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Meta-Analysis of Pre-Post Studies: Why Standardised Mean Difference Should Be Avoided

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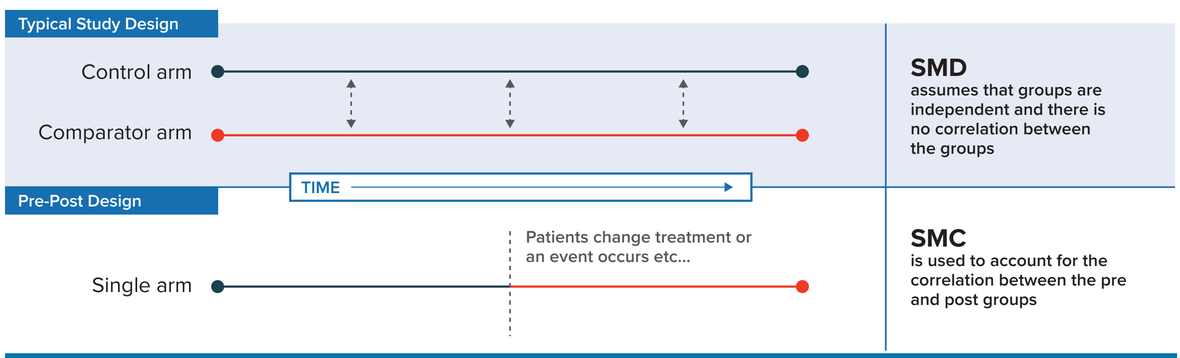
INTRODUCTION

- Single-group studies may measure an outcome at 2 timepoints, with the change between timepoints determined. Pre-post studies (sometimes known as before and after studies) may be used to assess the impact of an intervention, policy change, or other adjustment, by comparing results before and after the change or event in the same group of patients. Pre-post studies with a single arm are subjected to multiple limitations (e.g., lack of a comparator control arm, regression to the mean, and correlation between the pre- and post-measures).[1,2]
- Commonplace methods, such as standardised mean difference (SMD) and mean difference, are inappropriate for the analysis of single-arm pre-post studies, as they do not account for the correlation between the pre- and post-measures. Previous literature[3,4] has proposed that single-arm pre-post studies should be analysed with standardised mean change (SMC), which accounts for the correlation between the pre- and post-measures. Figure 1 presents an infographic outlining the study designs that are appropriate for analysis with SMC or SMD.
- This study re-analyses a published meta-analysis of pre-post studies to assess the impact of ignoring correlations in the analysis of pre-post data. Furthermore, this research explores the conditions under which the use of SMD, which inappropriately ignores correlations, would result in differing conclusions in analyses of pre-post data using SMC.
- Accordingly, our primary objective is to showcase the differences between SMC and SMD and the need to implement correct methods when analysing pre-post data.

Figure 1. Study Designs Suitable for Analysis With SMC or SMD



METHODS

Re-analysis of data from Farooq et al.[5]

- Desktop research was utilised to identify a meta-analysis based on pre-post data. The identified publication[5] assesses the change in moderate-to-vigorous intensity physical activity (MVPA) in children and adolescents.
- We independently performed random-effects (RE) meta-analyses based on the MVPA data for studies presenting data from 12-year-old males. Meta-analyses used SMC, which appropriately considers the correlation between the pre- and post-measures, and SMD, which ignores such correlation. Only those studies that reported data for the same number of patients at both timepoints were included, a requirement of the use of SMC.
- As correlation coefficients were not available in the data extraction provided by Farooq et al.,[5] the original publications were consulted to identify correlation coefficients. If this information was not identified, it was estimated as the mean correlation coefficient reported by the other included studies.

Simulations

- A total of 1,470,000 datasets were simulated across 147 combinations of post-change measure and correlation between the pre- and post-measures (i.e., 10,000 replicate datasets per combination). All other variables (e.g., pre-change measure, standard deviations, and number of patients) were held constant.
- Across each dataset, data were simulated for the included studies, each of which was separately analysed by SMC and SMD, and RE meta-analyses were performed. For each dataset, whether the pooled estimate reported by SMC and SMD meta-analyses was statistically significant was recorded.
- For each combination, the percentage of meta-analyses that were statistically significant when using SMC but not SMD (or vice versa) was determined.
- This allowed for the identification of conditions under which meta-analyses using SMD and SMC produce contrasting results, as well as the variables that determine such differences.

DISCUSSION

- Through the meta-analysis performed on the example dataset and simulations, we have shown that SMC and SMD cannot be assumed to be equivalent for the analysis of single-arm pre-post studies. Furthermore, we have clearly illustrated how the use of incorrect methods (e.g., SMD) to analyse single-arm pre-post studies can lead to erroneous results and invalid conclusions.
- Additionally, many studies choose an arbitrary value for the correlation between the pre- and post-measures when using SMC.[1] However, our findings show that the choice of correlation coefficient can have ramifications for the statistical significance of any meta-analysis using SMC.
- As such, where studies do not report the correlation between the pre- and post-measures, it is important that the selected correlation coefficient is based on clinical rationale and not selected arbitrarily.
- Further limitations of pre-post studies also should be considered when performing analysis, such as the possibility of temporal effects on changes between measurements taken before and after an intervention.

