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Supplementary Material

Variability in meta-analysis estimates of continuous outcomes using different standardization and scale-specific re-expression methods

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Supplementary Material 1. Standardization methods

In this supplementary material we present the standardization processes that we followed to obtain our data. For this purpose, we illustrate each standardization method using one study that reported SPPB outcomes (i.e., Campo, 2019).

Study-specific 1 and 2: Dividing the MDs and SEs by the pooled sample SD of each study at baseline and post-interventions time points, respectively. The example presented below corresponds to the study-specific 1 standardization method.

$$SD_{pooled} = \sqrt{\frac{{SD_t}^2 * (n_t - 1) + {SD_c}^2 * (n_c - 1)}{n_t + n_c - 2}}$$

So, Campo (2019) pooled sample SD was:

$$SD_{pooled} = \sqrt{\frac{2.25^2 * (117 - 1) + 2.25^2 * (117 - 1)}{117 + 117 - 2}} = 2.25$$

Then, we divided the MDs and corresponding SEs by 2.25:

$$SMD = {MD}/{SD_{pooled}} = {2}/{2.25} = 0.888$$

$$SE_{SMD} = {SE}/{SD_{pooled}} = {0.291}/{2.25} = 0.129$$

Internal reference: Using an internal SD reference standard (i.e., the average of the pooled SDs at baseline for each scale). First, we calculated all pooled SDs of each study as in method 1. Second, we calculated the average of pooled SDs for each scale. Third, we standardized each studies' MD by the resulting value.

For the SPPB scale the internal reference SD is obtained as

$$Internal\ SD\ ref_{SPPB} = \frac{2.25 + 2.702 + 2.602 + 1.617 + 2.707 + 2.579 + 2.498}{7} = 2.42$$

For the BI scale the internal reference SD is obtained as

$$Internal\ SD\ ref_{BI} = \frac{26 + 16.508 + 11.997 + 9.861 + 17}{5} = 16.62$$

So, the standardized mean difference and SE of Campo (2019) using this method for the SPPB scale is:

$$SMD = {MD}/{SD_{pooled}} = {2}/{2.42} = 0.826$$

$$SE_{SMD} = {SE}/{SD_{pooled}} = {0.291}/{2.42} = 0.120$$

External reference: Using an external SD reference. We extracted SD references from a large retrospective cohort study that could be representative of our sample: acutely hospitalized older adults (Urquiza et al., 2020). For SPPB we used a SD = 3.14, and for BI outcomes we used a SD = 25.39. So, the standardized mean difference and SE of Campo (2019) study using this method (SPPB scale) would be:

$$SMD = {}^{MD}/_{SD_{pooled}} = {}^{2}/_{3.14} = 0.637$$

$$SE_{SMD} = {}^{SE}/_{SD_{pooled}} = {}^{0.291}/_{3.14} = 0.093$$

Supplementary Material 2. Weighted internal SD references calculation

Cochrane methodological guidelines state that an acceptable option for re-expressing SMDs using a familiar instrument is to calculate a weighted average across all intervention groups of all studies hat used the selected instrument (in our case, we used the pre-intervention SDs).

$$Weighted\ internal\ SD\ ref_{SPPB} = \sqrt{\frac{2.25^2 * (234-1) + 2.702^2 * (348-1) + 2.602^2 * (370-1) + 1.617^2 * (200-1) + 2.707^2 * (250-1) + 2.579^2 * (118-1) + 2.498^2 * (103-1)}{234 + 348 + 370 + 200 + 250 + 118 + 103 - 7}} = 2.484$$

$$Weighted\ internal\ SD\ ref_{BI} = \sqrt{\frac{26^2 * (167-1) + 16.508^2 * (370-1) + 11.997^2 * (200-1) + 9.861^2 * (118-1) + 17^2 * (103-1)}{167 + 370 + 200 + 118 + 103 - 5}} = 17.201$$

