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Multilevel meta-analysis of complex single-case designs

Raw data versus effect sizes

Lies Declercq, Laleh Jamshidi & Wim Van den Noortgate

IMEC – ITEC

KU Leuven, Belgium

Overview

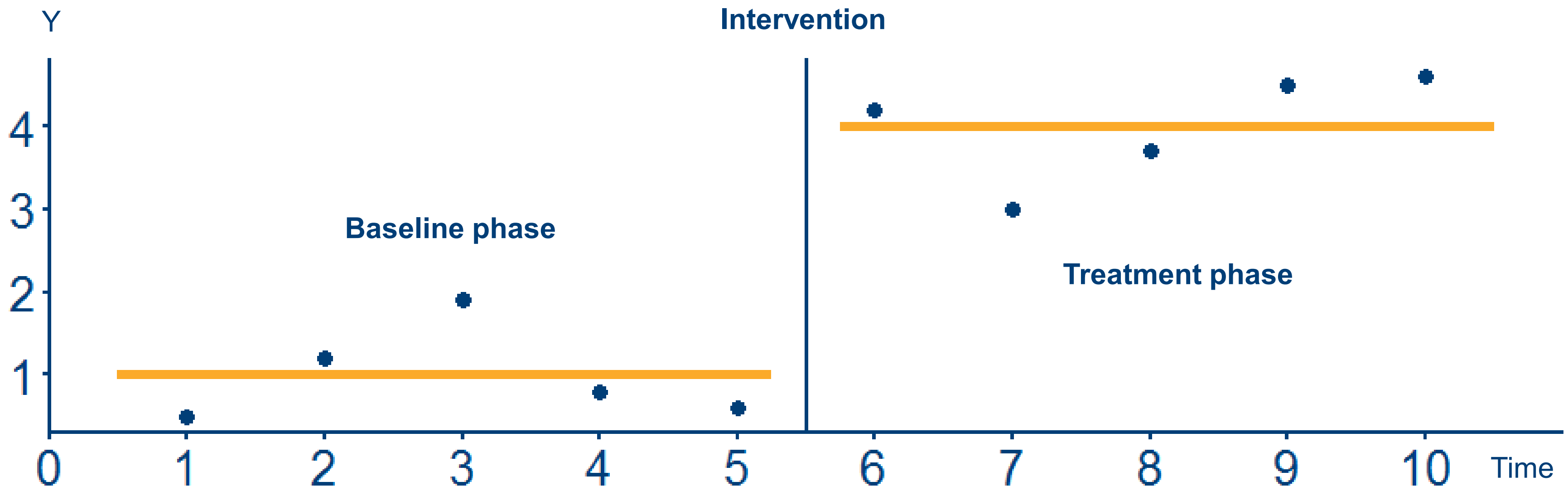
- Single-case experimental designs (SCEDs)
  - What & why
  - Multilevel meta-analysis of SCEDs
- Handling complex SCED designs
  - Motivation
  - Simulation study
- Results & conclusions

