Sample Size calculations for Stepped Wedge Trials

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(Joint work with Rumana Omar, Andrew Copas, Emma Beard, James Hargreaves and Gareth Ambler)

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Objectives of the project/paper

Work supported by a NIHR Research Methods Opportunity Funding Scheme Grant (**RMOFS-2013-03-02**)

- Critically investigate the conditions under which applying a stepped wedge design can result in potential gains in terms of
  - Efficiency
  - Statistical power
  - Financial/ethical implications

- Produce a toolbox to perform power calculations
  - Simulation-based approach
  - Extension to more general models

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- Have lots of fun working in the "Special Issue Crew"!

Analytical formulæ

Modelling & sample size calculations

Analytical formulæ

- *Hussey & Hughes (2007) + "Reprise": Hughes et al (2015)*
  - Specifically for cross-sectional data. Defines cluster- and time-specific average outcome as $\mu_{ij} = \mu + \alpha_i + \beta_j + X_{ij}\theta$
  - Can compute

$$\text{Power} = \Phi\left(\frac{\theta}{\sqrt{V(\theta)}} - z_{\alpha/2}\right)$$

    where $V(\theta) = f(\boldsymbol{X}, I, J, \sigma^2_e, \sigma^2_\alpha)$
  - Can use asymptotic normality, eg for binary or count outcomes

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- Design Effect (DE) — *Wortman et al (2013) + Hemming & Taljaard (2015)*
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- Some generalisations (*Hemming et al 2014*)
  - "Multiple layers of clustering" + "incomplete" SWT

Modelling & sample size calculations

Simulation-based calculations *Baio et al (2015)*

- Can directly model different types of outcomes (eg binary or counts)
  - The linear predictor is just defined using a suitable transformation $g(\cdot)$
- Can extend model to account for specific features of the SWT
  - Repeated measurements (eg closed-cohort) — add extra random effect

$$v_{ik} \sim \text{Normal}(0, \sigma^2_v)$$

  - Specify time trends (eg quadratic or polynomial)
  - Include cluster-specific intervention effects

$$X_{ij}(\theta + u_i) \qquad \text{with} \qquad u_i \sim \text{Normal}(0, \sigma^2_u)$$

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- Helps alignment of **design** and **analysis** model
  - This is one of the issues identified by the literature review
  - More flexibility at design stage to match complexity of data generating process as well as analysis model (mixed effects, GEE, etc)

Simulation-based vs analytical calculations

ICC	Analytical power based on HH $K = 20, J = 6$	Simulation-based calculations $K = 20, J = 6$
Continuous outcome[a]		
0	9	9
0.1	13	13
0.2	14	13
0.3	14	14
0.4	14	14
0.5	14	14
Binary outcome[b]		
0	11	15
0.1	17	16
0.2	18	17
0.3	18	18
0.4	18	18
0.5	18	18
Count outcome[c]		
0	8	8
0.1	13	12
0.2	13	12
0.3	13	12
0.4	13	11
0.5	13	11

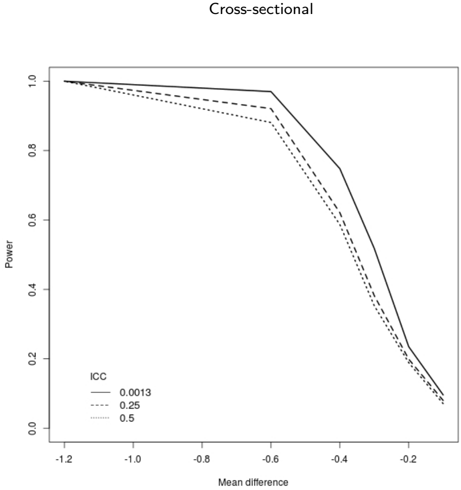
[a] Intervention effect $= -0.3785$; $\sigma_e = 1.55$.
[b] Baseline outcome probability $= 0.26$; OR $= 0.56$.
[c] Baseline outcome rate $= 1.5$; RR $= 0.8$.

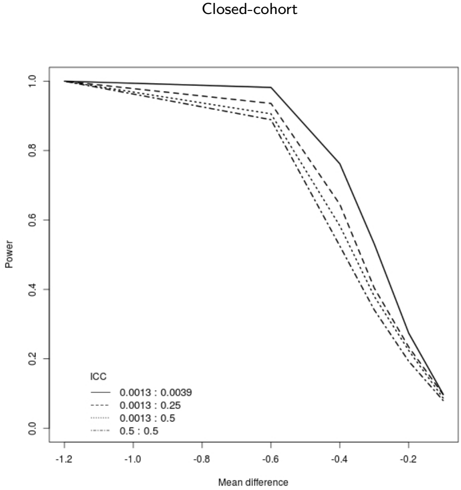
Notation: K = number of subjects per cluster; J = total number of time points, including one baseline.

The cells in the table are the estimated number of clusters as a function of the ICC and outcome type, to obtain 80% power

Cross-sectional vs closed-cohort data

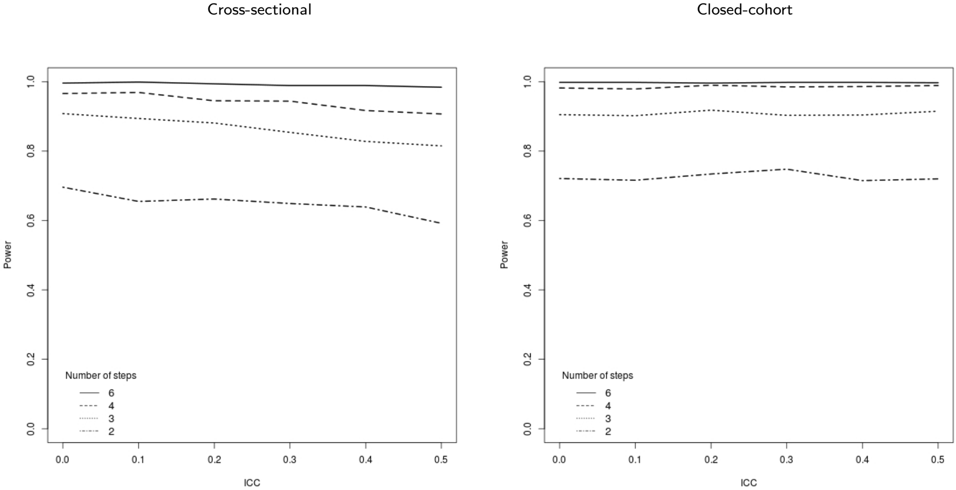
Effect size & ICC — Continuous outcome





$I = 25$ clusters, each with $K = 20$ subjects; $J = 6$ time points ($\equiv$ measurements) including one baseline

Number of steps — Binary outcome



$I = 24$ clusters, each with $K = 20$ subjects; individual-level ICC$= 0.0016$ for closed-cohort

R package SWSamp

- Will allow the user to run simulations for a set of "basic" models
  - Cross-sectional + closed-cohort data
  - Continuous (normal), binary and count outcome
- Provide template for custom data-generating models
- Include Bayesian alternative (based on `INLA`)
  - Comparable computational time to REML
  - Can use default priors but can also customise
- Explore issues with open-cohorts & time-to-event outcomes

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- Can use the name "Samp"...

(Only a very few!) References

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Thank you!