

Item Performance and Structural Validity of the Quick Motor Function Test among Late Onset Pompe Disease Patients

Armstrong NM, PhD¹; Kruijshaar ME, PhD²; Sjöström-Bujacz A, PhD³; Daskalopoulou C, PhD⁴; Papageorgiou DP, MS⁴; An Haack K, MD⁵; Gallego V, MD¹; DasMahapatra P, MD, MPH¹; Thibault N, PharmD, RPh¹; Zaher A, MD⁶; van der Ploeg A, MD, PhD²; van der Beek N, MD, PhD²

¹Sanofi, Cambridge, MA, USA; ²Erasmus MC University Medical Center, Center for Lysosomal and Metabolic Diseases, Rotterdam, The Netherlands; ³IQVIA, Solna, Sweden; ⁴IQVIA, Athens, Greece, ⁵Sanofi, Chilly-Mazarin, France; ⁶Sanofi, ON, Canada

INTRODUCTION

- Pompe disease is a rare inheritable metabolic disorder caused by a deficiency of the acid alpha-glucosidase (GAA) enzyme¹
- In late-onset Pompe disease (LOPD), the ability to perform tasks requiring limb and girdle muscle strength, such as walking, running, and climbing stairs is progressively impaired²
- To evaluate motor function, the Quick Motor Function Test (QMFT) is a 16-item scale constructed for Pompe disease for which content and construct validity have been previously established³, but not structural validity. An evaluator scores the items on a 5-point ordinal scale (0–4)
- We can use the QMFT to determine whether there is improvement in motor function over time

OBJECTIVE

- To evaluate QMFT’s structural validity and individual items’ performance and thus determine the appropriateness of the current unidimensional scoring

METHODS

Data Source

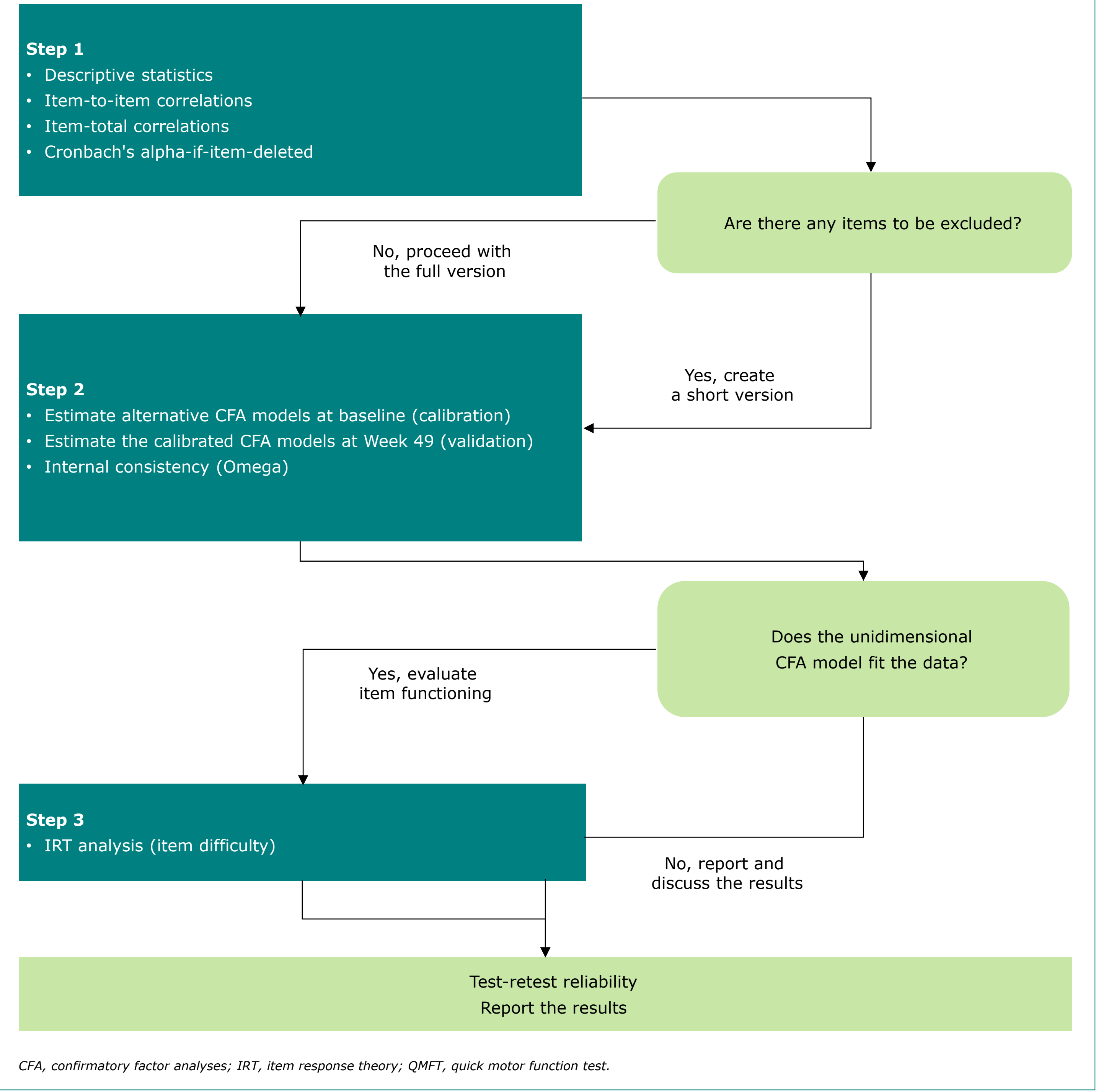
- Blinded pooled data from baseline (n=97) and Week 49 (n=91) of the COMET study (NCT02782741), a Phase 3 randomized trial of patients with LOPD were analyzed
- The study included modified intention-to-treat population [at least 1 (partial) infusion]
 - ≥18 years of age
 - Able to ambulate 40 meters without stopping and without assistive device

