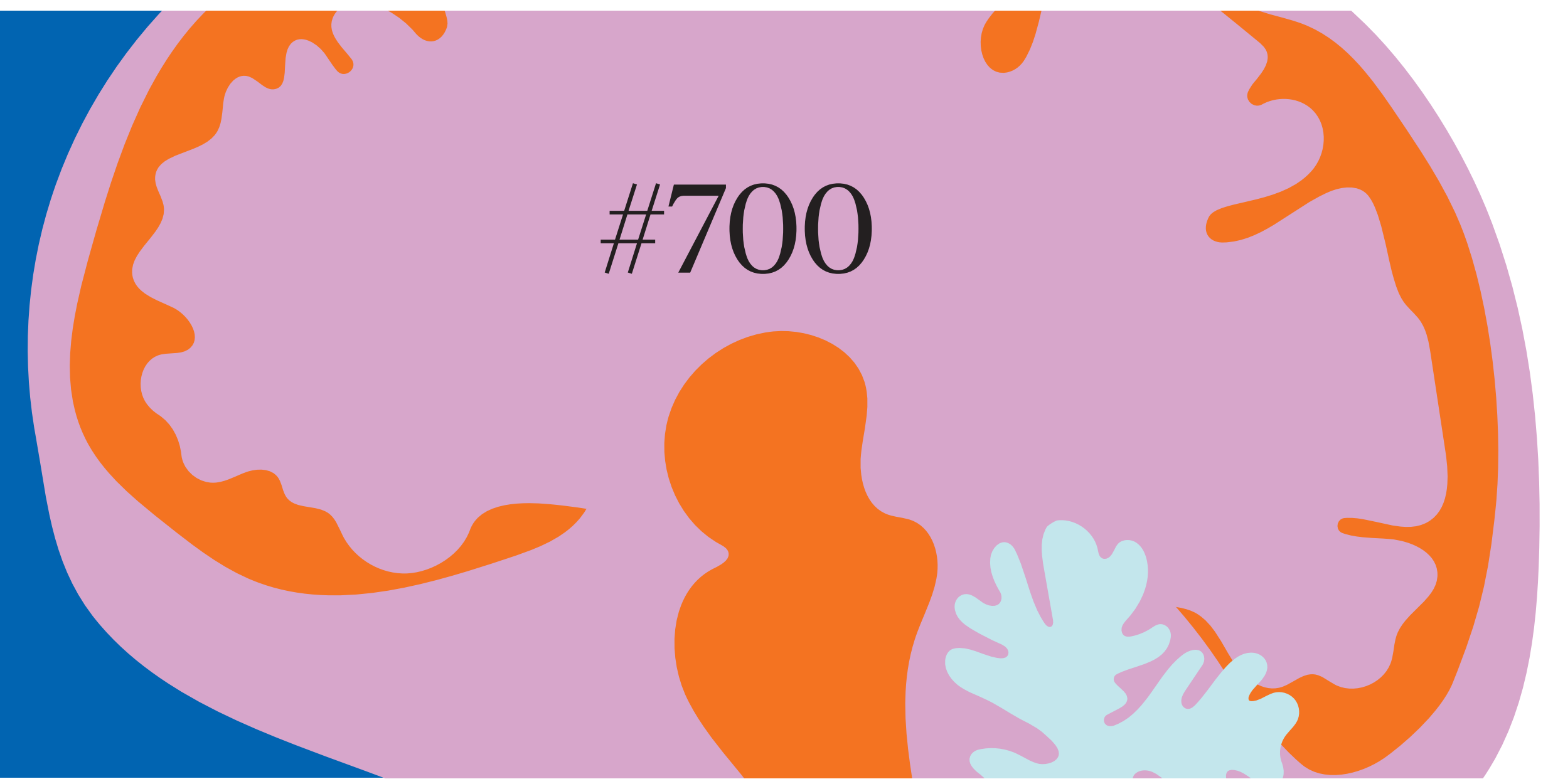


Huntington's Disease Everyday Functioning – Short Form (Hi-DEF-SF) Scale: Validation Analyses Results

