Stepped-Wedge Design (SWD) for HIV Trials

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Introduction to SWD

SWD is a variation of the cluster-randomized trials. All clusters begin in the control group, and subsequently a random cluster or clusters are crossed over to the intervention group at predefined time points or intervals. Consequently, all clusters will be in the intervention group by the end of the trial.

Benefits for Large-Scale Community Trials

- ✓ Expanded access to intervention for all participants
- ✓ Efficient use of study resources during implementation
- ✓ Flexible cross-sectional or longitudinal follow up
- ✓ Accommodation of different types of outcomes

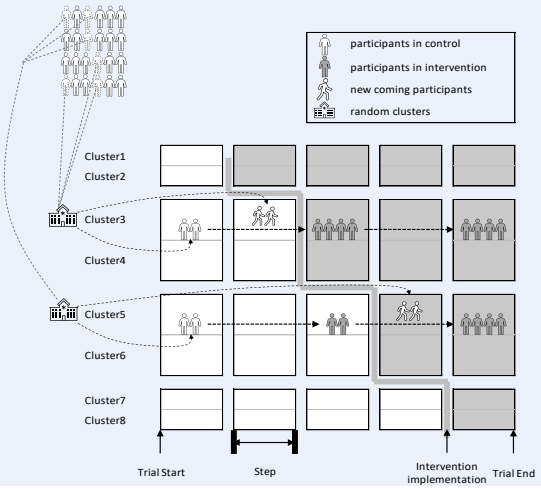
Open Cohort SWD

Description: While most eligible participants are identified at the beginning of the study, the cohort is allowed to be dynamic during the trial: some individuals may leave trial early, while others may become eligible and enter the trial later.

Example in HIV Research: THRio is a stepped wedge cluster randomized trial designed to determine the impact of isoniazid preventive therapy on rates of tuberculosis and death in HIV-infected patients with access to antiretroviral therapy in Brazil. In this study, 29 clinics were randomly allocated a date to begin the intervention period with two clinics beginning the intervention every 2 months. Results showed that the intervention had a modest impact on tuberculosis incidence (13% reduction) and a larger impact on tuberculosis/death (24% reduction).

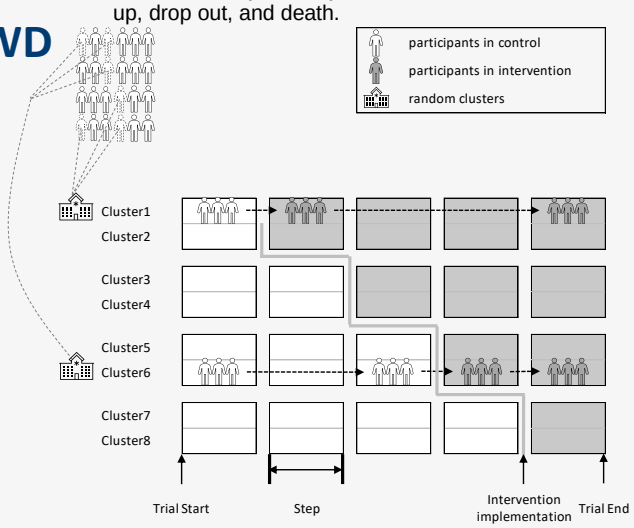
A stepped wedge design was chosen for an operational simplicity and to ensure that all patients eventually received the efficacious intervention.

Reference: Durovni, B., Saraceni, V., Moulton, L. H., Pacheco, A. G., Cavalcante, S. C., King, B. S., Cohn, S., Efron, A., Chaisson, R. E., & Golub, J. E. (2013). Effect of improved tuberculosis screening and isoniazid preventive therapy on incidence of tuberculosis and death in patients with HIV in clinics in Rio de Janeiro, Brazil: a stepped wedge, cluster-randomised trial. The Lancet. Infectious diseases, 13(10), 852–858. https://doi.org/10.1016/S1473-3099(13)70187-7



Closed Cohort SWD

Description: All eligible participants are identified and enrolled at the beginning of the trial. Subjects are exposed to control and intervention sequentially. The number of subjects may decline due to loss to follow-up, drop out, and death.



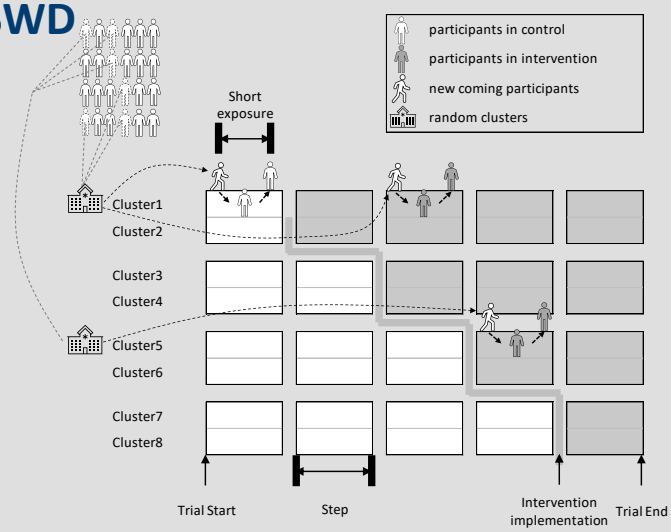
Example in HIV Research: Previous studies suggest that crowdsourcing may be a promising approach to increase HIV testing among men who have sex with men (MSM) in China, but few studies have formally evaluated it in a real-world setting. A closed SWD trial was conducted in 8 Chinese cities from 2 provinces to test the effectiveness of a crowdsourced intervention. Results showed that the intervention was effective for developing and strengthening community-based HIV testing services for MSM.

Withholding intervention from a subgroup of participants would be difficult in MSM. SWD addresses this concern by ensuring that all participants receive the intervention and by allowing each city to serve as its own control.

Reference: SESH Study Group, & Tucker, J. D. (2017). Crowdsourcing to promote HIV testing among MSM in China: study protocol for a stepped wedge randomized controlled trial. Trials, 18(1), 447. https://doi.org/10.1186/s13063-017-2183-1

Cross-Sectional SWD

Description: Eligible participants can enter the study at different times during trial, and are not followed over time. Participants are only exposed to a particular treatment for a relatively short period, either the control or the intervention, but not both.



Example in HIV Research: In Africa, up to 30% of HIV-infected patients who are eligible for antiretroviral therapy (ART) do not start timely treatment. Streamlined ART Strategy (START-ART) was designed to influence health systems to provide ART more efficiently. A SWD trial was implemented in Uganda to evaluate START-ART intervention, in a population of 12,024 patients from 20 health clinics. Results showed that 80% of ART-eligible patients exposed to the intervention started ART by 2 weeks compared to 38% in the standard practice (control).

A large-scale implementation of a life-saving intervention using a roll-out of intervention across clinics allowed for successful incorporation of intervention into the Ugandan health system.

Reference: Amanyire, G., Semitala, F. C., Namusobya, J., Katuramu, R., Kampiire (2016). Effects of a multicomponent intervention to streamline initiation of antiretroviral therapy in Africa: a stepped-wedge cluster-randomised trial. The lancet. HIV, 3(11), e539–e548. https://doi.org/10.1016/S2352-3018(16)30090-X

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