

## Article

# HD-PRO-TRIAD™ Validation: A Patient-reported Instrument for the Symptom Triad of Huntington's Disease

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## Abstract

**Background:** Few valid, disease-specific measures of health-related quality of life (HRQOL) capture the spectrum of symptoms associated with Huntington's disease (HD). The HD-PRO-TRIAD™ is a new, HD-specific, patient-reported outcome (PRO) instrument of the HD symptom triad (cognitive decline, emotional/behavioral dyscontrol, and motor dysfunction) designed for clinical research and practice. The objective was to validate the HD-PRO-TRIAD™ through a cross-sectional sample of individuals with HD and caregivers.

**Methods:** Development of the HD-PRO-TRIAD™ has been described elsewhere. A total of 132 individuals with HD and 40 HD caregivers, comprising 29 dyads, participated in the cross-sectional psychometric validation of this instrument. Participants provided responses to the HD-PRO-TRIAD™ and other HRQOL and disease severity instruments (EuroQOL 5D, Short Form 12, Neuro-QOL Item Banks, PROMIS Global Health, and self-reported Unified Huntington's Disease Rating Scale Total Functional Capacity and Independence Scales). Internal consistency, construct validity, and patient-caregiver proxy consistency were evaluated.

**Results:** Internal consistency of the three domains and overall HD-PRO-TRIAD™ instrument was supported by Cronbach's alpha values  $\geq 0.94$ . Construct validity was supported by significant correlations between HD-PRO-TRIAD™ domain scores and other measures of the same domains (e.g., significant positive correlations between HD-PRO-TRIAD™ Anxiety with Neuro-QOL Anxiety), as well as slightly weaker but still strong correlations with other HRQOL instruments (e.g., HD-PRO-TRIAD™ Anxiety and UHDRS Independence; all  $p < 0.01$ ). Consistency between patient self-report and caregiver proxy report was supported by an intra-class correlation coefficient  $\geq 0.92$  for all three domains and the overall instrument.

**Discussion:** These data indicate that HD-PRO-TRIAD™ is a reliable and valid HRQOL instrument that captures the typical triad of HD symptoms.

**Keywords:** Huntington's disease, quality-of-life scale, psychometric validation, patient-reported outcome, health-related quality of life, HD-PRO-TRIAD™

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## Introduction

Huntington's disease (HD) is an autosomal-dominant neurodegenerative disease caused by a CAG trinucleotide repeat expansion in the huntingtin gene on the short side of chromosome 4. HD is an insidious, progressive disorder that causes deficits in the symptom triad of cognitive, behavioral, and motor functioning.<sup>1,2</sup> Symptoms gradually appear and worsen over time, leading to a clinical diagnosis of HD (currently based on unequivocal motor symptoms) often when affected individuals reach their mid-40s. Death occurs approximately 20 years after clinical diagnosis.<sup>1</sup> Coping with the progressive symptoms of the disease obviously affects an individual's health-related quality of life (HRQOL), a multidimensional construct used to determine the impacts of HD and its symptoms on emotional, cognitive, social, and physical well-being.<sup>3</sup>

Several qualitative studies<sup>4-7</sup> have examined HRQOL in individuals with HD by employing either semi-structured interviews or focus groups. Three semi-structured interview studies identified that concerns with physical, emotional, cognitive, social, and day-to-day functioning (including driving ability, interactions with others, household chores, conversing on the telephone, shopping, managing finances, ability to work, and cooking) had a significant impact on HRQOL.<sup>4-6</sup> Similarly, a focus group study provided support for five general HRQOL themes: emotional health (anxiety/fear, stigma, anger, psychiatric/behavioral changes, positive psychological function, resilience, and depression); social participation (interpersonal relationships, leisure, vocation, and independence/autonomy); physical/mental health (gene testing, involuntary movements/chorea, mobility/ambulation, speech and swallowing difficulties, medications, health promotion, upper extremities, and weight loss); cognitive health (learning/memory, executive function, and communication/comprehension); and end-of-life issues (planning, interactions with others with HD, forward comparison).<sup>7</sup> Collectively, these studies highlight the multifaceted areas of HRQOL affected in individuals with HD.

