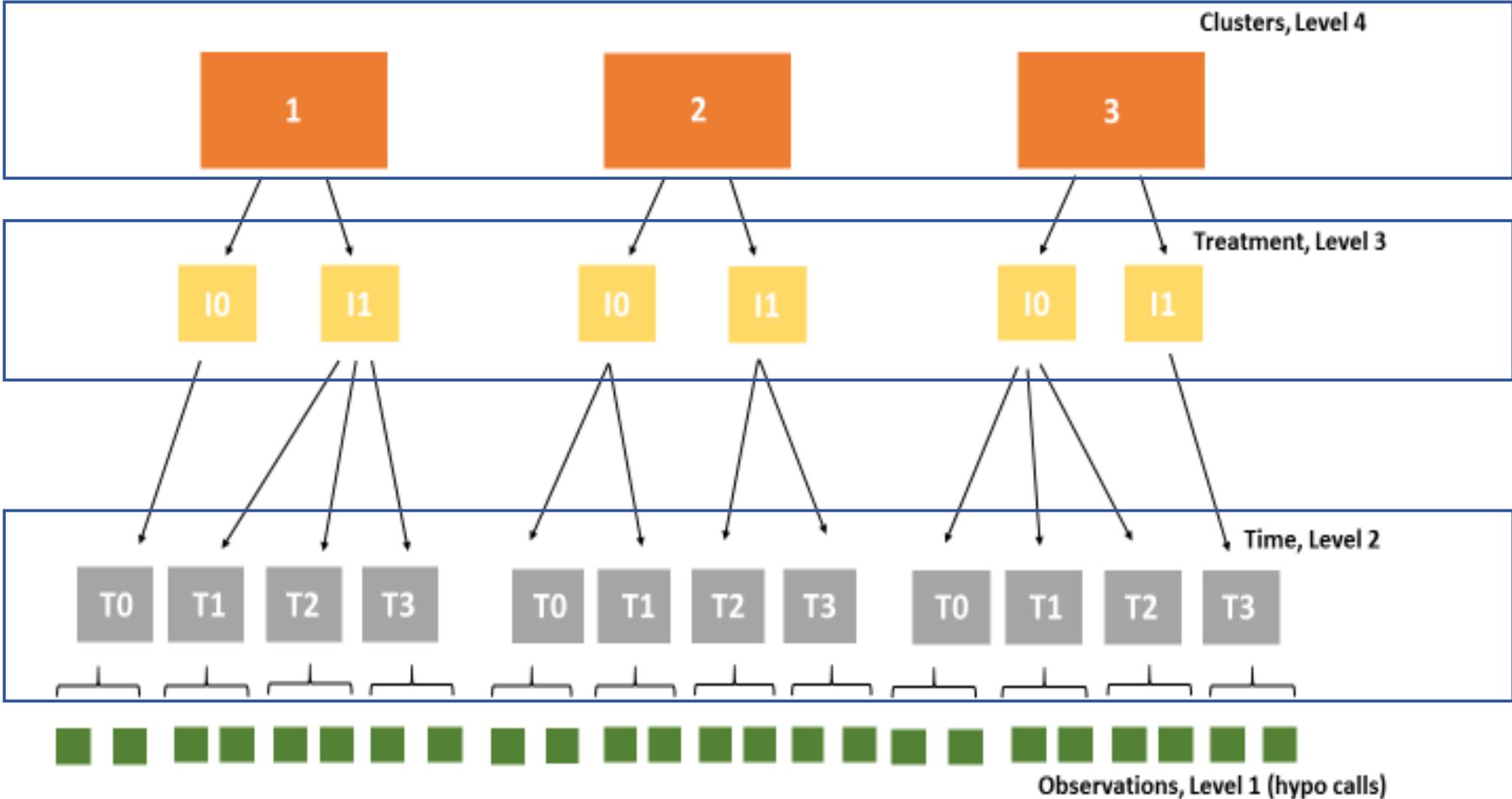

Fixed effects *Random effects*

Generalised Linear Mixed Models (GLMM)

- An extension of linear mixed models
- Outcome variables from other distributions (e.g. binary responses)
- Analyse individual level data
- Unequal cluster sizes are acceptable

Stepped Wedge Design

Cluster	Time			
	T0	T1	T2	T3
1 st Cluster L&N	Light Green	Dark Green	Dark Green	Dark Green
2 nd Cluster N&D	Light Green	Light Green	Dark Green	Dark Green
3 rd Cluster L	Light Green	Light Green	Light Green	Dark Green