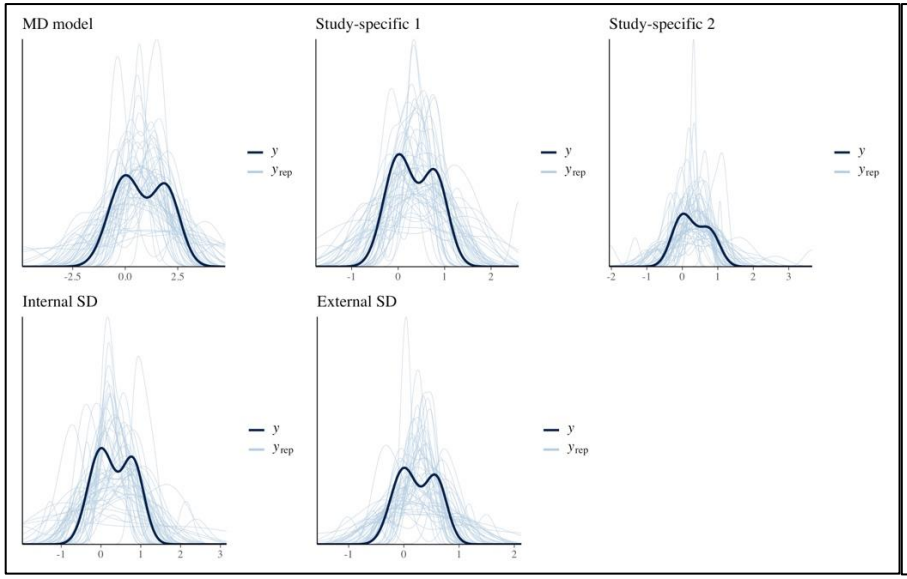
So, the standardized mean difference and SE of Campo (2019) study using this method (SPPB scale) would be:

$$SMD = {}^{MD}/_{SD_{pooled}} = {}^{2}/_{2.484} = 0.805$$

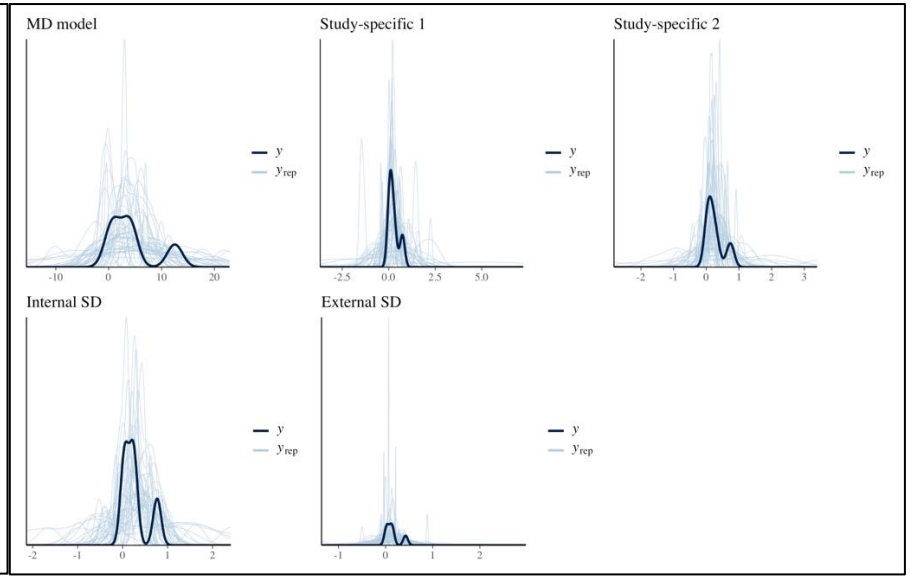
$$SE_{SMD} = {}^{SE}/_{SD_{pooled}} = {}^{0.291}/_{2.484} = 0.117$$

Supplementary Material 3. Convergence analysis: posterior predictive checking

In this supplementary material we show the posterior predictive checking of our models to observe how well predicted data fitted our observed data for both outcomes. The thicker dark blue lines represent the observed data, and the thinner light blue lines are the posterior draws of the effect size estimates. The more similar both types of densities, the more probability of model convergence.



Supplementary Figure 1. Posterior predictive checking for SPPB outcomes



Supplementary Figure 2. Posterior predictive checking for BI outcomes

Supplementary Table 1. Model fit results

Outcome	Model	Residual deviance*	DIC
Short Physical Performance Battery	Study-specific 1	7.35	9.39
	Study-specific 2	7.30	7.76
	Internal reference	7.34	9.32
	External reference	7.17	4.54
Barthel Index	Study-specific 1	5.12	4.67
	Study-specific 2	5.12	4.63
	Internal reference	5.12	4.74
	External reference	5.04	–1.44

Note. *Compared with 7 data points for Short Physical Performance Battery outcomes, and 5 data points for Barthel Index outcomes. Lower DIC values indicate better model fit. Differences between 5 and 10 are substantial.

