

# Optimal allocation of clusters in staircase cluster randomised trial designs

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# Things change...

Staircase designs:

- optimal allocation of clusters

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- comparison to stepped wedge designs

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- comparison to stepped wedge designs
- optimal allocation of control and intervention periods

# The usual stepped wedge

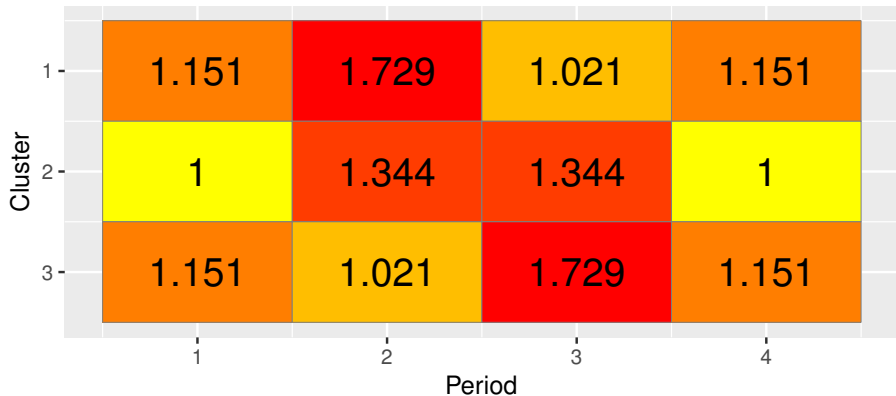
	Period 1	Period 2	Period 3	Period 4
Sequence 1	0	1	1	1
Sequence 2	0	0	1	1
Sequence 3	0	0	0	1

# The usual stepped wedge

	Period 1	Period 2	Period 3	Period 4
Sequence 1	0	1	1	1
Sequence 2	0	0	1	1
Sequence 3	0	0	0	1

The “information content” of sequence-period cells describes how much each cell contributes to the estimation of the treatment effect.

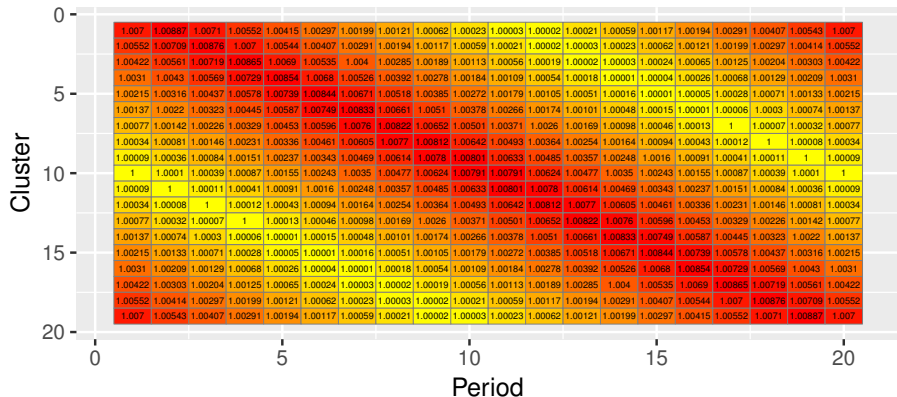
# Information content of SW sequence-period cells



3-sequence stepped wedge



# Information content of SW sequence-period cells



19-sequence stepped wedge

# The suggestion of a staircase...

	Period 1	Period 2	Period 3	Period 4
Sequence 1	0	1	1	1
Sequence 2	0	0	1	1
Sequence 3	0	0	0	1

# The suggestion of a staircase...

	Period 1	Period 2	Period 3	Period 4
Sequence 1	0	1		
Sequence 2		0	1	
Sequence 3			0	1

## ...and the extension of a dog leg

	Period 1	Period 2	Period 3	Period 4
Sequence 1	*	1		
Sequence 2		0	1	
Sequence 3			0	*