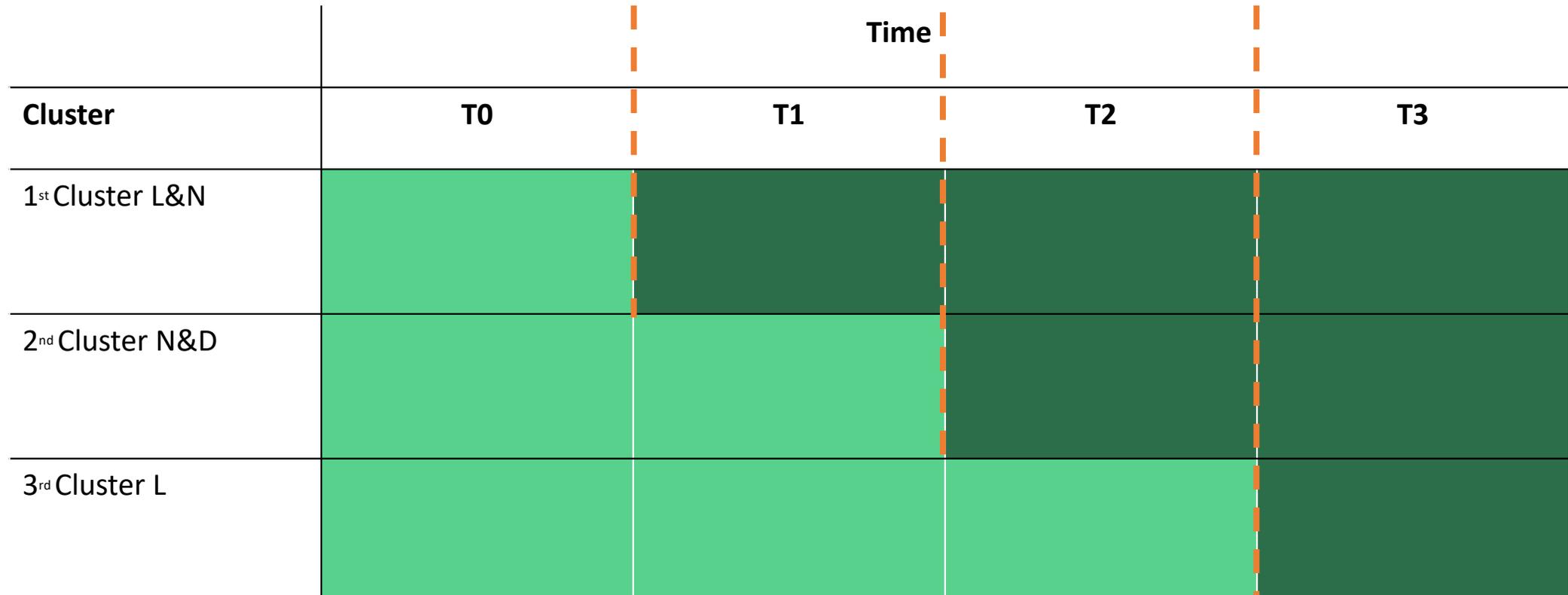


GLMM summary of results

	Odds Ratio	95% Confidence Interval	P value
Intervention	1.04	0.74, 1.48	0.797
T1	1.06	0.82, 1.36	0.671
T2	0.74	0.52, 1.06	0.103
T3	0.50	0.33, 0.76	0.001
Deprivation	0.94	0.91, 0.97	0.001
Month	1.01	0.99, 1.03	0.307
Age	0.97	0.93, 1.01	0.078
Gender	1.19	1.02, 1.38	0.023
ICC		0.006 (95% CI: 0.000, 0.116)	

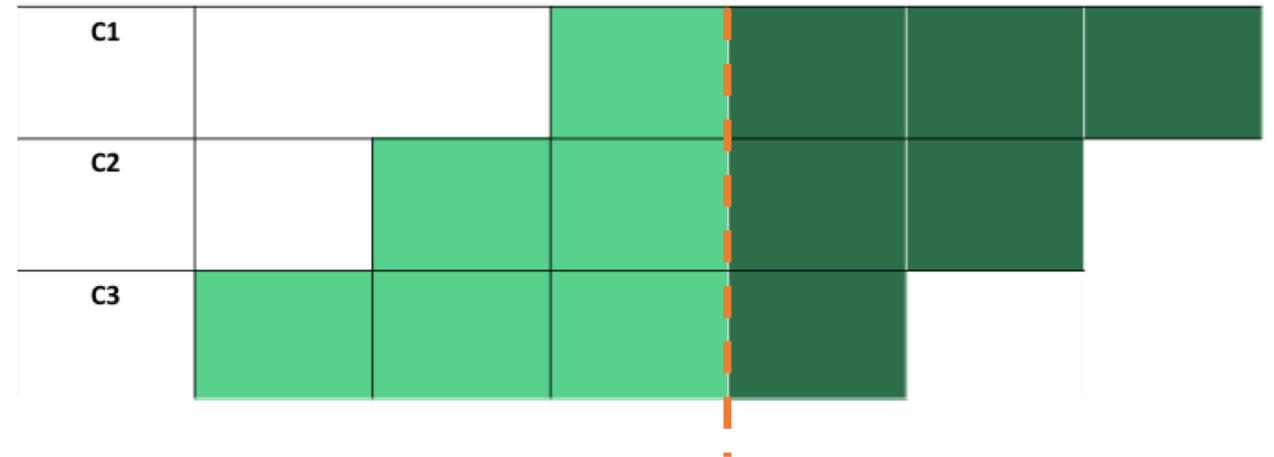
Interrupted time series analysis

Each 'step' as an interruption in time.



