ABSTRACT

A stepped wedge cluster randomized trial is a type of longitudinal cluster design that sequentially switches clusters to intervention over time until all clusters are treated. While the traditional posttest-only parallel design requires adjustment for a single intraclass correlation coefficient, the stepped wedge design allows multiple outcome measurements from the same cluster and so additional correlation parameters are necessary to characterize the within-cluster dependency structure. Although a number of studies have differentiated between the concepts of within-period and inter-period correlations, few studies have allowed the inter-period correlation to decay over time. In this article, we consider the proportional decay correlation structure for a cohort stepped wedge design, and provide a matrix-adjusted quasi-least squares (MAQLS) approach to accurately estimate the correlation parameters along with the intervention effect. We further develop a corresponding sample size procedure accounting for the correlation decay, and numerically validate it for continuous outcomes in a simulation study. We show that the empirical power agrees well with the prediction even with a small number of clusters, when data are analyzed with MAQLS concurrently with a suitable bias-corrected sandwich variance. Two trial examples are provided to illustrate the new sample size procedure.

KEY WORDS: Group-randomized trial; stepped wedge design; proportional decay; generalized estimating equations; quasi-least squares; finite-sample correction
1 Introduction

A unique feature of cluster randomized trials (CRTs) is that intact clusters, such as schools or clinics, are randomized to intervention arms (Murray, 1998; Donner and Klar, 2000). Randomization at the cluster level often carries pragmatic considerations, for example, administrative convenience, political reasons and prevention of treatment contamination (Turner et al., 2017a). A stepped wedge CRT is a type of longitudinal design that sequentially switches clusters to intervention during the study course until all clusters are treated (Hussey and Hughes, 2007). Such designs have become increasingly popular due to their logistical flexibility and ethical benefits. Because individual outcomes within the same cluster tend be more similar than those in different clusters, the concept of intraclass correlation coefficient (ICC) plays a central role in designing CRTs. While the traditional posttest-only parallel design requires adjustment for a single ICC, the stepped wedge design allows multiple outcome measurements from the same cluster and so naturally requires additional correlation parameters to characterize the within-cluster dependence. Correspondingly, sample size and power calculations for stepped wedge designs necessitate the specification of more than one correlation parameters. For example, Hemming et al. (2015) considered both the within-period and between-period ICCs in their sample size procedure for a cross-sectional design. Hooper et al. (2016) and Li et al. (2018) examined a three-correlation structure that additionally accounts for within-individual repeated measurements in a closed-cohort design.

Despite existing development of multi-parameter correlation structures for designing stepped wedge trials, most of them assumed a constant between-period ICC. For example, in a cross-sectional design, Hemming et al. (2015) allowed the between-period ICC to be different from the within-period ICC, but restricted the between-period ICC to be constant irrespective of the distance between periods. Relaxing the constant between-period ICC assumption for a cross-sectional design, Kasza et al. (2017) studied a non-uniform correlation structure with a decay parameter and concluded that sample size is sensitive to correlation decay. From the design standpoint, if correlation decay is present, a sample size framework accounting for such decay would provide adequate power. From the analysis standpoint, efficiency gain could be achieved by appropriately modeling the decayed correlation. Similar considerations carry over
to cohort designs. Particularly, the constant between-period ICC assumption of Hooper et al. (2016); Li et al. (2018) may not always be realistic and it is therefore necessary to develop alternative design and analysis strategies accounting for correlation decay in cohort studies.

In this article, we focus on the cohort stepped wedge design and consider a population-averaged model with a decayed correlation structure. The parameter estimates from a population-averaged model can be interpreted as the marginal intervention effect for the participating individuals combined over all periods, and may be preferred over the cluster-specific models (i.e., random-effects models) for trials conducted in the health policy or health services settings. The population-averaged model is fitted with quasi-least squares (QLS; Chaganty 1997; Chaganty and Shults 1999), which is an extension of generalized estimating equations (GEE; Liang and Zeger 1986), to accommodate non-standard correlation structures. Since CRTs frequently include a small number of clusters, we refine the QLS approach by incorporating appropriate finite-sample bias-corrections to both the estimation of correlation parameters and the variance of the intervention effect. Finally, we derive a new closed-form variance expression to facilitate sample size and power determination; the new variance expression accounts for the correlation decay and extends the previous results from Hussey and Hughes (2007). Based on the derived variance expression, we obtain a new design effect and study how the power depends on the correlation parameters. Finally, we validate the proposed sample size procedure in a simulation study and illustrate the proposed methods using two stepped wedge CRTs.

2 Methods

We consider a cohort stepped wedge design, where a closed cohort of individuals are enrolled at each of the participating clusters at the start of the trial. We mainly focus on cohort designs to inform the applications in Section 3.2, and will defer the discussion of cross-sectional designs to Section 4. We assume the trial involves a total of $T$ time periods. All clusters are under the control condition in the baseline period ($t = 1$), and will be randomly chosen to switch to intervention during the course of the study, until all clusters are treated at the end of the $T$th period. Individual participants will be
scheduled for outcome measurement during each period, and so each individual has a total of $T$ repeated measurements. Denote $y_{ijt}$ as the outcome for individual $j$ ($j = 1, \ldots, N_i$) from cluster $i$ ($i = 1, \ldots, I$) at period $t$ ($t = 1, \ldots, T$). We assume a complete design in the terminology of [Hemming et al., 2015] such that outcome measurements are taken for all individuals during each period. A step is defined as the pre-planned time point when at least one cluster crosses over from control to intervention. We denote the total number of steps by $S$ ($2 \leq S \leq T - 1$), and assume that $m_s$ clusters cross over at step $s$ such that $\sum_{s=1}^{S} m_s = I$. Typically for each individual, there are $b \geq 1$ baseline measurements taken under the control condition, and $c_s \geq 1$ measurements taken between step $s$ and step $s + 1$ (or end of study). Therefore, each measurement time point is associated with a distinct period and the total number of periods $T = b + \sum_{s=1}^{S} c_s$. A standard stepped wedge design is given by $b = c_s = 1$ for all $s$, and $T = S + 1$ ($T \geq 3$). A tabular illustration of a standard design with $I = 8$ clusters and $T = 5$ periods is provided in Table 1.

**Table 1:** A tabular illustration of a standard stepped wedge design with $I = 8$ clusters and $T = 5$ periods. Each cell with a zero entry indicates a control cluster-period and each cell with a one entry indicates an intervention cluster-period.

|             | $T = 1$ | $T = 2$ | $T = 3$ | $T = 4$ | $T = 5$ |
|-------------|---------|---------|---------|---------|---------|
| Cluster 1   | 0       | 1       | 1       | 1       | 1       |
| Cluster 2   | 0       | 1       | 1       | 1       | 1       |
| Cluster 3   | 0       | 0       | 1       | 1       | 1       |
| Cluster 4   | 0       | 0       | 1       | 1       | 1       |
| Cluster 5   | 0       | 0       | 0       | 1       | 1       |
| Cluster 6   | 0       | 0       | 0       | 1       | 1       |
| Cluster 7   | 0       | 0       | 0       | 0       | 1       |
| Cluster 8   | 0       | 0       | 0       | 0       | 1       |
2.1 Matrix-Adjusted QLS Analyses

The population-averaged model relates the marginal mean, $\mu_{ijt}$, with the time trend and the intervention effect by

$$g(\mu_{ijt}) = \beta_t + X_{it}\delta,$$  \hspace{1cm} (1)

where $g$ is the link function and $\beta_t$ is the $t$th period effect. Further, $X_{it}$ is the intervention status, which equals 1 or 0 depending on whether cluster $i$ receives intervention during period $t$, and $\delta$ describes the intervention effect on the link function scale. We write the collection of model parameters as $\theta = (\beta_1, \ldots, \beta_T, \delta)'$, the collection of intervention status for cluster $i$ (a sequence of ones preceded by zeros) as $X_i = (X_{i1}, \ldots, X_{iT})'$, and define $v(\mu_{ijt})$ as a known variance function. To allow for potential decay in the between-period ICC, we define the proportional decay correlation structure similar to Lefkopoulou et al. (1989). Specifically, we define (i) the within-period correlation as the correlation between outcomes for two distinct individuals from the same cluster during the same period, i.e. $\text{corr}(y_{ijt}, y_{ij't}) = \tau$, (ii) the within-individual correlation as the correlation between outcomes measured at time $t$ and $t'$ for the same individual, i.e. $\text{corr}(y_{ijt}, y_{ij't}) = \rho^{\vert t-t'\vert}$, and (iii) the between-period correlation as the correlation between outcome measured at time $t$ for individual $j$ and outcome measured at time $t'$ for individual $j'$, i.e. $\text{corr}(y_{ijt}, y_{ij't'}) = \tau \rho^{\vert t-t'\vert}$. In other words, the correlation structure is defined through two parameters, $\tau$ and $\rho$, with the former resembling the traditional ICC in a parallel design and the latter controlling for the degree of correlation decay. Although model (1) excludes additional baseline covariates, an extension to covariate-adjusted analysis is straightforward.

