Design Challenges for Multilevel Interventions

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Multilevel Intervention Research Methodology
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Multilevel Interventions

- Multilevel interventions address more than one level of influence for the targeted outcome.
- Multilevel interventions pose special challenges in terms of design and analysis.
  - Respondents who share the same source for any level of influence will share some physical, social, or other connection.
  - Such connections create a positive intraclass correlation among the observations taken from those respondents.
  - That correlation invalidates the usual analytic procedures.
  - This must be considered in the planning stage to ensure a valid analysis and adequate power.
- Many different design and analytic alternatives have been proposed for the evaluation of multilevel interventions.

Three Kinds of Randomized Trials

- Randomized Clinical Trials (RCTs)
  - Individuals randomized to study conditions with no interaction among participants after randomization
    - Most surgical and drug trials
    - Some behavioral trials
- Group-Randomized Trials (GRTs)
  - Groups randomized to study conditions with interaction among the members of the same group before and after randomization
    - Many trials conducted in communities, worksites, schools, etc.
    - Also known as cluster-randomized trials
- Individually Randomized Group Treatment Trials (IRGTs)
  - Individuals randomized to study conditions with interaction among participants after randomization
    - Many behavioral trials

Impact on the Design

- Randomized clinical trials and individually randomized group-treatment trials
  - There is usually good opportunity for randomization to distribute all potential sources of bias evenly.
  - If well executed, bias is not usually a concern.
- Group-randomized trials
  - GRTs often involve a limited number of groups.
  - In any single realization, there is limited opportunity for randomization to distribute all potential sources of bias evenly.
  - Bias is more of a concern in GRTs than in RCTs.

Impact on the Analysis

- Observations on randomized individuals who do not interact are independent and are analyzed with standard methods.
- The members of the same group in a GRT will share some physical, geographic, social or other connection.
- The members of groups created for an IRGT will develop similar connections.
- Those connections will create a positive intraclass correlation that reflects extra variation attributable to the group.

$$ICC_{m:g:c} = corr\left(y_{i:k:l}, y_{i':k:l}\right)$$

Impact on the Analysis

- Given m members in each of g groups...
  - When group membership is established by random assignment,

$$\sigma^2_{\bar{y}_g} = \frac{\sigma^2_y}{m}$$

  - When group membership is not established by random assignment,

$$\sigma^2_{\bar{y}_g} = \frac{\sigma^2_e}{m} + \sigma^2_g$$

  - Or equivalently,

$$\sigma^2_{\bar{y}_g} = \frac{\sigma^2_y}{m}\left(1 + \left(m - 1\right) \mathrm{ICC}\right)$$

Impact on the Analysis

- The variance of any group-level statistic will be larger.
- The df to estimate the group-level component of variance will be based on the number of groups, and so often limited.
  - This is almost always an issue in a GRT.
  - This can be an issue in an IRGT, especially if there are small groups in all study conditions.
- Any analysis that ignores the extra variation or the limited df will have a Type I error rate that is inflated, often badly.
  - Type I error rate may be 30-50% in a GRT, even with small ICC
  - Type I error rate may be 15-25% in an IRGT, even with small ICC
- Extra variation and limited df limit power, so they must be considered at the design stage.

The Need for GRTs and IRGTs

- A GRT remains the best comparative design available whenever the investigator wants to evaluate an intervention that…
  - operates at a group level
  - manipulates the social or physical environment
  - cannot be delivered to individuals without contamination
- An IRGT is the best comparative design whenever...
  - Individual randomization is possible without contamination
  - There are good reasons to deliver the intervention in small groups

What About Alternative Designs?

- Many alternatives to GRTs have been proposed.
  - Multiple baseline designs
  - Time series designs
  - Quasi-experimental designs
  - Dynamic wait-list or stepped-wedge designs
  - Regression discontinuity designs
- Murray et al. (2010) compared these alternatives to GRTs for power and cost in terms of sample size and time.

- Murray DM, Pennell M, Rhoda D, Hade E, Paskett ED. Designing studies that would address the multilayered nature of health care. Journal of the National Cancer Institute Monographs, 2010, 40:90-96.

