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Methods: Mind the Gap
Webinar Series

Power Calculations for Stepped Wedge Designs with Binary Outcomes: Methods and Software

Presented by:

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National Institutes of Health
Office of Disease Prevention

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Power Calculations for Stepped Wedge Designs with Binary Outcomes: Methods and Software

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Department of Biostatistics

Yale School of Public Health

Yale SCHOOL OF PUBLIC HEALTH

Center for Methods in Implementation and Prevention Science

- Promotes the adoption of research findings into clinical practice and develops and assesses sustainable interventions to improve public health
- Serves as an international leader in methods innovation for public health, providing biostatistical and methodological expertise on new implementation science projects

CMIPS Biostatistics Team

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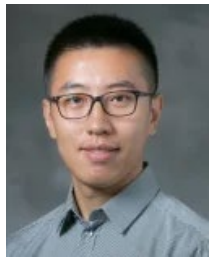


Laura Forastiere, PhD, Assistant Professor of Biostatistics

Additional CMIPS primary and associate faculty specialize in qualitative research and ethnography, health economics, maternal and child health promotion, global mental health promotion, cervical cancer prevention, and other areas of priority for the Center.

Outline

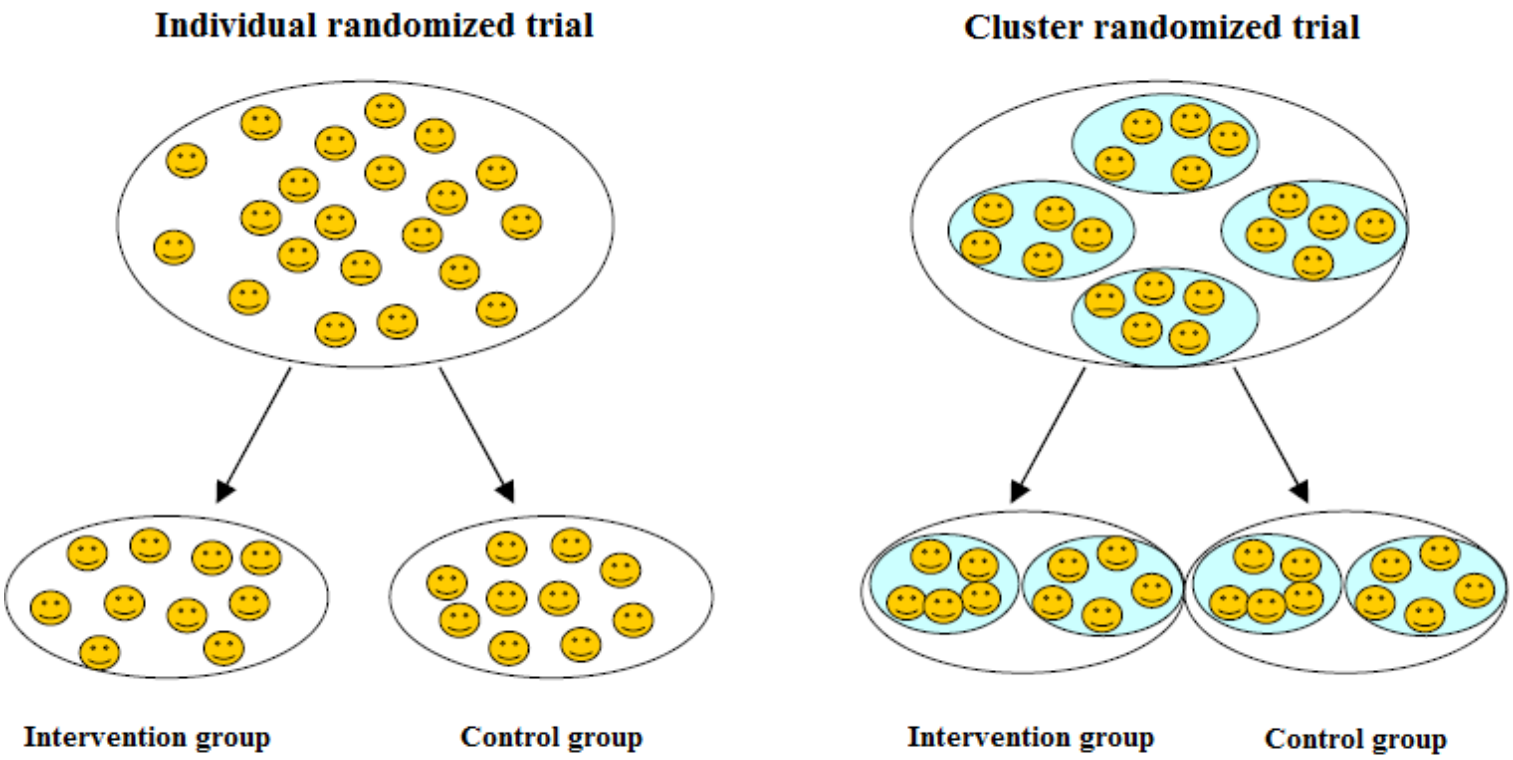
- Introduction of stepped wedge designs (SWDs)
- Existing power calculation methods for SWDs with binary outcomes
- Power calculation using a maximum likelihood approach for SWDs with binary outcomes
- Power calculation using generalized estimating equations for SWDs with binary outcomes
- Software

Motivating example

- During the year following the birth of a child, 40% of women are estimated to have an unmet need for contraception.
- Postpartum intrauterine device (PPIUD) meets women's need for contraceptive protection following childbirth
  - Long-term contraceptive protection
  - Reversible
  - Safe, effective and convenient
  - Does not interfere with breastfeeding during the postpartum period
- Uptake of PPIUD is low
  - PPIUD insertion should be performed by a trained provider in the early postpartum period
  - The services are not widely available
- The International Federation of Gynaecology and Obstetrics (FIGO) implements an intervention that institutionalize PPIUD services
  - as a routine part of antenatal counselling
  - as a part of delivery room services

Canning, D. et al. (2016) Institutionalizing postpartum intrauterine device (PPIUD) services in Sri Lanka, Tanzania, and Nepal: study protocol for a longitudinal cluster-randomized stepped wedge trial. BMC Pregnancy and Childbirth 16, 362.