We use the quasi-least squares (QLS) approach described in Shults and Morrow (2002) to simultaneously estimate the intervention effect in model (1) and the correlations. The QLS modifies the traditional GEE by providing an alternative estimation procedure for correlation parameters including those from non-standard correlation structures; other statistical advantages of using QLS over the traditional GEE could be found in Shults and Hilbe (2014). Write $y_{ij} = (y_{ij1}, \ldots, y_{ijT})'$, $\mu_{ij} = (\mu_{ij1}, \ldots, \mu_{ijT})'$, $y_i = (y_{i1}, \ldots, y_{iN_i})'$ and $\mu_i = (\mu_{i1}, \ldots, \mu_{iN_i})'$. Further define $D_i(\theta) = \partial \mu_i / \partial \theta'$, and let the working covariance of $y_i$ be $V_i = \phi A_i^{1/2}(\theta) R_i(\alpha_0, \alpha_1) A_i^{1/2}(\theta)$, where $\phi$ is the dispersion parameter, $A_i(\theta) =$
Therefore, valid correlation values that ensure positive definite $R \times \text{angular region}$ working correlation parameterized by unknown parameters $\alpha$ and $\t$. It is straightforward to see that the proportional decay structure induces separability between $y$ among elements of $\text{diag}$. Finally, the inverse of the $R \times T$ first-order autoregressive (AR1) correlation matrix. We could verify that the determinant

$$\det \{ R_i(\tau, \rho) \} = \det \{ G_i(\tau) \}^T \det \{ F(\rho) \}^{N_i} = (1 - \tau)^T(N_i-1) \{ 1 + (N_i - 1)\tau \}^T(1 - \rho^2)^{(N_i-1)}. $$

Therefore, valid correlation values that ensure positive definite $R_i(\tau, \rho)$ should be contained in the triangular region

$$ S = \left\{ (\tau, \rho) : -\frac{1}{\max\{N_i : i = 1, \ldots, I\} - 1} < \tau < 1, -1 < \rho < 1 \right\}. $$

Finally, the inverse of the $R_i$ also exists in closed form and is given by $R_i^{-1}(\tau, \rho) = G_i^{-1}(\tau) \otimes F_i^{-1}(\rho)$, where

$$ G_i^{-1}(\tau) = (1 - \tau)^{-1}\{ I - \tau /\{ (1 - \tau)\{ (1 + (N_i - 1)\tau) \} \} \} J, $$

$$ F_i^{-1}(\rho) = (1 - \rho^2)^{-1}\{ I + \rho^2 C_2 - \rho C_1 \}. $$

$J$ is a square matrix of ones, $C_2 = \text{diag}(0, 1, \ldots, 1, 0)$, and $C_1$ is a tridiagonal matrix with zeros on the main diagonal and ones on the two sub-diagonals.

To introduce the QLS estimating equations, we further define $r_{ij}(\theta) = A_i^{-1/2}(\theta)/(y_{ij} - \mu_{ij})$, and write $r_i(\theta) = (r_i(\theta), \ldots, r_{iN_i}(\theta))^T$. The first-stage QLS estimates for $\theta$, $\alpha_0$ and $\alpha_1$ are obtained by alternating between the following estimating equations until convergence

$$ \sum_{i=1}^I D_i'(\theta) A_i^{-1/2}(\theta) R_i^{-1}(\alpha_0, \alpha_1) r_i(\theta) = 0, $$

$$ \sum_{i=1}^I \frac{\partial}{\partial \alpha_0} \{ r_i'(\theta) R_i^{-1}(\alpha_0, \alpha_1) r_i(\theta) \} = 0, $$

$$ \sum_{i=1}^I \frac{\partial}{\partial \alpha_1} \{ r_i'(\theta) R_i^{-1}(\alpha_0, \alpha_1) r_i(\theta) \} = 0. $$
In particular, (2) is the usual GEE coupled with the proportional decay structure, and (16), (17) are scalar equations for the first-stage correlation estimates. Further, closed-form solutions exist for \( \hat{\alpha}_0 \) and \( \hat{\alpha}_1 \) (within an iterative step) and are provided in Web Appendix A. Chaganty and Shults (1999) showed that \( \hat{\alpha}_0 \) and \( \hat{\alpha}_1 \) are asymptotically biased for \( \tau \) and \( \rho \), hence the following two second-stage estimating equations are used to obtain \( \hat{\tau} \), \( \hat{\rho} \) and eliminate the large-sample bias in the first-stage correlation estimates

\[
\sum_{i=1}^{I} \text{tr} \left\{ \frac{\partial G_i^{-1}(\hat{\alpha}_0)}{\partial \alpha_0} G_i(\tau) \right\} = 0 \quad (5)
\]

\[
\text{tr} \left\{ \frac{\partial F_i^{-1}(\hat{\alpha}_1)}{\partial \alpha_1} F(\rho) \right\} = 0 \quad (6)
\]

The closed-form solution for (5) is provided by Shults and Morrow (2002) as

\[
\hat{\tau} = \left[ \sum_{i=1}^{I} \frac{N_i(N_i - 1)}{1 + (N_i - 1)\hat{\alpha}_0^2} \right]^{-1} \sum_{i=1}^{I} \frac{N_i(N_i - 1)\hat{\alpha}_0^2}{1 + (N_i - 1)\hat{\alpha}_0^2} \]

and Chaganty and Shults (1999) showed that \( \hat{\rho} = 2\hat{\alpha}_1/(1 + \hat{\alpha}_1^2) \) solves (6).

Below we refine the existing QLS approach with finite-sample bias-corrections by utilizing cluster-leverage, \( H_i = D_i(\theta)(\sum_{i=1}^{I} D'_i(\theta)D_i(\theta))^{-1}D'_i(\theta)V_i \) (Preisser and Qaqish, 1996). Because stepped wedge CRTs usually include a small number of clusters \( I \leq 30 \), the QLS estimators for the correlations may be subject to finite-sample bias (even after correcting for the large-sample bias using the second-stage estimating equations). This is due to the known fact that \( r_i(\hat{\theta}) \) tends to be close to zero when \( I \) is small. For this reason, we replace the first-stage estimating equations (16) and (17) by

\[
\sum_{i=1}^{I} \frac{\partial}{\partial \alpha_0} \text{tr} \left[ R_i^{-1}(\alpha_0, \alpha_1) \tilde{R}_i(\theta) \right] = 0 \quad (7)
\]

\[
\sum_{i=1}^{I} \frac{\partial}{\partial \alpha_1} \text{tr} \left[ R_i^{-1}(\alpha_0, \alpha_1) \tilde{R}_i(\theta) \right] = 0 \quad (8)
\]

where \( \tilde{R}_i(\theta) = A_i^{-1/2}(I - H_i)^{-1}A_i^{1/2}r_i(\theta)r'_i(\theta) \) represents the “matrix-adjusted” moment estimator for the correlation structure (Preisser et al., 2008). The solutions obtained from (7) and (8) could effectively reduce the finite-sample bias in \( \hat{\alpha}_0 \) and \( \hat{\alpha}_1 \), which would in turn decrease the bias in the QLS estimators.
for τ and ρ. Accurately estimating the correlation parameters have practical implications since these estimates could be used to guide the design of future trials (Murray, 1998). The derivation of the matrix-adjusted estimating equations, (7) and (8), along with the closed-form updates are provided in Web Appendix B.

