Information content of cluster-period cells in stepped wedge designs with unequal cell sizes

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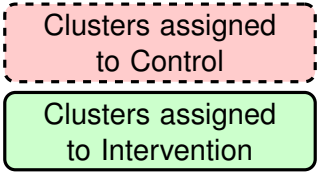
The standard cluster randomised trial



- *Clusters (groups)* of participants assigned to treatments. (Why?)
- Clusters could be hospitals, intensive care units, schools, neighbourhoods...
  - Clustering inflates required sample size over that required for an individually-randomised trial.

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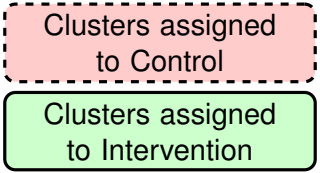

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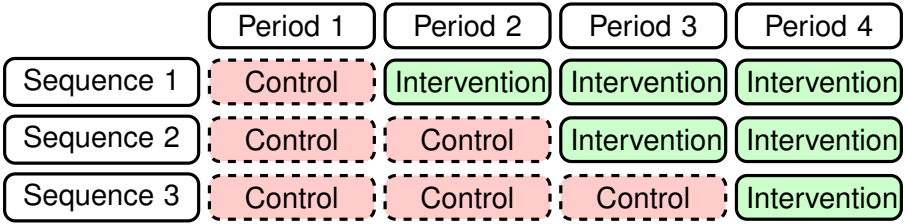
Can reduce required sample size by considering *longitudinal (multiple period)* cluster randomised trials.

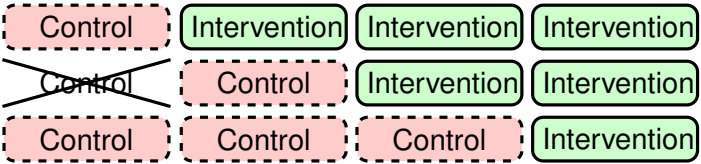
The stepped wedge cluster randomised trial design



- Stepped wedge designs can be useful when all clusters need to receive the intervention, or the intervention is going to be rolled out anyway.
- Different numbers of clusters may be assigned to each sequence;
- Might be different numbers of participants in each cluster in each period.

Each cluster-period pair is a **cell** of the design.

Does each *cell* contribute the same amount of information?



- Which participants contribute the most information about the treatment effect?
- Do we really need to include all cluster-period cells? (What about *incomplete* designs?)

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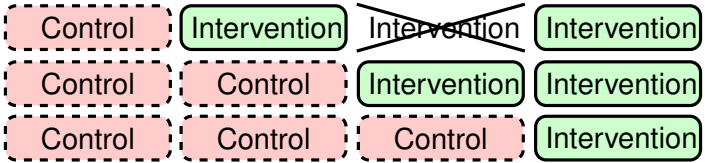

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- Do we really need to include all cluster-period cells? (What about *incomplete* designs?)

Need a model for the outcomes to answer this question!

A model for continuous outcomes:

$$\text{Outcome} = \text{Period effect} + \textbf{Treatment effect} + \text{random effects} + \text{error}$$

- **Treatment effect** is of most interest: θ
  - $\hat{\theta}$ is the weighted least squares estimator of θ.
  - $var(\hat{\theta})$ is the variance of this estimator: key ingredient in sample size calculations.

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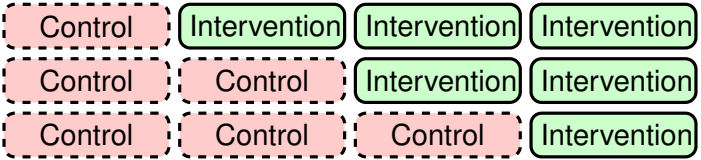
How much does $var(\hat{\theta})$ increase if observations from a given cell are omitted?