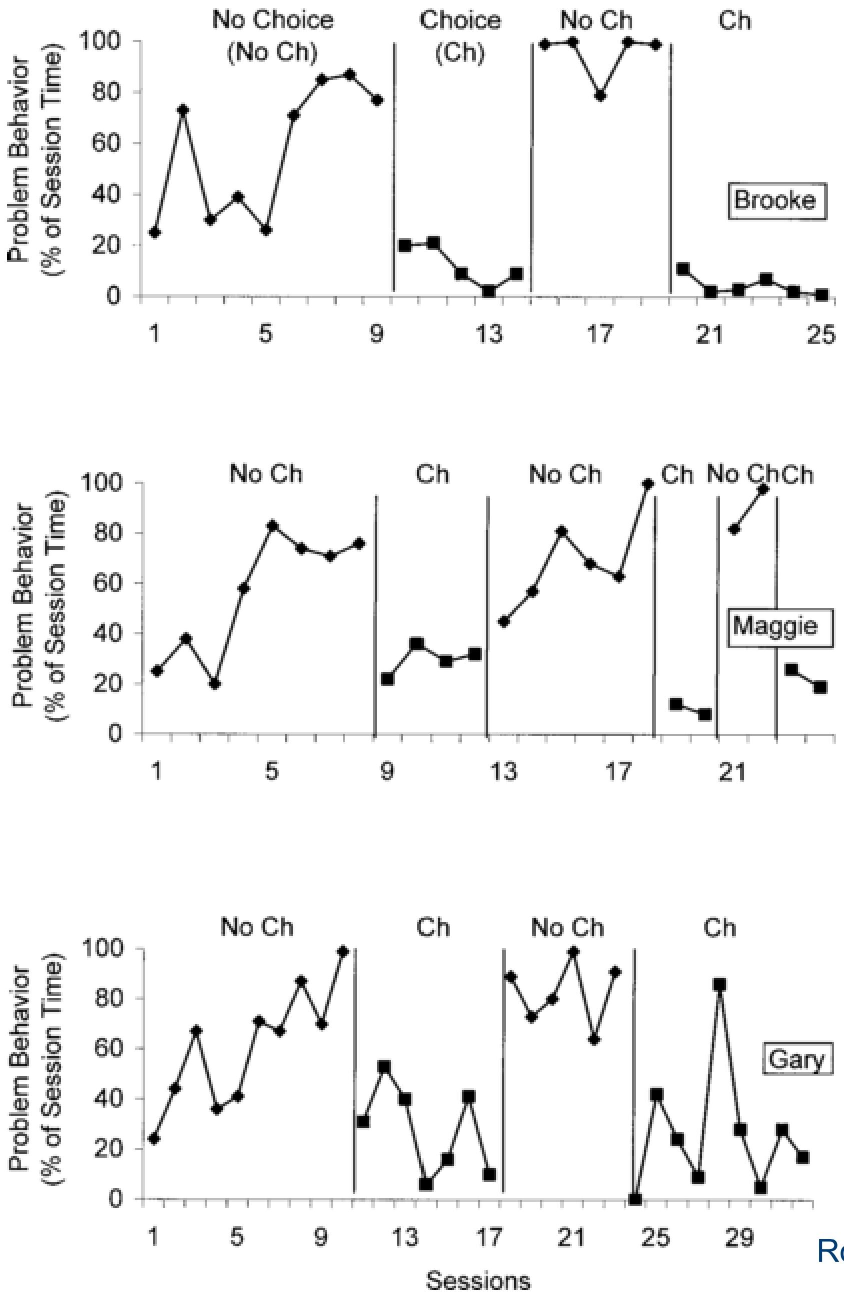
Single-case experimental designs

How to analyze SCED data?

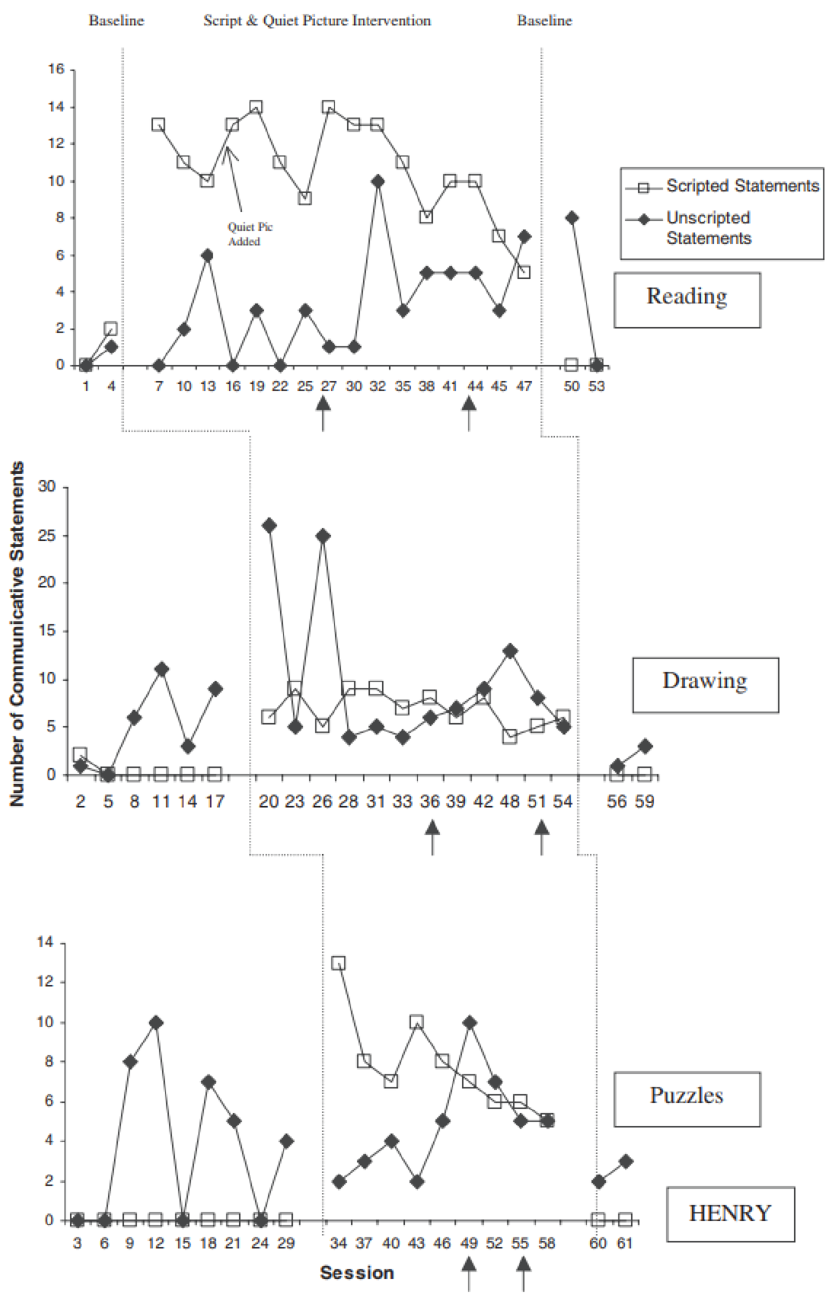
Single-case experimental design (SCED)