Many quantitative studies have also examined generic (not HD-specific) measures of HRQOL in HD, most using a single instrument.<sup>5,8-16</sup> However, generic HRQOL instruments do not fully capture the triad of symptoms characteristic of HD, nor are they sensitive to change over time, which requires a more sensitive HRQOL assessment in this population.

To address these shortcomings, two instruments have been recently developed that target HD-specific HRQOL issues, the Huntington Quality of Life Instrument (H-QoL-I)<sup>17</sup> and the Huntington's Disease Health-Related Quality of Life questionnaire (HDQoL).<sup>17,18</sup> The H-QoL-I<sup>17</sup> is an 11-item self-report instrument examining three HRQOL dimensions: Motor Functioning, Psychology, and Socializing. The HDQoL<sup>18</sup> is a 40-item self-report instrument designed to evaluate six subdomains: Cognitive, Hopes and Worries, Services, Physical and Functional, Mood State, and Self and Vitality. The initial publication for the H-QoL-I indicates it has acceptable internal consistency (Cronbach's alpha > 0.84), as well as satisfactory construct, discriminant, and external validity.<sup>17</sup> Similarly, the initial publication on the HDQoL indicates high reliability, stability, and internal consistency,

good unidimensionality, and good construct validity.<sup>18</sup> However, these findings have not been replicated in independent samples, and neither instrument has been examined over time. The H-QoL-I is also limited by its narrow scope, as it only evaluates two of the three symptom domains characteristic of HD (motor and behavioral/emotional). Although the HDQoL covers a wide range of HRQOL items, none are chorea-specific. The HDQoL also takes approximately 20 minutes to complete, which is acceptable in a research context, but might be difficult to administer in a clinical setting.

The purpose of the current study was to develop and validate a new instrument of HRQOL that 1) is specific to HD, 2) assesses fully the triad of symptoms characteristic of HD, and 3) can be administered in a clinical or research setting.

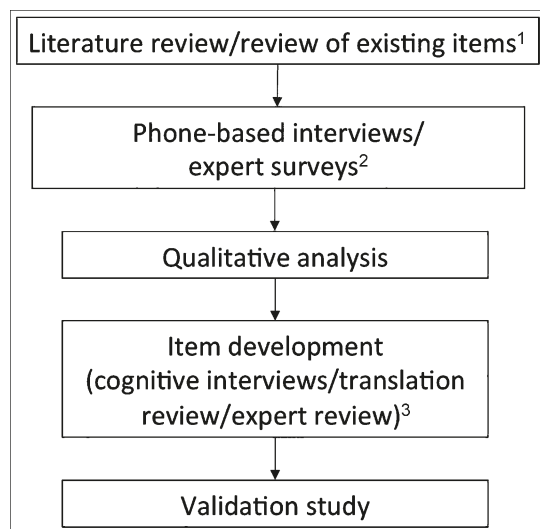
## Methods

The development of the framework and content for the new HD-specific HRQOL instrument (HD-PRO-TRIAD™) has been fully described elsewhere.<sup>4</sup> First, a literature review was conducted to identify the triad of symptoms relevant to an HD-specific HRQOL instrument. Individual phone-based interviews with individuals with HD and caregivers, as well as an expert survey, were then conducted to identify HRQOL issues important to individuals with HD and develop items for a preliminary version of HD-PRO-TRIAD™. To capitalize on advances from recent federally funded measurement science efforts, we received permission to examine and include relevant item content from Neuro-QOL,<sup>19</sup> Traumatic Brain Injury-QOL,<sup>20,21</sup> HDQLIFE™,<sup>7</sup> and the Functional Assessment of Chronic Illness Therapy (FACIT)<sup>22</sup> measurement systems. Specifically, we considered items from Neuro-QOL's Cognition and Emotional and Behavioral Dyscontrol item banks,<sup>23</sup> and from Traumatic Brain Injury-QOL.<sup>20,21</sup> Motor-related items were considered from the HDQLIFE item banks<sup>7</sup> and from the FACIT<sup>22</sup> system. After selecting and content matching available items with patient, caregiver, and provider perspectives, we drafted a preliminary instrument that was then cognitively tested in 10 individuals with HD.<sup>4</sup> The resulting HD-PRO-TRIAD™ (Version 1), consisting of 47 items, was administered to 172 participants (132 individuals with HD and 40 caregivers) for psychometric testing. These data were used to determine internal consistency, construct validity with existing HRQOL measures, and determine consistency between individuals with HD and their caregivers of HD-PRO-TRIAD™.

