Sensitivity analyses of primary outcome analyses using multiple imputation

(Supplement to *The efficacy of a transdiagnostic emotion focused treatment for chronic pain patients with comorbid anxiety and depression. A randomized controlled trial. Boersma, K, Södermark, M, Hesser, H, Flink, IK, Gerdle, B, Linton, SJ)*

Methods

Given that baseline anxiety was associated with propensity for missing data in the study, we reanalyzed the data using multiple imputation as a sensitivity analysis [2]. The results from the regression models were pooled across 50 imputed data sets (each saved at the 500th imputation cycle). Estimates and standard errors were averaged across the 50 imputed data sets using Rubin's [3] pooling equations. Although both multiple imputation and full information maximum likelihood (FIML) work under the same missing data assumption (MAR) and yield similar results in large samples with the same set of variables, an inclusive strategy with more variables is often preferred in order to reduce bias and increase efficiency [1]. In addition, MAR assumes that all observed variables associated with missing data are include in the model to produce accurate results. Given this and due to that multiple imputation model used all outcome variables measured at pre-treatment, including baseline anxiety, results (i.e., estimates, standard errors, *p*-values) from multiple imputation were compared with those obtained in FIML.

Results

Results of sensitivity analyses using multiple imputation

Supplementary Table 1 provides the main results of the regression analysis for continuous and categorical outcomes that were rerun using multiple imputation. Regression models that were rerun using multiple imputation did not alter the results materially and produced overall

similar results in terms of estimates, standard errors and *p*-values as those presented in the main text. However, in three instances the *p*-values changed slightly which lead to another qualitative interpretation of the results in terms of significance. There was a statistically significant difference between conditions on the continuous outcome measure MADRS-S at post-assessment (*p*=.038 vs. *p* =.061) and the difference on MADRS-S at 9-month follow-up approached but did not reach predetermined significance level using multiple imputation (*p* =.054 vs. *p* =.043). The difference between treatments in the proportions of the participants who showed a reliable recovery on at least one of the outcome variables at post-assessment was statistically significant using multiple imputation (*p* = .049 vs. *p* = .055).

Overall the results from the sensitivity analyses were comparable and we therefore conclude that analytic models that were presented in the main text were not unduly influenced by the approach used to handle missing data, i.e. FIML versus multiple imputation.

Supplementary Table 1. Results from maximum likelihood robust regression analyses of continuous and categorical outcomes (clinically significant improvement) evaluating treatment differences at post-assessment and 9-month follow-up.

Outcome	Post-assessment		9-month follow-up	
	b (SE)	*p*	*b* (SE)	*p*
Continuous outcomes				
MADRS-S	-2.92 (1.41)	.038	-2.92 (1.52)	.054
GAD-7	-0.60 (0.95)	.524	-0.87 (1.04)	.403
PCS	-4.24 (1.52)	.005	-2.86 (1.72)	.096
MMPI-pain intensity	-0.12 (0.44)	.789	0.55 (0.44)	.213

MPI-pain interference	-6.72(1.82)	<.001	-6.34 (2.36)	.007
Categorical outcomes (clinically significant improvement)				
MADRS-S	1.01 (0.72)	.162	0.54 (0.58)	.359
GAD-7	0.17 (0.58)	.77	0.11 (0.56)	.848
PCS	1.82 (1.07)	.089	0.68 (0.59)	.255
MMPI-pain intensity	0.61 (1.25)	.626	-0.55 (1.23)	.66
MPI-pain interference	1.03 (0.85)	.229	1.00 (0.63)	.113
Any measure	0.88 (0.44)	.049	0.68 (0.43)	.112

Note. Missing data were handled using multiple imputation and all results are based on all individuals who were randomized (N =115). MPI; West Haven-Yale Multidimensional Pain Inventory, PCS; Pain Catastrophizing Scale, MADRS-S; Montgomery Åsberg Depression Rating Scale, GAD-7; Generalized Anxiety Disorder 7-item Scale.

References

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[2] Enders, CK. Applied missing data analysis. New York: Guilford Press, 2010.

[3] Rubin, DB. Multiple imputation for nonresponse in surveys. Hoboken, NJ: Wiley, 1987.