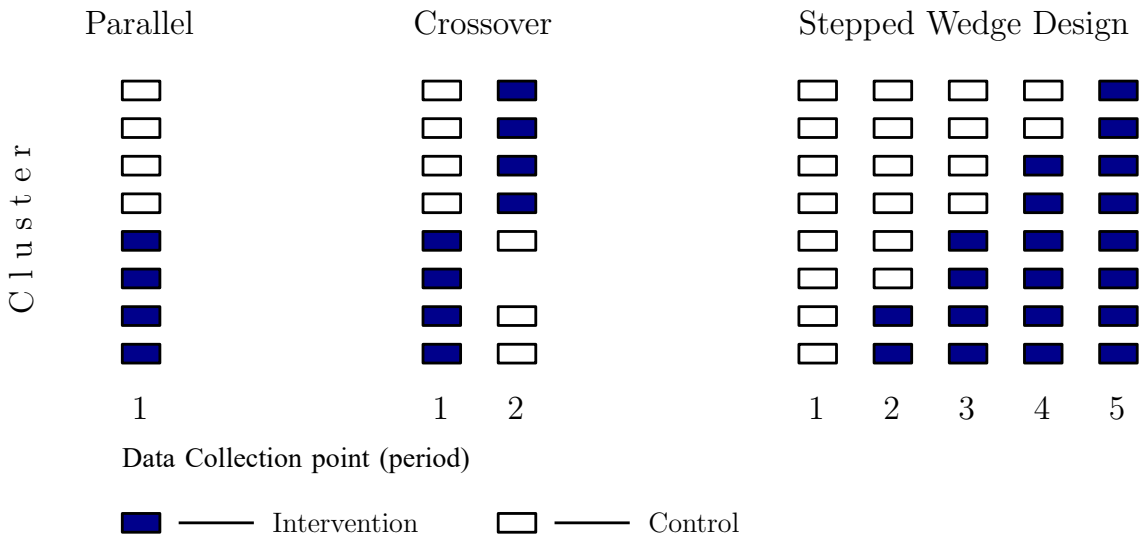
Cluster randomized trials



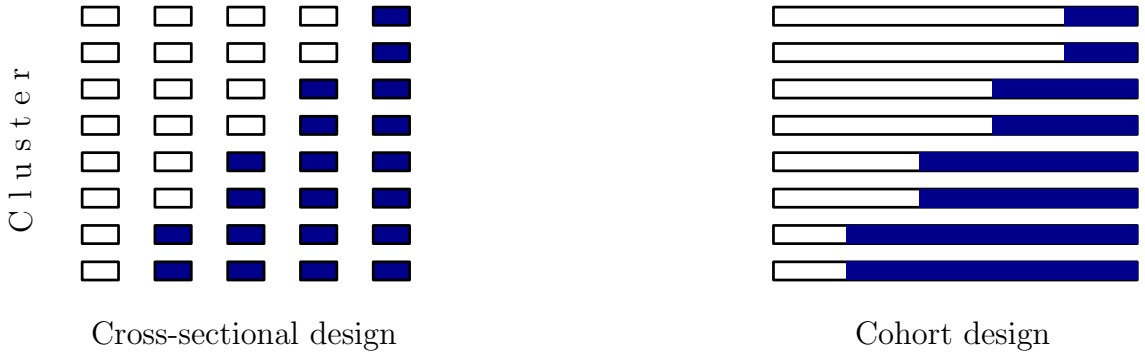
- Intervention requires application at a cluster level
- Avoid contamination (e.g. sharing medication or health messages)

Cluster randomized trials

- Different types of cluster randomized trials (CRT)

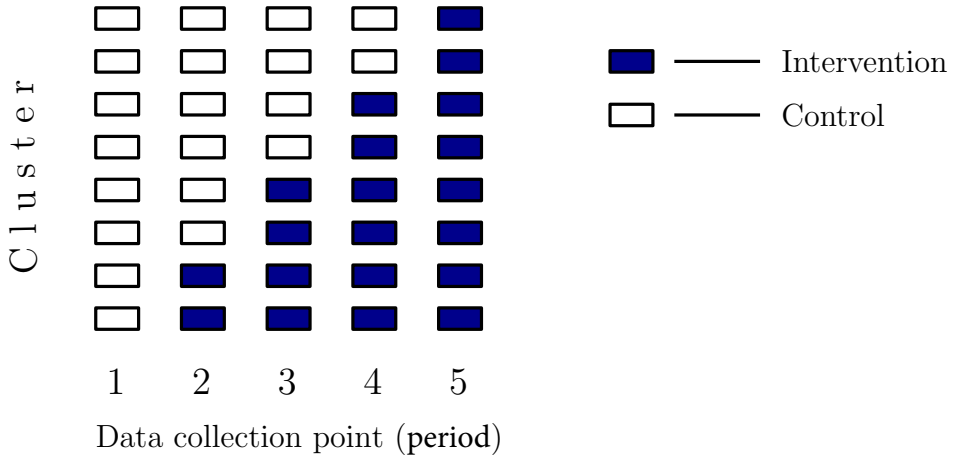


- Cross-sectional v.s. cohort designs



Stepped wedge design

- Stepped Wedge Design (SWD)



Ethics: all clusters need to get the potentially efficacious treatment
Feasibility: not able to give the intervention simultaneously to many clusters

Spiegelman, D. (2016) Evaluating public health interventions: 2. Stepping up to routine public health evaluation with the stepped wedge design. Am J Public Health 106(3), 453-457.

Motivating example

Postpartum intrauterine device (PPIUD) study design

- Collaboration with

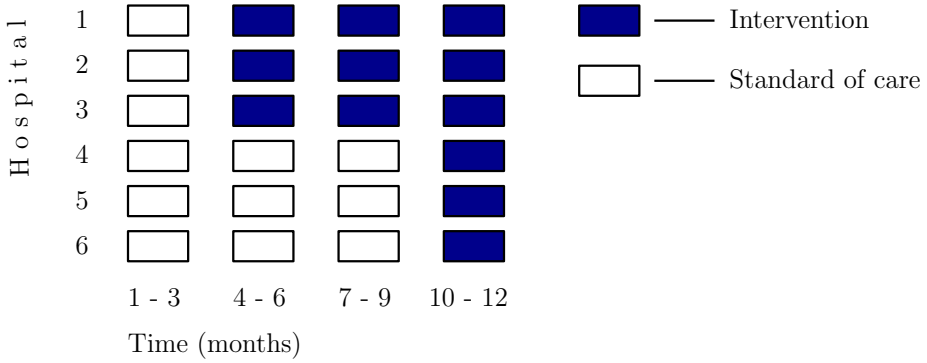
  International Federation of Gynaecology and Obstetrics (FIGO)
  Association of Gynaecologists and Obstetricians of Tanzania (AGOTA)
  Harvard T.H. Chan School of Public Health (HSPH)

- Impact of PPIUD use in Tanzania

Motivating example

Postpartum intrauterine device (PPIUD) study design

- Power to detect the effectiveness of PPIUD in preventing unintended pregnancy for 1.5 years following the index birth
- Enrollment is one year long.
- There are 6 clusters (hospitals), and 4 time periods.
- Each time period is 3 months long for enrollment.
- Approximately 900 women join each hospital in three months
- The cluster size is expected to be 900*4=3,600.