The availability of a small number of clusters may also have implications for estimating the variance using GEE-based approaches (Turner et al., 2017b). In general, the variance of the marginal mean model parameter \( \hat{\theta} \) can be estimated using the model-based variance \( \Omega_1^{-1} \) or the sandwich variance \( \Omega_0^{-1} \Omega_1^{-1} \), where

\[
\Omega_0 = \sum_{i=1}^{I} C_i D_i V_i^{-1} B_i (y_i - \mu_i) (y_i - \mu_i)^t B_i^t V_i^{-1} D_i C_i, \tag{9}
\]

and both \( \Omega_0 \), \( \Omega_1 \) are evaluated at (\( \hat{\theta}, \hat{\tau}, \hat{\rho} \)). When both \( C_i \) and \( B_i \) are identity matrices, equation (9) reduces to the uncorrected sandwich estimator of Liang and Zeger (1986) which we denote as BC0. BC0 provides valid inference regardless of the correct specification of the working correlation \( R_i \), as long as the number of clusters is sufficiently large (\( I \geq 30 \)), while the consistency of the model-based variance requires the correct specification of the correlation structure. As \( r_i(\hat{\theta}) \) is biased towards zero with a limited number of clusters, BC0 is likely to underestimate the variance and alternative choices of matrices \( C_i \) and \( B_i \) may be necessary to provide a partial correction to the finite-sample bias. We consider three approaches for bias-corrections: the finite-sample correction due to Kauermann and Carroll (2001), or BC1, is given by \( C_i = I \) and \( B_i = (I - H_i)^{-1/2} \); the finite-sample correction due to Mancl and DeRouen (2001), or BC2, is given by \( C_i = I \) and \( B_i = (I - H_i)^{-1} \); the finite-sample correction due to Fay and Graubard (2001), or BC3, given by \( C_i = \text{diag}\{(1 - \min\{\zeta, [D_i^t V_i^{-1} D_i \Omega_1^{-1}]_{jj}\})^{-1/2}\} \) and \( B_i = I \), where the bound parameter \( \zeta \) is a user-defined constant (\(< 1\)) with a default value 0.75. Because the matrix elements of the cluster leverage are between 0 and 1, we generally have BC0 < BC1 < BC2 (Preisser et al., 2008). Further, Scott et al. (2017) have shown that BC3 tends to be close to BC1. Finally, the estimation of dispersion parameter should only affect the model-based variance. Similar to Liang and Zeger (1986), the dispersion parameter could be consistently updated from iteration \( s \) to \( s + 1 \) by

\[
\hat{\phi}^{(s+1)} = \frac{\sum_{i=1}^{I} \hat{\phi}^{(s)} \text{tr}(\tilde{R}_i)}{\sum_{i=1}^{I} TN_i - (T+1)},
\]
2.2 Sample Size and Power Calculation

Under the null hypothesis $H_0 : \delta = \delta_0$, the large-sample variance of $\sqrt{n}(\hat{\delta} - \delta_0)$ is provided by the $(T + 1, T + 1)$ element of the large-sample covariance matrix of $\sqrt{n}(\hat{\theta} - \theta_0)$. Since the QLS estimator $\hat{\delta}$ is asymptotically normal, we could use the $z$-test statistic $\frac{\hat{\delta}}{\sqrt{\text{var}(\hat{\delta})}}$ to test the null of no intervention effect $H_0 : \delta = 0$, and the power to detect an intervention effect of size $\delta \neq 0$ with a prescribed type I error rate $\alpha$ is approximately

$$\text{power} = \Phi \left( z_{\alpha/2} + \frac{|\delta|}{\sqrt{\text{var}(\hat{\delta})}} \right), \quad (10)$$

where $\Phi$ is the standard normal cumulative distribution function and $z_{\alpha/2}$ is the normal quantile such that $\Phi(z_{\alpha/2}) = 1 - \alpha/2$. Because there is uncertainty in estimating the asymptotic variance $\text{var}(\hat{\delta})$, an alternative two-sided test uses the same statistic but refers to the $t$-distribution with $I - (T + 1)$ degrees of freedom. With the same effect size $\delta$ and prescribed type I error rate $\alpha$, the power of the $t$-test is approximately

$$\text{power} = \Psi_{I - (T + 1)} \left( t_{\alpha/2, I - (T + 1)} + \frac{|\delta|}{\sqrt{\text{var}(\hat{\delta})}} \right), \quad (11)$$

where $\Psi_{I - (T + 1)}$ is the $t$-distribution function with degrees of freedom $I - (T + 1)$ and the quantile $t_{\alpha/2}$ is chosen such that $\Psi_{I - (T + 1)}(t_{\alpha/2}) = 1 - \alpha/2$. We notice that because the $t$-distribution has a heavier tail compared with the standard normal distribution, the QLS $z$-test is more likely to result in an inflated type I error rate with the use of BC0 than the corresponding QLS $t$-test. As the bias-corrected sandwich variance estimators (BC1, BC2, and BC3) provide different degrees of inflation relative to the uncorrected variance BC0, an investigation of the two tests coupled with the collection of alternative variance estimators could help inform the practical choice among the analytical options for stepped wedge CRTs.

To assist the design of stepped wedge trials allowing for correlation decay, we next derive a new closed-form variance expression for $\hat{\delta}$ assuming the outcome is continuous and $g$ is the identity link function. We will return to categorical outcomes and nonlinear link functions in Section 4. To do so, we follow Shih \cite{Shih1997} and assume the covariance of $Y_i$ to be known as $\text{var}(Y_i) = V_i$. Therefore,
var(ˆδ) is the (T + 1, T + 1) element of the model-based variance Ω_{1}^{-1}. We further assume a balanced design such that an equal number of participants will be recruited in each cluster prior to the first period, so that N_i = N. Such a simplification assumption is routinely made in designing stepped wedge trials.

Under a balanced design, we could write the design matrix corresponding to cluster i as Z_i = 1_N ⊗ (I_T, X_i), where 1_N is a N-vector of ones. Then the variance of the intervention effect ˆδ equals to the lower-right element of φ{∑_{i=1}^{I} Z_i R_i^{-1}(τ, ρ)Z_i}^{-1}, where φ is the marginal variance. We show in Web Appendix C that a closed-form variance expression for ˆδ is

\[
\text{var}(ˆδ) = \frac{(φI/N)(1 − ρ^2)[1 + (N − 1)τ]}{(IU − W)(1 + ρ^2) − 2(IV − Q)ρ},
\]

where the design constant U = ∑_{i=1}^{I} ∑_{j=1}^{T} X_{ij} is the total number of cluster-periods exposed under the intervention condition, W = ∑_{j=1}^{T} (∑_{i=1}^{I} X_{ij})^2 is the squared number of clusters receiving the intervention summed across periods, V = ∑_{i=1}^{I} ∑_{j=1}^{T−1} X_{ij}X_{i,j+1} and Q = ∑_{j=1}^{T−1} (∑_{i=1}^{I} X_{ij})(∑_{i=1}^{I} X_{i,j+1}) are cross-product terms resulting from the decayed correlation structure. It is interesting to see that this variance expression does not depend on the magnitude of the period effect β_j as long as they are controlled for in the marginal mean model. Noticeably, the QLS-based variance (12) extends the variance by Hussey and Hughes (2007) to cohort designs with decayed correlation. In addition, variance expression (12) extends the formula due to Liu et al. (2002) to longitudinal cluster designs with staggered randomization. Further, as the cohort size N becomes large, the variance expression converges

\[
\lim_{N \to \infty} \text{var}(ˆδ) = \frac{φI(1 − ρ^2)τ}{(IU − W)(1 + ρ^2) − 2(IV − Q)ρ},
\]

which is a finite constant since |ρ| < 1 and τ > 0 for large N. Therefore, the limit of the variance is a positive constant determined by available design resources I, T and two correlation values τ, ρ, and cannot be made arbitrarily small. In other words, the power of the stepped wedge design may not be increased to one by solely increasing the cohort size, which is consistent with the known results for parallel cluster randomized designs (Murray, 1998). For this reason, when N is large, variance (13) could be used in the design stage to approximate the variance (12).

