The validity and applicability of a new PROMIS® physical function short form for use in relapsing and progressive multiple sclerosis

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Jeffrey Johns,, Kevin N. Alschuler, Gloria von Geldern and Rod Middleton
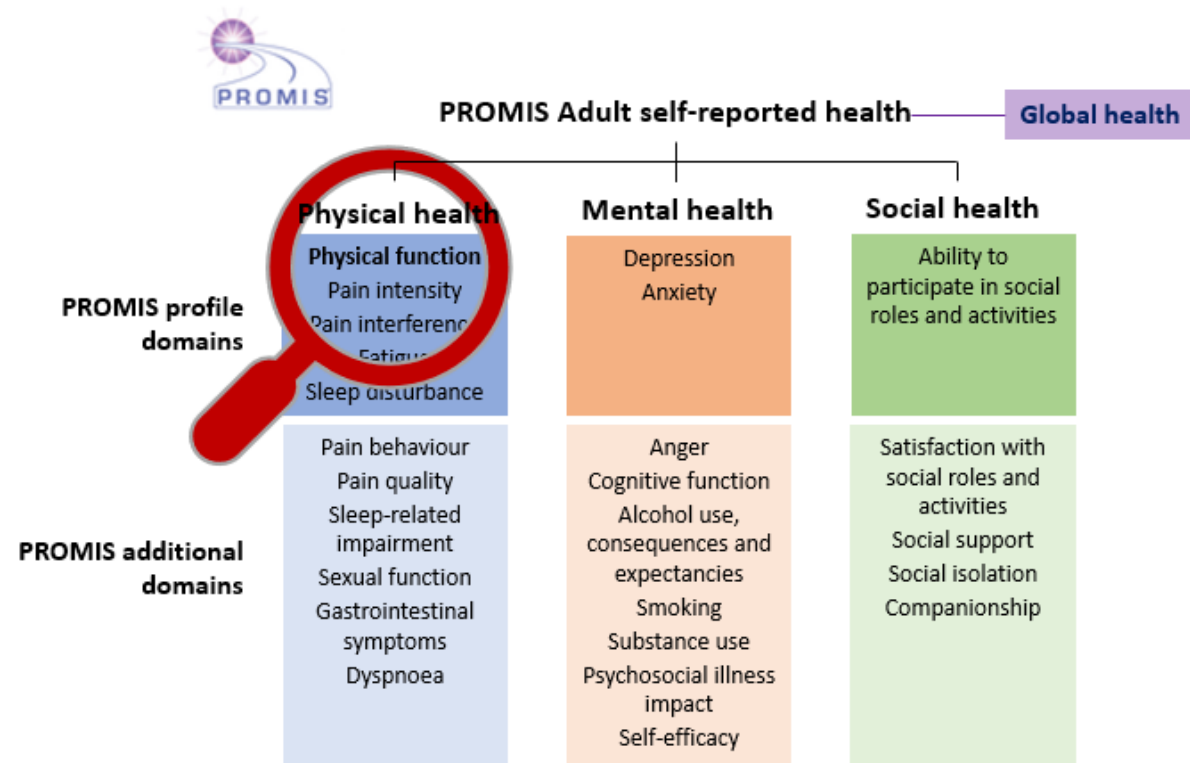
- Nothing to disclose

Background

- There is a pressing need to develop a robust measurement technique that will enable people living with multiple sclerosis (MS) to self-report their level of physical functioning in order to help healthcare teams identify suitable strategies to improve their outcomes

- The emergence of the NIH PROMIS item banks has opened new possibilities for the development of health outcome measures that are brief and optimally targeted

- We carried out mixed methods research to derive a novel physical function measure from the PROMIS physical function item bank, for use in MS populations, that would be capable of capturing subtle changes in physical disability

Objective

- To describe the development, validity and applicability of a MS-specific PROMIS short form for use in relapsing and progressive MS types, the **PROMIS SF v2.1 – Physical Function (MS) 15a**

MS, multiple sclerosis; **NIH**, National Institutes of Health

Figure 1. Adult NIH PROMIS item banks

Source: http://www.healthmeasures.net/explore-measurement-systems/promis/intro-to-promis

Methods

Study design: A mixed-methods sequential design was followed in this research:

Study participants

Inclusion criteria

- Clinician-confirmed MS diagnosis
- 18–65 years of age
- Able to read and write in English

Exclusion criteria

- Cognitive or other impairment (visual) that would interfere with questionnaire completion (steps 3 & 4 only)
- Use of a wheelchair or scooter as the main form of mobility (steps 3 & 4 only)
- Patient-reported WebEDSS scores >6.5 (step 4)

WebEDSS, patient-reported Expanded Disability Status Scale available at: https://edss.clinicspeak.com/en/#!/welcome

Key steps

Concept elicitation interviews (CEI) were performed with MS patients (n=14)

CEI results mapped to the PROMIS physical function item bank, with input from a panel of measurement experts (including PROMIS investigators), to identify items relevant for MS patients

Cognitive interviews were performed with MS patients to confirm the comprehensiveness, relevance and language clarity of the draft short form (n=48)

Further item reduction and psychometric evaluation was performed in two observational studies:

(1) a cross-sectional study at two MS tertiary centers in the US, n=296 [US sample]

(2) a 96-week longitudinal study in the UK MS Register cohort in the UK, n=558 [UK sample]

Analysis

Step 1 & 3

- Modified grounded theory methods were applied to thematic analysis

Step 4

- Item-level analysis e.g. item-item correlations, item response distribution
- Convergence validity
- Known groups validity
- A T-score map, generated as a heatmap showing the most likely response for each item, for each PROMIS Physical Function (MS) T-score
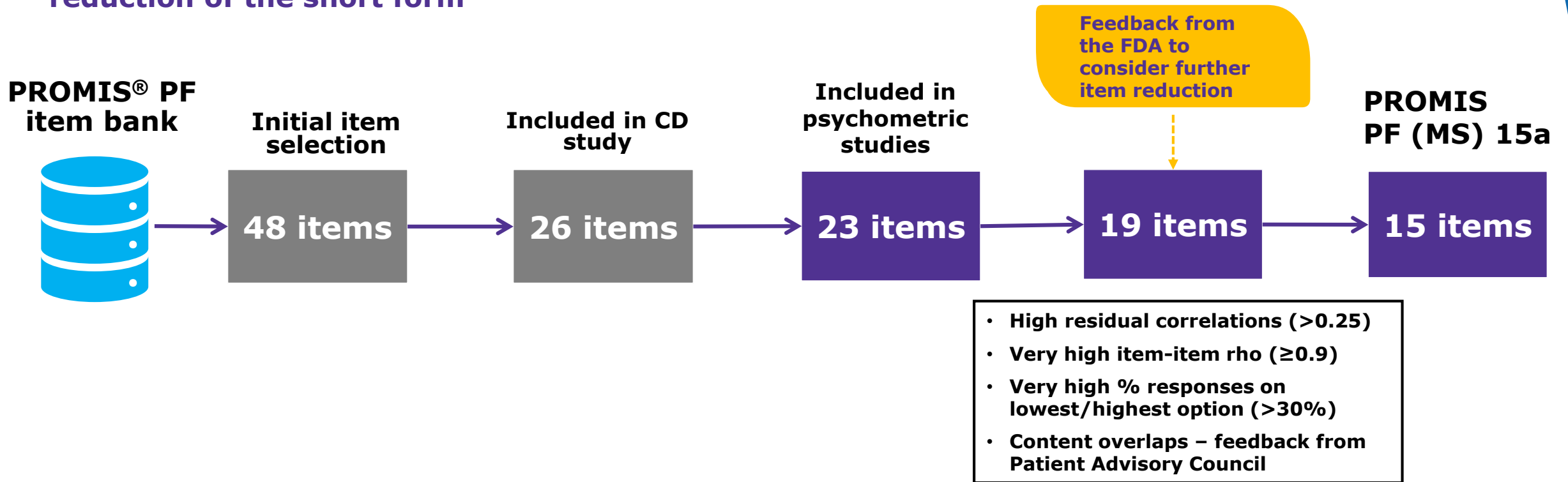
Results 1/5: Cognitive interviews

Table 1. Summary of cognitive interview findings (26 RRMS and 15 PPMS patients)