Power calculation

- Statistical power is an important component of study design

The **power** of a statistical test H_0 v.s. H_A :

Power = Pr(reject H_0 | H_A is true)

Type I error (false positive) : the error of rejecting H_0 when it is actually true.	$\alpha = \Pr(\text{Type I error})$
Type II error (false negative) : the error of failing to reject H_0 when H_A is true.	$\beta = \Pr(\text{Type II error})$

$$\text{Power} = 1 - \beta$$

Existing power calculation method

Hussey and Hughes (2007)

- Apply a linear mixed model (LMM) for continuous outcomes

$$Y_{ijk} = \mu + X_{ij}\beta + \gamma_j + b_i + \epsilon_{ijk},$$

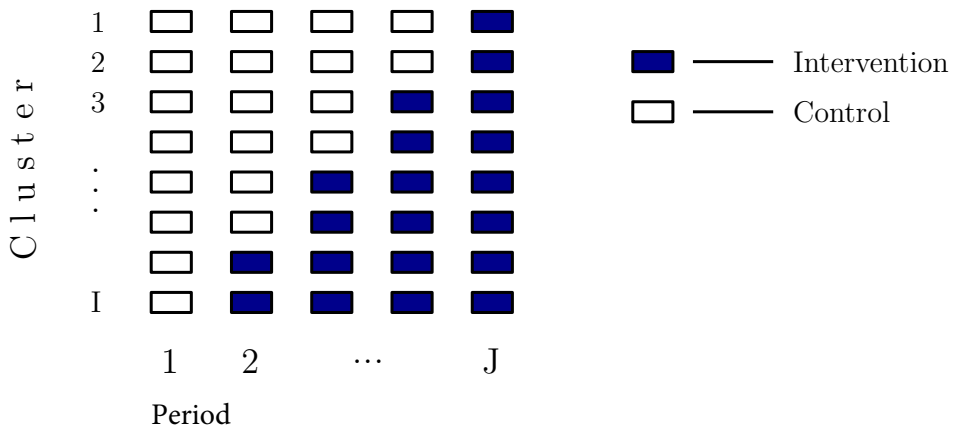
where Y_{ijk} is the outcome of individual $k(\in \{1, \cdots, K\})$ at time period $j(\in \{1, \cdots, J\})$ from cluster $i(\in \{1, \cdots, I\})$,

X_{ij} is an indicator of the treatment (1=intervention; 0=control),

μ is the expected outcome at baseline (control at period 1), β is the treatment effect,

γ_j is the time effect corresponding to period j ($\gamma_1 = 0$ for identifiability),

$\epsilon_{ijk} \sim N(0, \sigma_e^2)$ is the error term, $b_i \sim N(0, \tau^2)$ is the random effect for cluster i



Hussey, M.A. and Hughes, J.P. (2007) Design and analysis of stepped wedge cluster randomized trials. Contemporary Clinical Trials 28(2) 182-191

Existing power calculation method

Hussey and Hughes (2007)

- Power calculation is based on a Wald test for

$$H_0 : \beta = 0 \text{ versus } H_A : \beta = \beta_A.$$

- The power for conducting a two-tailed test of size α is

$$power = \Phi\left(\frac{|\beta_A|}{\sqrt{Var(\widehat{\beta})}} - Z_{1-\alpha/2}\right),$$

where $\Phi(\cdot)$ is the cumulative standard Normal distribution,
$Z_{1-\alpha/2}$ is the $(1-\alpha/2)$'th quantile of the standard Normal distribution.

- The estimated treatment effect $\widehat{\beta}$ is obtained from a weighted least squares (WLS) analysis, assuming that σ_e^2 and τ^2 are known.

Existing power calculation method

Hussey and Hughes (2007)

- The linear mixed model (LMM) for continuous outcomes

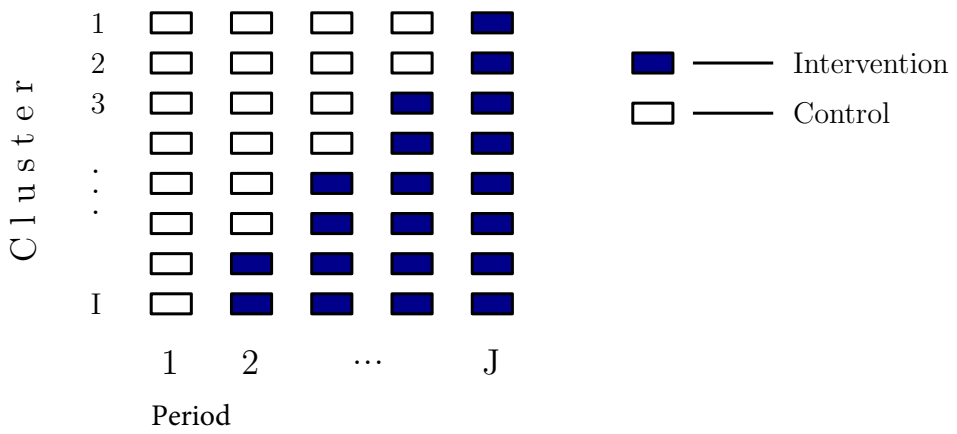
$$Y_{ijk} = \mu + X_{ij}\beta + \gamma_j + b_i + \epsilon_{ijk},$$

where $\epsilon_{ijk} \sim N(0, \sigma_e^2)$ is the error term, $b_i \sim N(0, \tau^2)$ is the random effect for cluster i.

