Cluster Randomized Trial designs for time-varying intervention effects

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KEY POINTS:

- We derived and compared the variance estimators of exposure time varying effects (**TOI effects**) between different CRT designs.
- The **SW-CRT** has the most efficient estimator for the **early TOI effect**.
- The **PB-CRT** typically has the most efficient estimator for the **long-term** and **time-averaged TOI effects**.

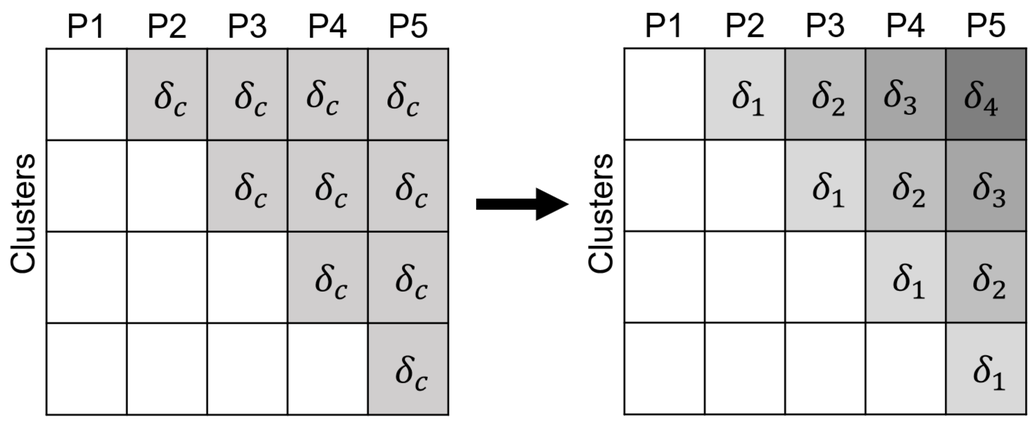
INTRODUCTION:

Cluster randomized trials (**CRTs**) are a useful alternative to the individually randomized controlled trial. In CRTs, clusters of individuals (e.g. schools, hospitals wards, communities) are randomized to receive the intervention.

The stepped-wedge cluster randomized trial (**SW-CRT**) is a popular type of CRT where clusters are randomized into sequences to begin receiving the intervention at different periods.

This design was recently used to study a novel co-rounding palliative care intervention on patient length of stay in the Singapore General Hospital (**SGH**).

The SGH study assumed a constant effect δ_c for the novel intervention. However, in practice, the intervention effect may vary as a function of exposure time. Such effects are referred to as time-on-intervention (**TOI**) effects δ_x where $x = 1, \ldots, d$.



The TOI effect estimands of interest are the:

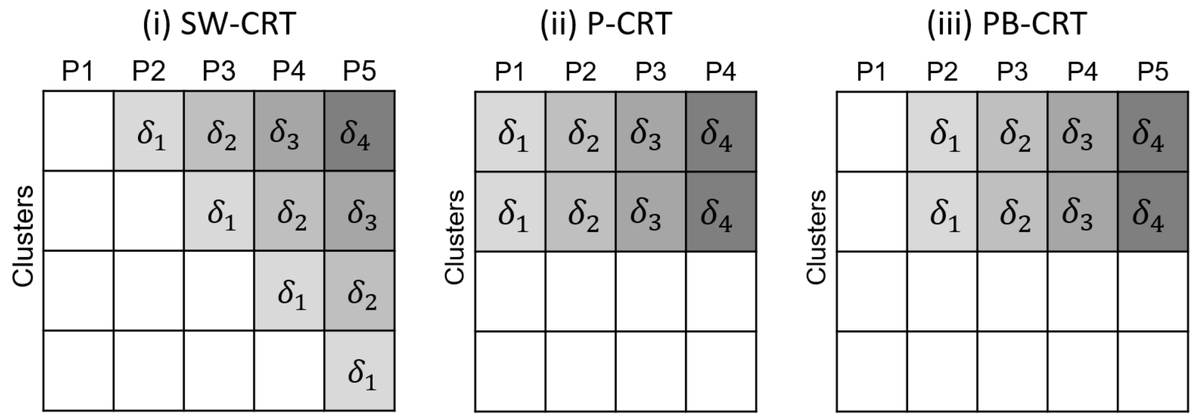
- **Early TOI effect:** δ_1
- **Long-term TOI effect:** $\delta_d = \delta_4$
- **Time-averaged TOI effect:** $\delta_{TA} = \left[\sum_{x=1}^{d} \delta_x\right]/d$

HYPOTHESIS:

- Due to the design's staggered crossover, estimates of long-term effects δ_d are less efficient than estimates of earlier TOI effects.
- Alternative CRT designs may be more efficient at modelling certain TOI effects than the SW-CRT.