Information content of each cell

Calculate $var(\hat{\theta})$ given the complete design:



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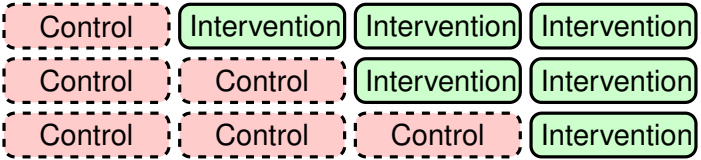
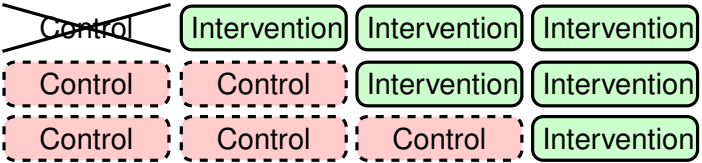


Calculate $var(\hat{\theta})_{[kt]}$ from the incomplete design, omitting period t of cluster k:



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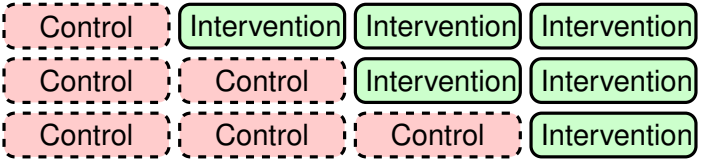

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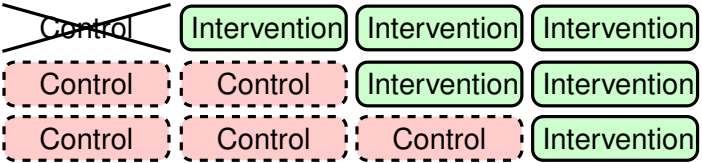

Information content of cell (k, t)**:** $IC(k,t) = var(\hat{\theta})_{[kt]} / var(\hat{\theta})$

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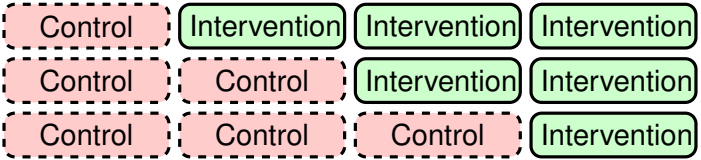

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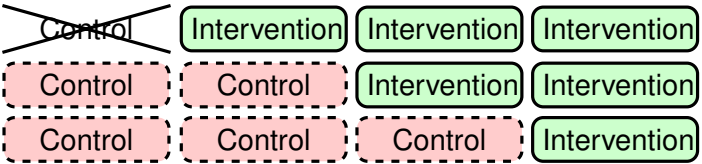

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$IC(k,t) = 1$ implies no information loss; $IC(k,t) > 1$ implies loss of information.