- The variance of $\widehat{\beta}$ is [1]

$$Var(\widehat{\beta}) = \frac{I\sigma^2(\sigma^2 + J\tau^2)}{(IU - W)\sigma^2 + (U^2 + IJU - JW - IV)\tau^2},$$

where $\sigma^2 = \sigma_e^2/K$, $U = \sum_{ij} X_{ij}$, $W = \sum_j (\sum_i X_{ij})^2$, and $V = \sum_i (\sum_j X_{ij})^2$.



[1] Hussey, M.A. and Hughes, J.P. (2007) Design and analysis of stepped wedge cluster randomized trials. Contemporary Clinical Trials 28(2), 182-191.

Existing power calculation method

Hussey and Hughes (2007)

- Pros

  closed-form formula for power calculation
  Simple and fast

- Cons

  Not designed for binary outcomes

- SWD power calculation software for binary outcomes

  Excel spreadsheet

  - For binary outcomes: http://faculty.washington.edu/jphughes/Power%20for%20stepped%20wedge.xls

  - Normal approximation: $\sigma_e^2 = [0.5(p_1 + p_2)][1 - 0.5(p_1 + p_2)]$.

  PASS Sample Size Software: several options on the approximation of the variance

  $\sigma_e^2 = p_1(1 - p_1)$
  $\sigma_e^2 = [0.5(p_1 + p_2)][1 - 0.5(p_1 + p_2)]$
  $\sigma_e^2 = 0.5p_1(1 - p_1) + 0.5p_2(1 - p_2)$

Existing power calculation method

Hussey and Hughes' approximation method for binary outcomes

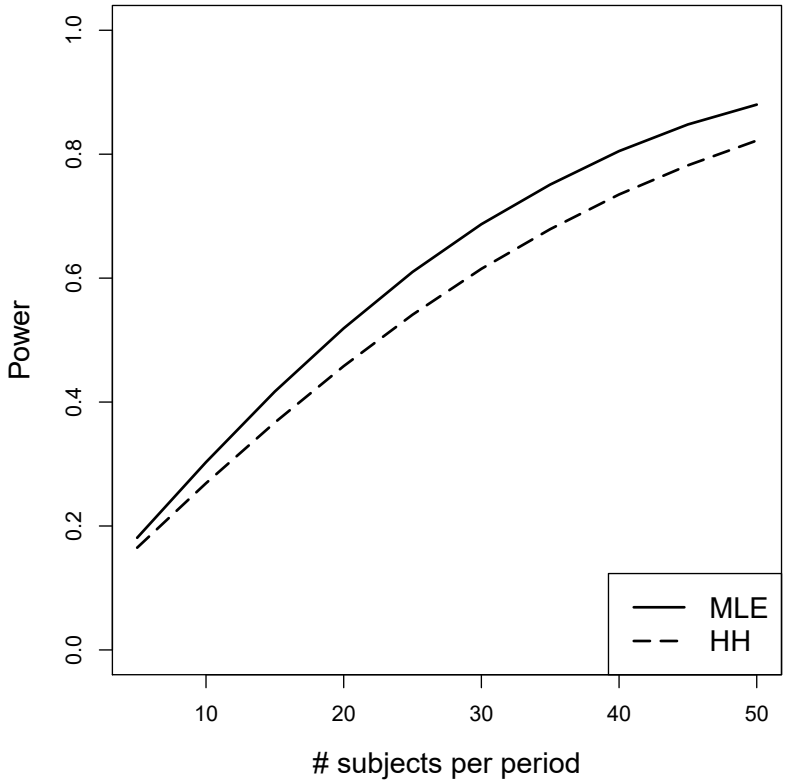
- It is inaccurate.[1]

- A toy example

  24 Clusters
  3 time periods
  Baseline proportion:
  $p_1 = 50\%$
  Proportion after intervention: $p_2 = 40\%$
  ICC ρ=0.1

- To achieve 80% power

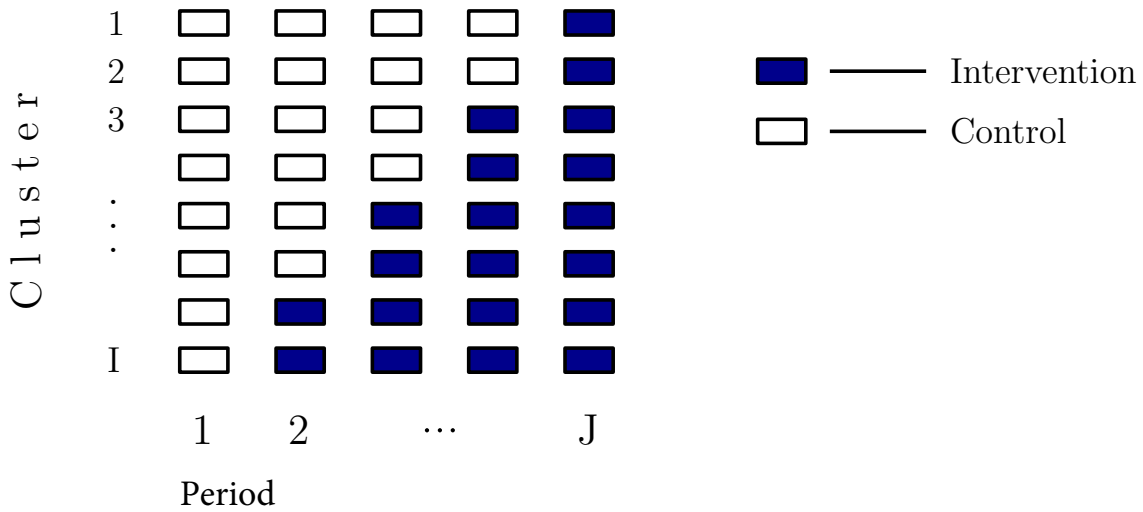
  H&H: required sample size 3,456
  MLE: required sample size 2,880



[1] Zhou, X., Liao, X., Kunz, L.M., Normand, S.L.T. and Spiegelman, D. (2020) A maximum likelihood approach to power calculations for stepped wedge designs of binary outcomes. Biostatistics 21(1), 102-121.