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





Romaniuk et al. (2002)



Ganz et al. (2002)

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)

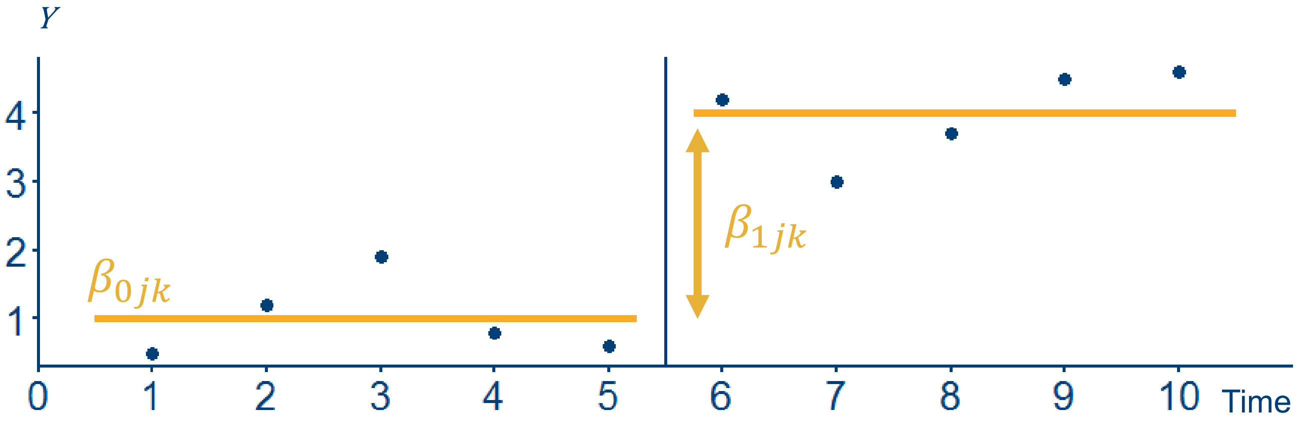
Van den Noortgate & Onghena (2007)