This process is summarized in Figure 1.

### Individual phone-based interviews with HD patients and caregivers

We conducted individual, semi-structured phone-based interviews with 15 individuals with HD and 16 HD caregivers. Six pairs of participants were patient-caregiver dyads. Audio recordings and notes were taken during individual interviews, which were transcribed and analyzed via NVivo 9.0 (QSR International Pty Ltd, Doncaster, Australia), a qualitative data analysis and management software package. Detailed results from the phone-based interviews are published in Victorson et al.<sup>4</sup> Content of the individual phone-based



**Figure 1. Development Framework and Process for HD-PRO-TRIAD™.** <sup>1</sup>To identify the triad of symptoms relevant to an HD-specific HRQOL instrument; <sup>2</sup>To identify HRQOL issues important to individuals with HD; <sup>3</sup>Item development is an iterative process that includes the listed components. HD, Huntington's disease; HRQOL, Health-related quality of life.

interviews was synthesized into a hierarchical domain framework, which was used to identify HD-specific HRQOL themes and dimensions. Items were developed to reflect three domains of HRQOL: cognition, emotional/behavioral, and motor functioning. This triad provided the basis for the item selection process.

#### HD-PRO-TRIAD™ content selection process

**Cognitive functioning items.** The phone-based interviews indicated that both individuals with HD and their caregivers expressed concerns with cognition, including difficulties with executive functioning, memory, and attention concentration. These concepts are captured by the Neuro-QOL Cognition item banks<sup>24</sup> and the TBI-QOL Cognition items.<sup>20,21</sup> Therefore, 31 Neuro-QOL Cognition items (13 Executive Function and 18 General Concerns) and 32 TBI-QOL items were included for consideration in the development of this measure.

**Emotional/behavioral functioning items.** The phone-based interviews also highlighted concerns with emotional/behavioral functioning including anger, depression, anxiety, and disinhibition, as well as concepts captured by the Emotional and Behavioral Dyscontrol item bank from the Neuro-QOL.<sup>24</sup> Therefore, all 18 Neuro-QOL Emotional and Behavioral Dyscontrol items were included for consideration in development of this domain.

**Motor functioning items.** Furthermore, interview data highlighted concerns with motor functioning, especially with regard to chorea. To this end, we maintained the linkage to an HD-specific extension of the Neuro-QOL system on motor functioning, which is also currently under development.<sup>25</sup> As such, we determined that the HDQLIFE chorea items would be considered for inclusion in this measure, in addition to other motor items from FACIT.<sup>22</sup>

**Reading level and translations reviews.** All items for the Neuro-QOL, TBI-QOL, and HDQLIFE were written at or below a fifth-grade level through the Lexile Framework™.<sup>26</sup> In addition, all Neuro-QOL, TBI-QOL, and HDQLIFE items have undergone translatability review to facilitate future translation of the final items into other languages, particularly Spanish. New items underwent forward and backward translation by two independent, native Spanish-speaking translation science experts from different countries of origin.

**Item review.** All items were reviewed by experts in HD, including physicians and nurse practitioners. Experts reviewed, revised, and removed items as appropriate. Items were selected for deletion if they were redundant, vague, or double-barreled, or if they were not representative of the HD triad. The item pool was narrowed to 47 items (14 Cognition, 14 Emotional and Behavioral Dyscontrol, 19 Motor Function) during this process.

Each item in HD-PRO-TRIAD™ was scored on a scale of 1–5, with greater scores indicating worse functioning or HRQOL on each domain. The total score for each domain was computed as a mean based on the sum of scores of item responses divided by the number of items answered. The possible maximum total score for each domain was therefore 5 if the patient answered 5 to all items. The HD-PRO-TRIAD™ total score was computed as the sum of the three domain total scores, with a possible maximum of 15.