For determining the required sample size based on equation (10) and (11), it is straightforward to solve N by fixing the required number of clusters I but not the other way around. However, with a
pre-determined cohort size $N$ for each cluster, we would postulate a series of values for $I$ and find the smallest value such that the estimated power is at least equal to the prescribed level. Additionally, in the following case as in [Woertman et al. (2013)], we could derive a simple expression for the design effect (DE) relative to an individually randomized trial to simplify sample size calculation. Specifically, we assume that an equal number of clusters switch to intervention at each step so that $m_s = m$, and further an equal number of measurements are taken between steps such that $c_s = s$ for all $s = 1, \ldots, S$. In this case, we have the total number of clusters $I = Sm$ and total number of periods $T = b + Sc$, and the design constants become

$$U = \frac{1}{2}S(S + 1)mc, \quad W = \left(\frac{1}{3}S^3 + \frac{1}{2}S^2 + \frac{1}{6}S\right)m^2c, \quad V = U - Sm, \quad Q = W - \frac{1}{2}S(S + 1)m^2.$$

Plugging the design constants back into the variance formula (12), and dividing by the variance of the two-sample mean difference $4\phi/(NSm)$, we obtain

$$DE = \frac{3S}{2(S - 1)} \left[ \frac{(1 - \rho^2)}{(S + 1)c(1 - \rho)^2 + 6\rho} [1 + (N - 1)\tau]. \right. \quad (14)$$

Similar to [Woertman et al. (2013)], this design effect allows us to study how the design resources affect the statistical efficiency relative to individual randomization and how the correlation parameters affect the statistical power. For example, since the design effect is free of $b$, the relative design efficiency does not change according to the number of baseline periods. However, for fixed values of the correlation parameters, increasing the number of steps $S$ and number of measurements between steps $c$ decreases the design effect and increases the efficiency. On the other hand, for fixed design resources, larger values of the within-period correlation $\tau$ increases the design effect, confirming that $\tau$ functions as the traditional ICC of a parallel cluster randomized trial. By contrast, the role of the decay parameter $\rho$ is characterized by $f(p) = (1 - \rho^2)/[(S+1)c(1 - \rho)^2 + 6\rho]$, which is monotonically increasing on $(-1, r)$ and decreasing on $(r, 1)$, where

$$r = 1 + \frac{\sqrt{3} - \sqrt{2(S + 1)c - 3}}{(S + 1)c - 3} \in (0, 1).$$

Since it is more plausible that $\rho \in (0, 1)$, the above result suggests that with an increasing level of correlation decay, the design effect first increases to its largest value and then decreases, with the maximum
A numeric illustration of the design effect as a function of $\rho$ is provided in Figure 1.

**Figure 1:** The design effect as a function of the degree of correlation decay $1 - \rho$. The x-axis is $1 - \rho$ so that the degree of decay increases from left to right. For illustration, the cohort size and the within-period correlation are fixed at $N = 20$ and $\tau = 0.1$. Corresponding to the analytical result in Section 2.3, the maximum design effect is attained when $\rho = r$ (gray square dot), a value between 0 and 1 and determined by the number of steps $S$ and the number of measurements between steps $c$. 

![Figure 1: Design effect as a function of correlation decay](image)
3 Numerical Results

3.1 A Simulation Study

We carry out a simulation study (1) to compare the correlation estimators from the regular QLS and the proposed matrix-adjusted QLS (MAQLS), and (2) to evaluate the utility of the proposed power formula for QLS-based analyses of stepped wedge CRTs. For the second objective, we first determine the empirical type I error rates for the QLS-based tests coupled with alternative variance estimators, and then identify valid tests (those with a close-to-nominal type I error rate) whose empirical power corresponds well with the predicted power from the proposed formula. Findings specific to the second objective are informative for practical data analysis since we prefer tests that maintain a valid size and meanwhile demonstrate empirical power that is at least the magnitude of the analytical prediction.

Within-cluster correlated continuous outcomes were generated from a multivariate normal distribution with mean given by \( \mu_{ijt} = \beta_t + X_{it} \delta \) and covariance \( \phi R(\tau, \rho) \), where \( R(\tau, \rho) \) is the proportional decay structure defined in Section 2.1. For illustrative purposes, we set the marginal variance \( \phi = 1 \) and assumed a gently increasing period effect such that \( \beta_1 = 0 \) and \( \beta_{t+1} - \beta_t = 0.1 \times (0.5)^{t-1} \) for \( t \geq 1 \). As discussed before, the predicted power should be insensitive to the magnitude of the period effects as long as they are accounted for in the QLS analyses. We fix the effect size \( \delta/\phi^{1/2} \) at zero for studying test size and choose \( \delta/\phi^{1/2} \) from \( \{0.2, 0.3, 0.4, 0.5\} \) for studying power. We choose the within-period correlation \( \tau \in \{0.03, 0.1\} \), which represent typical ICC values reported in the parallel CRTs (Murray, 1998). We further chose \( \rho \in \{0.2, 0.8\} \), representing large and moderate degree of correlation decay over time. The number of clusters are varied from 9 to 24 as stepped wedge CRTs usually include a limited number of clusters. The number of periods and cohort size are specified from \( 3 \leq T \leq 8 \) and \( 5 \leq N \leq 24 \) to ensure that the predicted power is at least 80%. For illustration, we focus on standard stepped wedge designs so that there is only one baseline period and the number of steps \( S = T - 1 \). In other words, an equal number of \( I/S \) clusters cross over to intervention during each step, and the outcome is measured only once for each individual between consecutive steps. For each scenario, 1000 data replications were generated and analyzed using both QLS and MAQLS. For the first objective, we
report the percent relative bias in estimating $\tau$ and $\rho$. In general, an unbiased approach for estimating the correlation parameters is preferred since accurate reporting of correlations is critical for planning future trials. The convergence rates are similar between QLS and MAQLS, and all exceed 95% except for a few cases. For the second objective, we consider both the $z$-tests and the $t$-tests for testing the null hypothesis of no intervention effect, coupled with five different variance estimators for $\hat{\delta}$, i.e., the model-based variance, BC0, BC1, BC2 and BC3. The nominal type I error rate is held fixed at 5%, and we consider an empirical type I error rate between 3.6% and 6.4% to be acceptable based on the margin of error from a binomial model with 1000 replications. By a similar reasoning, since the predicted power in each scenario is at least 80%, we consider an empirical power that differs by no more than 2.6% from the predicted value to be acceptable.

For the first objective, we summarize in Table 2 and Table 3 the percent relative bias in estimating the correlations with QLS and MAQLS. It is evident that the percent bias in estimating the within-period correlation $\tau$ is much larger than that in estimating the decay parameter $\rho$, without respect to the incorporation of matrix-adjustment to the first-stage estimating equations (16) and (17). However, the QLS estimator for $\tau$ exhibits noticeable downward bias, especially when the number of clusters is not large. By contrast, MAQLS substantially reduces such finite-sample bias and improves the estimation of $\tau$. On the other hand, the QLS estimator for the decay parameter $\rho$ seems more accurate in that the absolute percent bias only occasionally exceeds one percent. Nevertheless, MAQLS still mildly improves the estimation of $\rho$ in that the absolute percent bias is always maintained under one percent. The comparative findings between QLS and MAQLS are consistent regardless of the magnitude of intervention effect $\delta$.

For the second objective, we present in Figure 2 the empirical type I error rates of the $z$-tests and $t$-tests for the QLS and MAQLS analyses. Overall, we observe that the matrix-adjustment to the correlation estimation mildly affects the tests with the model-based variance but has virtually no impact on the tests with the sandwich variance. This is in accordance with [Lu et al. (2007)], who observed similar patterns for the traditional GEE analyses of pretest-posttest CRTs. Since MAQLS provides more accurate estimation of the correlations, we will mostly focus on this approach in the following discussion.
Table 2: Percent relative bias of the correlation parameters based on uncorrected quasi-least squares (QLS) and matrix-adjusted quasi-least squares (MAQLS) for each simulation scenario when the treatment effect is zero.