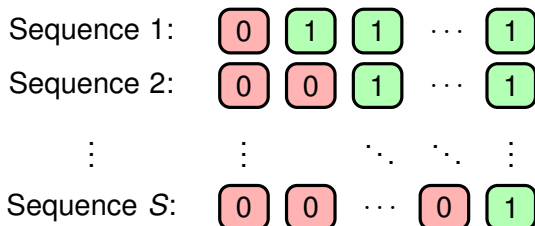
## ...and the extension of a dog leg

	Period 1	Period 2	Period 3	Period 4
Sequence 1	*	1		
Sequence 2		0	1	
Sequence 3			0	*

\*: when categorical terms for period are included, these cells contribute nothing to the estimation of the treatment effect, and the staircase and dog leg are equivalent.

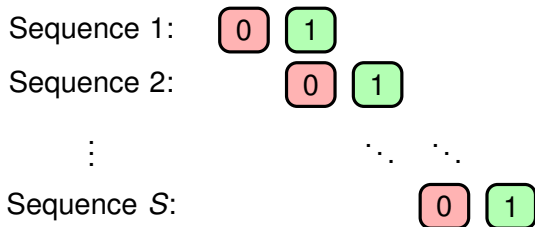
# Staircases embedded in stepped wedges

- Each stepped wedge contains a staircase...



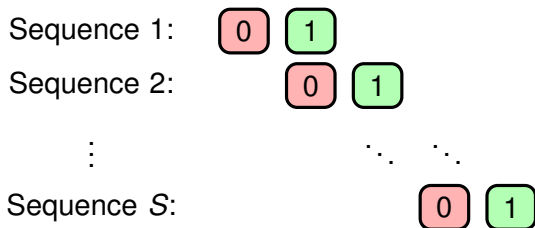
# Staircases embedded in stepped wedges

- Each stepped wedge contains a staircase...



# Staircases embedded in stepped wedges

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How much information do we lose when we only consider the staircase?



# Staircases versus stepped wedges

$var(\hat{\theta})$  : variance of the treatment effect estimator

$$\frac{var(\hat{\theta})_{SC}}{var(\hat{\theta})_{SW}} = \frac{\text{Staircase design}}{\text{Stepped wedge design}}$$

- Continuous outcomes, 100 subjects in each cluster in each period.
- For two subjects in the same cluster:

$$cov(\text{measured in same period}) = \rho$$

$$cov(\text{measured in different periods}) = r\rho$$

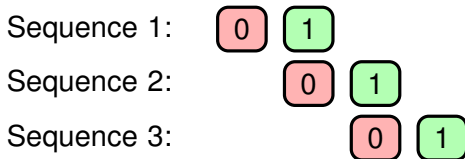
- Within-period intra-cluster correlation  $\rho = 0.005, \dots, 0.50$ ;
- cluster auto-correlation  $r = 0.50, \dots, 0.99$ .

## 3-sequence SW and SC

Sequence 1:	0	1	1	1
Sequence 2:	0	0	1	1
Sequence 3:	0	0	0	1

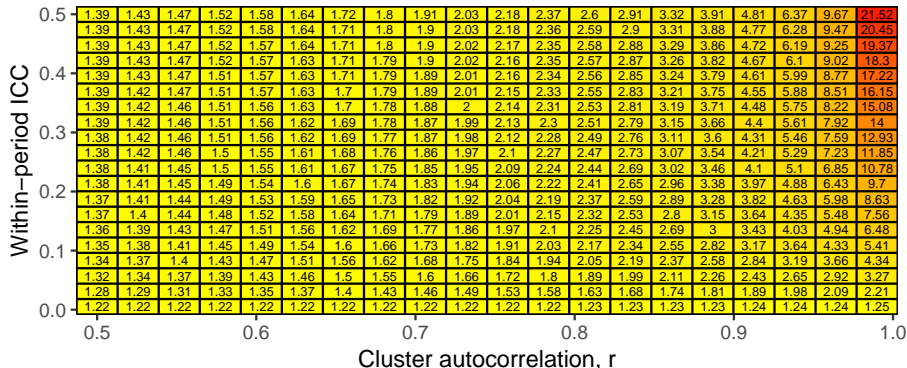
Stepped wedge: 12 cluster-period cells  
Staircase: 6 cluster-period cells.