#### HD-PRO-TRIAD™ (version 1) psychometric validation

**Participants.** Participants were recruited through an online panel testing company, OP4G (op4g.com), and through an exhibit/display table at the 2012 annual meeting of the Huntington's Disease Society of America (HDSA). Inclusion criteria were prior diagnosis of HD (for individuals with HD) or past or current role as a caregiver for someone diagnosed with HD (for caregivers); age ≥18 at the time of study participation; ability to actively participate in an online questionnaire; and ability to read, write, speak, and understand English. Participants completed the HD-PRO-TRIAD™ instrument and the HRQOL and disease severity tools described below. They accessed and completed the self-reported instruments independently online via the Assessment Center<sup>SM</sup> (an online data capture system). The institutional review board at Northwestern University approved this study.

**Concurrent and divergent validation measures.** The construct validity of HD-PRO-TRIAD™ was assessed against the following established external HRQOL instruments (all completed by the patients and caregivers).

**EuroQOL 5D.** The EuroQOL 5D (EQ-5D)<sup>27</sup> is a five-item, standardized, self-report instrument designed to evaluate general health status (mobility, self-care, usual activities, pain/discomfort, anxiety/depression). It was scored from 0 to 1, with greater scores representing better QOL.<sup>28</sup>

**Short Form 12.** The Short Form 12 (SF-12)<sup>29</sup> is a 12-item self-report instrument designed to evaluate HRQOL. Both the mental and

physical scales were assessed in this study. For each scale, the SF-12 was scored from 0 to 100, with greater scores indicating better QOL.

**Neuro-QOL Item Banks.** Neuro-QOL<sup>19</sup> is a patient-related outcome (PRO) measurement system designed to evaluate HRQOL in individuals with neurologic diseases. Five-item banks were administered from the Neuro-QOL: Anxiety, Depression, Ability to Participate in Social Roles, Lower Extremity Function, and Upper Extremity Function. Neuro-QOL item banks were administered as static short forms. All Neuro-QOL scales were scored such that a greater score represented more of the domain being measured. That is, greater scores for Anxiety and Depression represented worse QOL, while greater scores for Ability to Participate in Social Roles, Lower Extremity Function, and Upper Extremity Function represented better QOL. The T-score metric for all Neuro-QOL scales has a mean of 50 and standard deviation (SD) of 10.

**PROMIS Global Health.** Patient-Reported Outcomes Measurement Information System (PROMIS®)<sup>30,31</sup> is a PRO measurement system designed to evaluate HRQOL. The 10-item PROMIS Global Health instrument yields two summary scores — Physical Health and Mental Health. The PROMIS Global Health measures were scored according to the PROMIS scoring algorithm. The T-score metric for all PROMIS measures has a mean of 50 and SD of 10.

**Self-reported functional capacity.** The Unified Huntington's Disease Rating Scale (UHDRS) Total Functional Capacity (TFC) Scale, designed as a clinician-administered and rated scale,<sup>31</sup> was modified to capture self-reported functional capacity (Appendix 1). This modified self-report measure assessed functional capacity across five domains: Occupation, Finances, Domestic Chores, Activities of Daily Living (ADL), and Requirements for Unskilled or Skilled Care. Self-reported functional capacity was computed as a sum of the scores for the five domains (each ranging from 0 to 2 or 0 to 3), for a total score of 13, with greater scores indicating better functioning.

**Self-reported functional independence.** We modified the UHDRS Independence Scale (a clinician-rated scale) to be administered as a self-report measure designed to evaluate functional independence (Appendix 2).<sup>32</sup> The scoring criteria for clinicians provided the anchors for a 10-item scale assessing functional independence. Scores range from 1 to 10, with greater scores indicating lesser functional independence.

As referenced above, all items included in the HD-PRO-TRIAD were existing items selected from either the Neuro-QOL/PROMIS, TBI-QOL, or HDQLIFE measurement systems. Measures selected from PROMIS/Neuro-QOL for validation purposes did not include any overlap in items, as both measurement systems include multiple assessments across several different domains of functioning.