Method – a Maximum Likelihood Approach

- We consider a binary treatment X_{ijk} and a binary outcome Y_{ijk} for individual k in cluster i at time period j, where $i \in \{1, \cdots, I\}$, $j \in \{1, \cdots, J\}$, and $k \in \{1, \cdots, K\}$.
- The cluster size is $N = J \cdot K$, and the sample size is $I \cdot J \cdot K$.
- Two cases: without time effects and with time effects.



Zhou, X., Liao, X., Kunz, L.M., Normand, S.L.T. and Spiegelman, D. (2020) A maximum likelihood approach to power calculations for stepped wedge designs of binary outcomes. Biostatistics 21(1), 102-121.

Method – a Maximum Likelihood Approach

The model with time effects

- Apply a generalized linear mixed model (GLMM) for binary outcomes

$$g(p_{ijk}) = \mu + X_{ijk}\beta + \gamma_j + b_i,$$

where μ is the probability of the outcome at baseline (control at period 1),
β is the treatment effect
γ_j is the time effect corresponding to period j ($\gamma_1 = 0$ for identifiability)
$b_i \sim N(0, \tau^2)$ is the random effect for cluster i,
$p_{ijk} = E(Y_{ijk}|X_{ijk}, b_i) = Pr(Y_{ijk} = 1|X_{ijk}, b_i)$

- The parameters $\boldsymbol{\theta} = (\mu, \beta, \gamma_2, \cdots, \gamma_J, \tau^2)$.

- Link function $g(\cdot)$

Identity link – parameter of interest is the risk difference
Log link – parameter of interest is the risk ratio (relative risk)
Logit link – parameter of interest is odds ratio

Method – a Maximum Likelihood Approach

The model without time effects

- Apply a generalized linear mixed model (GLMM) for binary outcomes

$$g(p_{ijk}) = \mu + X_{ijk}\beta + b_i,$$

where μ is the probability of the outcome at baseline (control at period 1),
β is the treatment effect
$b_i \sim N(0, \tau^2)$ is the random effect for cluster i,
$p_{ijk} = E(Y_{ijk}|X_{ijk}, b_i) = Pr(Y_{ijk} = 1|X_{ijk}, b_i)$

- The parameters $\boldsymbol{\theta} = (\mu, \beta, \tau^2)$.

Method – a Maximum Likelihood Approach

Power calculation

- The asymptotic power for $H_0 : \beta = 0 \text{ versus } H_A : \beta = \beta_A$

$$power = \Phi\left(\frac{|\beta_A|}{\sqrt{Var(\widehat{\beta})}} - Z_{1-\alpha/2}\right).$$

- In the likelihood theory, $Var(\widehat{\beta})$ can be obtained by the inverse of information matrix.

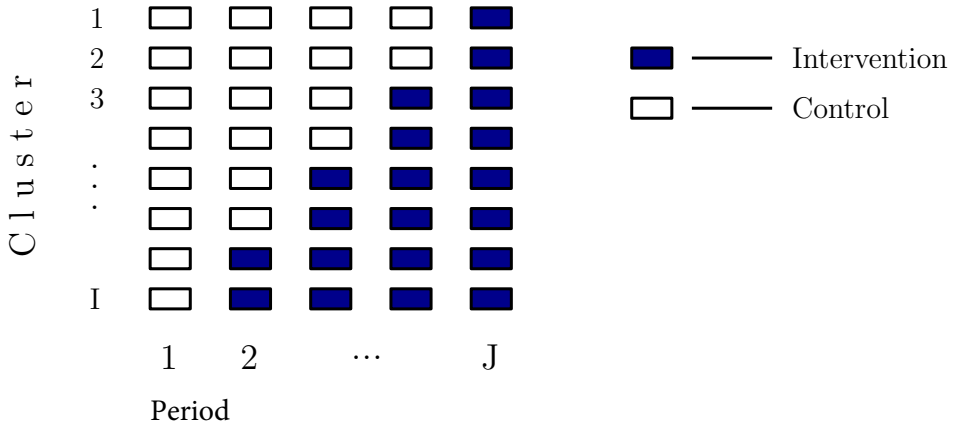
Method – Generalized Estimating Equations

GEE model with time effects

- Apply a generalized estimating equations model (GEE) for binary outcomes

$$g(p_{ijk}) = \mu + X_{ijk}\beta + \gamma_j,$$

  where γ_j is the time effect corresponding to time period j ($\gamma_1 = 0$ for identifiability)
- $p_{ijk} = P(Y_{ijk} = 1|X_{ijk})$.
- The link function $g(\cdot)$ can choose from: identity, log and logit links.
- The parameters $\boldsymbol{\theta} = (\mu, \beta, \gamma_2, \cdots, \gamma_J)$.



Li, F., Turner, E.L. and Preisser, J.S. (2018) Sample size determination for GEE analyses of stepped wedge cluster randomized trials. Biometrics 74, 1450-1458.

Method – Generalized Estimating Equations

- A correlation structure R_i with three levels of correlation is employed:

  α_0, within-period correlation ($\text{corr}(Y_{ijk}, Y_{ijk'}) = \alpha_0,\ k \neq k'$)
  α_1, inter-period correlation ($\text{corr}(Y_{ijk}, Y_{ij'k'}) = \alpha_1,\ j \neq j'$)
  α_2, within-individual correlation ($\text{corr}(Y_{ijk}, Y_{ij'k}) = \alpha_2,\ j \neq j'$)

$$
\begin{array}{c|cccc|cccc|cccc}
 & Y_{111} & Y_{112} & Y_{113} & Y_{114} & Y_{121} & Y_{122} & Y_{123} & Y_{124} & Y_{131} & Y_{132} & Y_{133} & Y_{134} \\
\hline
Y_{111} & 1 & \alpha_0 & \alpha_0 & \alpha_0 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 \\
Y_{112} & \alpha_0 & 1 & \alpha_0 & \alpha_0 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 \\
Y_{113} & \alpha_0 & \alpha_0 & 1 & \alpha_0 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 \\
Y_{114} & \alpha_0 & \alpha_0 & \alpha_0 & 1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 \\
Y_{121} & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & 1 & \alpha_0 & \alpha_0 & \alpha_0 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 \\
Y_{122} & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_0 & 1 & \alpha_0 & \alpha_0 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 \\
Y_{123} & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_0 & \alpha_0 & 1 & \alpha_0 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 \\
Y_{124} & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_0 & \alpha_0 & \alpha_0 & 1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 \\
Y_{131} & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & 1 & \alpha_0 & \alpha_0 & \alpha_0 \\
Y_{132} & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_0 & 1 & \alpha_0 & \alpha_0 \\
Y_{133} & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_0 & \alpha_0 & 1 & \alpha_0 \\
Y_{134} & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_0 & \alpha_0 & \alpha_0 & 1
\end{array}
$$