# 3-sequence SW and SC

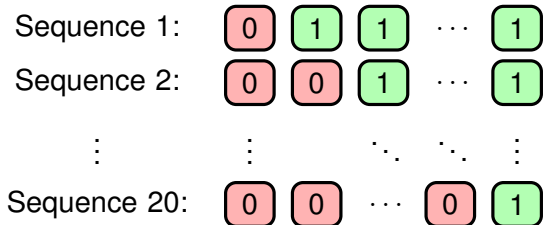


Stepped wedge: 12 cluster-period cells  
Staircase: 6 cluster-period cells.

# 3 sequences, constant between-period ICC



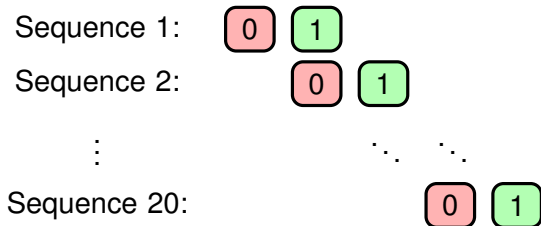
# 20-sequence SW and SC



Stepped wedge: 420 cluster-period cells

Staircase: 40 cluster-period cells.

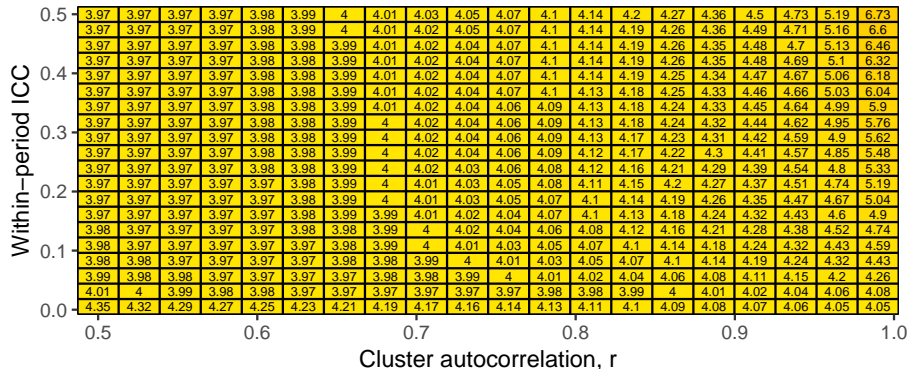
# 20-sequence SW and SC



Stepped wedge: 420 cluster-period cells

Staircase: 40 cluster-period cells.

# 20 sequences, constant between-period ICC



# Staircase vs. Stepped wedge

- Can lose a lot of information about the treatment effect
  - Why? Stepped wedge “hot spots”.
- Loss can be out of proportion to the reduction in the number of measurements.
  - 3 sequence design:  
50% of the measurements, up to  $20\times$  increase in variance.
  - 20 sequence design:  
10% of the measurements, but only up to  $7\times$  increase.