| Correlations | Effect Size | Resources | % bias for $\tau$ | % bias for $\rho$ |
|--------------|-------------|-----------|------------------|------------------|
| $\tau$ | $\rho$ | $\delta$ | $I$ | $N$ | $T$ | QLS | MAQLS | QLS | MAQLS |
| 0.03 | 0.2 | 0 | 18 | 10 | 7 | -29.0 | 1.2 | -0.4 | 0.3 |
| 0.03 | 0.2 | 0 | 18 | 24 | 4 | -16.8 | 4.5 | -0.4 | 0.1 |
| 0.03 | 0.2 | 0 | 20 | 14 | 5 | -19.8 | 4.0 | -0.6 | -0.1 |
| 0.03 | 0.2 | 0 | 21 | 8 | 4 | -31.1 | 1.4 | -0.4 | 0.2 |
| 0.03 | 0.2 | 0 | 15 | 8 | 4 | -42.5 | 3.2 | -0.5 | 0.5 |
| 0.03 | 0.8 | 0 | 16 | 12 | 5 | -23.3 | 6.7 | -0.5 | -0.2 |
| 0.03 | 0.8 | 0 | 24 | 7 | 5 | -28.4 | -0.7 | -0.5 | -0.1 |
| 0.03 | 0.8 | 0 | 12 | 8 | 5 | -52.0 | 4.3 | -2.6 | -0.5 |
| 0.03 | 0.8 | 0 | 12 | 5 | 4 | -86.5 | -2.7 | -2.6 | -0.3 |
| 0.03 | 0.8 | 0 | 10 | 5 | 3 | -97.4 | -3.8 | -1.3 | -0.6 |
| 0.10 | 0.2 | 0 | 21 | 11 | 8 | -9.4 | 3.6 | -0.8 | 0.4 |
| 0.10 | 0.2 | 0 | 24 | 11 | 7 | -8.4 | 3.2 | -0.7 | 0.3 |
| 0.10 | 0.2 | 0 | 15 | 16 | 6 | -11.8 | 7.2 | -0.7 | 1.1 |
| 0.10 | 0.2 | 0 | 18 | 8 | 7 | -14.7 | 1.7 | -0.7 | 0.9 |
| 0.10 | 0.2 | 0 | 16 | 7 | 5 | -16.8 | 3.7 | -1.0 | 0.8 |
| 0.10 | 0.8 | 0 | 20 | 18 | 5 | -8.1 | 4.9 | -0.1 | 0.2 |
| 0.10 | 0.8 | 0 | 15 | 9 | 4 | -16.3 | 1.7 | -0.2 | 0.1 |
| 0.10 | 0.8 | 0 | 10 | 20 | 3 | -17.3 | 6.2 | -0.1 | 0.3 |
| 0.10 | 0.8 | 0 | 12 | 5 | 5 | -27.6 | 2.7 | -1.0 | 0.0 |
| 0.10 | 0.8 | 0 | 9 | 7 | 4 | -30.3 | 2.8 | -0.9 | -0.1 |
Table 3: Percent relative bias of the correlation parameters based on quasi-least squares (QLS) and matrix-adjusted quasi-least squares (MAQLS) for each simulation scenario when the treatment effect is nonzero.

| Correlations | Effect Size | Resources | % bias for $\tau$ | % bias for $\rho$ | QLS | MAQLS | QLS | MAQLS |
|--------------|-------------|-----------|-------------------|-------------------|-----|-------|-----|-------|
| $\tau$       | $\rho$      | $\delta$  | $I$ | $N$ | $T$ | QLS | MAQLS | QLS | MAQLS |
| 0.03 0.2     | 0.3         | 18 10 7   | -29.2 | 1.0 | -0.4 | 0.3 |
| 0.03 0.2     | 0.3         | 18 24 4   | -16.8 | 4.8 | -0.4 | 0.0 |
| 0.03 0.2     | 0.3         | 20 14 5   | -19.8 | 3.8 | -0.6 | -0.1 |
| 0.03 0.2     | 0.4         | 21 8 4    | -31.5 | 0.9 | -0.3 | 0.2 |
| 0.03 0.2     | 0.5         | 15 8 4    | -42.8 | 3.0 | -0.3 | 0.6 |
| 0.03 0.8     | 0.2         | 16 12 5   | -23.3 | 6.9 | -0.5 | -0.2 |
| 0.03 0.8     | 0.2         | 24 7 5    | -28.1 | 0.2 | -0.5 | 0.1 |
| 0.03 0.8     | 0.3         | 12 8 5    | -51.9 | 4.6 | -2.6 | 0.4 |
| 0.03 0.8     | 0.4         | 12 5 4    | -86.9 | -2.6 | -2.4 | -0.4 |
| 0.03 0.8     | 0.5         | 10 5 3    | -94.0 | -4.0 | -1.5 | -0.5 |
| 0.10 0.2     | 0.3         | 21 11 8   | -9.5  | 3.6 | -0.8 | 0.4 |
| 0.10 0.2     | 0.3         | 24 11 7   | -8.4  | 3.1 | -0.6 | 0.4 |
| 0.10 0.2     | 0.4         | 15 16 6   | -11.8 | 7.1 | -0.7 | 0.9 |
| 0.10 0.2     | 0.4         | 18 8 7    | -14.9 | 1.6 | -0.7 | 0.8 |
| 0.10 0.2     | 0.5         | 16 7 5    | -16.9 | 3.6 | -1.0 | 0.7 |
| 0.10 0.8     | 0.2         | 20 18 5   | -8.1  | 4.8 | -0.1 | 0.2 |
| 0.10 0.8     | 0.3         | 15 9 4    | -16.4 | 1.7 | -0.2 | 0.1 |
| 0.10 0.8     | 0.4         | 10 20 3   | -17.2 | 6.3 | -0.1 | 0.3 |
| 0.10 0.8     | 0.4         | 12 5 5    | -27.4 | 2.9 | -1.1 | 0.2 |
| 0.10 0.8     | 0.5         | 9 7 4     | -30.4 | 2.9 | -1.0 | -0.2 |
Figure 2: Empirical type I error rates for (a) QLS z-tests, (b) QLS t-tests, (c) MAQLS z-tests and (d) MAQLS t-tests. MB: model-based variance; BC0: uncorrected sandwich variance; BC1: KC-corrected sandwich variance; BC2: MD-corrected sandwich variance; BC3: FG-corrected sandwich variance. The acceptable bounds are shown with the dashed horizontal lines. For each value of $I$, there may be multiple points with the same symbol indicating results with different combinations of design resources and correlation parameters.
Firstly, the MAQLS $z$-tests are much more liberal than the corresponding MAQLS $t$-tests. The type I error rates of the MAQLS $z$-tests coupled with the model-based variance or BC2 are close to nominal, while the MAQLS $z$-tests coupled with BC0, BC1 or BC3 are frequently liberal. By contrast, only the MAQLS $t$-tests with BC0 remain occasionally liberal, while MAQLS $t$-tests with BC1 or BC3 maintain close-to-nominal size and MAQLS $t$-tests with model-based variance or BC2 are often conservative. Figure 3 presents the differences between the empirical and the predicted power for each simulation scenario. Among all MAQLS $z$-tests, only the choice of BC2 provides lower power than predicted. While the choices of the remaining variance estimators guarantee adequate power for the $z$-tests, one should be cautious in using the sandwich variance estimators (BC0, BC1 and BC3) with a small number of clusters (e.g. $I \leq 20$) since they may carry an inflated test size. On the other hand, the empirical power for MAQLS $t$-tests coupled with the model-based variance, BC1 or BC3 corresponds reasonably well with the analytical prediction from the proposed formula, while the empirical power for MAQLS $t$-tests with BC2 still tends to be lower than predicted.

3.2 Illustrative Examples

3.2.1 The AEP Study

We illustrate the proposed sample size procedure to design a cohort stepped wedge CRT that aims to study the effect of an exercise intervention on the physical function of patients with end-stage renal disease [Bennett et al., 2013]. The intervention was an accredited exercise physiologist (AEP) coordinated resistance exercise program, offered at hemodialysis clinics to improve the quality of life for dialysis patients. During the planning phase, it was determined that $I = 15$ clinics (clusters) were available, and would be randomized over $T = 4$ periods evenly spaced across 48 weeks. At baseline, no exercise programs were offered to any clinic. At week 12, 36 and 48, a random subset of 5 clinics cross over from control to intervention. A closed cohort of patients were recruited at baseline, and would be followed up during the study period. The primary patient-level outcome was the 30-second sit-to-stand (STS) test, recording the number of times a patient could rise from and return to a seated position in a 30-second
Figure 3: Differences between the empirical power and the predicted power of (a) QLS z-tests, (b) QLS t-tests, (c) MAQLS z-tests and (d) MAQLS t-tests. MB: model-based variance; BC0: uncorrected sandwich variance; BC1: KC-corrected sandwich variance; BC2: MD-corrected sandwich variance; BC3: FG-corrected sandwich variance. The acceptable bounds are shown with the dashed horizontal lines. For each value of $I$, there may be multiple points with the same symbol indicating results with different combinations of design resources and correlation parameters.
The 30-second STS test was conducted at the end of each period, resulting in 4 outcome measurements per patient. Based on a prior study within a similar context, a conservative estimate of the effect size was given by $\delta/\phi = 0.325$ (Cappy et al., 1999), and the within-period correlation was estimated to be $\tau = 0.03$ (Littenberg and MacLean, 2006). With $I = 15$ clusters, the simulations suggest the MAQLS $z$-test with the model-based variance could provide close-to-nominal size and adequate power; we illustrate the power calculation based on the $z$-test statistic as it is often more powerful than the corresponding $t$-test.