Patient Global Impression of Change (PGIC)

- PGIC was used for test-retest reliability
- PGIC consisted of 4 items concerning disease-related symptoms, daily activities, mobility, and respiratory issues
- A 7-point scale was used to rate improvement on each PGIC item from -3 (a great deal worse) through 0 (no change) to 3 (a great deal better)

An overview of the analytical strategy is presented in **Figure 1**

Figure 1: The analysis process of the psychometric evaluation of the QMFT



ACKNOWLEDGMENTS

The study is sponsored by Sanofi and the medical writing support was provided by Deepa Warriier, PhD from Sanofi.

DISCLOSURES

Armstrong N, An Haack K, Gallego V, DasMahapatra P, Thibault N, and Zaher A are employees of Sanofi and may own Sanofi stock. **Kruijshaar ME** declares no conflicts of interest. **Sjöström-Bujacz A, Daskalopoulou C and Papageorgiou DP** are employees of IQVIA and serve as consultants to Sanofi. **van der Ploeg A** received funding for research, clinical trials, and advisory fees from Sanofi-Genzyme, Amicus Therapeutics, BioMarin, Ultragenyx, Sarepta, Audentes, and Spark Therapeutics working on enzyme replacement therapy or next-generation therapies in the field of Pompe disease, other lysosomal storage diseases, or neuro-muscular disorders, under agreements with the Erasmus MC University Medical Center and the relevant industry. **van der Beek N** has received consulting fees, speaking fees, and fees for attending meetings and advisory boards by Sanofi.

Poster presented at ISPOR 2024, Atlanta, Georgia, USA; May 5–8, 2024.

RESULTS

Item Performance

- Item-to-item correlations ranged from 0.04–0.80 (**Table 1**), while the majority of item-total correlations were sufficiently strong (≥0.50) (**Table 2**)

Table 1: Item-to-item correlations for QMFT at two timepoints: baseline and Week 49

Item-to-item correlations: r																
Week 49	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Baseline																
1		0.287	0.074	0.350	0.422	0.317	0.333	0.385	0.317	0.400	0.398	0.337	0.234	0.286	0.383	0.303
2	0.267		0.239	0.165	0.304	0.212	0.412	0.253	0.234	0.278	0.311	0.207	0.204	0.287	0.268	0.281
3	0.168	0.258		0.214	0.128	0.263	0.446	0.139	0.246	0.238	0.274	0.301	0.159	0.191	0.357	0.298
4	0.175	0.190	0.265		0.678	0.606	0.335	0.499	0.571	0.457	0.617	0.470	0.079	0.338	0.549	0.451
5	0.275	0.194	0.325	0.671		0.430	0.265	0.440	0.500	0.470	0.561	0.374	0.044	0.259	0.440	0.378
6	0.376	0.093	0.261	0.340	0.417		0.355	0.344	0.437	0.447	0.505	0.414	0.226	0.411	0.460	0.383
7	0.358	0.230	0.369	0.358	0.296	0.344		0.292	0.306	0.241	0.310	0.244	0.231	0.375	0.327	0.251
8	0.304	0.226	0.204	0.438	0.356	0.260	0.198		0.690	0.704	0.775	0.741	0.224	0.421	0.593	0.583
9	0.359	0.247	0.279	0.507	0.488	0.407	0.251	0.613		0.724	0.728	0.661	0.352	0.480	0.699	0.641
10	0.314	0.213	0.253	0.413	0.395	0.390	0.208	0.621	0.637		0.800	0.650	0.356	0.478	0.696	0.688
11	0.303	0.275	0.332	0.522	0.443	0.281	0.256	0.646	0.607	0.732		0.706	0.311	0.426	0.673	0.691
12	0.343	0.225	0.358	0.432	0.414	0.397	0.301	0.750	0.580	0.553	0.572		0.297	0.429	0.621	0.596
13	0.518	0.283	0.248	0.276	0.261	0.453	0.329	0.273	0.348	0.387	0.362	0.349		0.430	0.404	0.398
14	0.249	0.203	0.230	0.374	0.374	0.359	0.252	0.389	0.422	0.283	0.275	0.497	0.388		0.440	0.433
15	0.330	0.228	0.323	0.550	0.502	0.490	0.359	0.613	0.759	0.687	0.595	0.652	0.430	0.475		0.767
16	0.358	0.148	0.212	0.519	0.440	0.396	0.239	0.626	0.612	0.661	0.543	0.677	0.448	0.437	0.754	