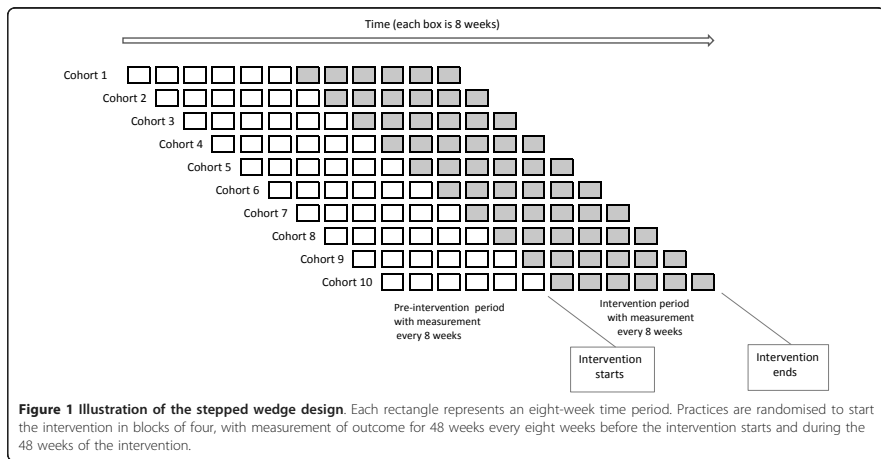
# Staircase designs in practice?

													Type of centre		
Step	2017				2018								Medium recruiter	Low recruiter	
1	Sep	Oct	Nov	Dec											
2		Oct	Nov	Dec	Jan										
3			Nov	Dec	Jan	Feb									
4				Dec	Jan	Feb	Mar								
5					Jan	Feb	Mar	Apr							
6						Feb	Mar	Apr	May						
7							Mar	Apr	May	Jun					
8								Apr	May	Jun	Jul				
9									May	Jun	Jul	Aug			
10										Jun	Jul	Aug	Sep		
11											Jul	Aug	Sep	Oct	
	60-day running-in period														
	60-day post-intervention period														

**Fig. 2** The randomised, stepped-wedge cluster design for the ERUTECC study. In ERUTECC, we use a stepped-wedge cluster design. First the centre is classified as low or medium recruiting. Second, the centres are randomised in each class ensuring that at least one low and one medium recruiting centre is included in every step. Each centre has a 60-day running-in period (yellow), followed by a 60-day post-intervention period (blue). The intervention (teleconference) is done after the 60-day running-in period, and every step provides data before and after intervention, but not at the same point in time. We will add up all patients for all 11 steps in the 60-day running-in period and compare this with the inclusion rate for all centres' 60-day post randomisation period

Lundström et al, Enhancing Recruitment Using Teleconference and Commitment Contract (ERUTECC): study protocol for a randomised, stepped-wedge cluster trial within the EFFECTS trial. *Trials*. 2018.

# Another staircase design...

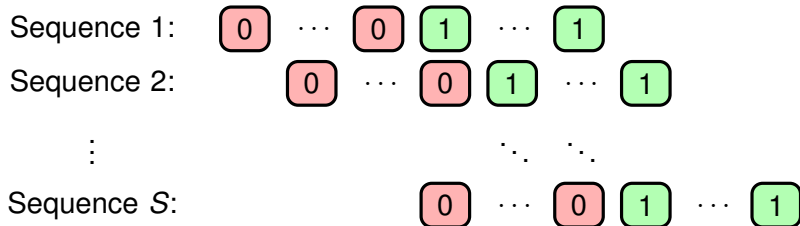


Dreischulte et al, A cluster randomised stepped wedge trial to evaluate the effectiveness of a multifaceted information technology-based intervention in reducing high-risk prescribing of non-steroidal anti-inflammatory drugs and antiplatelets in primary medical care: The DQIP study protocol. *Trials*, 2012.

