Sample Size Methodology for Stepped Wedge Design and its Application in HIV Research

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Background & Introduction

- **Sankofa pediatric HIV disclosure study**

The 'Sankofa' pediatric HIV disclosure study (2013–2017) was an intervention that aimed to address the low prevalence of disclosure of pediatric HIV status in Ghana.

'Sankofa 1' was a 2-site cluster-randomized trial, which provided evidence for the efficacy and safety of the intervention. 'Sankofa 2' will examine the effectiveness of the intervention in real-world clinic conditions in Ghana.

- **Stepped wedge designs (SWD)**

The stepped wedge design (SWD) is a variation of the cluster randomized trials. All clusters begin in the control group, and subsequently a random cluster is crossed over to the intervention group at predefined time points or intervals. After switching, the clusters will remain in the intervention group until the end of the study. Consequently, all clusters will be in the intervention group by the end of the trial.

Evidence-based Approaches

- **Sample size methodology**

In this project, we did a comprehensive review of the existing sample size methodologies for SWD trials, and categorized them according to different sources of data (an open cohort, a closed cohort, cross-sectional sample) and different types of outcomes (continuous, discrete, time-to-event). We also conducted a systematic review on HIV trials with SWD, examining the sample size and statistical power approaches described in the methods of these studies.

- **Simulation**

Simulation studies in R and SAS for statistical power calculation of a time-to-event outcome can be used by the research community in the future.

Target Community Needs

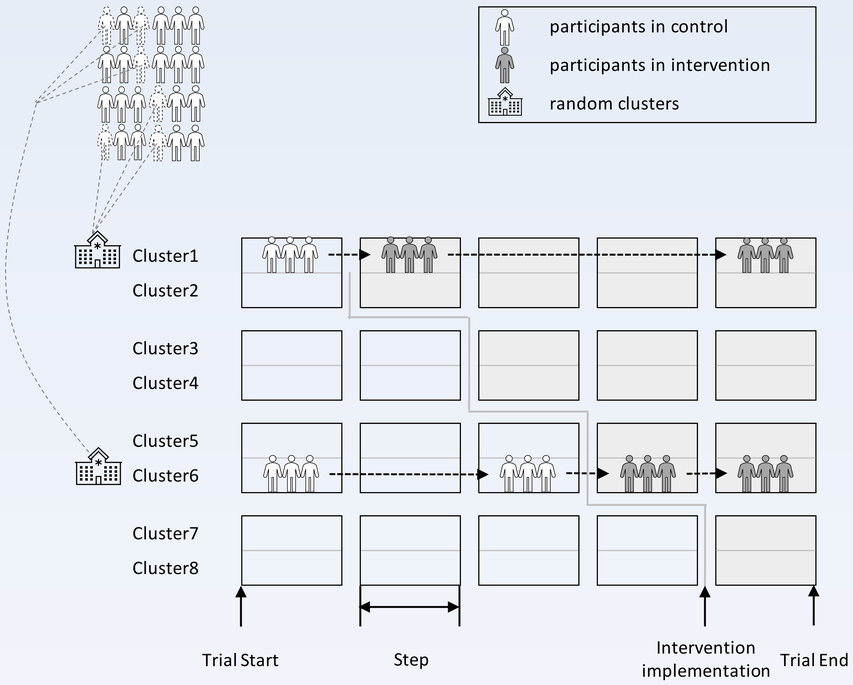
When designing a trial to examine the effectiveness of the Sankofa pediatric HIV disclosure intervention in real-world clinic conditions in Ghana, we realized that traditional randomized controlled trials are impracticable in large communities due to both ethical and practical considerations. A pragmatic trial should ensure that everyone has access to an efficacious intervention and should accommodate implementational challenges of a large-scale community trial.

Research Questions

SWD has become very popular in large-scale pragmatic trials, but there is very limited literature with regard to the sample size methodologies for SWD. The size of a sample influences the precision of our estimates, the power of the study to draw conclusions, and economic expense. Therefore, studying the sample size methods for SWD is of great significance for the community.

Methods & Results

In order to link the academic research achievements to the real-world pragmatic trials setting, we first did a review of the the existing sample size methods for different types of SWD trials and different outcomes; then we conducted a systematic review of the application of SWD in HIV-related trials. In conclusion, we synthesized the state of the art in SWD sample size methods and provided practical guidance for the HIV-research community, especially for the non-statistician audience.



This figure illustrates how a SWD with an open cohort works. We also created a series of figures to explain to non-statisticians the different types of SWD trials, and provided available examples of each type in the field of HIV research through a comprehensive literature review.

Public Health Significance

- **Pediatric HIV intervention**

HIV infection is a major public health issue. Sub-Saharan Africa has been disproportionately affected by the HIV epidemic, and it is home to nearly 90% of children and adolescents living with HIV.

Preliminary data shows that intervention-assisted disclosure had a positive impact on rate of disclosure without detrimental sequelae. If the effectiveness of the intervention in large-scale community can be proven, it will be yet another tool in the fight against healthcare disparities.

- **Stepped wedge designs (SWD)**

SWDs are very commonly used in pragmatic clinical trials. Different from RCT, in an SWD trial, all clusters will receive the intervention by the end of the study. Therefore, SWDs can alleviate ethical concerns about the use of control groups.

Furthermore, SWDs are advantageous in studies with large number of clusters where simultaneous intervention roll-outs may be logistically impractical due to the limited resources or geographical constraints.

Community Engagement

- **Target Community**

Our research directly benefits the community in Greater Acra (12 HIV treatment centers) and Ashanti (9 HIV treatment centers) regions in Ghana.

We designed the study schema for an open cohort SWD with no repeated within-person observations for the time-to-event primary outcome.

- **Academic Community**

During the internship, I worked closely with Prof. Shabanova from Yale School of Medicine and Prof. Ciarleglio from Yale School of Public Health. Under their instruction, I gained real-life experience of working with researchers in an applied setting; and learning how to work in that environment is a valuable skill to a new biostatistician.

- **Research Community**

We summarized up-to-date HIV-related SWD trials, discussing the limitations in their study design and sample size calculation methods, and providing guidance to non-statistician researchers on appropriate methods when calculating sample size for these types of studies.

Future plans include creating an R package with functions that can be used by the research community at large in their research proposals, which will benefit the SWD trials in the future.

Acknowledgement

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