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June 28, 2023
Acknowledgement


• The presentation is based on the above paper and the presentations.

• The project was initiated and supervised by Dr. Mariola Moeyaert and received invaluable input from Dr. Panpan Yang.
Outline

1. Conceptual Framework
   1.1 Single-Case Experimental Research
   1.2 Two-Stage IPD Meta-Analysis
2. Empirical Validation: Monte Carlo Simulation
3. Conclusion and Future research
4. Questions
1. Conceptual Framework

Single-case experimental designs (SCED) is a scientifically rigorous alternative to randomized controlled trial (RCT) designs.
1. Conceptual Framework

The are a variety of SCEDs that can be considered as extensions of the basic AB design, such as the multiple-baseline design (MBD).

- MBD is one of the most used SCED in practice (Shadish & Sullivan, 2011).

- Using motivational general-mastery imagery to improve the self-efficacy of youth squash players (Munroe-Chandler et al., 2014).
  - **Participants**: 5 youth squash athletes
  - **Outcome**: Squash-specific self-efficacy
  - **Intervention**: Motivational general-mastery imagery intervention
1. Conceptual Framework

Single-case experimental designs

Multiple-Baseline Design (MBD)

- Suitable for conditions when a return-to-baseline performance is not feasible.
- The start of the intervention are staggered across participants.
- Multiple participants are included as within-study replications to provide multiple demonstrations of intervention effectiveness.
1. Conceptual Framework

Meta-Analysis of SCED Data

- Using meta-analysis for SCED data, several key questions can be answered.

<table>
<thead>
<tr>
<th>Purposes of Using Meta-Analysis</th>
<th>Research Questions to be Answered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Summarizing magnitude of intervention effects.</td>
<td>What is the overall average treatment effect across studies?</td>
</tr>
<tr>
<td>Investigating intervention heterogeneity.</td>
<td>Do the intervention effects vary across participants and studies?</td>
</tr>
<tr>
<td>Identifying moderators to explain intervention heterogeneity.</td>
<td>What participant factors and study factors are related to various intervention effects?</td>
</tr>
</tbody>
</table>
1. Conceptual Framework
IPD Meta-Analysis: What?

- Individual Patient/Participant Data (IPD) meta-analysis is also called raw SCD data meta-analysis (Declercq et al. 2022, Moeyaert & Fingerhut, 2022).
- Raw data from multiple participants and studies are extracted and synthesized.
- Three-level structure:

   ![Diagram of three-level structure]

   - Level 1: Measurements
   - Level 2: Participants
   - Level 3: Studies
1. Conceptual Framework
IPD Meta-Analysis: Why?

<table>
<thead>
<tr>
<th>Aggregated data meta-analysis</th>
<th>Individual Participant Data meta-analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic analytic unit: aggregated intervention effectiveness per study.</td>
<td>Basic analytic unit: a measurement score for each participant at each timepoint in each study (hierarchical structure).</td>
</tr>
<tr>
<td>Between-participant variance in intervention effectiveness cannot be estimated.</td>
<td>Between-participant and between-study variance can be estimated.</td>
</tr>
<tr>
<td>No participant-specific moderators can be included.</td>
<td>Moderators at both the participant and study level can be investigated to explain intervention heterogeneity.</td>
</tr>
<tr>
<td>Easy to be understood, applied, and interpreted.</td>
<td>Demands some experience with statistical modeling.</td>
</tr>
</tbody>
</table>
1. Conceptual Framework

IPD Meta-Analysis: Statistical Models

Statistical Model - IPD Meta-Analysis Approaches

A three-level modeling for IPD meta-analysis of SCED data Without Moderators

<table>
<thead>
<tr>
<th>Level 1</th>
<th>( Y_{ijk} = \beta_{0jk} + \beta_{1jk} D_{ijk} + e_{ijk} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>with ( e_{ijk} \sim N(0, \sigma^2_e) )</td>
</tr>
</tbody>
</table>

Assuming the data below comes from participant 3 (\( j = 3 \)) from Study 2 (\( k = 2 \)):

\[ Y_{i32} = \beta_{032} + \beta_{132} D_{132} + e_{i32} \]

\( D_{132} = 0 \) when the data point comes from the baseline phase, and \( D_{132} = 1 \) when the data point comes from the intervention phase.
1. Conceptual Framework