The darker colors reflect stronger correlations, while the lighter colors reflect weaker correlations
QMFT, quick motor function test; r, Spearman correlation coefficient.
Item 1: Prone, raising the torso; Item 2: Supine, neck flexion; Item 3: Supine, hand across midline; Item 4: Supine, hip and knee flexion; Item 5: Supine, extending the legs; Item 6: Supine, sit up; Item 7: Sit, extending the arms; Item 8: Standing up from a chair; Item 9: Standing up from half-knee; Item 10: Squatting; Item 11: Standing up from a squatting position; Item 12: Picking up an object; Item 13: Standing on one leg; Item 14: Walking ten meters; Item 15: Jumping; Item 16: Walking up step

Table 2: Item-to-total correlations for QMFT at baseline and at Week 49

Item	Baseline	Week 49
	QMFT Total score (N=97) r	QMFT Total score (N=91) r
1 Raising the torso	0.448	0.490
2 Neck flexion	0.333	0.365
3 Hand across midline	0.389	0.339
4 Hip and knee flexion	0.600	0.650
5 Extending the legs	0.591	0.579
6 Sit up	0.517	0.576
7 Extending the arms	0.419	0.421
8 Standing up from a chair	0.669	0.749
9 Standing up from half-knee	0.752	0.782
10 Squatting	0.703	0.788
11 Standing up from a squatting position	0.702	0.845
12 Picking up an object	0.713	0.717
13 Standing on one leg	0.502	0.383
14 Walking ten meters	0.507	0.538
15 Jumping	0.816	0.788
16 Walking up steps	0.742	0.732

The darker colors reflect stronger correlations, while the lighter colors reflect weaker correlations
N, number of patients; QMFT, quick motor function test; r, Spearman correlation coefficient.

CONCLUSIONS

- Our study has empirically demonstrated that the QMFT is a unidimensional measure of motor function characterized by high measurement precision
- The psychometric evidence established in this work offers support for the application of the QMFT total score in assessments of motor function in patients with LOPD

Structural Validity

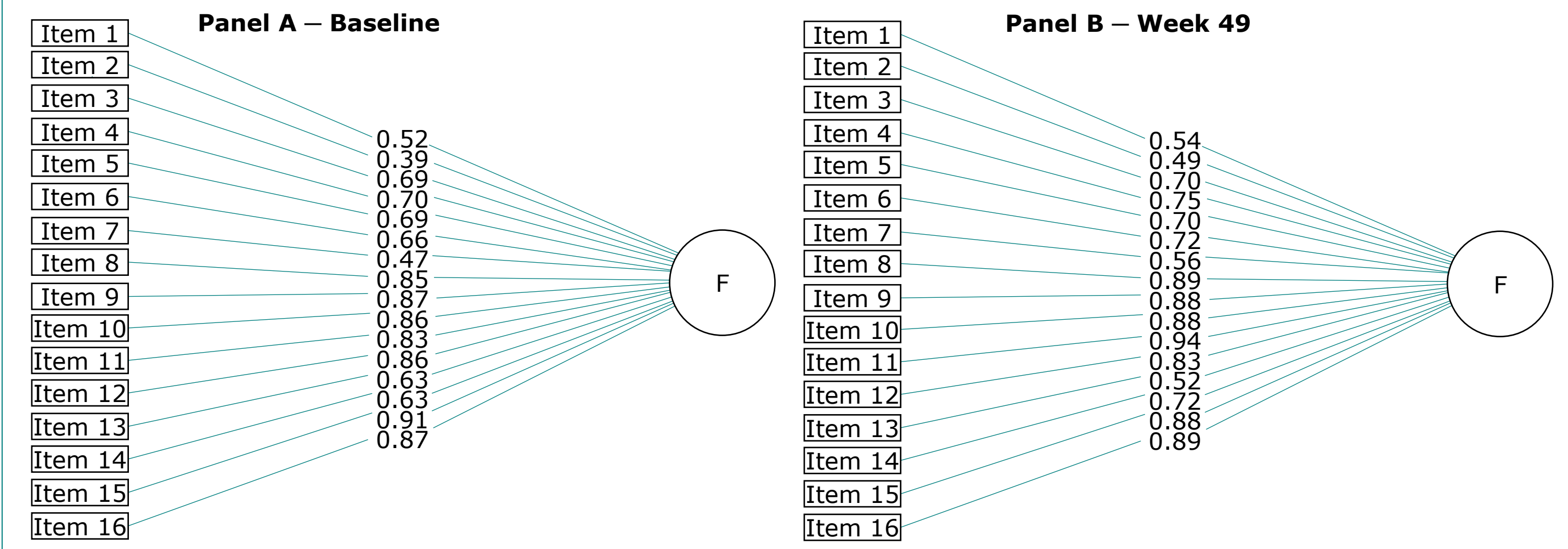
- The goodness-of-fit indices were slightly better for the bifactor model, yet further check of the appropriateness of the factor solution revealed that the bifactor model resulted in an irregular pattern of factor loadings. These factor loadings cannot be interpreted as consistent representations of any specific subdimension.
 - Thus, the bifactor model results, similar to the second-order factor model, suggest that the proposed subdimensions are not appropriate representations of the QMFT’s internal structure.