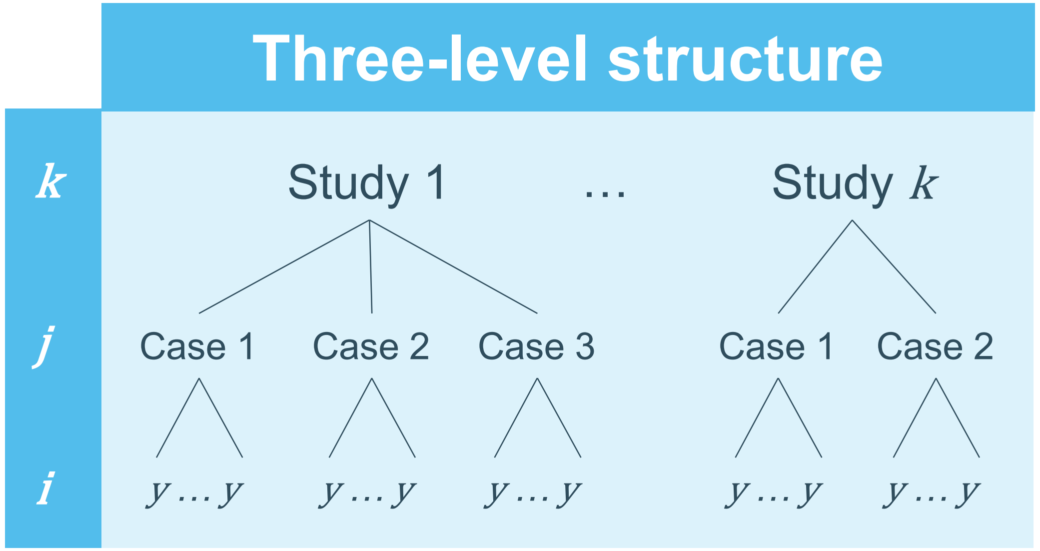
Multilevel meta-analysis of SCED data

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

$$\begin{cases} \beta_{0jk} = \gamma_{000} + u_{0jk} + v_{00k} \\ \beta_{1jk} = \gamma_{100} + u_{1jk} + v_{10k} \end{cases}$$

$$\boldsymbol{u}_{.jk} \sim N(\boldsymbol{0}, \Sigma_u),\ \boldsymbol{v}_{.0k} \sim N(\boldsymbol{0}, \Sigma_v),\ e_{ijk} \sim N(0, \sigma_e^2)$$



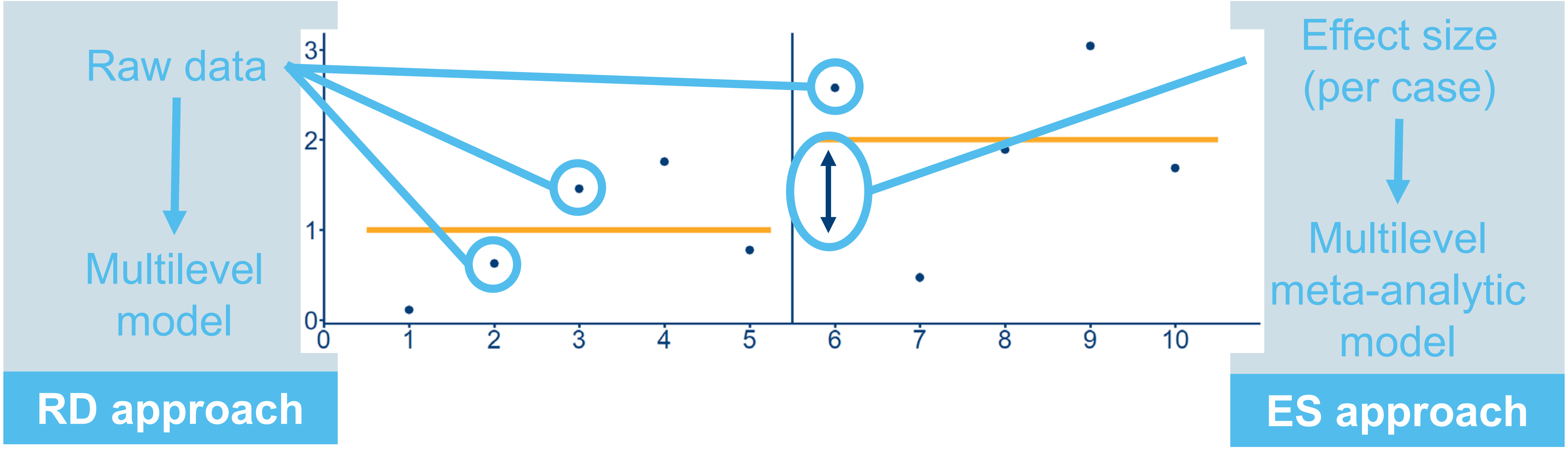


Moeyaert et al. (2014)

Handling complex SCED designs

A simulation study

Raw data versus effect sizes



Raw data versus effect sizes

RD approach	ES approach

RD approach

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

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

$$\boldsymbol{u}_{.\boldsymbol{jk}} \sim N(\boldsymbol{0}, \Sigma_u),\ \boldsymbol{v}_{.\boldsymbol{0k}} \sim N(\boldsymbol{0}, \Sigma_v),\ e_{ijk} \sim N(0, \sigma_e^2)$$

