Multilevel meta-analysis of complex single-case designs

Raw data versus effect sizes

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Overview

• Single-case experimental designs (SCEDs)
  • What & why
  • Multilevel meta-analysis of SCEDs
• Handling complex SCED designs
  • Motivation
  • Simulation study
• Results & conclusions
Single-case experimental designs

How to analyze SCED data?
Single-case experimental design (SCED)

- 1 ‘case’ (participant, classroom, facility, petri dish, …)
- Time series
- Intervention
- Baseline vs. treatment phase

![Diagram showing baseline and treatment phases with intervention points.](image-url)
Combining SCED data

- Across cases & across studies: meta-analysis
- Multilevel modeling
  - Yields estimates of
    - Individual case and study effects (empirical Bayes)
    - Overall population average
    - Heterogeneity across cases and across studies
- Flexible & adaptable
  - Time trends
  - Case, study, setting or treatment characteristics
  - Complex phase designs
  - Discrete data (GLMM)

Van den Noortgate & Onghena (2007)
Multilevel meta-analysis of SCED data

\[ Y_{ijk} = \beta_{0jk} + \beta_{1jk}D_{ijk} + e_{ijk} \]
\[ \begin{cases} 
\beta_{0jk} = \gamma_{000} + u_{0jk} + v_{00k} \\
\beta_{1jk} = \gamma_{100} + u_{1jk} + v_{10k} 
\end{cases} \]

\[ u_{.jk} \sim N(0, \Sigma_u), \ v_{.0k} \sim N(0, \Sigma_v), \ e_{ijk} \sim N(0, \sigma_e^2) \]

Three-level structure

Moeyaert et al. (2014)
Handling complex SCED designs
A simulation study
Raw data versus effect sizes

Raw data 
Multilevel model
RD approach

Effect size (per case)
Multilevel meta-analytic model
ES approach
Raw data versus effect sizes

**RD approach**

\[ Y_{ijk} = \beta_{0jk} + \beta_{1jk}D_{ijk} + \beta_{2jk}T_{ijk} + \beta_{3jk}D_{ijk}T_{ijk} + e_{ijk} \]

\[ \begin{aligned}
\beta_{0jk} &= \gamma_{000} + u_{0jk} + v_{00k} \\
\beta_{1jk} &= \gamma_{100} + u_{1jk} + v_{10k} \\
\beta_{2jk} &= \gamma_{200} + u_{2jk} + v_{20k} \\
\beta_{3jk} &= \gamma_{300} + u_{3jk} + v_{30k}
\end{aligned} \]

\[ u_{jk} \sim N(0, \Sigma_u), \quad v_{0k} \sim N(0, \Sigma_v), \quad e_{ijk} \sim N(0, \sigma_e^2) \]

**ES approach**

**Step 1** – OLS per case \( jk \)

\[ Y_{ijk} = \beta_{0jk} + \beta_{1jk}D_{ijk} + \beta_{2jk}T_{ijk} + \beta_{3jk}D_{ijk}T_{ijk} + e_{ijk} \]

**Step 2** – Multivariate multilevel meta-analytic model

\[ \begin{aligned}
b_{1jk} &= \gamma_{100} + u_{1jk} + v_{10k} + r_{1jk} \\
b_{3jk} &= \gamma_{300} + u_{3jk} + v_{30k} + r_{3jk}
\end{aligned} \]

\[ u_{jk} \sim N(0, \Sigma_u), \quad v_{0k} \sim N(0, \Sigma_v), \quad r_{ijk} \sim N(0, \Sigma_b) \]

Van den Noortgate & Onghena (2008)
Raw data versus effect sizes

RD approach

\[ Y_{ijk} = \beta_{0jk} + \beta_{1jk}D_{ijk} + \beta_{2jk}T_{ijk} + \beta_{3jk}D_{ijk}T_{ijk} + e_{ijk} \]

\[
\begin{align*}
\beta_{0jk} &= \gamma_{000} + u_{0jk} + v_{00k} \\
\beta_{1jk} &= \gamma_{100} + u_{1jk} + v_{10k} \\
\beta_{2jk} &= \gamma_{200} + u_{2jk} + v_{20k} \\
\beta_{3jk} &= \gamma_{300} + u_{3jk} + v_{30k}
\end{align*}
\]

\[ u_{.jk} \sim N(\mathbf{0}, \Sigma_u), \ v_{.0k} \sim N(\mathbf{0}, \Sigma_v), \ e_{ijk} \sim N(0, \sigma^2_e) \]

2 fixed effects, 21 variance components

ES approach

Step 2 – Multivariate multilevel meta-analytic model

\[
\begin{align*}
b_{1jk} &= \gamma_{100} + u_{1jk} + v_{10k} + r_{1jk} \\
b_{3jk} &= \gamma_{300} + u_{3jk} + v_{30k} + r_{3jk}
\end{align*}
\]

\[ u_{.jk} \sim N(\mathbf{0}, \Sigma_u), \ v_{.0k} \sim N(\mathbf{0}, \Sigma_v), \ r_{ijk} \sim N(0, \Sigma_b) \]