Table 3: Goodness-of-fit indices of confirmatory factor analyses (CFA) models at baseline and Week 49

Time point	Model	χ ²	df	p-value	RMSEA	RMSEA (90% CI)	CFI	SRMR
Baseline	Unidimensional	228.61	104	<0.001	0.11	[0.09; 0.13]	0.95	0.08
	Second-order	165.82	103	<0.001	0.08	[0.06; 0.10]	0.98	0.07
	Bifactor	109.76	88	0.058	0.05	[0.00; 0.08]	0.99	0.05
Week 49	Unidimensional	216.55	104	<0.001	0.11	[0.09; 0.13]	0.97	0.09
	Second-order	178.08	103	<0.001	0.09	[0.07; 0.11]	0.98	0.08
	Bifactor	126.20	88	0.005	0.07	[0.04; 0.10]	0.99	0.08

CI, confidence interval; CFI, comparative fit index; df, degrees of freedom; RMSEA, root mean square error of approximation; SRMR, standardized root mean squared residual. The unidimensional model and the two comparison models (bifactor and second-order) showed acceptable model fit. The differences in model fit were relatively small, as indicated by similar values of CFI and SRMR, as well as overlapping confidence intervals for RMSEA. Considering the interpretability of model parameters, the unidimensional model was recommended as the most parsimonious representation of the QMFT’s internal structure.

Figure 2: Unidimensional CFA model of QMFT at baseline (A) and Week 49 (B)



F, factors; Latent variables (factors) are represented as ellipses and observed items as rectangles; Standardized factor loadings are presented. Item 1: Raising the torso; Item 2: Neck flexion; Item 3: Hand across midline; Item 4: Hip and knee flexion; Item 5: Extending the legs; Item 6: Sit up; Item 7: Extending the arms; Item 8: Standing up from a chair; Item 9: Standing up from half-knee; Item 10: Squatting; Item 11: Standing up from a squatting position; Item 12: Picking up an object; Item 13: Standing on one leg; Item 14: Walking ten meters; Item 15: Jumping; Item 16: Walking up steps

Reliability

Internal Consistency Reliability

- The unidimensional scoring of QMFT showed excellent internal consistency reliability both at baseline (Cronbach’s alpha=0.906; McDonald’s omega=0.946) and Week 49 (Cronbach’s alpha=0.917; McDonald’s omega=0.966)

Test re-test Reliability

Table 4: Across four stable patient groups defined by no change on PGIC, good test-retest reliability [i.e., intraclass correlation coefficient (ICC) ≥0.75] observed⁶

PGIC	Ability to perform daily activities		Disease-related symptoms		Change in ability to breathe		Mobility	
	N	ICC [95% CI]	N	ICC [5% CI]	N	ICC [95% CI]	N	ICC [95% CI]
QMFT score	28	0.854 [0.654, 0.936]	19	0.886 [0.676, 0.958]	28	0.875 [0.728, 0.942]	26	0.875 [0.738, 0.943]

CI, confidence interval; ICC, intraclass correlation coefficient; N, number of patients; PGIC, Patient Global Impression of Change.

Item-level Analysis with Item Response Theory

- QMFT items offered high level of information across the spectrum of motor function. Measurement precision was best at mid to high range of motor function, yet it varied by item (**Figures 3A, 3B**)

Figure 3: Item information functions and test information functions for the QMFT items