ES approach

Step 1 – OLS per case jk

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

$$b_{1jk} \quad b_{3jk} \quad \Sigma_b$$

Step 2 – Multivariate multilevel meta-analytic model

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

$$\boldsymbol{u}_{.\boldsymbol{jk}} \sim N(\boldsymbol{0}, \Sigma_u),\ \boldsymbol{v}_{.\boldsymbol{0k}} \sim N(\boldsymbol{0}, \Sigma_v),\ r_{ijk} \sim N(0, \Sigma_b)$$

Van den Noortgate & Onghena (2008)

Raw data versus effect sizes

RD approach

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

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

$$\boldsymbol{u}_{.jk} \sim N(\boldsymbol{0}, \Sigma_u),\ \boldsymbol{v}_{.0k} \sim N(\boldsymbol{0}, \Sigma_v),\ e_{ijk} \sim N(0, \sigma_e^2)$$

4 fixed effects,
21 variance components

ES approach

Step 2 – Multivariate multilevel meta-analytic model

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

$$\boldsymbol{u}_{.jk} \sim N(\boldsymbol{0}, \Sigma_u),\ \boldsymbol{v}_{.0k} \sim N(\boldsymbol{0}, \Sigma_v),\ r_{ijk} \sim N(0, \Sigma_b)$$

2 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` — Bates et al. (2015)
  - ES approach: `rma.mv` from `metafor` — Viechtbauer (2010)

Model 1 – No time trend

RD approach

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

$$\begin{cases} \beta_{0jk} = \gamma_{000} + u_{0jk} + v_{00k} \\ \beta_{1jk} = \gamma_{100} + u_{1jk} + v_{10k} \end{cases}$$

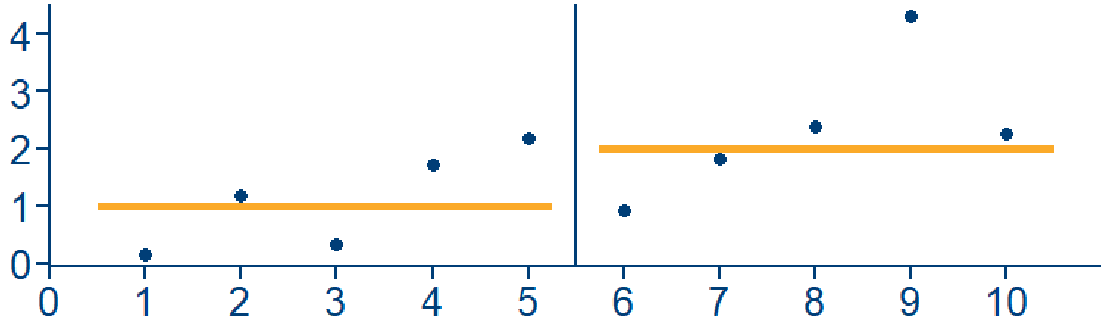
$$\boldsymbol{u}_{.jk} \sim N(\boldsymbol{0}, \Sigma_u), \;\; \boldsymbol{v}_{.0k} \sim N(\boldsymbol{0}, \Sigma_v), \;\; e_{ijk} \sim N(0, \sigma_e^2)$$

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

ES approach

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

$$u_{1jk} \sim N(0, \sigma_u^2), \;\; v_{.0k} \sim N(0, \sigma_v^2), \;\; r_{ijk} \sim N(0, \sigma_r^2)$$



Model 2 – Linear time trend

RD approach

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

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

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

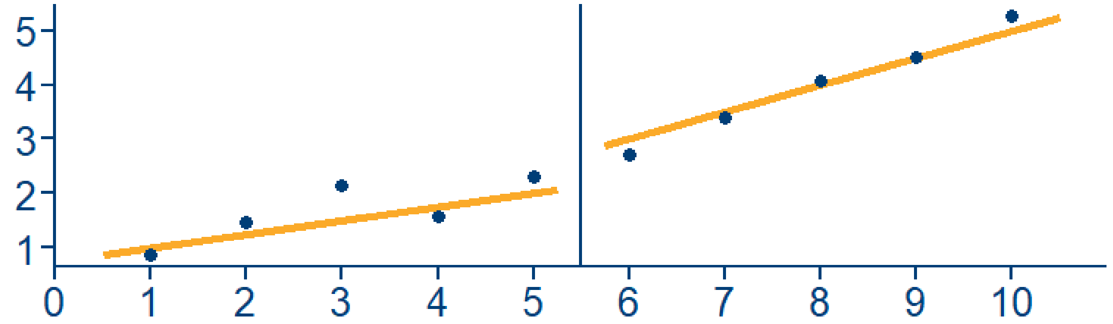
$$\Sigma_u, \Sigma_v \in \mathbb{R}^{4\times4}$$

