

Supplemental Table 1

Variable	Baseline				At 1 year				Adjusted Between-group Difference (95% CI)	P Value
	Levothyroxine		Placebo		Levothyroxine		Placebo			
	N	Mean±SD	N	Mean±SD	N	Mean±SD	N	Mean±SD		
Participants with higher fatigability at baseline ¹										
PFS physical score (SD) (n=88) ²	55	23.2±6.1	33	22.2±7.3	55	19.2±9.1	33	20.0±9.8	-0.4 (-3.6 to 2.8) ²	0.79 ³
PFS mental score (SD) (n=41)	27	20.0±5.7	14	19.5±7.5	27	9.8±9.9	14	15.4±12.2	-2.2 (-8.8 to 4.5) ²	0.51 ³
Participants with complete outcome data ⁵										
Complete data for PFS physical score (SD) (n=116)	112	15.1±9.0	104	11.5±9.1	112	14.5±9.7	104	12.2±9.3	-0.3 (-2.1 to 1.6) ²	0.77 ³
Complete data for PFS mental (SD) score (n=114)	111	7.6±8.0	103	5.3±7.0	111	5.6±7.7	103	5.8±7.8	-1.2 (-3.0 to 0.6) ²	0.18 ³

Per protocol analysis ⁶										
PFS physical score (SD) (n=205)	104	14.1±9.2	101	10.8±8.7	104	14.5±9.4	101	12.2±8.8	0.2 (-1.8 to 2.2) ²	0.86 ³
PFS mental score (SD) (n=205)	104	7.5±8.0	101	5.0±6.6	104	5.6±6.8	101	5.9±7.8	-1.4 (-3.2 to 0.4) ²	0.13 ³
Excluding participants with diabetes mellitus										
PFS physical score (SD) (n=200)	98	13.9±9.1	102	11.1±9.2	98	13.8±9.2	102	12.8±9.3	-0.7 (-2.7 to 1.2) ²	0.46 ³
PFS mental score (SD) (n=200)	98	7.3±7.5	102	5.1±6.8	98	5.9±7.7	102	6.1±8.2	-1.2 (-3.2 to 0.7) ²	0.20 ³
Adjusting for diabetes mellitus										
PFS physical score (SD) (n=230)	119	14.7±9.3	111	11.1 ±9.1	119	14.8±9.6	111	12.4±9.3	0.1 (-1.9 to 2.0) ⁴	0.95 ⁵
PFS mental score (SD) (n=230)	119	7.4±8.0	111	5.1±6.9	119	6.0±7.8	111	6.0±8.0	-1.0 (-2.9 to 0.8) ⁴	0.26 ⁵
Sqrt transformed data analysis ⁶										
PFS physical score (SD) (n=230)	119	3.6±1.4	111	3.0±1.5	119	3.6±1.4	111	3.2±1.5	0.1 (-0.2 to 0.4) ²	0.61 ³

PFS mental score (SD) (n=230)	119	2.2±1.6	111	1.7±1.5	119	1.9±1.6	111	1.8±1.7	-0.1 (-0.5 to 0.2) ²	0.49 ³
IPW-analysis ⁷										
PFS physical score (SD) (n=230)	119	14.7±9.3	111	11.1 ±9.1	119	14.9±9.6 ⁸	111	12.4±9.3 ⁸	-0.75 (-2.7 to 1.2) ²	0.45 ³
PFS mental score (SD) (n=230)	119	7.4±8.0	111	5.1±6.9	119	6.0±7.8 ⁸	111	6.0±7.9 ⁸	0.26 (-1.6 to 2.1) ²	0.78 ³
Participants with TSH values in the upper quartile ⁹										
PFS physical score (SD) (n=56)	28	11.5±8.5	28	6.3±6.3	28	13.0±8.5	28	10.3±7.5	-0.01 (-4.2 to 4.2)	0.10 ³
PFS mental score (SD) (n=56)	28	5.5±7.7	28	3.4±4.1	28	6.1±8.7	28	4.1±5.1	0.62 (-2.8 to 4.0)	0.72 ³

If not otherwise indicated, the crude means are reported. The Pittsburgh Fatigability Scale (PFS) physical and mental subscores range from 0-50 with higher scores indicating greater fatigability.

¹ Including only participants with higher fatigability at baseline (≥15 points in the PFS physical or ≥13 points in the PFS mental score)

² Between-group differences generated through multiple linear regression model for the follow-up scores adjusted for PFS baseline scores, sex, country and starting levothyroxine dose

³ P value generated through multiple linear regression model for the follow-up scores adjusted for PFS baseline scores, sex, country and starting levothyroxine dose.

⁴ Between-group differences generated through multiple linear regression model for the follow-up scores adjusted for PFS baseline scores, sex, country, starting levothyroxine dose and presence of diabetes mellitus

⁵ P value generated through multiple linear regression model for the follow-up scores adjusted for PFS baseline scores, sex, country, starting levothyroxine dose and presence of diabetes mellitus.

⁶ Square root transformation was performed prior to multiple linear regression model for the follow-up scores adjusted for the same variables as in the main analysis in order to correct for skewed distributions.

⁷ Inverse probability weighting (IPW) was performed in order to correct for missing data at 12 months follow-up. The covariables included in the logistic regression model to estimate IPWs were BMI, age, country, sex and the number of comorbidities.

⁸ Weighted means (IPW)

⁹ Including only participants with TSH levels in the upper quartile (≥ 6.76 mIU/L)