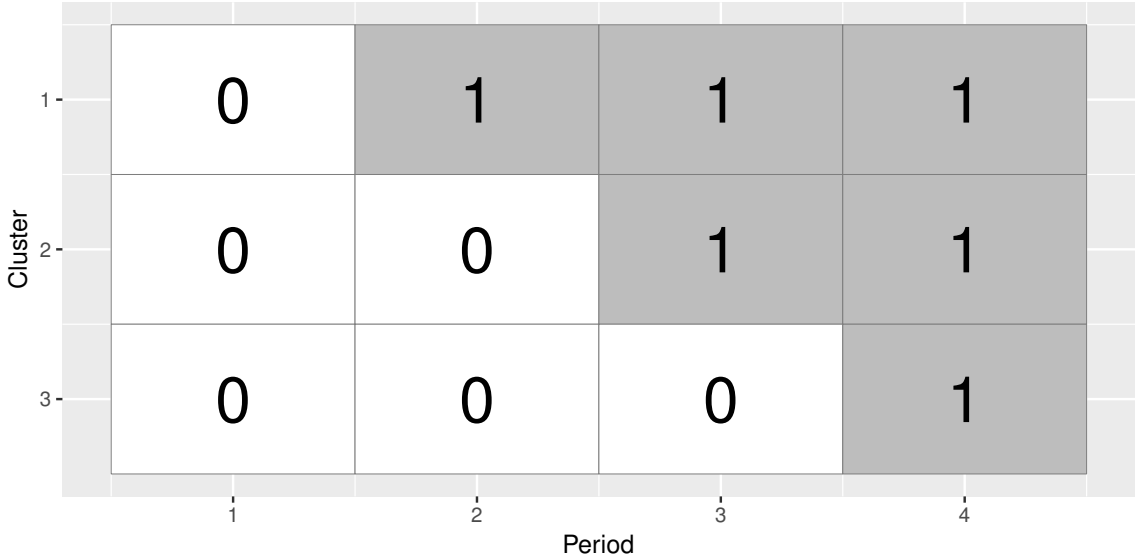
Information content of cells

- Previously explored the information content of stepped wedge cells when:
  - There are the same number of participants in each cluster in each period[1]
  - There are the same number of participants in each cluster in each period *and* there is treatment effect heterogeneity or implementation periods in the design[2]
- Most information in the cluster-period cells near the time of the treatment switch (and in “hotspots”)

[1] Kasza & Forbes, Biometrics, 2018

[2] Kasza, Taljaard, Forbes. Statistics in Medicine, 2019

Design matrix: equal numbers of participants in each cell



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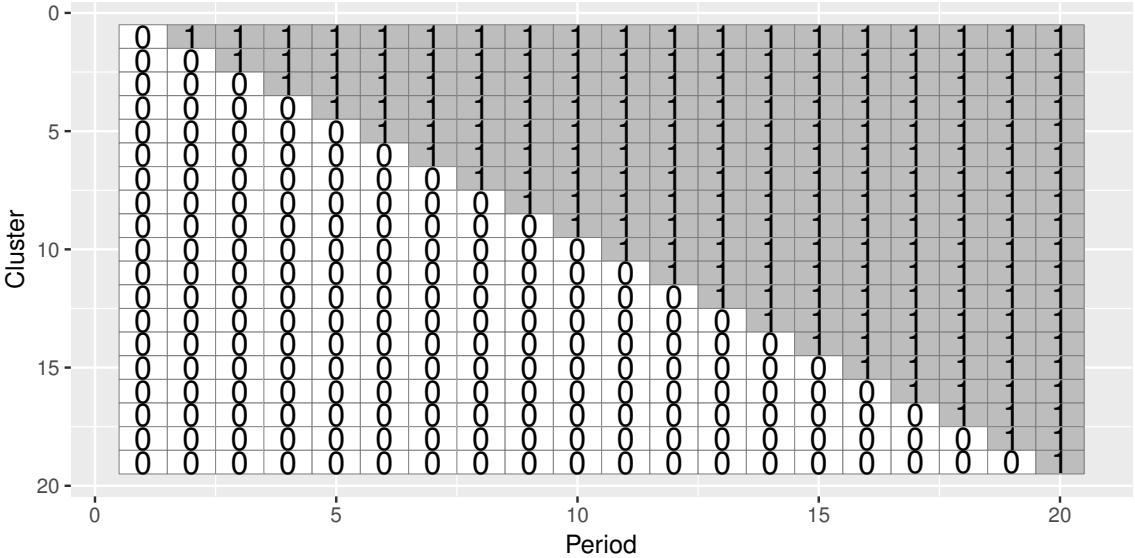
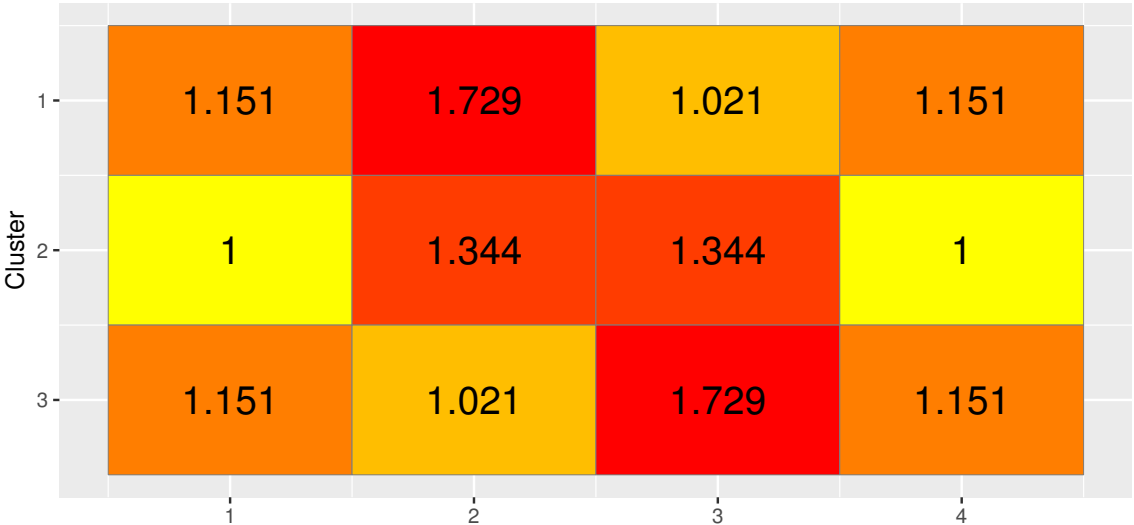