Multiple Baseline Designs

- Intervention introduced into groups one by one on a staggered schedule
  - Measurement in all groups with each new entry.
  - Often used with just a few groups, e.g., 3-4 groups.
  - Data examined for changes associated with the intervention.

Multiple Baseline Designs

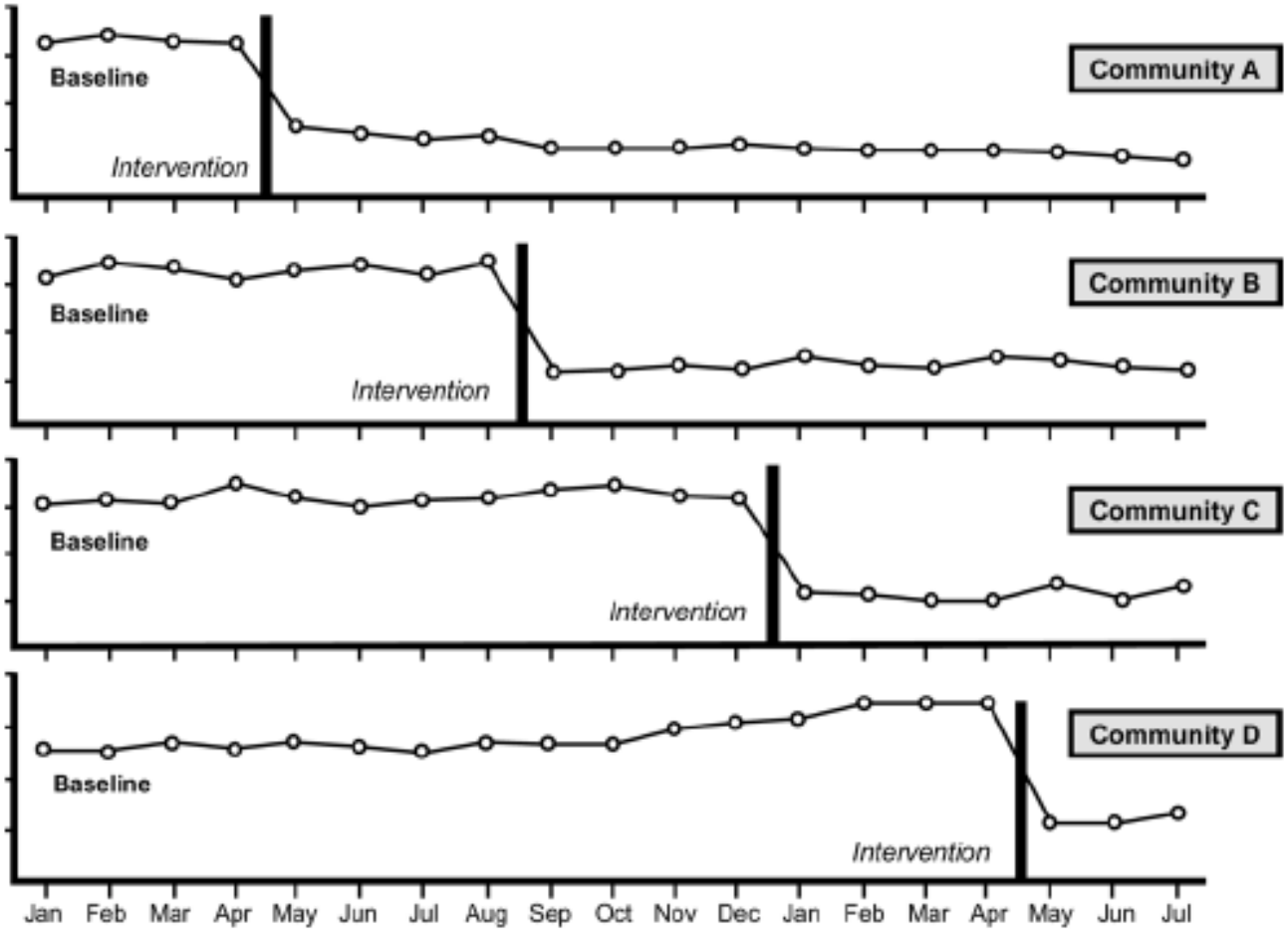


Figure 1. Hypothetical example of a multiple baseline design used to assess behavior change following an intervention in four communities.