(a) cross-sectional

$$
\begin{array}{c|cccc|cccc|cccc}
 & Y_{111} & Y_{112} & Y_{113} & Y_{114} & Y_{121} & Y_{122} & Y_{123} & Y_{124} & Y_{131} & Y_{132} & Y_{133} & Y_{134} \\
\hline
Y_{111} & 1 & \alpha_0 & \alpha_0 & \alpha_0 & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_1 \\
Y_{112} & \alpha_0 & 1 & \alpha_0 & \alpha_0 & \alpha_1 & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_1 & \alpha_1 \\
Y_{113} & \alpha_0 & \alpha_0 & 1 & \alpha_0 & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_1 \\
Y_{114} & \alpha_0 & \alpha_0 & \alpha_0 & 1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_2 \\
Y_{121} & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_1 & 1 & \alpha_0 & \alpha_0 & \alpha_0 & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_1 \\
Y_{122} & \alpha_1 & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_0 & 1 & \alpha_0 & \alpha_0 & \alpha_1 & \alpha_2 & \alpha_1 & \alpha_1 \\
Y_{123} & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_1 & \alpha_0 & \alpha_0 & 1 & \alpha_0 & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_1 \\
Y_{124} & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_0 & \alpha_0 & \alpha_0 & 1 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_2 \\
Y_{131} & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_1 & 1 & \alpha_0 & \alpha_0 & \alpha_0 \\
Y_{132} & \alpha_1 & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_0 & 1 & \alpha_0 & \alpha_0 \\
Y_{133} & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_1 & \alpha_0 & \alpha_0 & 1 & \alpha_0 \\
Y_{134} & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_1 & \alpha_1 & \alpha_1 & \alpha_2 & \alpha_0 & \alpha_0 & \alpha_0 & 1
\end{array}
$$

(b) closed cohort

Method – Generalized Estimating Equations

GEE model with time effects

- For cluster i, $Y_i = (Y_{i11}, Y_{i12}, \cdots, Y_{iJK})^T$ and $p_i = (p_{i11}, p_{i12}, \cdots, p_{iJK})^T$.
- The GEE estimator $\widehat{\boldsymbol{\theta}}$ is obtained by solving the equation

$$\sum_{i=1}^{I} \mathrm{D}_i^T \mathrm{V}_i{}^{-1}(Y_i - p_i) = 0.$$

$\mathrm{D}_i = \partial p_i / \partial \boldsymbol{\theta}$, $\mathrm{V}_i = A_i{}^{1/2} R_i A_i{}^{1/2}$
A_i is the N-dimensional diagonal matrix with elements $v(p_{ijk})$
The variance function is $v(p_{ijk}) = p_{ijk}(1 - p_{ijk})$.
R_i is the working correlation matrix for cluster i

- The covariance of $\widehat{\boldsymbol{\theta}}$ can be obtained by the model-based estimator $(\sum_i \mathrm{D}_i(\boldsymbol{\theta})^T \mathrm{V}_i^{-1}(\boldsymbol{\alpha}) \mathrm{D}_i(\boldsymbol{\theta}))^{-1}$. Hence, we can calculate the variance of $\widehat{\beta}$.

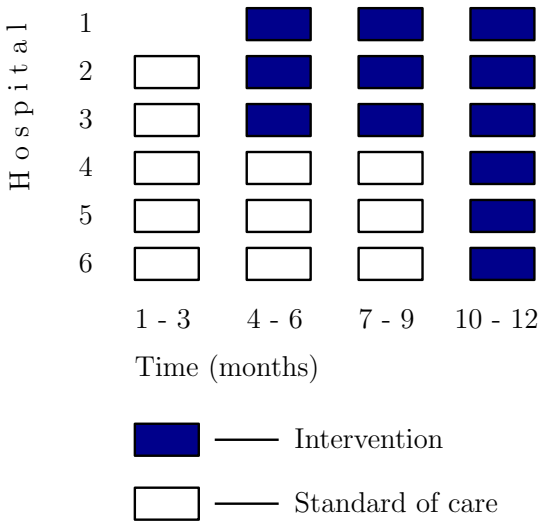
Design example

PPIUD study

- Outcome: unintended pregnancy within 1.5 years of the index birth
- 6 hospitals and 4 time periods
- K=900, cluster size $N = J \cdot K$=3600
- Baseline unintended pregnancy rate: 18.1%
- Expected unintended pregnancy rate after intervention

  14.5% – relative risk 0.8
  16.3% – relative risk 0.9
- ICC ρ=0.022
- Hypothetical time effects

  No time effects $\delta = 0$
  Negligible time effects $\delta = -0.01\%$
  5% reduction of the baseline unintended pregnancy rate $\delta = -0.91\%$
  10% reduction of the baseline unintended pregnancy rate $\delta = -1.81\%$



Design example

Expected pregnancy rate	Time effects							
	δ = 0		δ = -0.01%		δ = -0.91%		δ = -1.81%	
	RR=0.8	RR=0.9	RR=0.8	RR=0.9	RR=0.8	RR=0.9	RR=0.8	RR=0.9
MLE (conditional)	1	0.908	0.976	0.480	0.981	0.494	0.984	0.506
GEE (marginal)	1	0.859	0.945	0.423	0.957	0.449	0.967	0.474
Hussey & Hughes	1	0.850	0.935	0.412	0.935	0.412	0.935	0.412

Software

- Hussey and Hughes method is often inaccurate for binary outcomes. Power may be over- or under-estimated.
- To improve this approximation, Zhou et al. proposed a conditional method, and Li et al. proposed a marginal method for binary outcomes, respectively.
- The motivation for developing **swdpwr**:

  These new methods had not yet been implemented in publicly available software such as SAS and R.

  Additionally, existing software for SWDs focused on limited settings and did not have accurate power calculations for binary outcomes.
- We have developed user-friendly software **swdpwr** (SAS macro and R package) to implement power calculations for SWDs with both continuous and binary outcomes and incorporate as various settings as possible.