Information content: equal numbers of participants in each cell ($ICC = 0.05$, $m = 100$)



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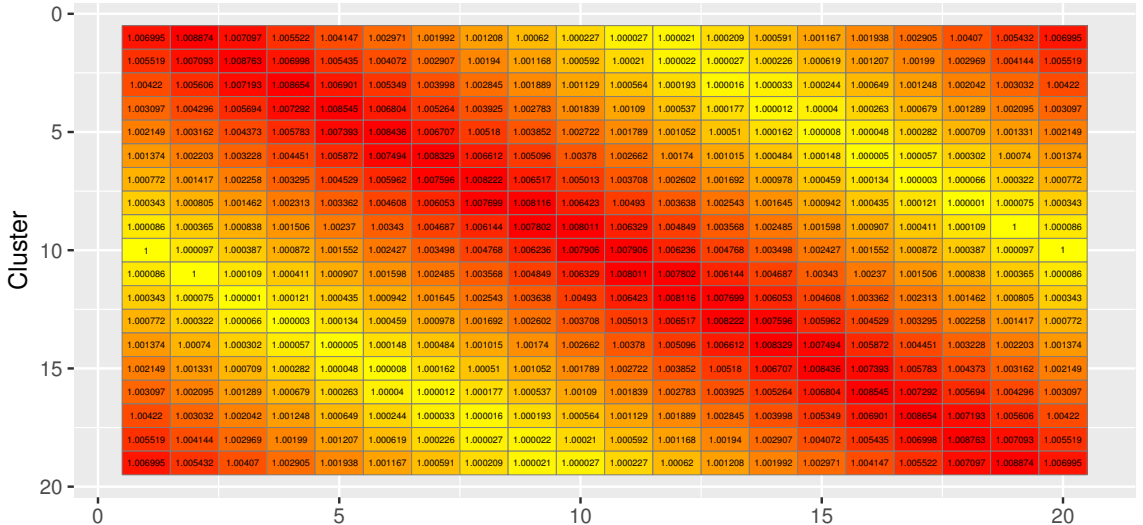


What happens when the number of participants in each cluster in each period varies?

Rehabilitation unit example:[3]

- Assess the impact of individual education in addition to usual care on fall rates in 8 hospital rehabilitation units
- 5-period stepped wedge design:

	Period 1	Period 2	Period 3	Period 4	Period 5
Sequence 1	Control	Intervention	Intervention	Intervention	Intervention
Sequence 2	Control	Control	Intervention	Intervention	Intervention
Sequence 3	Control	Control	Control	Intervention	Intervention
Sequence 4	Control	Control	Control	Control	Intervention