Multiple Baseline Designs

- Evaluation relies on logic rather than statistical evidence.
  - Replication of the pattern in each group, coupled with the absence of such changes otherwise, is taken as evidence of an intervention effect.
  - With just a few groups, there is little power for a valid analysis.
- Good choice if effects are expected to be large and rapid.
- Poor choice if effects are expected to be small or gradual.
- Very poor choice if the intervention effect is expected to be inconsistent across groups.

- Rhoda DA, Murray DM, Andridge RR, Pennell ML, Hade EM. Studies with staggered starts: multiple baseline designs and group-randomized trials. Am J Public Health 2011;101(11):2164-9.

Time Series Designs

- Often used to evaluate a policy change in a single group.
- Require repeated and reliable measurements.
  - Standard methods require ~50 observations before and again after the intervention.
- Rely on a combination of logic and statistical evidence.
  - Standard methods provide evidence for change in a single group.
  - One-group designs provide no statistical evidence for between-group comparisons.
- Best used in with an archival data collection system.
  - Could be a strong approach with archival data on many groups.
- May require several cycles of data.

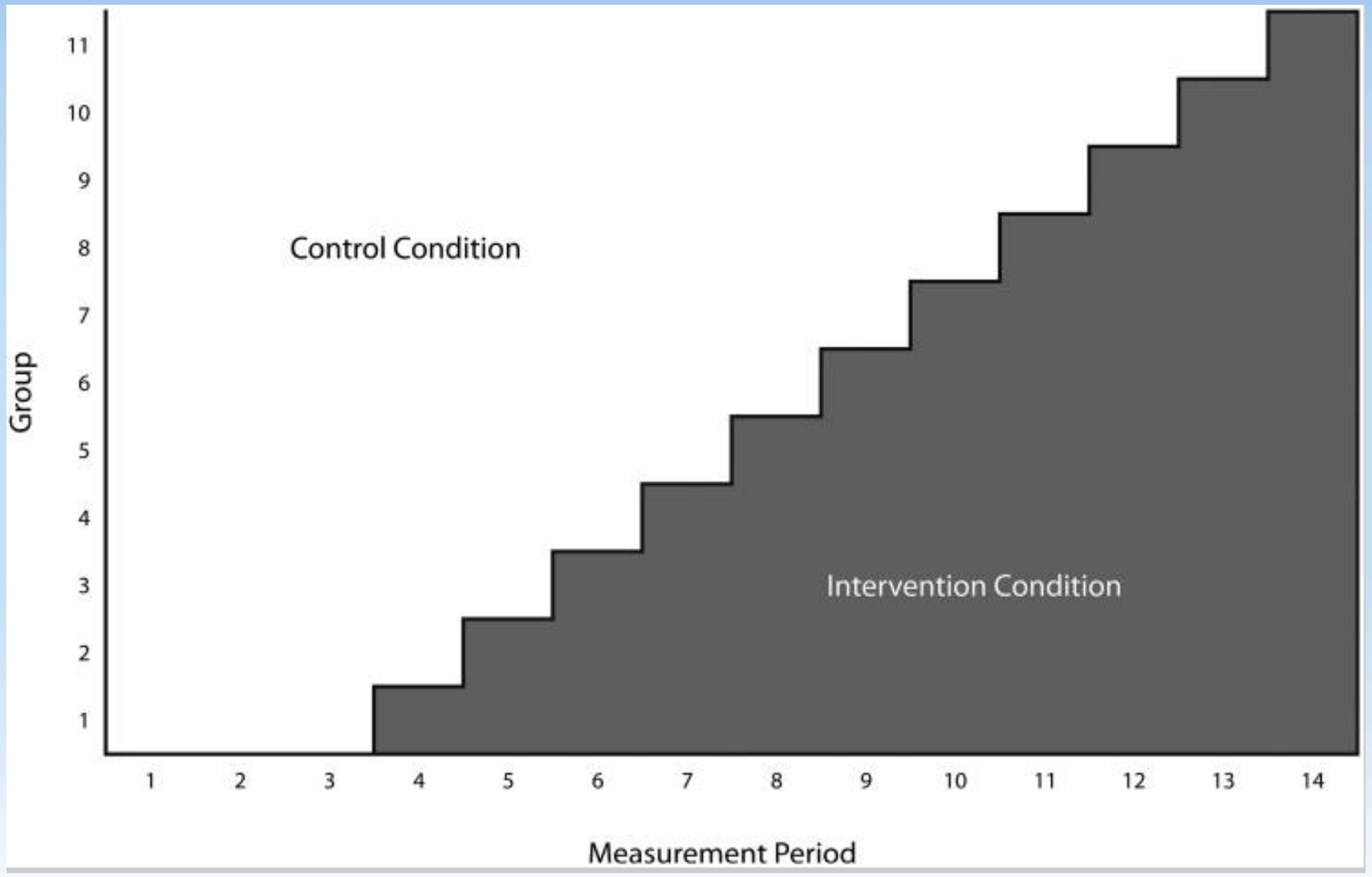
Quasi-Experimental Designs

- QEs have all the features of experiments except randomization.
  - Causal inference requires elimination of plausible alternatives.
- If groups are assigned and members are observed, analysis and power issues are the same as in GRTs.
- Useful when randomization is not possible.
  - Can provide experience with recruitment, measurement, intervention.
  - Can provide evidence of treatment effects if executed properly.
- Well-designed and analyzed QEs are usually more difficult and more expensive than well-designed and analyzed GRTs.

Stepped-Wedge Designs

- Sometimes called Dynamic Wait-List Designs
- Combine the features of multiple baseline designs and GRTs.
  - Measurement is frequent and on the same schedule in all groups.
  - Time is divided into intervals.
  - Groups selected at random for the intervention in each interval.
  - By the end of the study, all the groups have the intervention.