4 fixed effects, 6 variance components
Simulation study

- Generate SCED raw data and calculate effect sizes
  - 3 models of increasing complexity
  - Estimate multilevel model from raw data (RD approach)
  - Estimate meta-analytic uni- or multivariate multilevel model from effect sizes (ES approach)

- Using R
  - RD approach: `lmer` from `lme4`  
  - ES approach: `rma.mv` from `metafor`

Bates et al. (2015)  
Viechtbauer (2010)
Model 1 – No time trend

**RD approach**

\[ Y_{ijk} = \beta_{0jk} + \beta_{1jk}D_{ijk} + e_{ijk} \]

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

\[ u_{jk} \sim N(0, \Sigma_u), \quad v_{0k} \sim N(0, \Sigma_v), \quad e_{ijk} \sim N(0, \sigma_e^2) \]

\[ \Sigma_u, \Sigma_v \in \mathbb{R}^{2 \times 2} \]

**ES approach**

\[ b_{1jk} = \gamma_{100} + u_{1jk} + v_{10k} + r_{1jk} \]

\[ u_{1jk} \sim N(0, \sigma_u^2), \quad v_{0k} \sim N(0, \sigma_v^2), \quad r_{ijk} \sim N(0, \sigma_r^2) \]
Model 2 – Linear time trend

**RD approach**

\[ Y_{ijk} = \beta_{0jk} + \beta_{1jk}D_{ijk} + \beta_{2jk}T_{ijk} + \beta_{3jk}D_{ijk}T_{ijk} + e_{ijk} \]

\[ \beta_{0jk} = \gamma_{000} + u_{0jk} + \nu_{00k} \]

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

\[ \beta_{2jk} = \gamma_{200} + u_{2jk} + \nu_{20k} \]

\[ \beta_{3jk} = \gamma_{300} + u_{3jk} + \nu_{30k} \]

\[ u_{jk} \sim N(0, \Sigma_u), \quad v_{.0k} \sim N(0, \Sigma_v), \quad e_{ijk} \sim N(0, \sigma_e^2) \]

\[ \Sigma_u, \Sigma_v \in \mathbb{R}^{4 \times 4} \]

**ES approach**

\[ \begin{cases} 
    b_{1jk} = \gamma_{100} + u_{1jk} + \nu_{10k} + r_{1jk} \\
    b_{3jk} = \gamma_{300} + u_{3jk} + \nu_{30k} + r_{3jk} 
\end{cases} \]

\[ u_{.jk} \sim N(0, \Sigma_u), \quad v_{.0k} \sim N(0, \Sigma_v), \quad r_{ijk} \sim N(0, \Sigma_b) \]

\[ \Sigma_u, \Sigma_v \in \mathbb{R}^{2 \times 2} \]
Model 3 – Quadratic time trend

**RD approach**

\[ Y_{ijk} = \beta_{0jk} + \beta_{1jk}D_{ijk} + \beta_{2jk}T_{ijk} + \beta_{3jk}D_{ijk}T_{ijk} + \beta_{4jk}T_{ijk}^2 + \beta_{5jk}D_{ijk}T_{ijk}^2 + e_{ijk} \]

\[ \begin{align*} 
\beta_{0jk} &= \gamma_{000} + u_{0jk} + v_{00k} \\
\beta_{1jk} &= \gamma_{100} + u_{1jk} + v_{10k} \\
\beta_{2jk} &= \gamma_{200} + u_{2jk} + v_{20k} \\
\beta_{3jk} &= \gamma_{300} + u_{3jk} + v_{30k} \\
\beta_{4jk} &= \gamma_{400} + u_{4jk} + v_{30k} \\
\beta_{5jk} &= \gamma_{500} + u_{5jk} + v_{50k} 
\end{align*} \]

\[ \mathbf{u}_{jk} \sim N(0, \Sigma_u), \quad \mathbf{v}_{0k} \sim N(0, \Sigma_v), \quad e_{ijk} \sim N(0, \sigma_e^2) \]

\[ \Sigma_u, \Sigma_v \in \mathbb{R}^{6 \times 6} \]

**ES approach**

\[ \begin{align*} 
b_{1jk} &= \gamma_{100} + u_{1jk} + v_{10k} + r_{1jk} \\
b_{3jk} &= \gamma_{300} + u_{3jk} + v_{30k} + r_{3jk} \\
b_{5jk} &= \gamma_{500} + u_{5jk} + v_{50k} + r_{5jk} 
\end{align*} \]

\[ \mathbf{u}_{jk} \sim N(0, \Sigma_u), \quad \mathbf{v}_{0k} \sim N(0, \Sigma_v), \quad r_{ijk} \sim N(0, \Sigma_b) \]

\[ \Sigma_u, \Sigma_v \in \mathbb{R}^{3 \times 3} \]
Simulation study

**Conditions**

- Baseline fixed effects set to 0
- Treatment fixed effects simultaneously set to 0 or 2
- Compound symmetry structure for $\Sigma_u$ and $\Sigma_v$
  - Variances $\sigma^2$ set to 1 or 4
  - Correlations $\rho$ set to 0 or 0.5
- Number of measurements $I \in \{20, 28, 40\}$
- Number of cases $J \in \{3, 5, 10\}$
- Number of studies $K \in \{5, 7, 10\}$