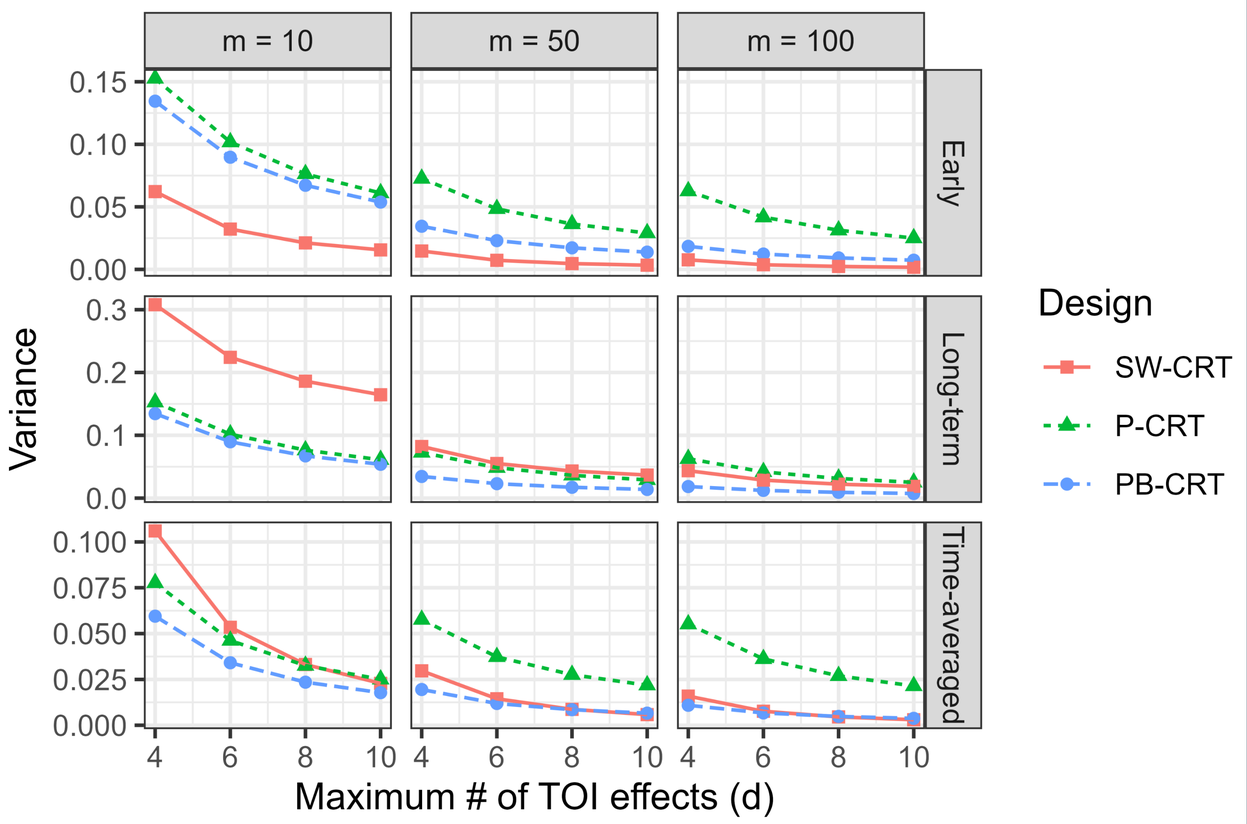
GOAL:

Derive and compare the variance estimators of TOI effects between different CRT designs.



NUMERICAL RESULTS:

The most efficient CRT design for estimating TOI effects (ICC = 0.05, m = cluster:period cell size).



SIMULATION RESULTS:

The simulation parameters were based on a SW-CRT exploring the impact of discontinuing weekend health services in hospital wards. Early $\delta_1 = 0.14$, long-term $\delta_d = 0.29$, and time-averaged $\delta_{TA} = 0.23$ TOI effects

Design	$\widehat{\delta}_1$ (SE)	$\widehat{\delta}_d$ (SE)	$\widehat{\delta}_{TA}$ (SE)
(i) SW-CRT	0.145 (0.034)	0.410 (0.093)	0.267 (0.048)
(ii) P-CRT	0.151 (0.182)	0.279 (0.182)	0.240 (0.178)
(iii) PB-CRT	0.168 (0.059)	0.296 (0.061)	0.258 (0.045)

CONCLUSIONS:

1. The **SW-CRT** has the most efficient estimator for the **early TOI effect**.
2. The **PB-CRT** typically has the most efficient estimator for the **long-term** and **time-averaged TOI effects**.
3. The **PB-CRT** with TOI effects can be a more appropriate CRT design for modelling TOI effects.

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