Cluster	Time			
1	Light Green	Dark Green	Dark Green	Dark Green
2	Light Green	Light Green	Dark Green	Dark Green
3	Light Green	Light Green	Light Green	Dark Green

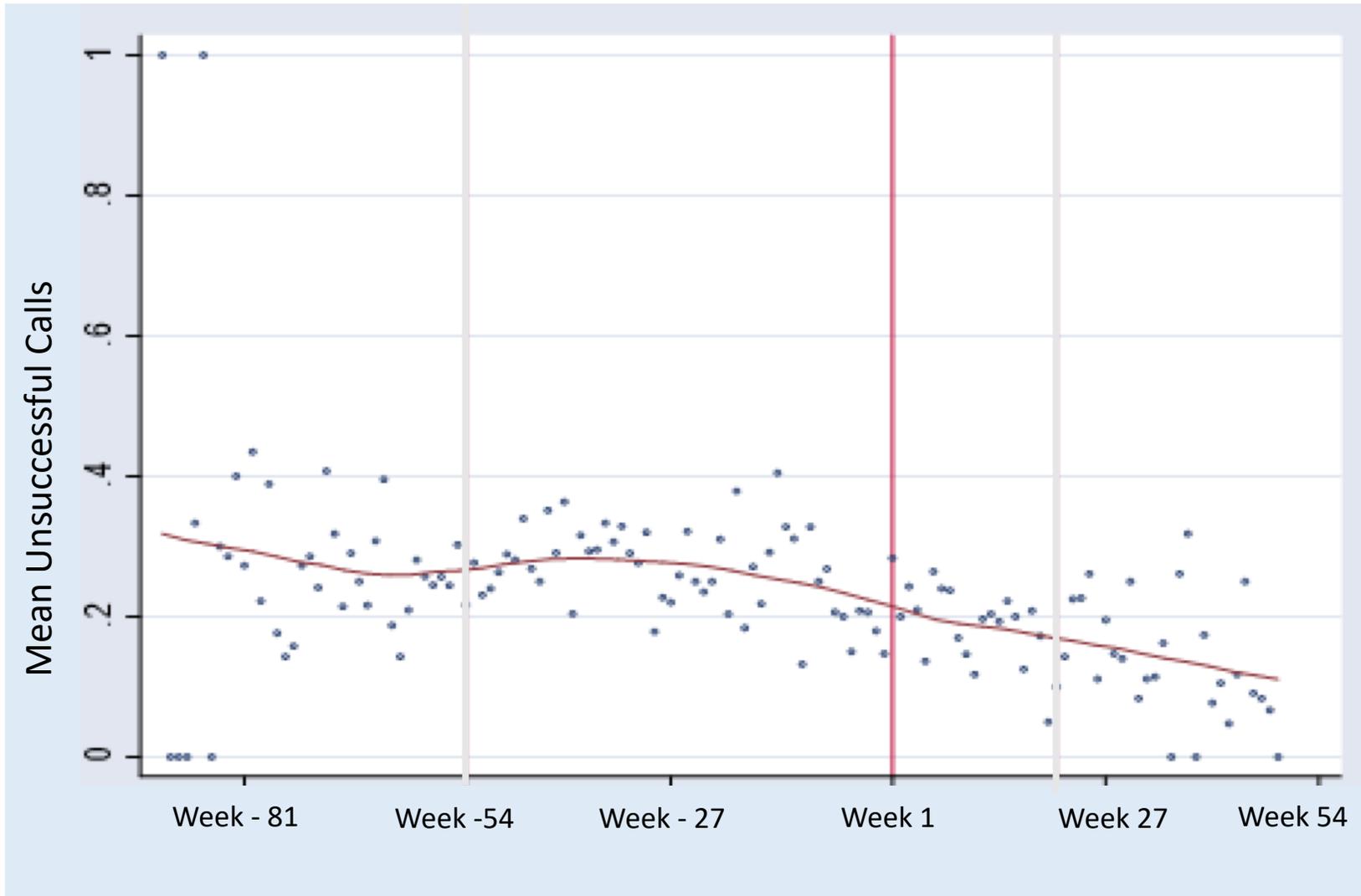
T0 – Intervention Start



- Clusters can be aligned based on the time elapsed before and after the intervention
- Or analysed separately.

All clusters aligned mean

T0 – Intervention Start



Summary

- In Stepped-Wedge Cluster designs, the intervention is introduced at different times (steps)
- All clusters are exposed to both control and intervention periods.
- Stepped-Wedge Cluster Designs have become very popular in the last three decades.
- They represent a good alternative to parallel cluster designs, especially when dealing with logistical and ethical concerns.
- Analyses and interpretation of results need to account for the two main limitations of this design: secular trends and contamination.

Thank you for listening!