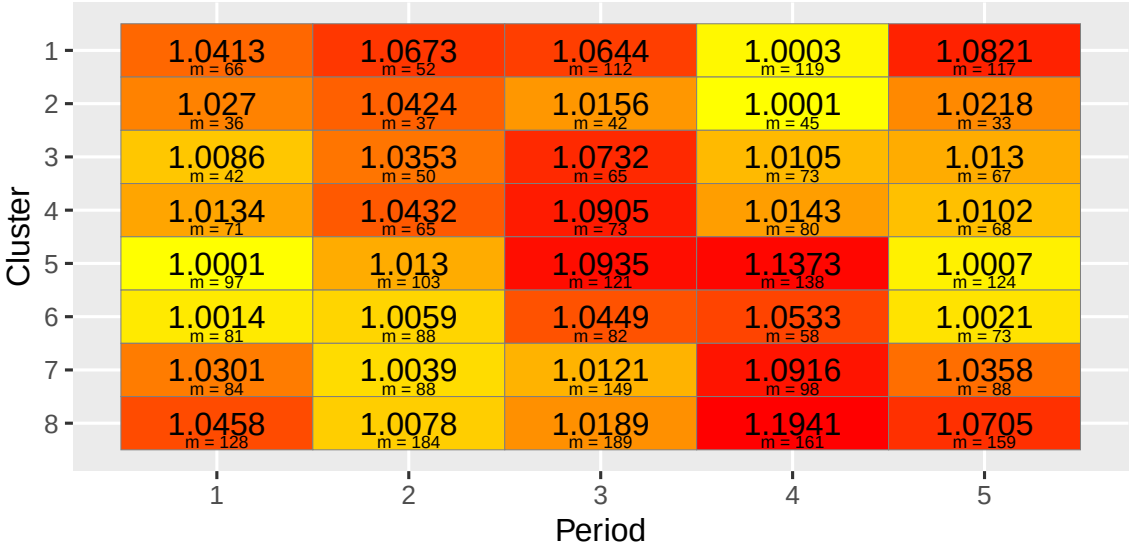
[3] Hill et al. The Lancet, 2015.

Differing numbers of patients in each cluster-period

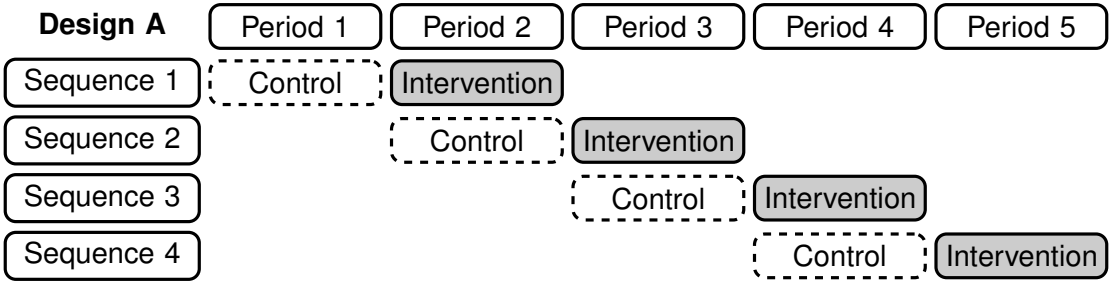
The trial did not contain equal numbers of patients in each hospital in each period!

	1	2	3	4	5
Cluster 1	66	52	112	119	117
Cluster 2	36	37	42	45	33
Cluster 3	42	50	65	73	67
Cluster 4	71	65	73	80	68
Cluster 5	97	103	121	138	124
Cluster 6	81	88	82	58	73
Cluster 7	128	184	189	161	159
Cluster 8	84	88	149	98	88

Information content of cluster-period cells in the rehab unit trial



What about incomplete designs for this trial?



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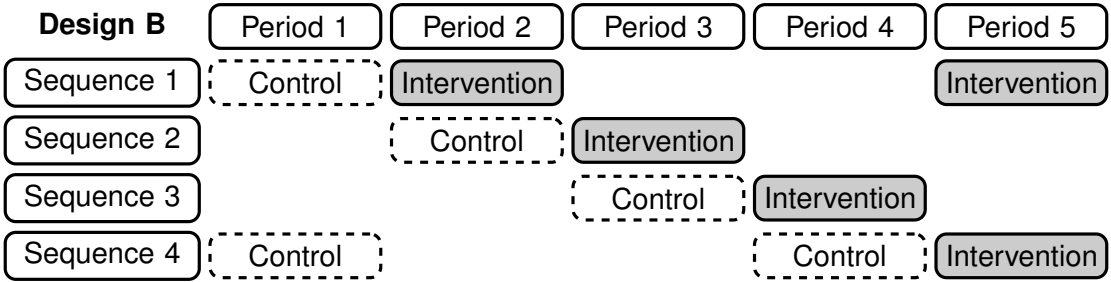