Supplementary Table 2. Model estimates and 95% CrI

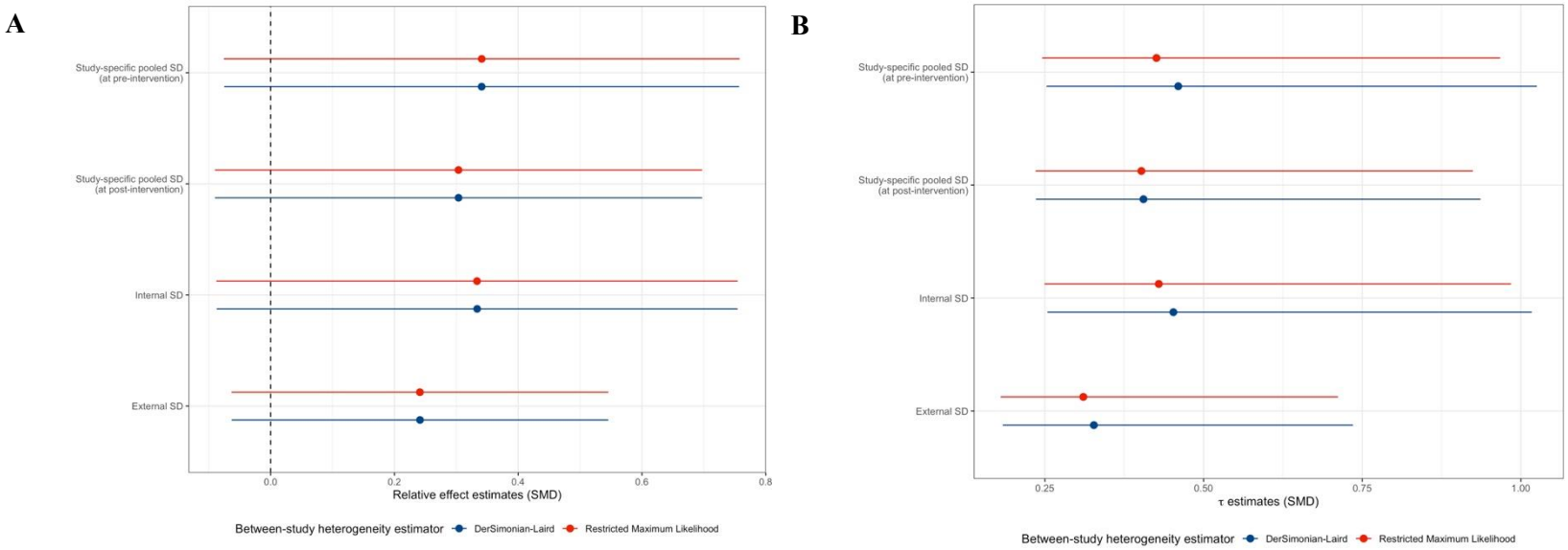
Outcome	Re-expression method*	Standardization**	MD (95% CrI)	τ (95% CrI)
Short Physical Performance Battery	Method 1	Pooled MD	0.82 (–0.50 to 2.16)	0.92 (0.06 to 2.79)
		Study-specific 1	0.85 (–0.51 to 2.24)	0.91 (0.06 to 2.85)
		Study-specific 2	0.85 (–0.60 to 2.35)	0.87 (0.06 to 2.73)
		Internal reference	0.82 (–0.51 to 2.24)	0.92 (0.06 to 2.95)
		External reference	0.75 (–0.59 to 2.11)	0.88 (0.05 to 2.83)
	Method 2	Pooled MD	0.82 (–0.50 to 2.16)	0.92 (0.06 to 2.79)
		Study-specific 1	0.87 (–0.52 to 2.30)	0.93 (0.06 to 2.92)
		Study-specific 2	0.76 (–0.53 to 2.11)	0.90 (0.06 to 2.80)
		Internal reference	0.84 (–0.55 to 2.28)	0.94 (0.06 to 3.02)
		External reference	0.59 (–0.47 to 1.67)	0.69 (0.04 to 2.24)
	Method 3	Pooled MD	0.82 (–0.50 to 2.16)	0.92 (0.06 to 2.79)
		Study-specific 1	1.10 (–0.66 to 2.91)	1.18 (0.07 to 3.69)
		Study-specific 2	0.96 (–0.68 to 2.67)	1.13 (0.07 to 3.54)
		Internal reference	1.07 (–0.69 to 2.89)	1.19 (0.07 to 3.82)
		External reference	0.75 (–0.59 to 2.11)	0.88 (0.05 to 2.83)
Barthel Index	Method 1	Pooled MD	3.75 (–2.15 to 10.20)	3.37 (0.17 to 12.10)
		Study-specific 1	4.04 (–7.13 to 16.70)	4.05 (0.20 to 26.60)
		Study-specific 2	4.02 (–6.26 to 15.90)	4.08 (0.19 to 23.50)
		Internal reference	3.92 (–7.39 to 15.50)	4.24 (0.22 to 24.20)
		External reference	3.42 (–7.13 to 13.40)	3.70 (0.19 to 32.30)
	Method 2	Pooled MD	3.75 (–2.15 to 10.20)	3.37 (0.17 to 12.10)
		Study-specific 1	4.27 (–7.54 to 17.60)	4.28 (0.21 to 28.20)
		Study-specific 2	4.25 (–6.62 to 16.80)	4.31 (0.20 to 24.80)
		Internal reference	4.15 (–7.82 to 16.40)	4.49 (0.23 to 25.60)
		External reference	2.32 (–4.83 to 9.08)	2.51 (0.13 to 21.90)
	Method 3	Pooled MD	3.75 (–2.15 to 10.20)	3.37 (0.17 to 12.10)
		Study-specific 1	6.30 (–11.10 to 26.00)	6.32 (0.31 to 41.60)