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Background

- Cognitive impairment in Huntington's disease (HD) is a key driver of functional impairment from the early stages of HD and is characterized by difficulties in higher-order cognitive tasks such as multi-tasking, organizing thoughts, planning, and decision making.^{1,2}
- The HD Everyday Functioning (Hi-DEF) scale is a novel, 40-item, patient-reported outcome (PRO) measure designed to assess the impact of cognitive symptoms. Previous analyses have demonstrated that the Hi-DEF scale is a valid and reliable measure of cognitive functioning in HD.³⁻⁶
- A short form of the scale was developed to enable ease of use in instances where using the full 40-item measure may not be feasible, or where less sensitive but more frequent administrations may be needed to track changes in functioning over time.

Objective

- To describe the development and validation of the Hi-DEF short form (Hi-DEF-SF) scale.

Methods

- The Hi-DEF-SF scale was developed by selecting a subset of items from the full 40-item Hi-DEF scale. Item selection for the Hi-DEF-SF scale was guided by comparing item locations (generated through Rasch measurement theory [RMT] analysis) vs. patient status (defined by five core Cambridge Neurological Test Assessment Battery [CANTAB] test scores and the Unified HD Rating Scale Total Functioning Capacity [TFC]). Items were selected to provide generalizability across tasks spanning the full range of the cognitive impairment scale.
- Psychometric properties of four different versions (i.e. item-combinations) of Hi-DEF-SF were analyzed in a non-interventional study using RMT and Classical Test Theory (CTT) analyses, and a final decision on which items to include was made by taking into account the relevance of the selected items across participants.
- The Hi-DEF-SF scale was scored using a crosswalk approach, which provides an equivalent Hi-DEF full scale total score for the raw score derived from the short-form scale.

RMT analysis evaluates the alignment between the study population and items, and the proposed scale

1 | Scale-to-sample targeting analysis

- Targeting** assesses relative distribution of patient scores and item ranges; if well matched, this indicates potential for precise measurement and ability to detect clinical changes
- Scale coverage** indicates whether the scale has the ability to measure different levels of executive functioning
- Reliability**, measured as Person Separation Index, expresses the ratio of the estimated true variance in the participant measures and their total variance

2 | Measurement continuum analysis

- Item thresholds** assess whether the response categories (i.e. no difficulty, a little difficulty, etc.) categorize individual responses in an ordered fashion. Ordered thresholds indicate that response options measure distinct categories
- Item fit** assesses whether the items converge on a single measurement construct
- Item dependency** assesses whether the response to one item biases the response to another

CTT is a traditional quantitative approach to testing the reliability and validity of a scale based on its items

1 | Reliability (internal consistency)

- Assesses the extent to which items across the scale measure the same concept. The Cronbach's α threshold for reliability is ≥ 0.7

2 | Validity

- Assesses alignment between Hi-DEF scores and scores produced by other instruments

Results

PARTICIPANT CHARACTERISTICS

- Participants (N=151) in the validation study had a mean age of 47 years (SD: ± 12). In total, 59% were women, 93% were White, the median TFC score was 12 (range: 8–13), and huntingtin cytosine-adenine-guanine (HTT CAG) repeat was in the range 39–55.

SELECTING SHORT-FORM SCALE ITEMS

- In selecting items from the full scale for inclusion in the Hi-DEF-SF, Work and Driving subscales were excluded. This was to provide maximum generalizability of the short-form scale across all people with HD, as driving and work status may vary across individuals. Items were selected from the Home and Communication subscales as the tasks/activities described under these subscales are applicable for all individuals.
- Amongst the four Hi-DEF-SF versions tested, the version that demonstrated the best psychometric properties was chosen. This included the seven items shown in **FIGURE 1**.