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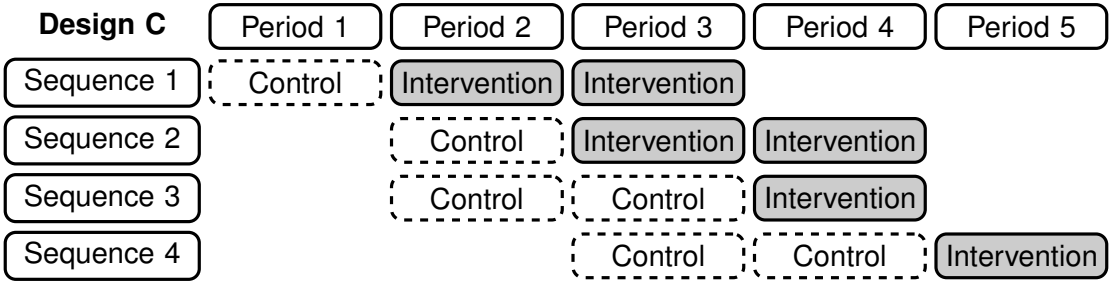

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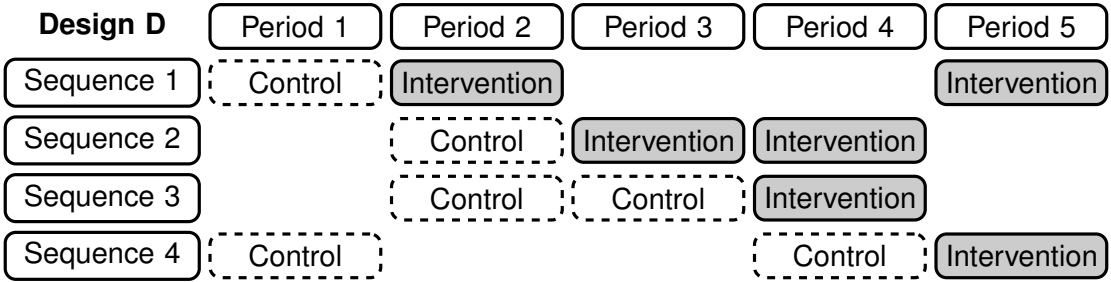

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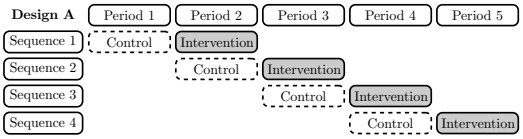
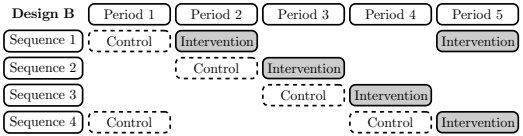
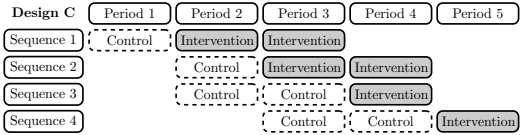
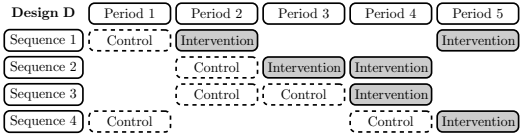