	Study-specific 2	6.27 (–9.76 to 24.70)	6.35 (0.30 to 36.50)
	Internal reference	6.12 (–11.50 to 24.10)	6.62 (0.34 to 37.70)
	External reference	3.42 (–9.76 to 24.70)	3.70 (0.19 to 32.30)

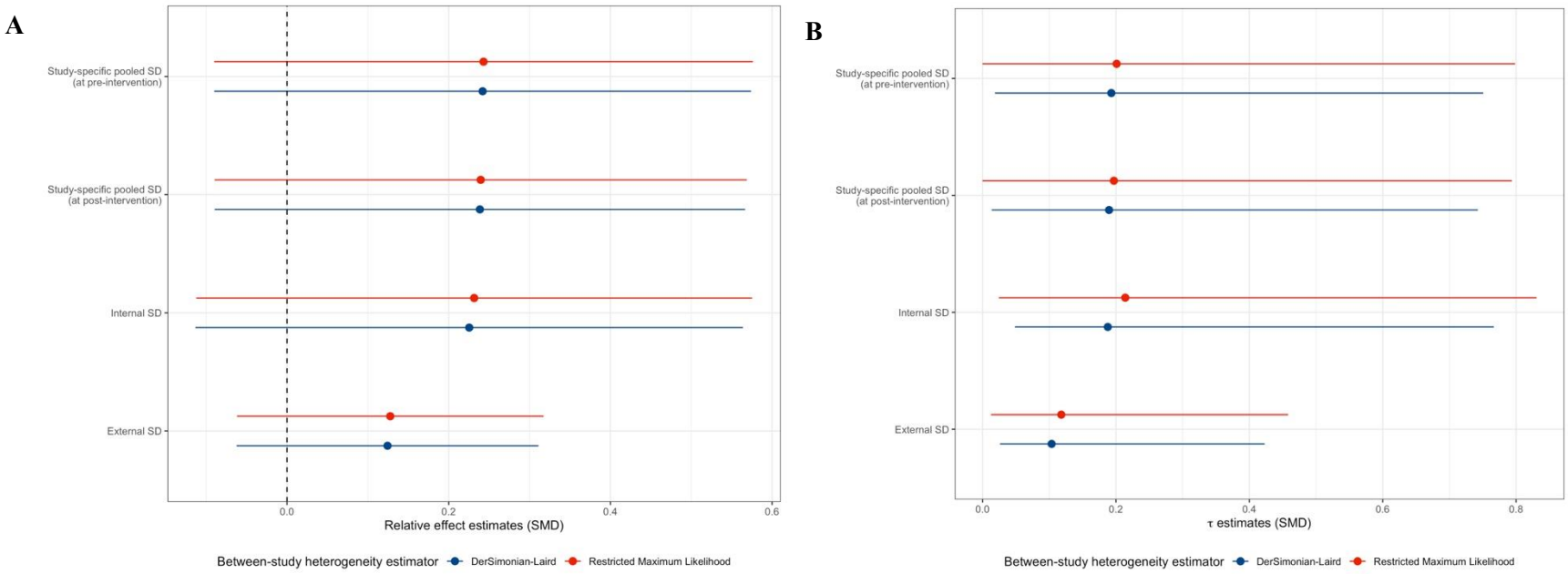
Note. *Method 1 corresponds to the re-expression process of using the same SD reference that was used for data standardization; method 2 corresponds to the re-expression method of using a weighted SD reference calculated as the average of pre-intervention SD values across all intervention groups of all studies that used the selected scale; method 3 corresponds to the re-expression method of using an external SD reference. **Pooled MD: original MD values (i.e., no standardization); Study-specific 1: data standardized by using the pooled sample SD of each study at the pre-intervention time point; Study-specific 2: data standardized by using the pooled sample SD of each study at the post-intervention time point; Internal reference: data standardized by using an internal SD reference calculated as the average of the pooled SDs at baseline for each scale; External reference: data standardized by using an existing SD from an external reference population that represents the patient population of the trials included in the meta-analysis.