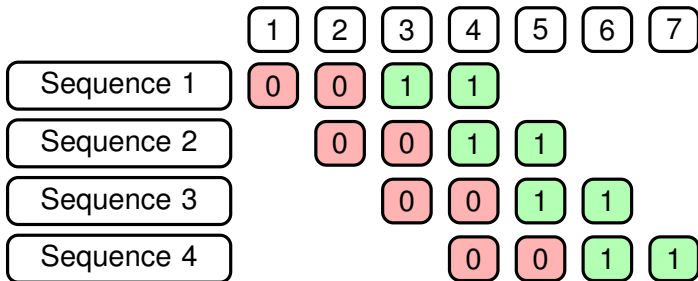
# An extended definition of a staircase design

An  $SC(S, T_0, T_1)$  is a (regular) staircase design:

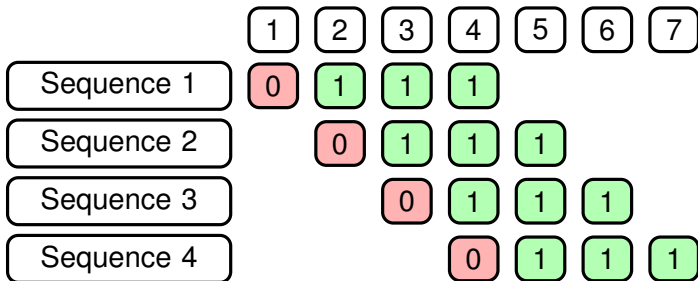
- on  $S$  treatment sequences;
- with  $T_0$  pre-switch control periods;
- and  $T_1$  post-switch intervention periods.



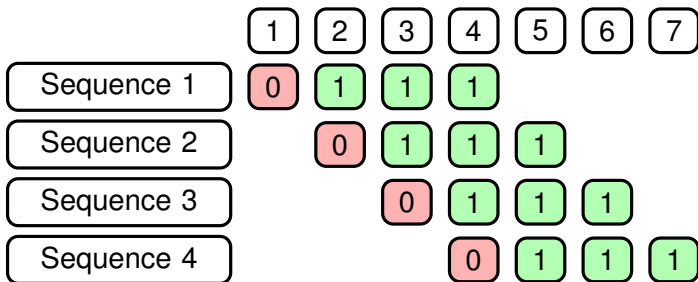
# SC(4, 2, 2): 4 sequences, 2 pre-, 2 post-switch periods