Chen, J., Zhou, X., Li, F. and Spiegelman, D. (2022) swdpwr: A SAS macro and an R package for power calculations in stepped wedge cluster randomized trials. Computer Methods and Programs in Biomedicine 213, 106522.

Software

Two Statistical Models

- Two statistical models can be used to account for the intra-class correlations in SWDs: conditional models and marginal models.
- Conditional models are based on mixed effects models, which accommodate the intra-class correlations via latent random effects.
- Marginal models describe the population-averaged response values across cluster-periods, and are usually fitted with the generalized estimating equations (GEE).
- The interpretations of regression parameters can be different under these two models, with the important exception of the identity and log links when random effects and the covariates are independent, as is typically assumed.

Software

Conditional Model - Binary Outcomes

For binary outcomes, consider a **cross-sectional** SWD which is modelled by a generalized linear mixed model (GLMM):

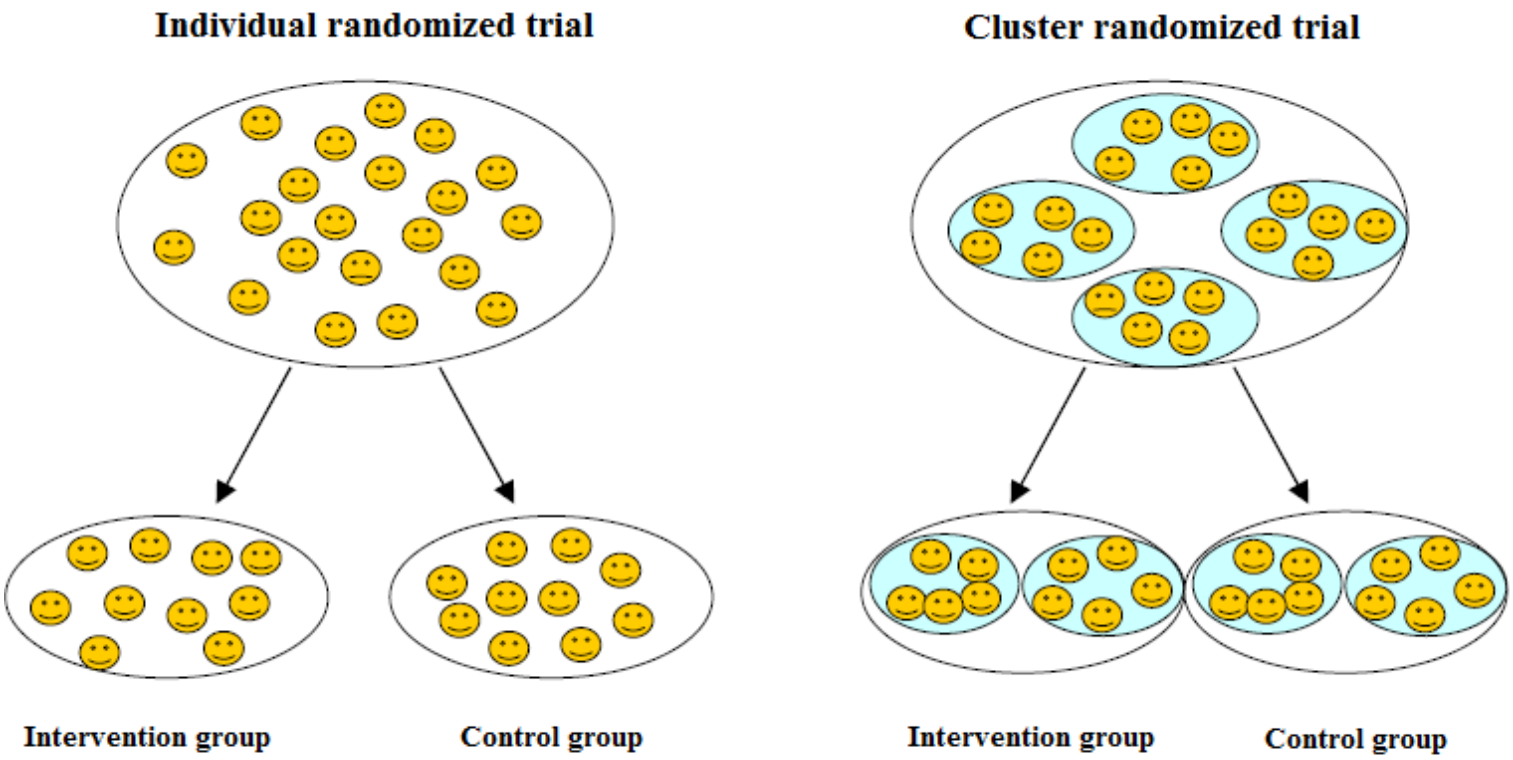
$$g(p_{ijk}) = \mu + X_{ijk}\beta + \gamma_j + b_i.$$

- $g(\cdot)$ can choose from: identity, log and logit links.
- $b_i \sim N(0, \tau^2)$ is the random effect.
- The correlation structure for this case is $\alpha_0 = \alpha_1 = \alpha_2$.
- $p_{ijk} = P(Y_{ijk} = 1|X_{ijk}, b_i)$ is the conditional probability of the outcome for each individual.
- Then we derive the likelihood of the observed outcomes based on the conditional probability under the specific link function. The calculation of the large-sample variance and power is then based on the theory of MLE.
- We also consider the case without time effects (all $\gamma_t = 0$). The model is

  $$g(p_{ijk}) = \mu + X_{ijk}\beta + b_i.$$

  The derivations of the likelihood formula and power are similar to the procedures with time effects.

Cluster randomized trials



- Intervention requires application at a cluster level
- Avoid contamination (e.g. sharing medication or health messages)

Software

Methods implemented:

- Conditional model [1]

  Only available for the cross-sectional design with $\alpha_0 = \alpha_1$
  Three link functions: identity, log, logit
  With time effects and without time effects
  Intensive computation

- Marginal model [2]

  available for the cross-sectional design and cohort design with flexible covariance structures
  Three link functions: identity, log, logit
  With time effects and without time effects
  Has closed-forms for power calculation.

[1] Zhou, X., Liao, X., Kunz, L.M., Normand, S.L.T. and Spiegelman, D. (2020) A maximum likelihood approach to power calculations for stepped wedge designs of binary outcomes. Biostatistics 21(1), 102-121.