Supplementary Material 4. Meta-analysis estimates under a frequentist approach

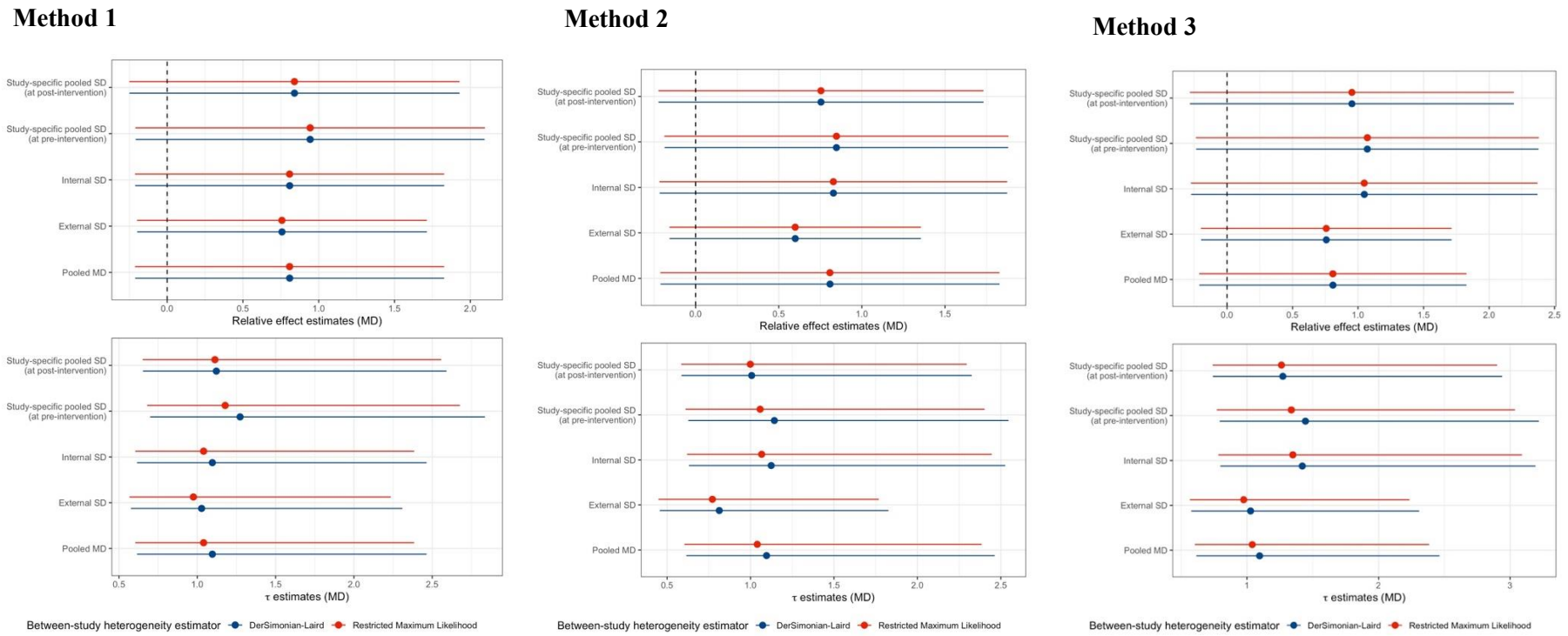
In this supplementary file we present our meta-analysis results under a frequentist approach. In the Supplementary Figure 3 appears the standardized mean and tau estimates with 95% Confidence Intervals (CI) for SPPB outcomes, and for BI outcomes in the Supplementary Figure 4. Re-expressed meta-analysis estimates using different re-expression methods for SPPB outcomes were plotted in the Supplementary Figure 5; and for BI outcomes in the Supplementary Figure 6.