IPD Meta-Analysis: Statistical Models

Statistical Model - IPD Meta-Analysis Approaches

A three-level modeling for IPD meta-analysis of SCED data Without Moderators

<table>
<thead>
<tr>
<th>Level</th>
<th>Equation Description</th>
</tr>
</thead>
</table>
| Level 1 | \( Y_{ijk} = \beta_{0jk} + \beta_{1jk}D_{ijk} + e_{ijk} \)  
with \( e_{ijk} \sim N(0, \sigma_e^2) \) |
| Level 2 | \( \beta_{0jk} = \theta_{00k} + u_{0jk}; \beta_{1jk} = \theta_{10k} + u_{1jk} \)  
with \((u_{0jk} \ u_{1jk}) \sim MVN \left[ \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_{u0}^2 & \sigma_{u01} \\ \sigma_{u01} & \sigma_{u1}^2 \end{pmatrix} \right] \) |
| Level 3 | \( \theta_{00k} = \gamma_{000} + v_{00k}; \theta_{10k} = \gamma_{100} + v_{10k} \)  
with \((v_{00k} \ v_{10k}) \sim MVN \left[ \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_{v0}^2 & \sigma_{v01} \\ \sigma_{v01} & \sigma_{v1}^2 \end{pmatrix} \right] \) |
| Combined | \( Y_{ijk} = \gamma_{000} + v_{00k} + u_{0jk} + (\gamma_{100} + v_{10k} + u_{1jk})D_{ijk} + e_{ijk} \)  
with \( e_{ijk} \sim N(0, \sigma_e^2), [u_{0jk} \ u_{1jk}] \sim MVN \left[ \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_{u0}^2 & \sigma_{u01} \\ \sigma_{u01} & \sigma_{u1}^2 \end{pmatrix} \right], \text{and} [v_{00k} \ v_{10k}] \sim MVN \left[ \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_{v0}^2 & \sigma_{v01} \\ \sigma_{v01} & \sigma_{v1}^2 \end{pmatrix} \right] \) |
### 1. Conceptual Framework

**IPD Meta-Analysis: Statistical Models**

#### Statistical Model - IPD Meta-Analysis approaches

**One-stage IPD meta-analysis**

\[ y_{ijk} = \beta_{0jk} + \beta_{1jk}D_{ijk} + e_{ijk} \text{ with } e_{ijk} \sim N(0, \sigma_e^2) \]

\[
\begin{align*}
\beta_{0jk} &= \gamma_{000} + u_{0jk} + \nu_{00k} \\
\beta_{1jk} &= \gamma_{100} + u_{1jk} + \nu_{10k}
\end{align*}
\]

\[
\begin{pmatrix}
u_{0jk} \\
u_{1jk}
\end{pmatrix} \sim MVN \left( \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_{u0}^2 & \sigma_{u1}^2 \\ \sigma_{u01} & \sigma_{u1}^2 \end{pmatrix} \right)
\]

\[
\begin{pmatrix} u_{0jk} \\
u_{1jk}
\end{pmatrix} \sim MVN \left( \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_{v0}^2 & \sigma_{v1}^2 \\ \sigma_{v01} & \sigma_{v1}^2 \end{pmatrix} \right)
\]

**Two-stage IPD meta-analysis**

**Stage 1**

\[ y_{ijk} = \beta_{0jk} + \beta_{1jk}D_{ijk} + e_{ijk} \text{ with } e_{ijk} \sim N(0, \sigma_e^2) \]

\[ b_{1jk} = \beta_{1jk} + r_{jk} \]

**Stage 2**

\[ \beta_{1jk} = \gamma_{100} + u_{1jk} + \nu_{10k} \]

\[ u_{1jk} \sim N \left( 0, \sigma_{u1jk}^2 \right) \]

\[ \nu_{10k} \sim N \left( 0, \sigma_{v10k}^2 \right) \]

---

2. Empirical Validation: Monte Carlo Simulation Study

Purpose:

• Statistical properties of IPD meta-analysis of multiple-baseline design data using three-level modeling.

• Empirically investigate under which realistic SCED conditions intervention and moderator effects can be estimated with appropriate statistical properties.