# SC(4, 1, 3): 4 sequences, 1 pre-, 3 post-switch periods

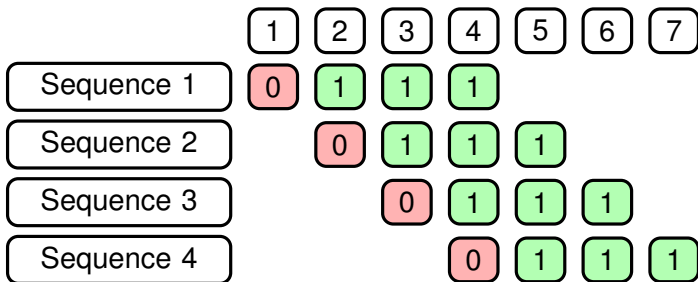


# SC(4, 1, 3): 4 sequences, 1 pre-, 3 post-switch periods



**Which is more efficient:  $SC(4, 2, 2)$  or  $SC(4, 1, 3)$ ?**

# $SC(4, 1, 3)$ : 4 sequences, 1 pre-, 3 post-switch periods

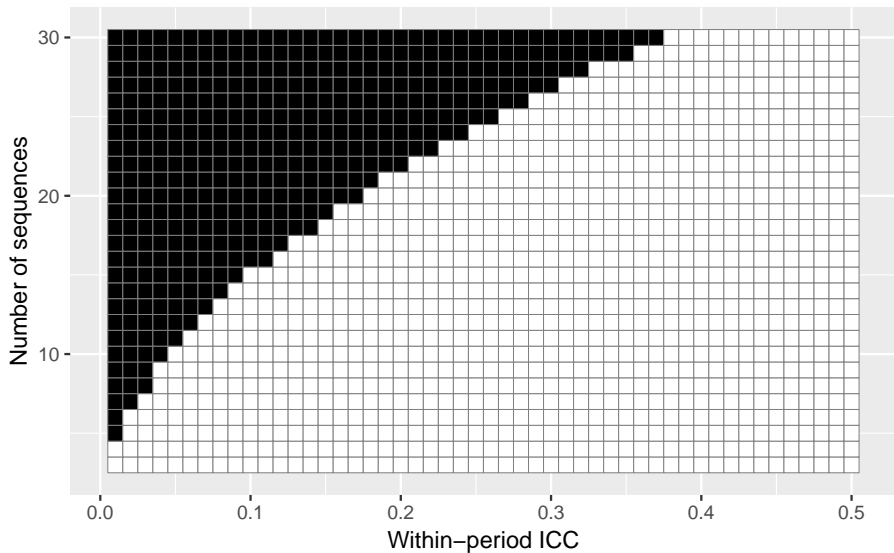


**Which is more efficient:  $SC(4, 2, 2)$  or  $SC(4, 1, 3)$ ?**

$SC(S, 2, 2)$  or  $SC(S, 1, 3)$  for  $S = 3, \dots, 30$ ?

Black =  $SC(S, 2, 2)$ ; White =  $SC(S, 1, 3)$

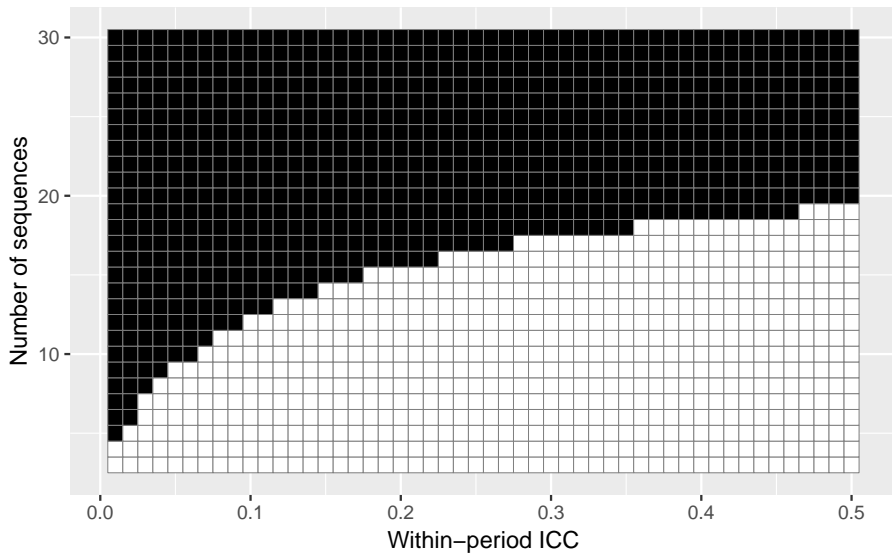
Constant BP ICC, CAC=0.99





Black =  $SC(S, 2, 2)$ ; White =  $SC(S, 1, 3)$

Constant BP ICC, CAC=0.95



# Take home messages

- Staircase designs less efficient than stepped wedge designs.
  - Can the lack of efficiency be overcome through recruitment of more clusters?
- Researchers **are** using staircase designs!
  - Tendency for *multiple* pre- and post-switch periods.
  - **BUT** a balanced number of pre- and post-switch periods is not always best!

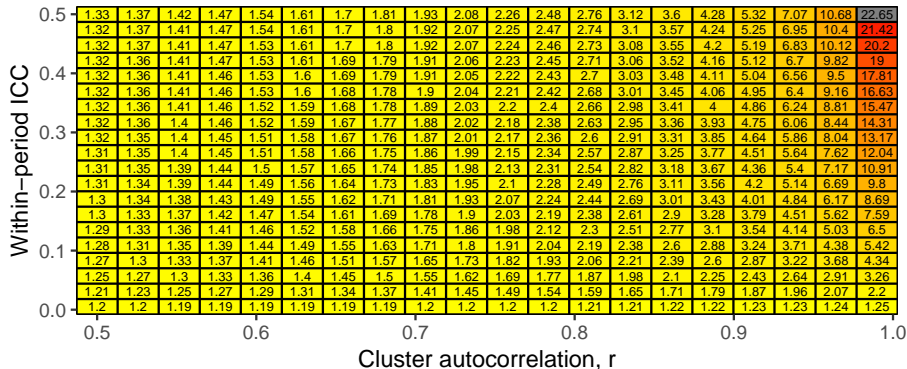
Explore our results at:

<https://monash-biostat.shinyapps.io/StaircaseDesign/>

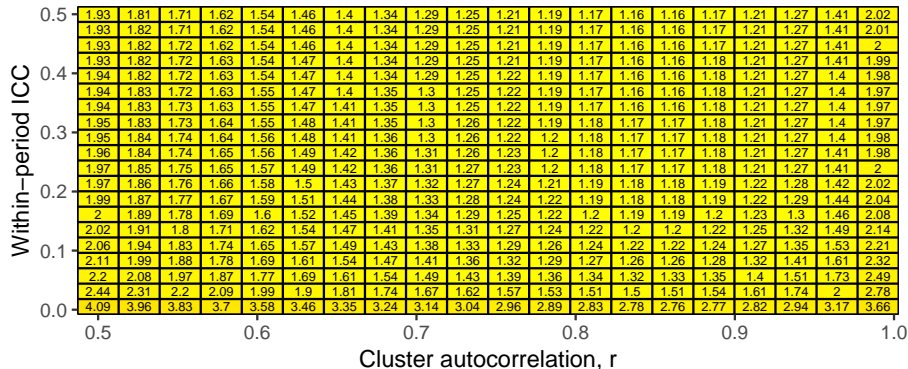
Future work:

- When is it possible to re-organise the observations in a stepped wedge design to come up with a **more efficient staircase**?
- Are there alternative incomplete stepped wedge designs that are better choices?

# 3 sequences, decaying between-period ICC

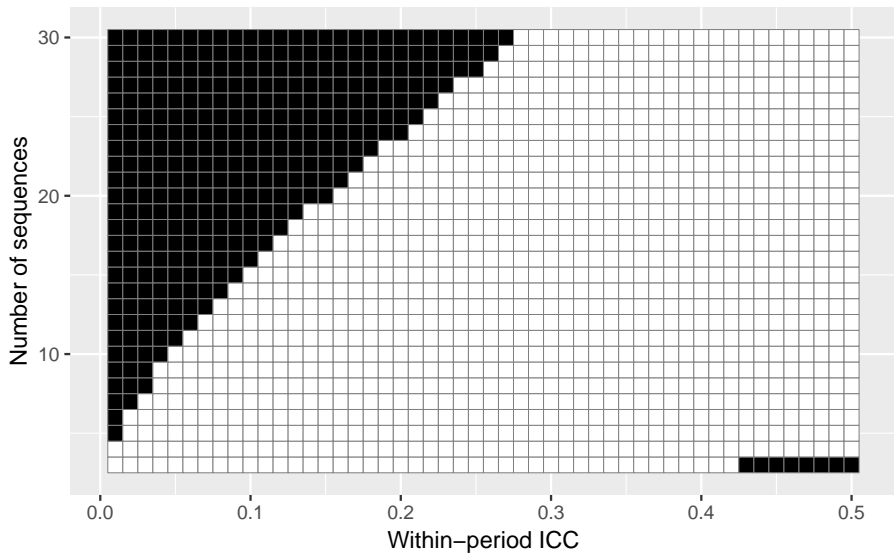


# 20 sequences, decaying between-period ICC



Black =  $SC(S, 2, 2)$ ; White =  $SC(S, 1, 3)$

Decaying BP ICC, CAC=0.99



Black =  $SC(S, 2, 2)$ ; White =  $SC(S, 1, 3)$

Decaying BP ICC, CAC=0.95