ES approach

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

$$\boldsymbol{u_{.jk}} \sim N(\boldsymbol{0}, \Sigma_u),\ \ \boldsymbol{v_{.0k}} \sim N(\boldsymbol{0}, \Sigma_v),\ \ r_{ijk} \sim N(0, \Sigma_b)$$

$$\Sigma_u, \Sigma_v \in \mathbb{R}^{2\times2}$$



Model 3 – Quadratic time trend

RD approach

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

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

$$\boldsymbol{u}_{.\boldsymbol{jk}} \sim N(\boldsymbol{0}, \Sigma_u),\ \boldsymbol{v}_{.\boldsymbol{0k}} \sim N(\boldsymbol{0}, \Sigma_v),\ e_{ijk} \sim N(0, \sigma_e^2)$$

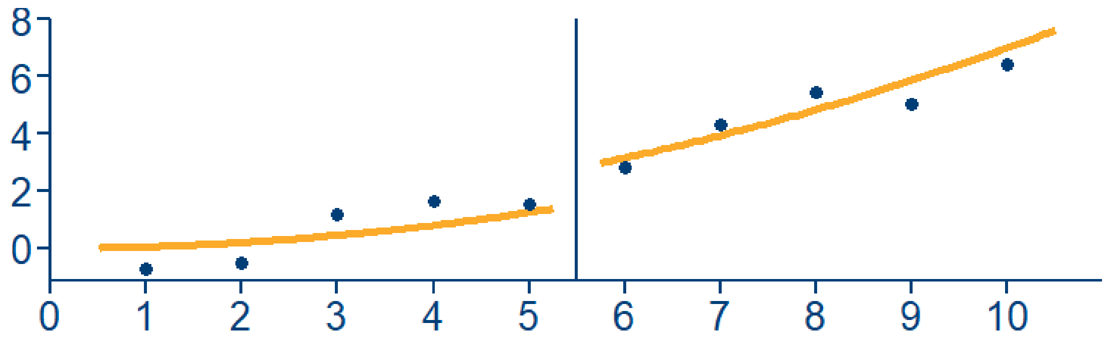
$$\Sigma_u, \Sigma_v \in \mathbb{R}^{6\times 6}$$

ES approach

$$\begin{cases} b_{1jk} = \gamma_{100} + u_{1jk} + v_{10k} + r_{1jk} \\ b_{3jk} = \gamma_{300} + u_{3jk} + v_{30k} + r_{3jk} \\ b_{5jk} = \gamma_{500} + u_{5jk} + v_{50k} + r_{5jk} \end{cases}$$

$$\boldsymbol{u}_{.\boldsymbol{jk}} \sim N(\boldsymbol{0}, \Sigma_u),\ \boldsymbol{v}_{.\boldsymbol{0k}} \sim N(\boldsymbol{0}, \Sigma_v),\ r_{ijk} \sim N(0, \Sigma_b)$$

$$\Sigma_u, \Sigma_v \in \mathbb{R}^{3\times 3}$$



Simulation study

Conditions

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

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.