FIGURE 1: HI-DEF ITEMS AND DOMAINS COVERED BY HI-DEF-SF

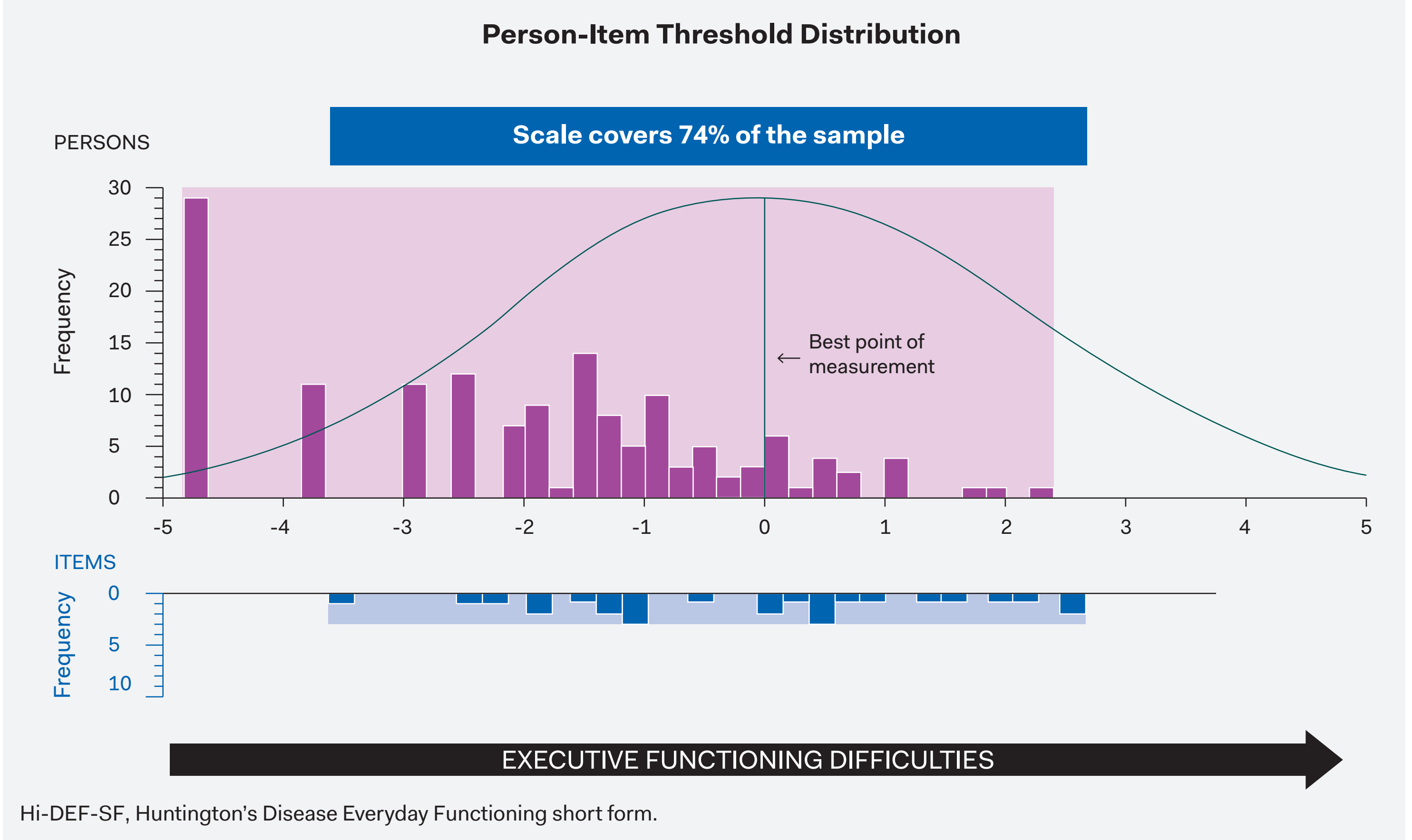
		Full 40-item Hi-DEF scale Items and domains	Hi-DEF short form
HOME	1	Completing a multi-step activity/task	1
	2	Starting a planned activity/task	
	3	Switching back and forth between two different activities	2
	4	Restarting an activity or task after interruption	
	5	Learning how to do a new activity/task	
	6	Following a written story	3
	7	Following a recipe	
	8	Following spoken instructions	4
	9	Acting on a written list of tasks	5
	10	Understanding e-mails	
	11	Completing logic puzzles	
	12	Filling out forms without mistakes	
	13	Doing basic math in your head	
	14	Managing day-to-day finances without mistakes	
	15	Responding to unexpected situations	
WORK	16 to 26	Not included	
DRIVING	27 to 34	Not included	
COMMUNICATION	35	Conveying thoughts in group conversations	6
	36	Conveying thoughts in writing	7
	37	Managing emotions in stressful situations	
	38	Participating in family activities	
	39	Participating in social interactions	
	40	Participating in recreational activities	

Hi-DEF, Huntington's Disease Everyday Functioning; Hi-DEF-SF, Huntington's Disease Everyday Functioning short form.