Given this is a standard stepped wedge design where an equal number of clinics switch to intervention at each step, we can write $U = IT/2$, $W = I^2T(2T - 1)/\{6(T - 1)\}$, $V = I(T - 2)/2$ and $Q = I^2T(T - 2)/\{3(T - 1)\}$. The variance expression (12) is then simplified to

$$\text{var}(\hat{\delta}) = \frac{6(\phi/N)(T - 1)(1 - \rho^2)[1 + (N - 1)\tau]}{I(T - 2)\{T(1 - \rho)^2 + 6\rho\}}. \quad (15)$$

If we anticipate large correlation decay so that $\rho = 0.2$, the power is estimated using equation (10) and (15) to be 78.8% if $N = 16$ and 80.4% if $N = 17$. Therefore at least $N = 17$ patients should be recruited in each clinic to achieve 80% power under this assumption of correlation decay. On the other hand, we could arrive at the same results by using the derived design effect (14). More specifically, in an individual randomized study, 298 patients would be required for the hypothesized effect size. Assuming 16 patients will be included in each clinic, the design effect is approximately 0.83, indicating a total of 248 patients in approximately 15.5 clinics would be required. Since the study affords to randomize only 15 clinics, we increase the cohort size to $N = 17$, resulting in a design effect 0.85. Therefore, 253 patients are required for a total of $253/17 \approx 14.9$ clinics, and we conclude that 17 patients in 15 clinics ensured 80% power.

While the within-period correlation estimate was available from prior studies, published estimates of the decay parameter $\rho$ were rare. For this reason, we carried out a sensitivity analysis on the power (Figure 4(a)) fixing the design resources but varying $\tau \in (0.03, 0.06)$ and $\rho \in (0, 1)$. Note that the upper bound of the within-period correlation $\tau$ was reported by Littenberg and MacLean (2006) and was used in this assessment. As expected, larger values of the within-period correlation reduces the
study power, and further, given a certain value of the within-period correlation, a greater magnitude of decay (smaller $\rho$) generally reduces the study power unless $\rho \approx 0$. For the hypothesized $\tau = 0.03$, the study power remained at least close to 80% regardless of the correlation decay. On the other hand, the amount of correlation decay could result in further power loss if the within-period correlation $\tau$ increases. Nevertheless, the power loss is at most around 10% even if the within-period correlation $\tau = 0.06$ approximates the upper bound.

**Figure 4:** Sensitivity analysis of study power for (a) the AEP study with $I = 15$ clusters and $N = 17$ individuals within each cluster, (b) the CORE study with $I = 11$ clusters and $N = 11$ individuals within each cluster, and (c) the CORE study with $I = 11$ clusters and $N = 30$ individuals within each cluster.

### 3.2.2 The CORE Study

We next illustrate the proposed sample size procedure by designing a non-standard stepped wedge trial, the CORE study. The CORE study is a cluster randomized trial which aims to evaluate the patient-centered service design in health providers to improve the psychosocial recovery outcomes for people with severe mental illness in Australia [Palmer et al., 2015]. The new service design intervention adopted the Experience Based Co-Design (EBCD) to identify users’ positive and negative experiences of the service, and involved patients’ participation to co-design solutions to the negative experiences. A total of $I = 11$ teams from four health service providers would be participating the study; each team involved a
number of service users who will be affected by the intervention. A stepped wedge design was considered appropriate for the study due to logistical constraint in simultaneously introducing the intervention to more than a few teams. The EBCD intervention will be delivered to the clusters in three waves, each with a duration of 9 months. Four teams will start the intervention in wave 1 and wave 2, respectively, while the remaining three teams receive the intervention in the final wave. In other words, the study includes four periods, with a baseline period lasting about 6 months.

The outcome of interest is the improvement in psychosocial recovery measured by the Recovery Assessment Scale Revised (RAS-R, Luszczakoski et al., 2014), and was measured for each user at the end of baseline period and each of the three follow-up period. The standardized effect size on the psychosocial recovery outcome was estimated to be $0.35$, and the within-period correlation was assumed to be $\tau = 0.1$ (Palmer et al., 2015). Since the study affords to randomize only 11 clusters, there may be a risk of inflated type I error rate with a $z$-test. For this reason, we determine the required cohort size based on a $t$-test using expressions (11) and (12). Assuming the correlation decay is only moderate so that $\rho = 0.8$, power is estimated to be 0.78 for $N = 10$ and 0.80 for $N = 11$, barring drop out. Therefore $N = 11$ is required to ensure 80% power given a 5% test size. We further conducted a sensitivity analysis to see how power changes according to the degree of correlation decay, and presented the power contour in Figure 4(b). Due to the small sample size and the heavy tail of the $t$ distribution, the study is sensitive to correlation decay ($\rho$) when $\tau = 0.1$, and remains so even if $\tau$ approaches zero. On the other hand, the actual study planned to recruit $N = 30$ users in each team. With this larger cohort size, Figure 4(c) suggests that the power becomes somewhat less sensitive to the correlation decay, especially as the within-period correlation approaches zero. For example, if $\tau \leq 0.02$, the study power remains at least around 80% regardless of the amount of correlation decay.

4 Discussion

This article expanded on the design and analysis considerations for cohort stepped wedge CRTs in the presence of correlation decay. Since a cohort design involves repeated outcome assessments for fixed
sets of individuals, we adopted the proportional decay structure of Lefkopoulou et al. (1989) to characterize the within-cluster dependency among the outcome measurements. Based on a marginal mean model accounting for the treatment and period effects, we developed a new sample size and power procedure to design stepped wedge CRTs accounting for the correlation decay. To apply this procedure, a key step is to obtain reasonable values for the correlation parameters. The within-period correlation, $\tau$, is similar to the traditional ICC in a parallel cluster randomized trial, and may often be found in previous studies with a similar endpoint. By contrast, the decay parameter, $\rho$, is rarely reported in the existing literature, and therefore the sensitivity of power should be investigated across a range of values for $\rho$, as illustrated in Section 3.2. Given that accurate reporting of correlations is vitally important for designing future stepped wedge trials, we also provided an improved, matrix-adjusted quasi-least squares (MAQLS) approach to estimate the correlation parameters along with the marginal mean parameters. The MAQLS has negligible impact on the estimation of the marginal mean parameters and the associated statistical tests coupled with the sandwich variance, but it substantially reduces the bias in estimating the within-period correlation $\tau$ and mildly improves the estimation of the decay parameter $\rho$, as confirmed in our simulation study.

A recent review of stepped wedge CRTs by Barker et al. (2016) indicated that both the cross-sectional and cohort designs were common in practice. Although we have developed the design and analysis strategies specifically for cohort stepped wedge CRTs, a parallel discussion for cross-sectional stepped wedge CRTs could be equally informative. In cross-sectional studies, the proportional decay correlation matrix $R_i(\tau, \rho)$ may no longer be appropriate to characterize the within-cluster dependency structure due to the absence of within-individual repeated measurements. Instead, the exponential decay structure of Kasza et al. (2017), $W_i(\tau, \rho) = (1 - \tau)I_{TN_i} + \tau J_N \otimes F(\rho)$, could be used, without changing the interpretation of $\tau$ and $\rho$ from the cohort setting. To estimate the correlation parameters, the MAQLS
approach could still be applied after replacing the second-stage estimating equations (5) and (6) by

$$\sum_{i=1}^{I} \text{tr} \left\{ \frac{\partial W_{i}^{-1}(\hat{\alpha}_0, \hat{\alpha}_1)}{\partial \alpha_0} W_{i}(\tau, \rho) \right\} = 0,$$

$$\sum_{i=1}^{I} \text{tr} \left\{ \frac{\partial W_{i}^{-1}(\hat{\alpha}_0, \hat{\alpha}_1)}{\partial \alpha_1} W_{i}(\tau, \rho) \right\} = 0.$$  

Such modifications are necessary because $\tau$ and $\rho$ are no longer separable in $W_{i}(\tau, \rho)$, and hence updates for $\tau$ and $\rho$ do not come in closed forms. Correspondingly, the inseparability between $\tau$ and $\rho$ also precludes the derivation of an analytical inverse $W_{i}^{-1}(\tau, \rho)$, and therefore one may not be able to obtain a simple algebraic expression for $\text{var}(\hat{\delta})$. As a result, sample size and power calculation requires numerically inverting the correlation matrix $W_{i}(\tau, \rho)$. In fact, with a continuous outcome and the identity link, it is straightforward to show that the QLS-based power procedure coupled with $W_{i}(\tau, \rho)$ coincides with the linear-mixed-model-based power procedure developed in Kasza et al. (2017) with exponential correlation decay.