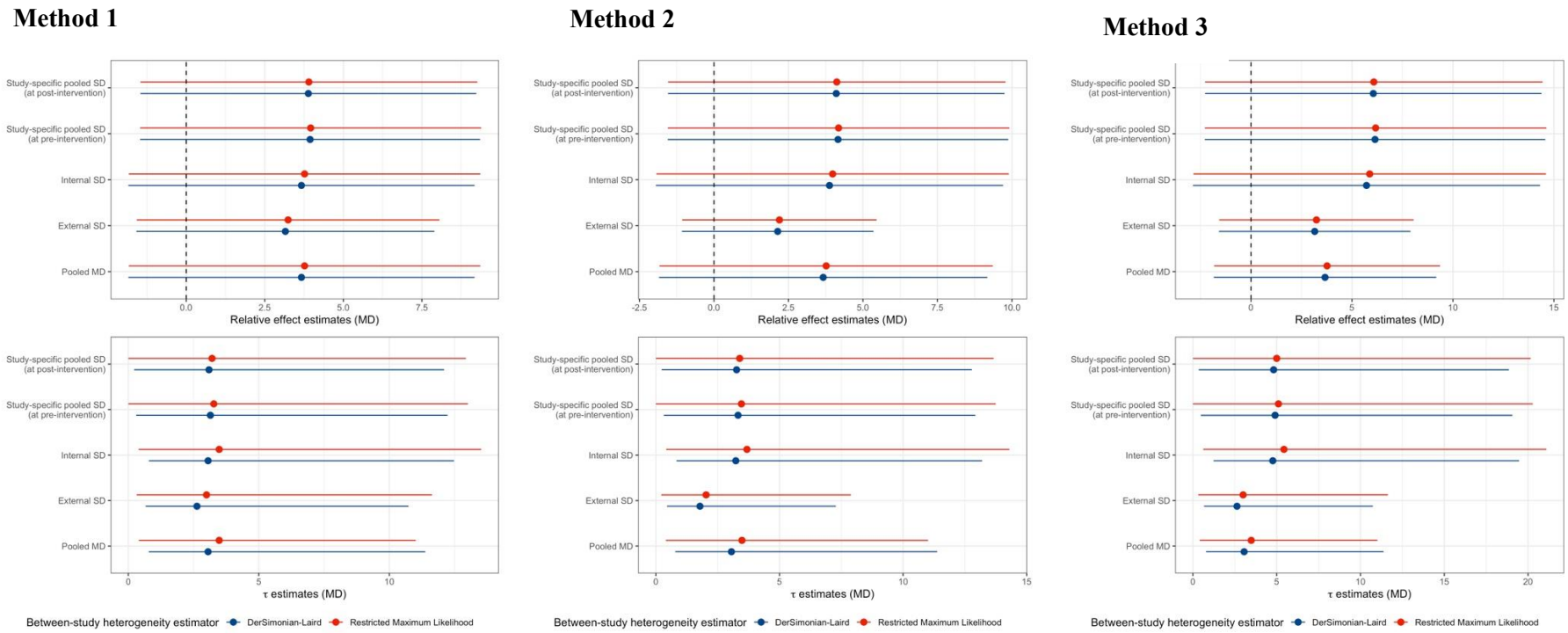
Supplementary Figure 3. A: Standardized mean estimates and 95% CI; and B: Heterogeneity estimates and 95% CI of SPPB outcomes



Supplementary Figure 4. A: Standardized mean estimates and 95% CI; and B: Heterogeneity estimates and 95% CI of BI outcomes



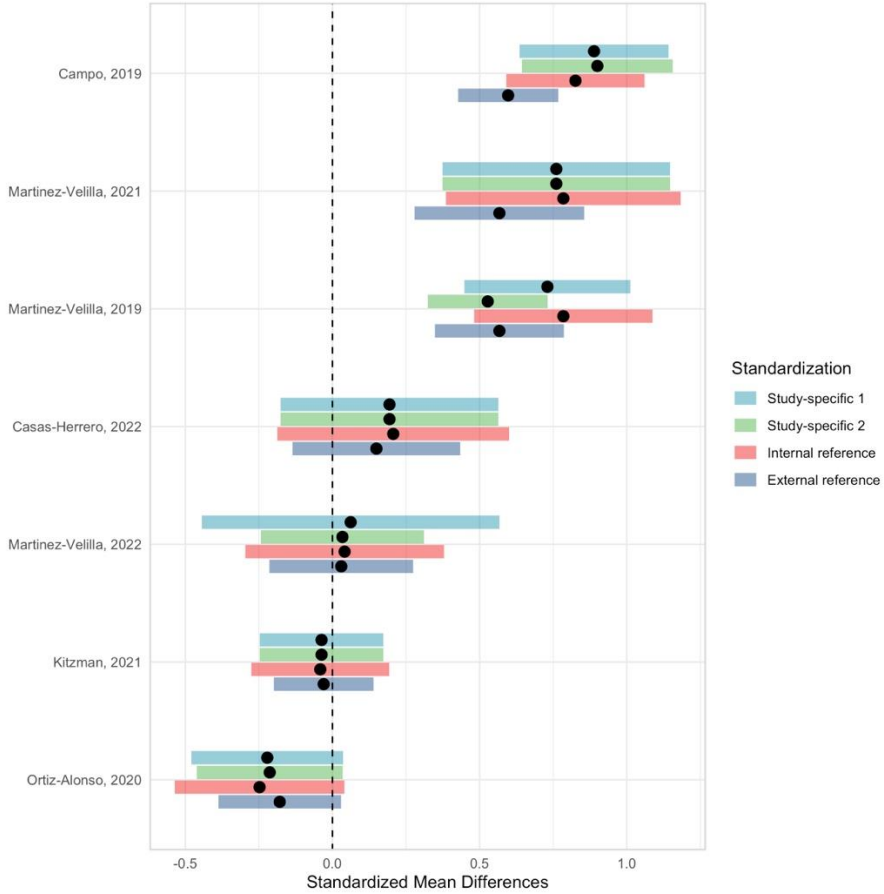
Supplementary Figure 5. Method 1: using the same SD reference for standardization. Method 2: using a weighted SD reference calculated as the average of pre-interventions SD values. Method 3: using an external SD reference from a representative observation study. Pooled MD refers to original MD values (i.e., no standardization).