RMT ANALYSIS

- Overall, Hi-DEF-SF demonstrated good reliability (Person Separation Index: 0.79/0.80).
- Sample coverage was good (74%), demonstrating broad ability to capture different levels of impact of HD despite the Hi-DEF-SF scale having fewer items than the full Hi-DEF scale (**FIGURE 2**).
- The response options measured distinct categories for all seven items with no dependency or item misfit.

FIGURE 2: HI-DEF-SF SCALE TARGETING AND RELIABILITY



CTT ANALYSIS

- The Hi-DEF-SF scale demonstrated high internal consistency (Cronbach's α : 0.91).
- Consistent with CTT results previously demonstrated for the Hi-DEF full scale,⁹ correlations between the short-form scale and TFC ($r=-0.51$) and HD-PRO TRIAD ($r=0.85$) were moderate-to-high, and correlations with key CANTAB test variables ($r=0.08-0.32$) were low-to-moderate (**TABLE 1**).
- Correlations between the Hi-DEF-SF scale and the Hi-DEF full scale were high ($r=0.95$), and consistent across all subscales ($r \geq 0.72$; **TABLE 1**).

TABLE 1: HI-DEF-SF CONVERGENT VALIDITY WITH KNOWN PROS AND FUNCTIONAL MEASURES AND THE 40-ITEM HI-DEF SCALE

	Hi-DEF-SF	Spearman's rank correlation coefficient
HD-PRO-TRIAD Total	0.85	High (>0.7)
HD-PRO-TRIAD Cognitive	0.89	Moderate (0.3-0.7)
HD-PRO-TRIAD Emotional	0.60	Low (<0.3)
HD-PRO-TRIAD Motor	0.55	
TFC	-0.51	
CANTAB key variables:		
PAL	-0.22	
ERT	-0.24	
OTS	0.08	
SWM (4-6-8)	0.31	
SWM (4 box)	0.22	
SWM (6 box)	0.18	
SWM (8 box)	0.32	
SSP	-0.19	
Hi-DEF scale		
Hi-DEF 40-item total	0.95	
Hi-DEF Home	0.95	
Hi-DEF Work	0.85	
Hi-DEF Driving	0.72	
Hi-DEF Communication	0.81	

PAL: first attempt memory score (high score=better performance). ERT: total hits (high score=better performance). OTS: mean choices to correct (low score=better performance). SWM: total errors (low score=better performance). SSP: forward span length (high score=better performance).

CANTAB, Cambridge Neurological Test Assessment Battery; ERT, Emotion Recognition Task; HD, Huntington's disease; Hi-DEF, Huntington's Disease Everyday Functioning; Hi-DEF-SF, Huntington's Disease Everyday Functioning short form; OTS, One Touch Stockings of Cambridge; PAL, Paired Associates Learning; PRO, patient-reported outcome; SSP, Spatial Span SWM, Spatial Working Memory; TFC, total functional capacity.

Conclusions

- The Hi-DEF-SF scale demonstrated strong reliability, construct validity, and targeting that is consistent with the full 40-item Hi-DEF scale and showed potential for use to capture the impact of cognitive impairment on functioning in participants with early HD.
- The short-form scale offers another option to clinicians, researchers, and patients to measure functioning associated with cognition when a seven-item measure is preferable to using the full scale.
- Further validation of the Hi-DEF-SF in HD patients across all stages is needed to confirm the findings and utility of the measure. The Hi-DEF-SF is currently being used as an outcome measure in an ongoing real-world HD study exploring the impact of HD across multiple aspects of patients' lives (Poster #705).

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