### Statistical analysis

HD-PRO-TRIAD™ and validation instruments, as well as socio-demographic and clinical characteristic questionnaires, were presented to participants online through Assessment Center<sup>SM</sup>. Descriptive

statistics were provided on socio-demographic and clinical characteristics for both the patient and caregiver cohorts. Descriptive statistics were calculated for HD-PRO-TRIAD™ and the validation instruments. Internal consistency of HD-PRO-TRIAD™ was evaluated using Cronbach's coefficient alpha, item-total correlations, and inter-item correlations. Construct validity (including convergent and divergent validity) was examined using Pearson correlation coefficients. We hypothesized that correlations between indices for similar constructs would be high (>0.70). That is, we expected that the HD-PRO-TRIAD™ Emotional/Behavioral Dysfunction and other measures of emotion such as Neuro-QOL Anxiety and Depression, PROMIS Global Mental Health, and SF-12 Mental Component would be highly correlated. Similarly, we anticipated we would observe high correlations between HD-PRO-TRIAD™ Motor Function and Neuro-QOL Lower Extremity Function and Upper Extremity Function, PROMIS Global Physical Health, and SF-12 Physical Component. We also anticipated HD-PRO-TRIAD™ Cognition would be highly correlated with measures of mental health, physical health, and social health (i.e., Neuro-QOL Ability to Participate in Social Roles). Intra-class correlation coefficients (ICCs) were computed to assess the degree of consistency between HD patient and caregiver proxy scores in the 29 HD patient-caregiver dyads.

### Results

The resulting HD-PRO-TRIAD™ (Version 1) is provided in Appendix 3 (Figures 2 and 3). The Cognition and Emotional and Behavioral Dysfunction domains consist of 14 items, and the Motor Function domain consists of 19 items. All items are rated 1 to 5. Each domain is scored separately as an average score of all items responded (1 to 5), and then added together for a total score. Total scores range from 3 (least affected) to 15 (most affected).

### Demographics and clinical characteristics

**HD patients.** A total of 132 individuals with HD and 40 HD caregivers (spanning 29 HD patient-caregiver dyads) participated (Table 2). One hundred and twenty-five of the HD individuals were recruited through OP4G, and seven were recruited at the 2012 HDSA annual meeting. Twenty-five caregivers were recruited through OP4G, and 15 were recruited at the HDSA meeting. Demographics did not vary notably between recruitment sources. Sixty-five percent of individuals with HD reported a positive gene test, with an average self-reported CAG repeat length of 44. Average self-reported time since HD diagnosis was 5 years, with individuals reporting the presence of motor symptoms for an average of 6 years. Most individuals with HD reported that a parent had HD (55% paternal and 23% maternal). Most individuals self-reported their health statuses as good (37%), very good (19%), or excellent (5%).

**Caregivers.** The 40 caregivers examined had an average age of 44 years and were primarily white and female (Table 1). Slightly more than 50% of caregivers were caring for spouses or partners. The remaining caregivers were caring for other family members (28%), HD

**Table 1.** Demographic Characteristics of Individuals with HD and Caregivers, and Clinical Characteristics of Individuals with HD as Reported by Individuals with HD or Their Caregivers

	HD Individuals N=132	Caregivers N=40
<b>Demographic characteristics</b>		
Age, mean (SD), years	40.8 (11.4)	43.9 (10.3)
Female, n (%)	63 (48%)	25 (63%)
<b>Language, n (%)</b>		
English speaking	130 (98%)	—
Spanish speaking	2 (2%)	—
Hispanic, n (%)	14 (11%)	4 (10%)
<b>Race, n (%)</b>		
Asian	7 (5%)	5 (13%)
Black	17 (13%)	6 (15%)
White	104 (79%)	27 (68%)
Other <sup>1</sup>	4 (3%)	2 (5%)
<b>Education, n (%)</b>		
Less than high school	1 (1%)	0 (0%)
High school	22 (17%)	2 (5%)
Partial college	30 (23%)	10 (25%)
College	53 (40%)	11 (28%)
Graduate degree	26 (20%)	17 (43%)
<b>Marital status, n (%)</b>		
Single	29 (22%)	3 (8%)
Married/Partnered	79 (60%)	35 (88%)
Divorced/Widowed	24 (18%)	2 (5%)
<b>Family income, n (%)</b>		
<\$5,000	2 (2%)	0 (0%)
\$5,000 to \$9,999	5 (4%)	0 (0%)
\$10,000 to \$19,999	8 (6%)	0 (0%)
\$20,000 to \$39,999	24 (18%)	5 (13%)
\$40,000 to \$74,999	41 (31%)	19 (48%)
\$75,000 to \$99,999	32 (24%)	7 (18%)
≥\$100,000	18 (14%)	8 (20%)