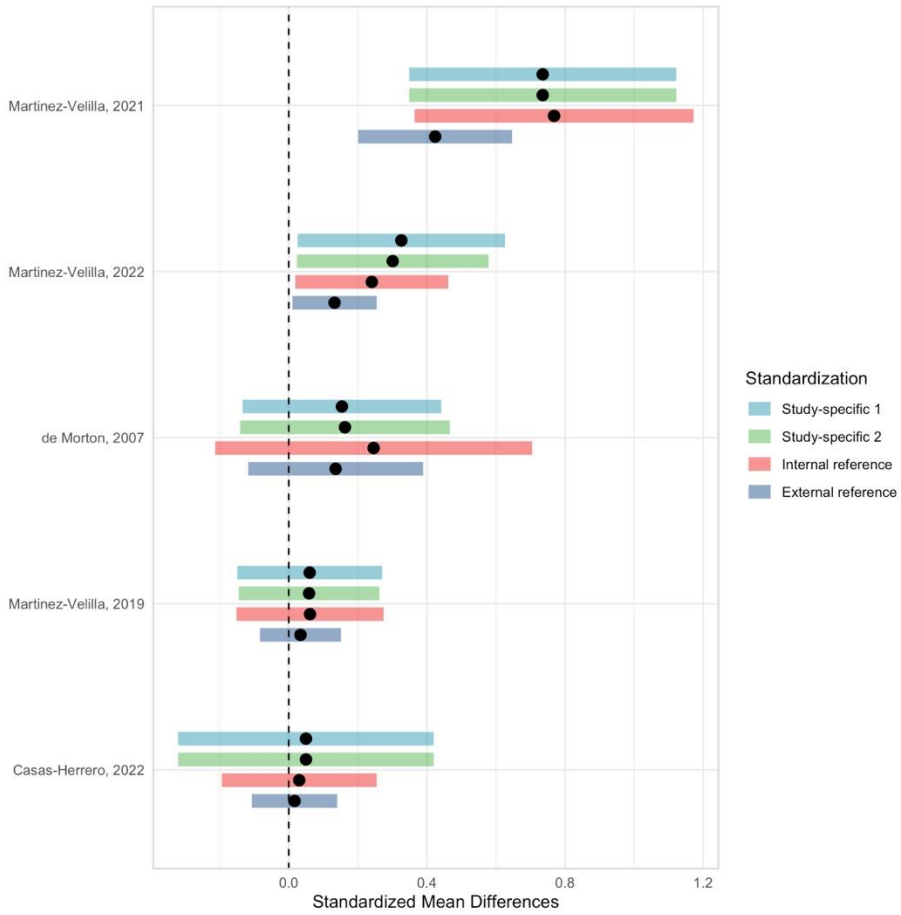
Supplementary Figure 6. Method 1: using the same SD reference for standardization. Method 2: using a weighted SD reference calculated as the average of pre-interventions SD values. Method 3: using an external SD reference from a representative observation study. Pooled MD refers to original MD values (i.e., no standardization).

Supplementary Material 5. Study-specific relative effect estimates

In this supplementary file we plot the observed study-specific relative effects for SPPB outcomes (Supplementary Figure 7) and for BI outcomes (Supplementary Figure 8). These plots give a visualization of how using different standardization methods could yield different estimates at the study level.



Supplementary Figure 7



Supplementary Figure 8

Supplementary Material 6. Real meta-analysis case simulation: pooling all effect sizes from different scales

In this supplementary material we simulate a real meta-analysis pooling all available effect sizes from different scales. This simulation is just for showing the standardization–meta-analysis–and–conversion back process that we recommend following in a real case.