One simplification we made in the sample size and power calculations was to assume equal cluster (cohort) sizes. It has been shown that cluster size imbalance leads to reduced power in parallel CRTs and therefore may be accounted for in the design phase (Eldridge et al., 2006). For a stepped wedge trial, Girling (2018) computed the relative efficiency of unequal versus equal cluster sizes by assuming a linear mixed model without correlation decay. It was concluded that the efficiency loss due to unequal cluster sizes is unlikely to exceed 12% across a wide range design of resources and correlation values. Nevertheless, a corresponding expression for the relative efficiency accounting for decayed correlation is currently not available and should merit additional study. The availability of such expressions for relative efficiency could inform the amount of additional design resources required to compensate the efficiency loss due to unequal cluster sizes. Another limitation of our design strategy is that we have assumed the proportional decay correlation is the correctly specified within-cluster dependency structure. However, both the QLS or MAQLS estimators for the intervention effect remain consistent even if the correlation structure is misspecified. If it is anticipated in the design phase that the working correlation may be misspecified, one could follow the general idea of Rochon (1998) to develop a modified sample size.
procedure based on the sandwich variance. Finally, we have assumed a continuous outcome and an identity link function, corresponding to the scenarios of the illustrative examples. In practice, binary outcomes are also common and Zhou et al. (2018) recently developed a suitable sample size procedure based on a generalized linear mixed model without correlation decay. In the presence of correlation decay, it is straightforward to extend the QLS-based sample size procedure to accommodate binary outcomes by following the strategy discussed in Li et al. (2018). However, we should note that the binomial variance is an explicit function of the marginal mean, and the magnitude of the period effects necessarily affects the variance for the intervention effect. Therefore, the variance of the intervention effect \( \text{var}(\hat{\delta}) \) does not have a closed form for binary outcomes, and the corresponding sample size procedure involves numerically computing the model-based variance that is a known function of the proportional decay structure.

Web Appendix A

We provide the closed-form solutions to \( \alpha_0, \alpha_1 \) based on the first-stage QLS estimating equations. These expressions were first introduced by Shults and Morrow (2002), and we review them in our notations for stepped wedge design. Specifically, the first-stage estimator for \( \alpha_0 \) is the solution to the scalar estimating equation

\[
\sum_{i=1}^{I} \frac{\partial}{\partial \alpha_0} \left[ r_i'(\theta) \left\{ G_i^{-1}(\alpha_0) \otimes F_i^{-1}(\alpha_1) \right\} r_i(\theta) \right] = 0
\]

(16)

This is equivalent to solving for \( f(\alpha_0) = 0 \), where

\[
f(\alpha_0) = \sum_{i=1}^{I} \left\{ [\alpha_0^2(N_i - 2)(N_i - 1) + 2\alpha_0(N_i - 1)] \sum_{j=1}^{N_i} r_{ij}'(\theta)F_i^{-1}(\alpha_1)r_{ij}(\theta) \right. \\
-2[1 + \alpha_0^2(N_i - 1)] \sum_{j=1}^{N_i-1} \sum_{j'=j+1}^{N_i} r_{ij}'(\theta)F_i^{-1}(\alpha_1)r_{ij'}(\theta) \left/ \left\{ (1 - \alpha_0)^2[1 + (N_i - 1)\alpha_0]^2 \right\} \right.
\]

For balanced cohort size such that \( N_i = N \), a closed-form expression for \( \alpha_0 \) is

\[
\alpha_0 = \frac{-(N - 1)a_1 + \sqrt{(N - 1)(N - 2)(N - 1)a_1 - 2a_2(a_1 + 2a_2)}}{(N - 1)(a_1(N - 1) - 2a_2)}
\]
where \( a_1 = \sum_{i=1}^{I} \sum_{j=1}^{N_i} r'_{ij}(\theta) F^{-1}(\alpha_1) r_{ij}(\theta) \), and \( a_2 = \sum_{i=1}^{I} \sum_{j=1}^{N_i} \sum_{j'=j+1}^{N_i} r'_{ij}(\theta) F^{-1}(\alpha_1) r_{ij}(\theta) \).

Similarly, the first-stage estimating equation for \( \alpha_1 \)

\[ \sum_{i=1}^{I} \frac{\partial}{\partial \alpha_1} \left[ r'_i(\theta) \left\{ G^{-1}_i(\alpha_0) \otimes F^{-1}(\alpha_1) \right\} r_i(\theta) \right] = 0. \quad (17) \]

is equivalent to the following expression

\[ \alpha_1 = \frac{b_m - \sqrt{b_m^2 - 4a_m^2}}{2a_m} \]

where

\[ a_m = \sum_{i=1}^{I} \left[ q_{i1} \sum_{j=1}^{N_i} \sum_{k=1}^{T-1} r_{ijk} r_{ik,k+1} + q_{i2} \sum_{j=1}^{N_i-1} \sum_{j'=j+1}^{N_i} \sum_{k=1}^{T-1} (r_{ij,k} r_{ij',k+1} + r_{ij',k} r_{ij,k+1}) \right] \]

\[ b_m = \sum_{i=1}^{I} \left[ q_{i1} \sum_{j=1}^{N_i} \sum_{k=1}^{T-1} (r^2_{ij,k} + r^2_{ij,k+1}) + 2q_{i2} \sum_{j=1}^{N_i-1} \sum_{j'=j+1}^{N_i} \sum_{k=1}^{T-1} (r_{ij,k} r_{ij',k+1} + r_{ij,k+1} r_{ij',k}) \right] \]

\[ q_{i1} = \frac{1 + (N_i - 2)\alpha_0}{(1 - \alpha_0)[1 + (N_i - 1)\alpha_0]} \]

\[ q_{i2} = \frac{-\alpha_0}{(1 - \alpha_0)[1 + (N_i - 1)\alpha_0]} \]

**Web Appendix B**

We justify the proposed matrix-adjusted correlation estimates as follows. Recall that the first-stage estimating equation (16) is equivalent to

\[ \sum_{i=1}^{I} \frac{\partial}{\partial \alpha_0} tr \left[ \left\{ G^{-1}_i(\alpha_0) \otimes F^{-1}(\alpha_1) \right\} r_i(\theta) r'_i(\theta) \right] = 0 \]

\[ (18) \]

and \( r_i(\theta) r'_i(\theta) \) is the nonparametric moment estimator for the correlation matrix. [Preisser et al., 2008] first noticed the finite-sample bias in the above moment estimator when \( I \) is small, and proposed to replace it by the “matrix-adjusted” estimator \( \tilde{R}_i(\theta) = A_i^{-1/2}(I - H_i)^{-1} A_i^{1/2} r_i(\theta) r'_i(\theta) \), within the traditional GEE routine. See also the Web Appendix B of [Li et al., 2018] for additional technical details. Therefore, estimating equation (18) could be replaced by

\[ \sum_{i=1}^{I} \frac{\partial}{\partial \alpha_0} tr \left[ \left\{ G^{-1}_i(\alpha_0) \otimes F^{-1}(\alpha_1) \right\} \tilde{R}_i(\theta) \right] = 0. \]

\[ (19) \]
When the true correlation is the proportional decay structure, we now provide the closed-form updates for the matrix-adjusted estimating equation. Write $\tilde{R}_i(\theta)$ as a block matrix with each block $\tilde{R}_{ij}$ corresponding to the repeated measurements for the same individual

$\tilde{R}_i(\theta) = \begin{pmatrix}
\tilde{R}_{i11} & \tilde{R}_{i12} & \ldots & \tilde{R}_{i1N_i} \\
\tilde{R}_{i21} & \tilde{R}_{i22} & \ldots & \tilde{R}_{i2N_i} \\
\vdots & \vdots & \ddots & \vdots \\
\tilde{R}_{iN_i1} & \tilde{R}_{iN_i2} & \ldots & \tilde{R}_{iN_iN_i}
\end{pmatrix}$.