[2] Li, F., Turner, E.L. and Preisser, J.S. (2018) Sample size determination for GEE analyses of stepped wedge cluster randomized trials. Biometrics 74, 1450-1458.

Software

The arguments of swdpower in the R package **swdpwr**

```
swdpower(K, design, family = "binomial",  model = "conditional",
    link = "identity", type = "cross-sectional", meanresponse_start = NA,
    meanresponse_end0 = meanresponse_start, meanresponse_end1 = NA,
    effectsize_beta = NA, sigma2 = 0, typeIerror = 0.05,
    alpha0 = 0.1, alpha1 = alpha0/2, alpha2 = NA)
```

Chen, J., Zhou, X., Li, F. and Spiegelman, D. (2022) swdpwr: A SAS macro and an R package for power calculations in stepped wedge cluster randomized trials. Computer Methods and Programs in Biomedicine 213, 106522.

Software

Argument	Description	Default
K	Number of individuals at each time period in a cluster, or the average cluster-period size under variable cluster-period sizes	
Design	I*J dimensional data set that describes the study design, unequal allocation of sequences and only complete designs with no transition periods are allowed	
family	Specify family="gaussian" for continuous outcome, family="binomial" for binary outcome	"binomial"
model	Specify model="conditional" for conditional model. Model="marginal" for marginal model	"conditional"
link	Choose link function from link="identity". Link="log" and link="logit"	"identity"
type	Specify type="cohort" for closed cohort study. Type="cross-sectional" for cross-sectional study	NA
meanresponse_start	The anticipated mean response ion the control group at the start of the study	"cross-sectional"
meanresponse_end0	The anticipated mean response in the control group at the end of the study	meanresponse_start
meanresponse_end1	The anticipated mean response in the intervention group at the end of the study	NA
effectsize_beta	The anticipated effect size	NA
sigma2	Marginal variance of the outcome (only allowed if is continuous outcome)	0
typeIerror	Two-sided Type I error	0.05
alpha0	Within-period intracluster correlation α_0	0.1
alpha1	Between-period intracluster correlation α_1	Alpha0/2
alpha2	Within-individual correlation α_2 (only allowed if type="cohort")	

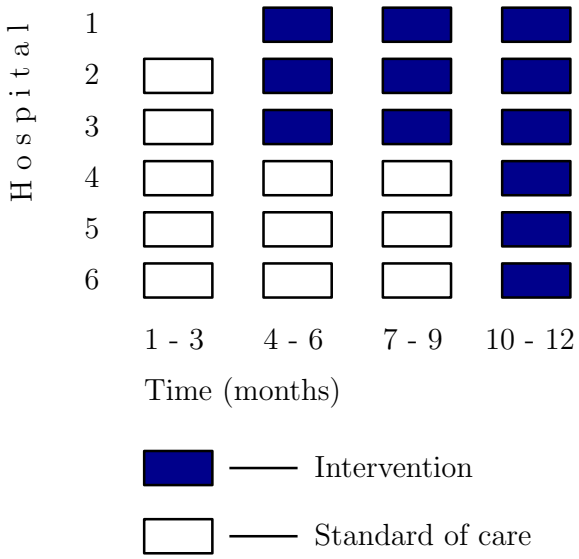
Software

Example: PPIUD study

- Outcome: pregnancy within 1.5 years of the index birth
- 6 hospitals and 4 time periods
- K=900, cluster size $N = J \cdot K$=3600
- Baseline pregnancy rate: 18.1%, and expected to be 16.3% after intervention
- ICC ρ=0.022
- Hypothetical time effects

  No time effects $\delta = 0$

  Negligible time effects $\delta = -0.01\%$



Software

Example: PPIUD study with no time effects

```
R> library("swdpwr")
R> data = matrix(c(rep(c(0, 1, 1, 1), times = 3),
+ rep(c(0, 0, 0, 1), times = 3)), nrow = 6, ncol = 4, byrow = TRUE)
R> swdpower(K = 900, design = data, family = "binomial",  model = "marginal",
+ link = "logit", type = "cross-sectional", meanresponse_start = 0.181,
+ meanresponse_end0 = 0.181, meanresponse_end1 = 0.163,
+ typeIerror = 0.05, alpha0 = 0.022, alpha1 = 0.022)

This cross-sectional study has total sample size of 21600
Power for this scenario is 0.859 for the alternative hypothesis treatment effect
beta = -0.126 ( two-sided Type I error =  0.05 )
```

Software

Example: PPIUD study with negligible time effects

```
R> library("swdpwr")
R> data = matrix(c(rep(c(0, 1, 1, 1), times = 3),
+ rep(c(0, 0, 0, 1), times = 3)), nrow = 6, ncol = 4, byrow = TRUE)
R> swdpower(K = 900, design = data, family = "binomial",  model = "marginal",
+ link = "logit", type = "cross-sectional", meanresponse_start = 0.181,
+ meanresponse_end0 = 0.1809, meanresponse_end1 = 0.163,
+ typeIerror = 0.05, alpha0 = 0.022, alpha1 = 0.022)

This cross-sectional study has total sample size of 21600
Power for this scenario is 0.423 for the alternative hypothesis treatment effect
beta = -0.126 ( two-sided Type I error =  0.05 )
```

Conclusion

- The Hussey and Hughes method is inaccurate for power calculation with binary outcomes. Power may be over- or under-estimated.
- Two methods using mixed effects models and GEEs can be used to calculate power of SWDs with binary outcomes.
- We have developed user-friendly software **swdpwr**, including a SAS macro and an R package, to implement power calculation methods for SWDs.

References

- Hussey, M.A. and Hughes, J.P. (2007) Design and analysis of stepped wedge cluster randomized trials. Contemporary Clinical Trials 28(2), 182-191.
- Zhou, X., Liao, X., Kunz, L.M., Normand, S.L.T. and Spiegelman, D. (2020) A maximum likelihood approach to power calculations for stepped wedge designs of binary outcomes. Biostatistics 21(1), 102-121.
- Li, F., Turner, E.L. and Preisser, J.S. (2018) Sample size determination for GEE analyses of stepped wedge cluster randomized trials. Biometrics 74, 1450-1458.
- Chen, J., Zhou, X., Li, F. and Spiegelman, D. (2022) swdpwr: A SAS macro and an R package for power calculations in stepped wedge cluster randomized trials. Computer Methods and Programs in Biomedicine 213, 106522.

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