<table>
<thead>
<tr>
<th>Design Factor</th>
<th>Notation</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of studies</td>
<td>$K$</td>
<td>10, 30, 40 or 50</td>
</tr>
<tr>
<td>Number of observations</td>
<td>$I$</td>
<td>20 or 40</td>
</tr>
<tr>
<td>Number of participants</td>
<td>$J$</td>
<td>4, 7, 12</td>
</tr>
<tr>
<td>Intervention effect</td>
<td>$\gamma_{100}$</td>
<td>0 or 2</td>
</tr>
<tr>
<td>Moderator effects</td>
<td>Gender, $\gamma_{110}$</td>
<td>0.75, 1.00, 1.50, 2.00</td>
</tr>
<tr>
<td></td>
<td>Age, $\gamma_{120}$</td>
<td>0.25 or 0.50</td>
</tr>
<tr>
<td></td>
<td>Study Quality, $\gamma_{101}$</td>
<td>0.75, 1.00, 1.50, 2.00</td>
</tr>
<tr>
<td></td>
<td>Physical Setting, $\gamma_{102}$</td>
<td>0.75, 1.00, 1.50, 2.00</td>
</tr>
<tr>
<td>Between-case variance</td>
<td>Baseline level, $\sigma_{\theta 0}^2$</td>
<td>2.00</td>
</tr>
<tr>
<td></td>
<td>Intervention effect, $\sigma_{\theta 1}^2$</td>
<td>2.00</td>
</tr>
<tr>
<td>Between-study variance</td>
<td>Baseline level, $\sigma_{\theta 2}^2$</td>
<td>2.00</td>
</tr>
<tr>
<td></td>
<td>Intervention effect, $\sigma_{\theta 1}^2$</td>
<td>2.00</td>
</tr>
<tr>
<td>Within-participant variance</td>
<td>$\sigma_e^2$</td>
<td>1.00</td>
</tr>
</tbody>
</table>

3. Methodological Research

Simulation Study – Data Generation

(1) **Model 0**: No Moderators

\[ Y_{ijk} = \gamma_{000} + v_{00k} + u_{0jk} + (\gamma_{100} + v_{10k} + u_{1jk})D_{ijk} + e_{ijk} \]

(2) **Model 1**: One Moderator at Level 2 and One Moderator at Level 3

\[ Y_{ijk} = \gamma_{000} + v_{00k} + u_{0jk} + (\gamma_{100} + \gamma_{110}\text{Gender}_{11k} + \gamma_{101}\text{Quality}_{101} + v_{10k} + u_{1jk})D_{ijk} + e_{ijk} \]

(3) **Model 2**: Two Moderators at Level 2 and One Moderator at Level 3

\[ Y_{ijk} = \gamma_{000} + v_{00k} + u_{0jk} + (\gamma_{100} + \gamma_{110}\text{Gender}_{11k} + \gamma_{120}\text{Age}_{11k} + \gamma_{101}\text{Quality}_{101} + v_{10k} + u_{1jk})D_{ijk} + e_{ijk} \]

(4) **Model 3**: Two Moderators at Level 2 and Two Moderators at Level 3

\[ Y_{ijk} = \gamma_{000} + v_{00k} + u_{0jk} + (\gamma_{100} + \gamma_{110}\text{Gender}_{11k} + \gamma_{120}\text{Age}_{11k} + \gamma_{101}\text{Quality}_{101} + \gamma_{102}\text{Setting}_{101} + v_{10k} + u_{1jk})D_{ijk} + e_{ijk} \]
3. Methodological Research
Simulation Study – Data Generation

• The number of conditions investigated depends on the specific model of interest.
• Model 0 is the only model that does not include 40 or 50 studies. The reason for this is that statistical properties are appropriate with as few as 30 studies (and there is already sufficient power across all conditions with 30 studies).

• Number of conditions per model:
  • Model 0: $2 \times 2 \times 3 \times 2 = 24$ conditions,
  • Model 1: $4 \times 2 \times 3 \times 2 \times 4 \times 4 = 768$ conditions,
  • Model 2: $4 \times 2 \times 3 \times 2 \times 4 \times 2 \times 4 = 1,536$ conditions
  • Model 3: $4 \times 2 \times 3 \times 2 \times 4 \times 2 \times 4 \times 4 = 6,144$ conditions.

- 4 conditions for Number of Studies
- 2 conditions for Number of Observations
- 3 conditions for Number of Participants
- 2 conditions for Intervention Effect
- 4 conditions for Magnitude of Gender Effect
- 4 conditions for Magnitude of Study Quality Effect
The number of conditions investigated depends on the specific model of interest.

Model 0 is the only model that does not include 40 or 50 studies. The reason for this is that statistical properties are appropriate with as few as 30 studies (and there is already sufficient power across all conditions with 30 studies).