Aspect	Findings
Instructions	• Well understood and interpreted correctly
Recall period *Non-explicit*	• Participants' interpretation of items, and their responses, demonstrated understanding of implied recall 'current status' • None of the participants was confused or asked for the recall period to be explicitly specified
Response options *5-point Likert Scale*	• Participants judged the response options as optimal, and were able to differentiate between the categories
Conceptual coverage	**Initial 26 items and final 22 items:** • All but one participant reported no missing concepts • One participant reported **difficulty sleeping** and **difficulty typing** as missing concepts/items (Round 1)
Language clarity	**Initial 26 items:** 3 items had language clarity issues (e.g. item *PFA3… bending, kneeling, stooping*)
	Final 22 items: All items were easy to understand and interpreted as intended
Modifications	**End of Round 1** • 3 items **DELETED** due to lack of relevance, and redundancy/overlaps with other items • 4 items **ADDED** to address walking ability and balance aspects
	End of Round 2 • 6 items **DELETED** due to language clarity issues, redundancy/content overlaps, and relevance • 1 item **ADDED** to address standing issues

PPMS, primary progressive multiple sclerosis; **RRMS**, relapsing–remitting multiple sclerosis

Figure 2. Results from qualitative research, item-item correlations, item distribution, factor analysis, item-response theory analyses facilitated further item reduction of the short form

PROMIS® PF item bank

Initial item selection

Included in CD study

Included in psychometric studies

Feedback from the FDA to consider further item reduction

PROMIS PF (MS) 15a

48 items → **26 items** → **23 items** → **19 items** → **15 items**

- **High residual correlations (>0.25)**
- **Very high item-item rho (≥0.9)**
- **Very high % responses on lowest/highest option (>30%)**
- **Content overlaps – feedback from Patient Advisory Council**

A panel of measurement experts (including PROMIS investigators) weighed the item-level analysis results as well as qualitative evidence from previous stages and agreed on deletion of items

CD, cognitive debriefing; **FDA**, Food and Drug Administration

Results 3/5: Psychometric analyses – score distribution

Table 2. The PROMIS PF (MS)15a shows optimal scaling, ceiling/floor effects are below critical threshold (i.e. <15%)

PROMIS PF T-scores	UK sample (n=558)	US sample (n=296)
Mean (SD)	37.6 (10.2)	44.8 (10.3)
Median (min, max)	35.2 (16.8, 63.3)	42.8 (23.7, 63.3)
Ceiling*,%	4.8	12.5
Floor*, %	0.2	0
T-scores distribution at baseline		
Cronbach's alpha	0.97	0.96

*Highest response option for all items; **Lowest response option for all items
SD, standard deviation

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Results 4/5: Psychometric analyses – convergence validity

The PROMIS PF (MS)15a scores showed correlations of expected magnitude and direction with measures of related concepts, across two study populations

Table 3. Spearman's correlation between PROMIS PF (MS) 15a and PRO measures

	UK sample (n=558)		US sample (n=296)	
	n	Spearman's coefficient	n	Spearman's coefficient
EDSS	–	–	258	-0.63
PR-WebEDSS	357	-0.86	296	-0.75
EQ-5D-3L mobility domain	534	-0.71	–	–
GHS physical health question (global03)	355	0.67	294	0.63
GHS health question (global01)	355	0.53	296	0.61
GHS fatigue question (global08)	355	0.50	296	0.65
GHS GPH summary (T-score)	299	0.80	294	0.84
MSIS-29 physical impact	357	-0.86	296	-0.89
MSWS-12	334	-0.91	–	–
FAMS mobility (total score)	–	–	295	0.85
FSS	532	-0.56	–	–
MFIS (physical)	–	–	296	-0.84

PROMIS PF (MS) 15a showed moderate-strong correlations with related PRO measures (Spearman's rho, range: ±0.5 to ±0.9), supporting convergence validity

EDSS, Expanded Disability Status Scale; **FAMS**, Functional Assessment Of Multiple Sclerosis; **FSS**, Fatigue Severity Scale; **GHS**, PROMIS Global Health Scale; **GPH**, Global Physical Health Component; **MFIS**, Modified Fatigue Impact Scale; **MSIS**, Multiple Sclerosis Impact Scale; **MSWS**, Multiple Sclerosis Walking Scale; **PRO**, patient-reported outcomes

Results 5/5: Psychometric analyses – known groups validity

Table 4. ANOVA test of PROMIS PF (MS) T-scores across patient groups

T-score differences across clinically-distinct patient groups, e.g. according to physical health and other criteria, were consistent with *a priori* expectations