Stepped Wedge Design



Stepped Wedge Design

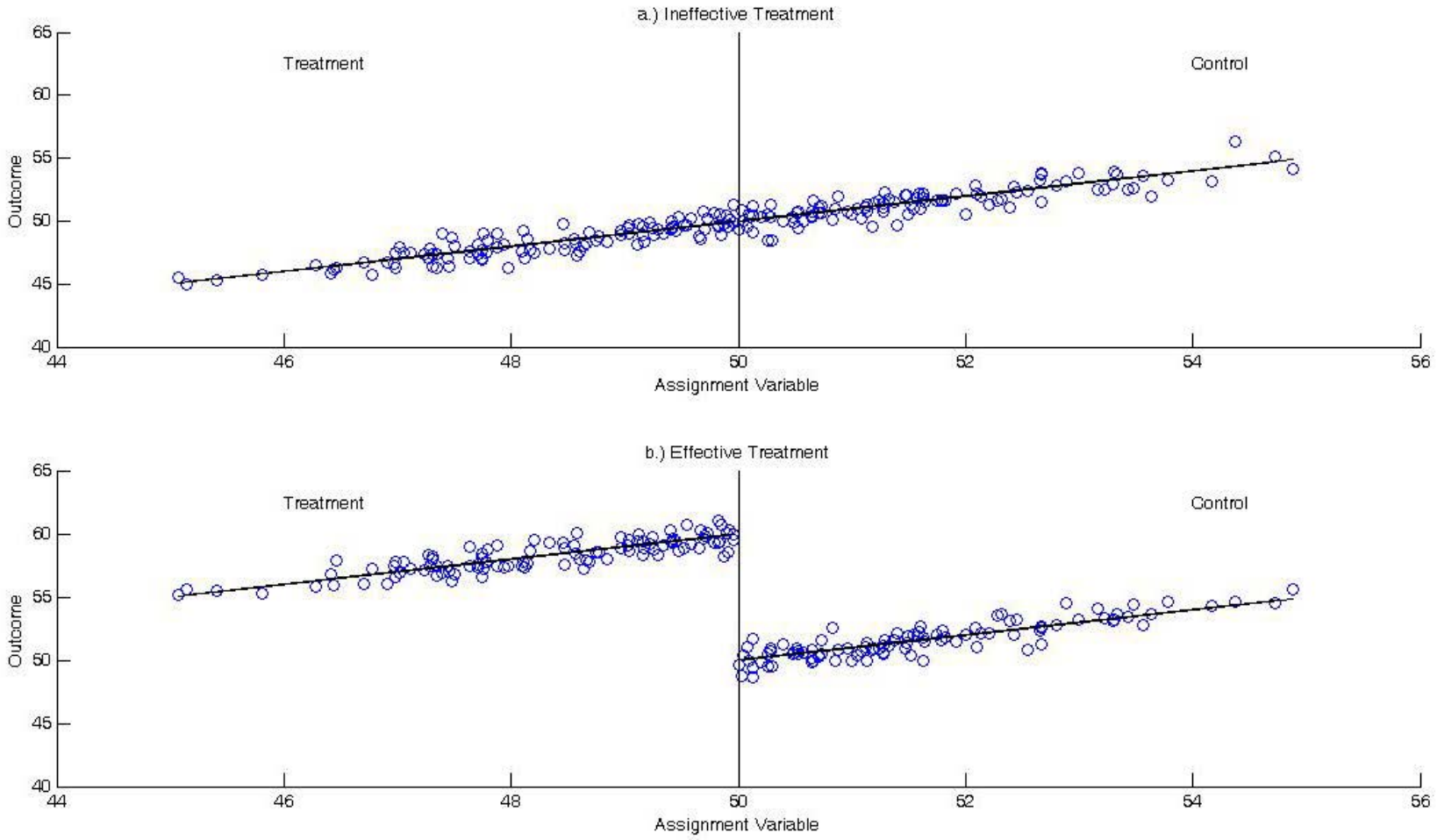
- The analysis estimates a weighted average intervention effect across the intervals.
  - Assumes that the intervention effect is rapid and lasting.
  - Not very sensitive to intervention effects that develop gradually or fade over time.
- These designs can be more efficient but usually take longer to complete and cost more than the standard GRT.

- Rhoda DA, Murray DM, Andridge RR, Pennell ML, Hade EM. Studies with staggered starts: multiple baseline designs and group-randomized trials. Am J Public Health 2011;101(11):2164-9.

Regression Discontinuity Designs

- Groups or individuals are assigned to conditions based on a score, often reflecting the need for the intervention.
- The analysis models the relationship between the assignment variable and the outcome.
  - The difference in intercepts at the cutoff is the intervention effect.

Regression Discontinuity Design



Regression Discontinuity Design

- Because assignment is fully explained by the assignment variable, proper modeling supports causal inference.
  - Rubin, Assignment to Treatment Group on the Basis of a Covariate, Journal of Educational and Behavioral Statistics, 1977, 2:1-26.
- RDs avoid randomization, but are as valid as a RCT or GRT.
- RDs are less efficient than the standard RCT or GRT.
  - Sample size requirements are usually doubled.

- Pennell ML, Hade EM, Murray DM, Rhoda DA. Cutoff designs for community-based intervention studies. Statistics in Medicine 2011;30(15):1865-1882.

Recommendations

- GRTs, IRGTs, stepped wedge, and regression discontinuity designs can provide the strongest evidence for causal inference if implemented and analyzed carefully.
  - Consider extra variation and limited df at the design stage.
  - Randomize with stratification on the baseline value of the primary outcome and group size.
  - Blind evaluation staff to the extent possible.
  - Analyze to account for extra variation and limited df.
- Other approaches can also provide evidence for causal inference, but rely on logic as much as statistics and face more threats to causal inference.

References

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  - Murray DM, Pals SP, Blitstein JL, Alfano CM, Lehman J. Design and analysis of group-randomized trials in cancer: a review of current practices. J Natl Cancer Inst. 2008;100(7):483-91.
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