Number of conditions per model:
- **Model 0**: $2 \times 2 \times 3 \times 2 = 24$ conditions,
- **Model 1**: $4 \times 2 \times 3 \times 2 \times 4 \times 4 = 768$ conditions,
- **Model 2**: $4 \times 2 \times 3 \times 2 \times 4 \times 2 \times 4 = 1,536$ conditions
- **Model 3**: $4 \times 2 \times 3 \times 2 \times 4 \times 2 \times 4 \times 4 = 6,144$ conditions.

For each condition, 1,000 datasets are examined. This resulted in a total of 8,472,000 datasets to be examined

$(24 + 768 + 1,536 + 6,144) \times 1,000 = 8,472,000$ datasets.
3. Methodological Research
Simulation Study - Results

<table>
<thead>
<tr>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MSE as a function of number of studies</strong></td>
<td><strong>MSE as a function of number of studies</strong></td>
<td><strong>MSE as a function of number of studies and cases</strong></td>
</tr>
</tbody>
</table>

**Intervention**

- Model 1
- Model 2
- Model 3

**Study Quality Moderator**

- Model 1
- Model 2
- Model 3

**Gender Moderator**

- Model 1 (K = 10, K = 30)
- Model 2 (K = 40, K = 50)

**Age Moderator**

- Model 1
- Model 2
- Model 3

(Same for the figures below)
3. Methodological Research
Simulation Study - Results

Relative Standard Error Bias as a function of number of studies

Model 1
- Intervention
- Gender Moderator
- Study Quality Moderator

Model 2
- Intervention
- Gender Moderator
- Study Quality Moderator

Model 3
- Intervention
- Gender moderator
- Study Quality Moderator
- Study Setting Moderator
### 3. Methodological Research

#### Simulation Study - Results

<table>
<thead>
<tr>
<th>Power as a function of number of studies</th>
<th>Power as a function of number of studies and Gender/Study Quality/Study Setting moderator effect</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td></td>
</tr>
<tr>
<td><img src="image1" alt="Graph for Model 1 Intervention" /></td>
<td><img src="image2" alt="Graph for Model 1 Gender Moderator" /></td>
</tr>
<tr>
<td><img src="image3" alt="Graph for Model 1 Study Quality Moderator" /></td>
<td><img src="image4" alt="Graph for Model 1 Study Setting Moderator" /></td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td></td>
</tr>
<tr>
<td><img src="image5" alt="Graph for Model 2 Intervention" /></td>
<td><img src="image6" alt="Graph for Model 2 Gender Moderator" /></td>
</tr>
<tr>
<td><img src="image7" alt="Graph for Model 2 Study Quality Moderator" /></td>
<td><img src="image8" alt="Graph for Model 2 Study Setting Moderator" /></td>
</tr>
<tr>
<td><strong>Model 3</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td></td>
</tr>
<tr>
<td><img src="image9" alt="Graph for Model 3 Intervention" /></td>
<td><img src="image10" alt="Graph for Model 3 Gender Moderator" /></td>
</tr>
<tr>
<td><img src="image11" alt="Graph for Model 3 Study Quality Moderator" /></td>
<td><img src="image12" alt="Graph for Model 3 Study Setting Moderator" /></td>
</tr>
</tbody>
</table>

(All figures are labeled with different colors for different values of K: K = 10, K = 30, K = 40, K = 50. The same figure is used for all models.)
4. Conclusion

- The impact of unit changes within the three-level modeling varies across different levels.
  - Unit changes at the level 3 (number of studies) and at level 2 (number of participants) tend to have larger influences on the statistical properties when compared to changes at the lower level, level 1 (number of measurement occasions).
- When the number of studies is large (k ≥ 30), the statistical properties of intervention and moderator effect estimates are appropriate, regardless of the number of participants, number of measurement occasions, and the magnitude of intervention and moderator effects.
- The only exception: for estimating the level 3 moderators (i.e., study quality and study setting), a substantial effect size is required in conjunction with a minimum of 30 studies.
- We do not recommend using IPD meta-analysis, with the inclusion of moderators, when the number of studies is small (k = 10).
4. Future Research

- Extending the basic three-level model introduced in this study by including more complexities (e.g., models with linear/non-linear time trends; imbalanced moderators; autocorrelation; count outcomes).
- Evaluating the robustness of IPD meta-analysis against violation of modeling assumptions such as non-normality of residuals.
- Dealing with situations when less studies are included for a meta-analysis.
References


Thank you for listening.

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June 28, 2023