	UK sample (n=558)				US sample (n=296)			
	N	**Mean (SE)**	**F-statistic**	**p-value**	**N**	**Mean (SE)**	**F-statistic**	**p-value**
EDSS score							50.36	p<0.001
Mild (0 to 4.0)	–	–			202	46.47 (0.72)		
Severe (4.5-6.5)	–	–			37	34.37 (0.71)		
Web EDSS score			699.23	p<0.001			166.11	p<0.001
Mild (0 to 4.0)	247	46.98 (0.56)			202	49.03 (0.64)		
Severe (4.5-6.5)	311	31.10 (0.30)			94	35.74 (0.64)		
GHS global03 (physical health)			83.01	p<0.001			85.47	p<0.001
Fair/poor (1,2)	192	32.14 (0.46)			96	37.90 (0.71)		
Excellent/very good/good (3,4,5)	172	44.72 (0.80)			198	48.31 (0.7)		
GHS global01 (general health)			40.49	p<0.001			49.04	p<0.001
Fair/poor (1,2)	142	32.33 (0.58)			59	37.01 (0.84)		
Excellent/very good/good (3,4,5)	219	41.89 (0.74)			237	46.76 (0.66)		
GHS global08r (fatigue)			42.62	p<0.001			67.37	p<0.001
Severe/very severe (1,2)	100	32.31 (0.73)			74	37.11 (0.72)		
None/mild/moderate (3,4,5)	264	40.27 (0.67)			222	47.38 (0.68)		
GHS GPH summary (T-score)			14.19	p < 0.001			188.95	p<0.001
<42.5	220	32.00 (0.39)			98	35.81 (0.51)		
≥42.5	144	47.38 (0.52)			196	49.46 (0.65)		
MSWS-12 (scale to 100)			392.77	p<0.001				
<25	162	50.26 (0.61)			–	–		
25 to <50	79	39.54 (0.53)			–	–		
≥50	164	31.63 (0.33)			–	–		
FAMS total score (mobility)							242.48	p<0.001
≤15	–	–			89	34.65 (0.49)		
16 through 22	–	–			77	42.09 (0.71)		
>22	–	–			129	53.52 (0.65)		
FSS scores			186.25	p<0.001				
<36	127	47.60 (1.01)			–	–		
≥36	411	35.02 (0.41)			–	–		
MS phenotype			87.7	p<0.001			0.00409	0.94926
RRMS(1)	374	41.75 (0.55)			280	45.14 (0.61)		
PPMS(2)	54	31.82 (0.84)			7	41.88 (5.29)		
SPMS(3)	130	30.32 (0.48)			9	37.01 (3.14)		

EDSS, Expanded Disability Status Scale; **FAMS**, Functional Assessment Of Multiple Sclerosis; **FSS**, Fatigue Severity Scale; **GHS**, PROMIS Global Health Scale; **GPH**, Global Physical Health Component; **MFIS**, Modified Fatigue Impact Scale; **MS**, multiple sclerosis; **MSIS**, Multiple Sclerosis Impact Scale; **MSWS**, Multiple Sclerosis Walking Scale; **PPMS**, primary progressive MS; **RRMS**, relapsing-remitting MS; **SPMS**, secondary progressive MS

Conclusions

A new PROMIS physical function short form for use in multiple sclerosis derived based on direct input from people with MS and clinical experts and validated in two observational studies is now available

- **The mixed-methods approach employed in this research, including the direct involvement of patients and clinicians ensured that the content of the PROMIS PF (MS) 15a is comprehensive and relevant for people with MS.**

- **Results from validation studies showed that the PROMIS PF (MS)15 is a reliable and valid measure of physical function – these findings were consistent across the UK and US populations**

- *A score interpretation guide has been developed to aid the integration of PROMIS scores into clinical decision-making **and** facilitate clinician–patient communication – please use QR code to download*

Please see our other poster at MS Virtual 2020: 8th Joint ACTRIMS–ECTRIMS Meeting
The interpretation and clinical application of the PROMIS® SF v1.0 - Fatigue (MS) 8b: a PROMIS short form for assessing fatigue in multiple sclerosis – Poster P1061

Acknowledgments

MID, minimal important difference

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