KEY POINTS

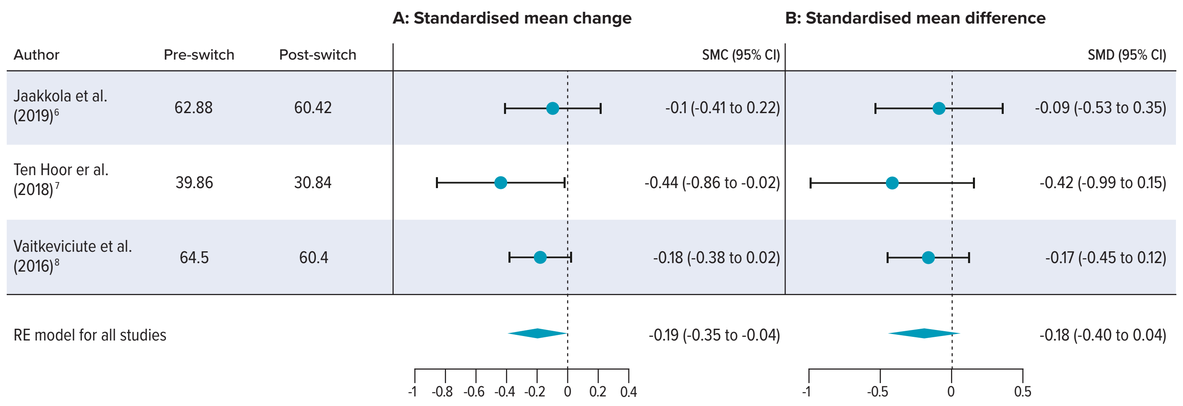
- Single-arm pre-post studies should be analysed with SMC and not SMD.
- Where studies do not report the correlation between pre- and post-measures, the estimated correlation coefficient should be based on clinical rationale and not selected arbitrarily. Sensitivity analyses also should be performed to determine the impact of the chosen correlation coefficient on the overall results.

RESULTS

Re-analysis of data from Farooq et al.[5]

- Of the 7 studies originally considered by Farooq et al.,[5] only 3 reported data for the same number of patients at both timepoints and were included in the meta-analyses. Of these, only 1 study[6] reported a correlation coefficient that was subsequently used across all included studies.
- The SMC meta-analysis (Figure 2A) reported a statistically significant pooled estimate (SMC = -0.19; 95% CI, -0.35 to -0.04), indicating a significant change in MVPA. In contrast, the SMD meta-analysis (Figure 2B) reported a statistically nonsignificant pooled estimate (SMD = -0.18; 95% CI, -0.40 to 0.04), indicating a nonsignificant reduction in MVPA.

Figure 2. Forest Plots of SMC and SMD for MVPA in 12-Year-Old Males



Simulations

- For each of the 1,470,000 simulated datasets, the percentage of meta-analyses that were statistically significant when using SMC but not SMD (or vice versa) is shown in Figure 3.
- As shown in Figure 3, differences in the statistical significance of meta-analyses using SMC and SMD are most likely to occur when there is a small to moderate change between pre- and post-measures and when large correlation coefficients are observed.
- Furthermore, where the correlation coefficient is positive, meta-analyses using SMC are more likely to report a statistically significant pooled estimate.
- In contrast, where correlation coefficients are negative, meta-analyses using SMD are more likely to report a statistically significant pooled estimate.

Figure 3. Significance Comparison of SMC and SMD From Simulations

Post-mean	-0.9	-0.6	-0.3	0.0	0.3	0.6	0.9
120	0.03	0.05	0.01	0.01	0.08	0.16	0.13
	0.24	0.14	0.11	0.07	0.15	0.25	0.46
	1.18	0.62	0.39	0.27	0.38	0.62	0.83
	3.86	2.44	1.04	0.74	0.85	1.29	1.71
	10.49	5.58	3.36	1.29	2.09	2.84	3.84
	18.77	11.38	5.79	1.92	4.23	6.82	7.79
110	23.21	16.11	8.08	2.62	7.17	11.64	13.51
	19.45	14.44	8.78	2.34	7.91	14.41	18.41
	11.82	9.33	5.46	1.66	6.54	13.18	18.59
	5.06	4.34	2.81	1.16	3.77	9.06	15.32
100	2.88	2.55	1.84	0.61	2.99	7.44	13.09
	5	4.48	2.91	0.9	4.06	10.08	15.22
	12.1	9.48	5.44	1.69	6.34	13.38	19.04
	19.56	14.06	8.45	2.45	7.89	14.34	18.65
90	23.76	15.18	7.96	2.49	6.93	11.62	14.29
	18.82	11.39	6.03	2.12	4.24	7.13	8.52
	10.18	5.73	3.06	1.2	2.18	3.06	3.79
	4.15	2.09	1.15	0.77	0.93	1.55	1.74
80	1.19	0.74	0.49	0.31	0.43	0.55	0.88
	0.33	0.12	0.11	0.16	0.17	0.22	0.34
	0.04	0.03	0.05	0.03	0.09	0.18	0.24

Correlation coefficient

Note: Blue cells represent more instances of SMC being statistically significant and SMD statistically nonsignificant; red cells, more instances of SMD being statistically significant and SMC statistically nonsignificant. Pre-means were held constant at 100; pre-mean and post-mean standard deviations were held constant at 35.

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