1) Standardization process using a specific SD reference to compute standardized mean differences and their standard errors.
2) Meta-analysis pooling all available evidence. In our case, combining standardized mean differences from both scales, SPPB and BI.
3) Back-conversion to scale-specific estimates multiplying the standardized mean differences by the same SD reference used for standardization. For example, using an external SD reference and REML estimator in the meta-analysis, the pooled effect was 0.31 (95% CI 0.07 to 0.54). So, multiplying the pooled effect by 3.14 (the external SD reference for SPPB scale), the scale-specific effect in SPPB units was 0.76 (95% CI 0.16 to 1.35).

All this procedure is represented in the organization chart below.

SPPB data
(*Mean Differences*)

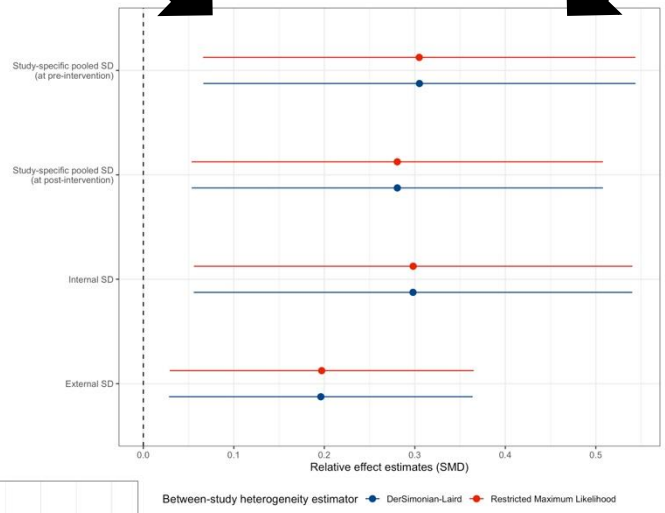
BI data
(*Mean Differences*)

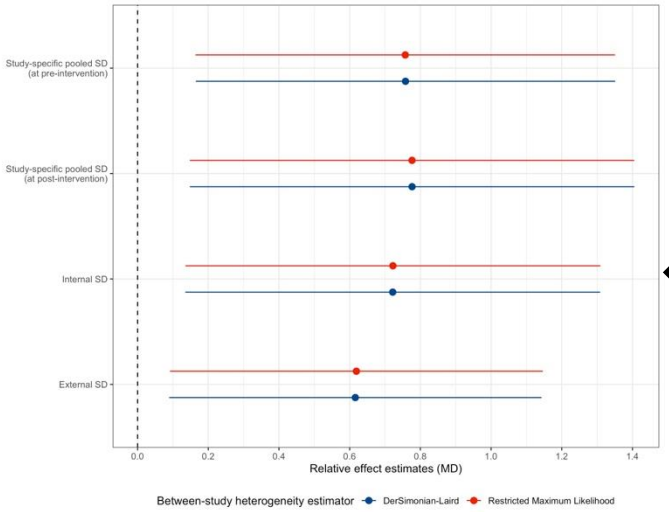
***Standardization**

SPPB data
(*Standardized Mean Differences*)

BI data
(*Standardized Mean Differences*)

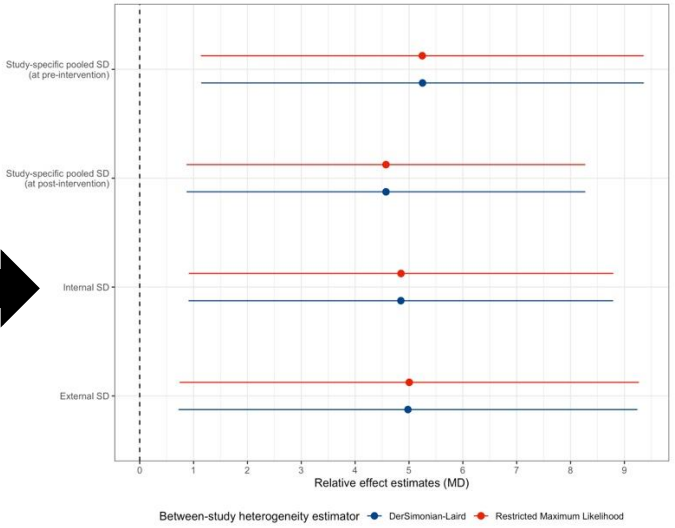
*We can use (in order of preference):
- **External** SD reference
- **Internal** SD reference
- **Study-specific** pooled SDs (at baseline and post-intervention time points)





SPPB

BI



****Back-conversion**

**Multiplying by the same SD reference used for standardization