**Steps**

1. For 216 conditions, 3 different models: generate 1000 datasets per condition and per model.
2. Calculate effect sizes via OLS per case.
3. Apply RD approach on raw data and ES approach on effect sizes.
Simulation study

Results & conclusions
## Convergence

<table>
<thead>
<tr>
<th></th>
<th>RD</th>
<th>ES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>99.2%</td>
<td>98%</td>
</tr>
<tr>
<td>Model 2</td>
<td>94.6%</td>
<td>99.9%</td>
</tr>
<tr>
<td>Model 3</td>
<td>42%</td>
<td>98.5%</td>
</tr>
</tbody>
</table>

Model 1 = No time trend  
Model 2 = Linear time trend  
Model 3 = Quadratic time trend
Speed

The graph shows the relationship between time (seconds) and a variable labeled 'J'. The graph includes different models (1, 2, 3) and approaches (ES, RD) represented by various markers and line styles. The x-axis represents the variable 'J', ranging from 3 to 10, while the y-axis represents time in seconds, ranging from 0 to 50.
Fixed effect parameter estimations

MSE

<table>
<thead>
<tr>
<th>( \sigma^2 )</th>
<th>( K )</th>
<th>Model 1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td>ES</td>
<td>RD</td>
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<tr>
<td>1</td>
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<td>0.25</td>
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<td>0.18</td>
<td>0.19</td>
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<td>0.13</td>
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<td>0.97</td>
<td>0.99</td>
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<tr>
<td></td>
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<td>0.69</td>
<td>0.69</td>
<td>0.71</td>
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<tr>
<td></td>
<td>10</td>
<td>0.48</td>
<td>0.48</td>
<td>0.50</td>
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</tbody>
</table>
## Fixed effect parameter estimations

### 95% CI coverage proportions

<table>
<thead>
<tr>
<th></th>
<th>Wald-type CI</th>
<th>RD</th>
<th>ES</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model 1</strong></td>
<td>Normal</td>
<td>90.39%</td>
<td>90.67%</td>
</tr>
<tr>
<td></td>
<td>Student’s $t$</td>
<td>95.09%</td>
<td>91.67%</td>
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<tr>
<td><strong>Model 2</strong></td>
<td>Normal</td>
<td>91.52%</td>
<td>90.72%</td>
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<tr>
<td></td>
<td>Student’s $t$</td>
<td>95.79%</td>
<td>91.24%</td>
</tr>
<tr>
<td><strong>Model 3</strong></td>
<td>Normal</td>
<td>92.56%</td>
<td>91.33%</td>
</tr>
<tr>
<td></td>
<td>Student’s $t$</td>
<td>96.44%</td>
<td>91.68%</td>
</tr>
</tbody>
</table>

*Using Satterthwaite df’s (1941) for the RD approach and Knapp and Hartung df’s (2003) for the ES approach.*
# Fixed effect parameter estimations

## Type I error rates (nominal $\alpha = .05$)

<table>
<thead>
<tr>
<th>Test</th>
<th>Model 1</th>
<th></th>
<th>Model 2</th>
<th></th>
<th>Model 3</th>
<th></th>
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<td>ES</td>
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<td>.08</td>
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<td>.08</td>
<td>.08</td>
<td>.07</td>
</tr>
<tr>
<td>Student’s t</td>
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<td>.05</td>
<td>.09</td>
<td>.04</td>
<td>.10</td>
<td>.03</td>
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<tr>
<td></td>
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<td>.05</td>
<td>.07</td>
<td>.05</td>
<td>.08</td>
<td>.04</td>
</tr>
</tbody>
</table>

$^a$ Using Satterthwaite df’s (1941) for the RD approach and Knapp and Hartung df’s (2003) for the ES approach.
Conclusions

• For more complex models, the ES approach obtained better convergence rates but that model estimation generally takes more time.

• The precision and the bias of the point estimates was very similar for both approaches and for all models. **Inference results** were consistently worse for the ES approach, although this might be due to the particular options implemented in the packages used in R.
Limitations & future research

• Model complexity
  • Model 3 is not the end point. Preliminary simulations with more complicated models took very long and were not feasible to simulate on larger scale.

• Alternative effect sizes
  • Non-overlap indices
  • Mean phase differences
  • Standardized mean differences
  • Other regression based indices

• Alternative complexities
  • Reversal designs
  • Discrete data
  • Case- or study characteristics as covariates
Take-away message

When confronted with convergence issues when estimating a multilevel model from the raw data, applied SCED researchers could try to simplify their model or turn to the ES approach instead. They should obtain reliable and valid point estimates but should interpret the corresponding inference results obtained from the multilevel analysis with caution.
Bibliography


Questions?
Thank you for your attention.

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