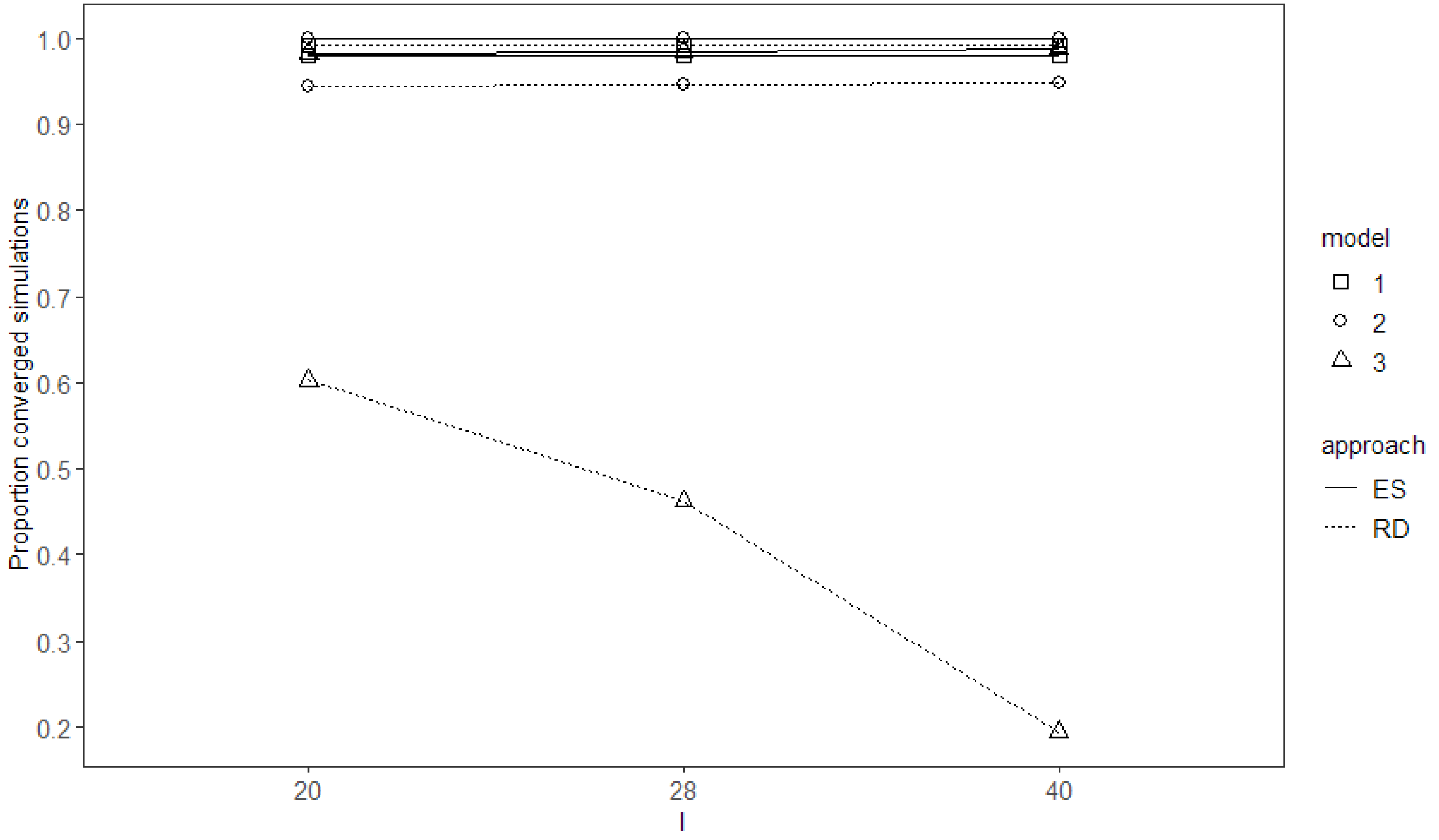
Simulation study

Results & conclusions

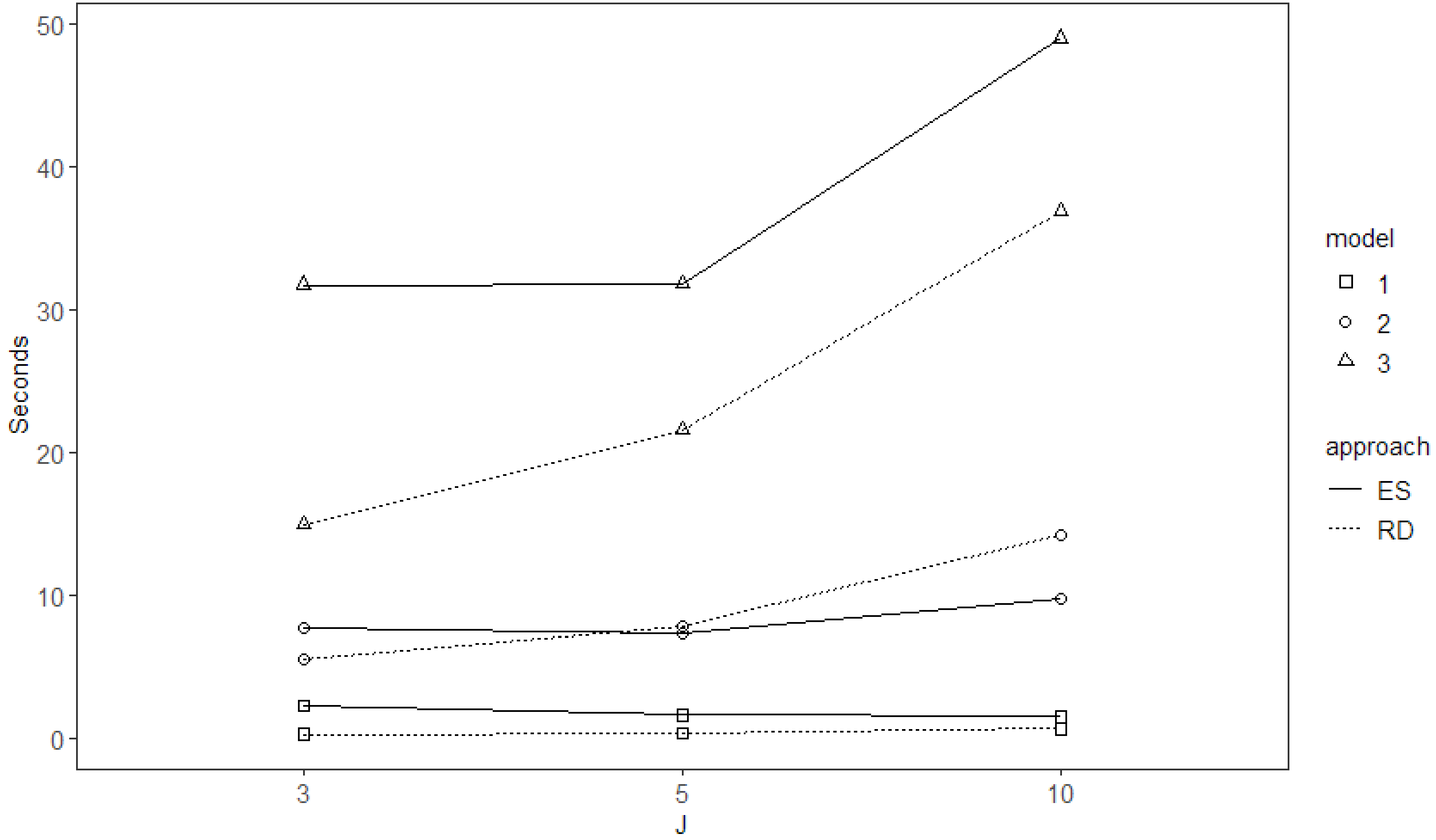
Convergence

	RD	ES
Model 1	99.2%	98%
Model 2	94.6%	99.9%
Model 3	42%	98.5%

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



Speed



Fixed effect parameter estimations

MSE

		Model 1		Model 2		Model 3	
σ^2	K	RD	ES	RD	ES	RD	ES
1	5	0,25	0,25	0,27	0,27	0,32	0,31
	7	0,18	0,18	0,19	0,19	0,22	0,22
	10	0,12	0,12	0,13	0,14	0,16	0,15
4	5	0,98	0,97	0,99	0,98	1,05	1,02
	7	0,69	0,69	0,71	0,71	0,79	0,74
	10	0,48	0,48	0,50	0,50	0,55	0,52

Fixed effect parameter estimations

95% CI coverage proportions

	Wald-type CI	RD	ES
Model 1	Normal	90.39%	90.67%
	Student's *t* [a]	95.09%	91.67%
Model 2	Normal	91.52%	90.72%
	Student's *t*	95.79%	91.24%
Model 3	Normal	92.56%	91.33%
	Student's *t*	96.44%	91.68%

[a] 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 $\alpha = .05$)

		Model 1		Model 2		Model 3	
Test	K	RD	ES	RD	ES	RD	ES
Normal	5	.11	.11	.10	.11	.08	.10
	7	.09	.09	.08	.09	.08	.09
	10	.08	.08	.08	.08	.07	.08
Student's *t* [a]	5	.05	.09	.04	.10	.03	.09
	7	.05	.08	.04	.09	.04	.09
	10	.05	.07	.05	.08	.04	.08

[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.

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Questions?

Thank you for your attention.

lies.declercq@kuleuven.be