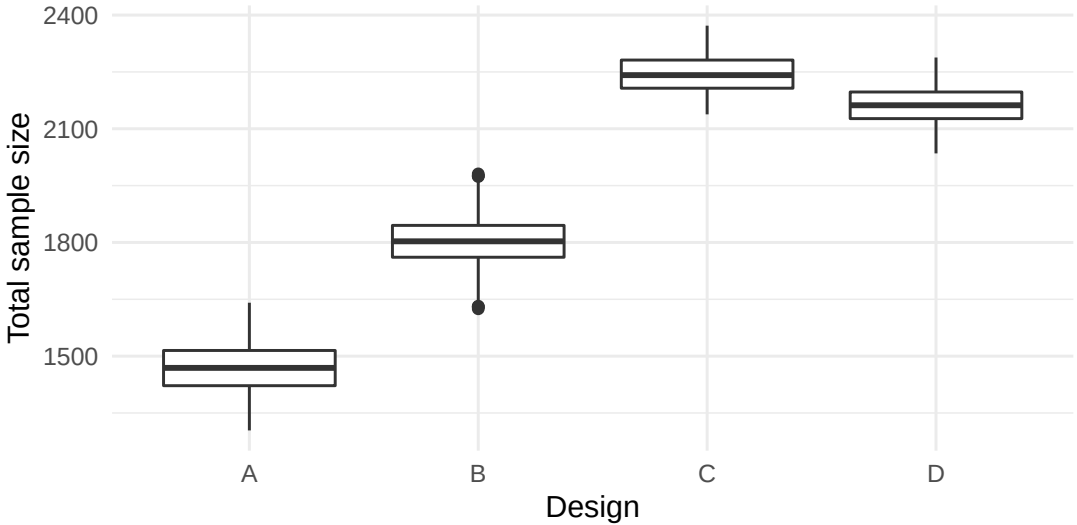




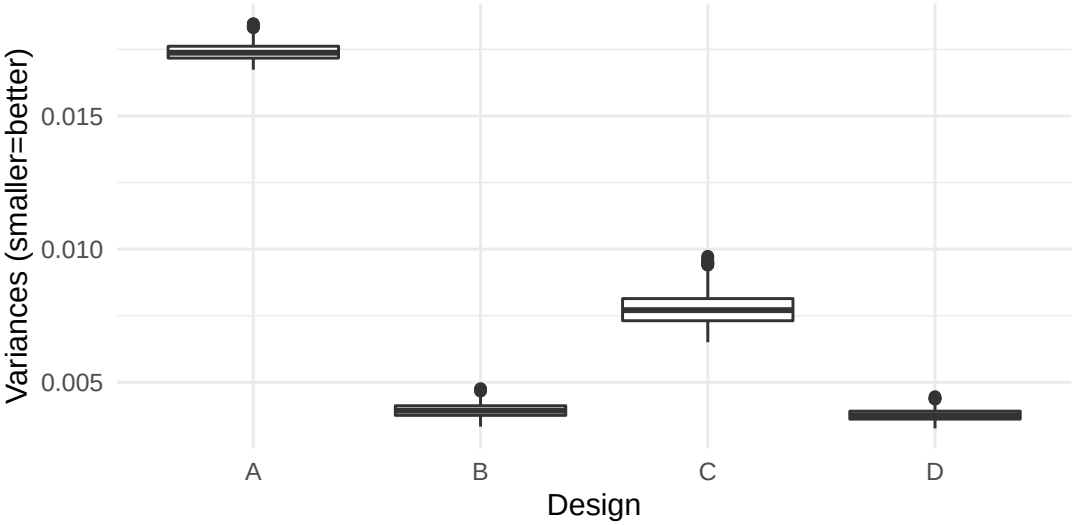


- Calculate $var(\hat{\theta})$ for each allocation of the 8 clusters to the 4 sequences (with 2 clusters per sequence)
  - 2520 possible allocations of clusters to sequences.

Total sample sizes of the incomplete Hill trials



The importance of “hot-spots” in the Hill et al. trial



What have we learned about the stepped wedge design?

- Periods near the treatment cross-over tend to be most valuable...
  - But the “hot corners” can add a lot of information (necessary to account for time effects)
- A cleverly constructed design with fewer observations can be more powerful than a design with more observations.
  - Logistical vs. statistical value of cells?

Future work: development of “optimal” incomplete designs.

You can explore the information content of cells in your own cluster randomised trial at:

`https://monash-biostat.shinyapps.io/ICvaryingclustersize/`