After some simplification algebra, we could express $\alpha_0$ as the solution to $g(\alpha_0) = 0$, where

$$g(\alpha_0) = \sum_{i=1}^{I} \left\{ [\alpha_0^2(N_i - 2)(N_i - 1) + 2\alpha_0(N_i - 1)] \sum_{j=1}^{N_i} \text{tr} \left( F^{-1}(\alpha_1) \tilde{R}_{ij} \right) ight\}$$

$$- \left\{ [1 + \alpha_0^2(N_i - 1)] \sum_{j \neq j'} \text{tr} \left( F^{-1}(\alpha_1) \tilde{R}_{ij} \tilde{R}_{ij} \right) \right\} / \left\{ (1 - \alpha_0)^2 [1 + (N_i - 1)\alpha_0]^2 \right\}$$

Similarly, we solve the following bias-corrected estimating equation for $\alpha_1$

$$\sum_{i=1}^{I} \frac{\partial}{\partial \alpha_1} \text{tr} \left[ \{ G_i^{-1}(\alpha_0) \otimes F^{-1}(\alpha_1) \} \tilde{R}_i(\theta) \right] = 0. \quad (20)$$

Recall that $F^{-1}(\rho) = (1 - \rho^2)^{-1}\{I + \rho^2C_2 - \rho C_1\}$, $C_2 = \text{diag}(0, 1, \ldots, 1, 0)$ and $C_1$ is a tridiagonal matrix with zeros on the main diagonal and ones on the two sub-diagonals. After some simplification algebra, we could express $\alpha_1$ as

$$\alpha_1 = \frac{e_m - \sqrt{e_m^2 - d_m^2}}{d_m}$$

where

$$d_m = \sum_{i=1}^{I} \left[ q_{i1} \sum_{j=1}^{N_i} \text{tr} \left( C_1 \tilde{R}_{ij} \right) + q_{i2} \sum_{j \neq j'} \text{tr} \left( C_1 \tilde{R}_{ij} \tilde{R}_{ij} \right) \right]$$

$$e_m = \sum_{i=1}^{I} \left[ q_{i1} \sum_{j=1}^{N_i} \text{tr} \left( \tilde{R}_{ij} \right) + q_{i1} \sum_{j=1}^{N_i} \text{tr} \left( C_2 \tilde{R}_{ij} \right) + q_{i2} \sum_{j \neq j'} \text{tr} \left( \tilde{R}_{ij} \tilde{R}_{ij} \right) + q_{i2} \sum_{j \neq j'} \text{tr} \left( C_2 \tilde{R}_{ij} \tilde{R}_{ij} \right) \right]$$
Web Appendix C

Recall that the $TN \times (T+1)$ design matrix corresponding to cluster $i$ as $Z_i = 1_N \otimes (I_T, X_i)$, where $1_N$ is a $N$-vector of ones. The variance of the intervention effect $\text{var}(\delta)$ equals to the lower-right element of $\phi(\sum_{i=1}^{I} Z_i' R_i(\tau, \rho) Z_i)^{-1}$, where $\phi$ is the marginal variance or dispersion. Notice that

$$
\sum_{i=1}^{I} Z_i' R_i^{-1} Z_i = \sum_{i=1}^{I} \left[ 1_N' \otimes \left( \begin{array}{c} I_T \\ X_i' \end{array} \right) \right] \left( G_i^{-1}(\tau) \otimes F^{-1}(\rho) \right) \left[ 1_N' \otimes \left( \begin{array}{c} I_T \\ X_i \end{array} \right) \right] = \left[ \begin{array}{c} \Lambda_{11} \\ \Lambda_{12} \\ \Lambda_{21} \\ \Lambda_{22} \end{array} \right],
$$

where $\Lambda_{11}$ is of dimension $T \times T$, $\Lambda_{12} = \Lambda_{21}'$ is of dimension $T \times 1$, and $\Lambda_{22}$ is a scalar. Define $c = (1 - \tau)^{-1}$ and $d = \tau / [(1 - \tau)\{(1 + (N - 1)\tau)\}]$, and after some algebra, we obtain

$$
\Lambda_{11} = I(1_N'1_N) \otimes (cF^{-1}) + I(1_N'1_N) \otimes (-dF^{-1}) = IN(c - Nd)F^{-1},
$$

$$
\Lambda_{12} = I(1_N'1_N) \otimes \sum_{i=1}^{I} (cF^{-1})X_i + (1_N'1_N) \otimes \sum_{i=1}^{I} (-dF^{-1})X_i = N(c - Nd) \sum_{i=1}^{I} F^{-1}X_i,
$$

and $\Lambda_{22} = N(c - Nd) \sum_{i=1}^{I} X_i F^{-1}X_i$. The variance of the intervention effect then becomes

$$
\text{var}(\delta) = \phi(\Lambda_{22} - \Lambda_{21}\Lambda_{11}^{-1}\Lambda_{12})^{-1}
$$

$$
= \phi \left\{ N(c - Nd) \sum_{i=1}^{I} X_i'F^{-1}X_i - I^{-1}N(c - Nd) \left( \sum_{i=1}^{I} X_i'F^{-1} \right) F \left( \sum_{i=1}^{I} F^{-1}X_i \right) \right\}^{-1}
$$

$$
= \phi IN^{-1}(c - Nd)^{-1} \left\{ I \sum_{i=1}^{I} X_i'F^{-1}X_i - \left( \sum_{i=1}^{I} X_i' \right) F^{-1} \left( \sum_{i=1}^{I} X_i \right) \right\}^{-1}.
$$

The key terms are further expanded as

$$
I \sum_{i=1}^{I} X_i'F^{-1}X_i = (1 - \rho^2)^{-1} \left\{ I \sum_{i=1}^{I} (X_{i1} + X_{iT}) + I(1 + \rho^2) \sum_{j=2}^{T-2} X_{ij} - 2\rho IV \right\}
$$

$$
= (1 - \rho^2)^{-1} \left\{ - I\rho^2 \sum_{i=1}^{I} (X_{i1} + X_{iT}) + (1 + \rho^2)IU - 2\rho IV \right\}
$$

$$
= (1 - \rho^2)^{-1} \left\{ - I^2\rho^2 + (1 + \rho^2)IU - 2\rho IV \right\},
$$

where $U = \sum_{i=1}^{I} \sum_{j=1}^{T} X_{ij}$ and $V = \sum_{i=1}^{I} \sum_{j=1}^{T-1} X_{ij}X_{i,j+1}$ are design constants that only depend on the stepped wedge assignment layout. In particular, the inner summation in $V$ reflects the between-
period autoregressive structure to the first order. Next,

$$\left( \sum_{i=1}^{I} X_i \right) F^{-1} \left( \sum_{i=1}^{I} X_i \right) = (1 - \rho^2)^{-1} \left\{ \left( \sum_{i=1}^{I} X_i \right)^2 + \left( \sum_{i=1}^{I} X_{iT} \right)^2 + (1 + \rho^2) \sum_{j=2}^{T-1} \left( \sum_{i=1}^{I} X_{ij} \right)^2 - 2\rho Q \right\}$$

$$= (1 - \rho^2)^{-1} \left\{ - \rho^2 \left( \sum_{i=1}^{I} X_i \right)^2 - \rho^2 \left( \sum_{i=1}^{I} X_{iT} \right)^2 + (1 + \rho^2) W - 2\rho Q \right\}$$

$$= (1 - \rho^2)^{-1} \left\{ - I^2 \rho^2 + (1 + \rho^2) W - 2\rho Q \right\},$$

where the design constants $W = \sum_{j=1}^{T} (\sum_{i=1}^{I} X_{ij})^2$ and $Q = \sum_{j=1}^{T-1} (\sum_{i=1}^{I} X_{ij})(\sum_{i=1}^{I} X_{i,j+1})$.

Again, the outer summation in $Q$ reflects the between-period autoregressive structure to the first order. Further note

$$c - Nd = \frac{1}{1 - \tau} - \frac{N\tau}{(1 - \tau)[1 + (N - 1)\tau]} = \frac{1}{1 + (N - 1)\tau}$$

Some further algebra leads to the following closed-form variance expression in Section 2.3,

$$\text{var}(\hat{\delta}) = \frac{(\phi I/N)(1 - \rho^2)[1 + (N - 1)\tau]}{(IU - W)(1 + \rho^2) - 2(IV - Q)\rho}.$$ 

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