Journal of Clinical Epidemiology 86 (2017) 160−167

Proposed variations of the stepped-wedge design can be used to accommodate multiple interventions

Vivian H. Lyons[a,b,*], Lingyu Li[c], James P. Hughes[c], Ali Rowhani-Rahbar[a,b]

[a]Department of Epidemiology, School of Public Health, University of Washington, Box 357236, Seattle, WA 98195-7236, USA
[b]Harborview Injury Prevention & Research Center, 401 Broadway Avenue, 4th Floor, Seattle, WA 98122, USA
[c]Department of Biostatistics, School of Public Health, University of Washington, Box 357232, Seattle, WA 98195-7232, USA

Accepted 4 April 2017; Published online 13 April 2017

Abstract

Objectives: Stepped-wedge design (SWD) cluster-randomized trials have traditionally been used for evaluating a single intervention. We aimed to explore design variants suitable for evaluating multiple interventions in an SWD trial.

Study Design and Setting: We identified four specific variants of the traditional SWD that would allow two interventions to be conducted within a single cluster-randomized trial: concurrent, replacement, supplementation, and factorial SWDs. These variants were chosen to flexibly accommodate study characteristics that limit a one-size-fits-all approach for multiple interventions.

Results: In the concurrent SWD, each cluster receives only one intervention, unlike the other variants. The replacement SWD supports two interventions that will not or cannot be used at the same time. The supplementation SWD is appropriate when the second intervention requires the presence of the first intervention, and the factorial SWD supports the evaluation of intervention interactions. The precision for estimating intervention effects varies across the four variants.

Conclusion: Selection of the appropriate design variant should be driven by the research question while considering the trade-off between the number of steps, number of clusters, restrictions for concurrent implementation of the interventions, lingering effects of each intervention, and precision of the intervention effect estimates.

Keywords: Cluster-randomized trial; Efficiency; Multiple interventions; Pragmatic trials; Stepped-wedge trial design; Study design

1. Introduction

The use of stepped-wedge designs (SWDs) in public health and clinical research has gained popularity since the Gambia Hepatitis Study [1]. The traditional SWD is a unidirectional crossover design in which time of the intervention implementation is randomized at the cluster level, with one or more clusters following the same randomization pattern within each cluster group (Fig. 1). The SWD offers a pragmatic approach where clusters initially serve as a control before receiving the intervention at a subsequent time step; eventually, all clusters receive the intervention [2]. This is a major departure from parallel cluster-randomized trials where assignments for intervention and control groups are decided at the beginning of the study and not changed subsequently [3].

In an SWD trial, the intervention effect is estimated using both within-cluster and between-cluster information. Indeed, one of the strengths of SWD is that by including within-cluster information, time-invariant confounding on the cluster level can be avoided and precision may be gained [3]. The stepped rollout can also increase logistic feasibility when simultaneous intervention implementation in many clusters may be prohibitive. An SWD can be the preferred design choice when it is necessary or desirable for all clusters to receive the intervention by the end of the study (e.g., when randomizing to a control group is unethical), thus precluding the parallel or bidirectional crossover cluster-randomized trial design. Another common motivation for using an SWD is having too few clusters for a parallel design. In these situations, an SWD can

Conflicts of interest: None.

Funding: V.H.L. was supported by the Maternal and Child Health Bureau, Health Resources and Services Administration (grant #T76 MC00011) and J.P.H. is the principal investigator of a grant from National Institute of Allergy and Infectious Diseases (grant #AI29168), which contributes to his salary. Neither funding agency had a role in the study design, analysis, the writing of the report, or the decision to submit the article for publication.

* Corresponding author. Tel.: +1-206-744-9430; fax: +1-206-744-9962.

E-mail address: vlyons@uw.edu (V.H. Lyons).

http://dx.doi.org/10.1016/j.jclinepi.2017.04.004
0895-4356/

What is new?

Key findings

- Evaluating multiple interventions using a stepped-wedge design is feasible.
- Investigators could use these four basic stepped-wedge designs (i.e., concurrent, replacement, supplementation, and factorial stepped-wedge designs) when evaluating multiple interventions with additional variations.

What this adds to what was known?

- Previous stepped-wedge studies have been limited to evaluation of a single intervention; investigators may evaluate multiple interventions using these four designs.

What is the implication and what should change now?

- Use of the replacement, supplementation, and factorial stepped-wedge designs allows investigators to assess the effect of multiple interventions within the same trial.
- Use of the factorial stepped-wedge design allows investigators to assess potential interactions between interventions.

provide higher quality evidence than purely observational studies or pre-post assessments [4–6]. Although some argue that two-arm parallel group or crossover cluster-randomized trial design, when possible, is preferable to a traditional SWD, an SWD can be more efficient than a parallel group cluster-randomized trial design under certain conditions [4,7,8]. Other scientific and logistical reasons for choosing an SWD are described in the study by Mdege et al. and elsewhere [5,7].

There are also inherent limitations to an SWD [4–11]. By design, the treatment effect in SWD is partially confounded by time, thus estimation of the intervention effect is often model dependent. When using an SWD, consideration must be given to both the amount of time required to begin the intervention rollout for each cluster as well as the length and placement of any wash-in or washout periods [12]. Other limitations have been discussed elsewhere [2,3].

	Time 0	Time 1	Time 2	Time 3
Group 1	0	1	1	1
Group 2	0	0	1	1
Group 3	0	0	0	1

Fig. 1. The traditional stepped-wedge study. 0 = control period; 1 = intervention period.

SWDs have traditionally been used to evaluate a single intervention. However, the need and desire to evaluate multiple interventions in a specific setting is not uncommon [13–15]. For example, to combat childhood obesity, a school might implement both a policy change to school lunch requirements and a new nutrition curriculum [16]. Evaluating multiple interventions in a single trial using an SWD has the potential to decrease the required time until each cluster receives an intervention, improve participant engagement, decrease total funding required, enhance efficiency, and allow for assessing potential interaction between the interventions as well as decrease total clusters needed compared with conducting two separate trials. Here, we propose new SWD variants that can be used for rolling out and evaluating multiple interventions and outline their features and efficiency. Note that these variants apply only in the context of multiple interventions, as without the second intervention, the models would essentially reduce to a single-intervention SWD. Examples from the existing literature where the proposed design variants could have been considered are provided throughout. The overarching goal is to provide a framework for researchers who plan to examine the effectiveness of multiple interventions using SWD in their work.

2. Methods

This study was motivated by the need to evaluate the effects of a new health care protocol in conjunction with a technological support piece. The technological support piece could only be applied following the implementation of the new health care protocol (described in Section 3.1.3), and we were interested not only in evaluating their joint effect but also the effect of the health care protocol by itself. Because of the cost of implementation per cluster, limited number of available clusters, and each cluster conditioning their participation on receiving the intervention, an SWD was chosen as the best design for this study, assuming it could be modified to accommodate the two interventions. In response to this identified gap in methodology, we developed four variants of SWD to support the evaluation of two interventions in one trial. We denote these variants as concurrent, replacement, supplementation, and factorial SWD. Each design uses unidirectional crossover, a hallmark of SWD. The designs are described in more detail in Section 3.

To understand the relative efficiency of the different design options, and as an aid to power calculation, we also developed methods to calculate the variance of each of the two interventions. We used the following equation which extends the original model proposed by Hussey and Hughes (i.e., intervention 1 and intervention 2) [12],