**Table 1.** Continued

	HD Individuals N=132	Caregivers N=40
Unknown	2 (2%)	1 (3%)
Currently employed, n (%)	61 (46%)	—
On disability, n (%)	62 (47%)	—
<b>Employed in same work as before HD, n (% of those currently employed)</b>		
Yes	44/61 (72%)	—
No	11/61 (18%)	—
Not applicable/unknown	6/61 (10%)	—
<b>Clinical Characteristics of HD individuals as reported by HD individuals and by caregivers</b>		
Gene testing, n (%)	86 (65%)	28 (70%)
CAG repeat length, mean (SD)	43.6 (4.4)	43.9 (4.9)
<b>HD status, mean (SD)</b>		
Years since HD diagnosis	4.8 (3.9)	—
Years with motor symptoms	5.7 (5.6)	—
Years with any symptoms	5.0 (3.5)	5.7 (4.3)
Physician confirmed showing of HD signs, n (%)	106 (80%)	—
<b>Family HD history, n (%)</b>		
Father with HD	72 (55%)	20 (50%)
Mother with HD	31 (23%)	14 (35%)
Unknown	29 (22%)	6 (15%)

<sup>1</sup>Other races include American Indian, Hawaiian Pacific Islander, and biraciality.  
 HD: Huntington's disease; SD, standard deviation.  
 Dashes denote that the characteristics were not measured in caregivers.

**Table 2.** Mean Scores on HD-PRO-TRIAD™ Instrument and Other Instruments by Patient and Caregiver Samples

Metric	HD individuals– self-reported mean (SD)	Caregiver-reported mean (SD)	ICC <sup>1</sup> (95% CI)
	N=132	N=40	N=29
<b>Cognition</b>			
HD-PRO-TRIAD™ Cognition <sup>2</sup>	3.2 (1.1)	3.3 (1.2)	0.92 (0.84, 0.96)
<b>Mental health</b>			
HD-PRO-TRIAD™ Emotional/Behavioral Dyscontrol <sup>2</sup>	2.7 (1.0)	2.4 (0.9)	0.93 (0.86, 0.97)
Neuro-QOL Anxiety <sup>3</sup>	57.5 (8.0)	54.9 (7.6)	0.87 (0.74, 0.94)
Neuro-QOL Depression <sup>3</sup>	54.1 (8.2)	51.6 (8.2)	0.86 (0.73, 0.93)
PROMIS Global Mental Health <sup>4</sup>	42.6 (9.7)	44.1 (9.7)	0.86 (0.73, 0.93)
SF-12 Mental Component <sup>5</sup>	41.3 (10.5)	43.6 (11.5)	0.83 (0.68, 0.91)
<b>Physical Health</b>			
HD-PRO-TRIAD™ Motor Function <sup>2</sup>	2.9 (1.0)	2.8 (1.1)	0.94 (0.88, 0.97)
Neuro-QOL Lower Extremity Function <sup>3</sup>	38.3 (10.9)	38.0 (11.2)	0.94 (0.88, 0.97)
Neuro-QOL Upper Extremity Function <sup>3</sup>	33.0 (11.6)	35.0 (14.3)	0.88 (0.77, 0.94)
PROMIS Global Physical Health <sup>4</sup>	39.0 (10.5)	41.1 (11.3)	0.90 (0.80, 0.95)
SF-12 Physical Component <sup>5</sup>	37.7 (10.8)	38.8 (12.5)	0.94 (0.88, 0.97)
<b>Social Health</b>			
Neuro-QOL Ability to Participate in Social Roles <sup>3</sup>	42.2 (7.4)	41.0 (8.8)	0.87 (0.75, 0.94)
<b>Overall HRQOL</b>			
HD-PRO-TRIAD™ Total <sup>2</sup>	8.8 (2.7)	8.5 (2.8)	0.95 (0.90, 0.98)
EQ-5D <sup>6</sup>	0.6 (0.3)	0.6 (0.3)	0.88 (0.77, 0.94)
<b>Index of HD severity</b>			
UHDRS TFC <sup>7</sup>	6.8 (4.3)	5.4 (4.2)	0.96 (0.92, 0.98)
UHDRS Independence <sup>8</sup>	3.5 (2.3)	3.8 (2.2)	0.71 (0.48, 0.85)

<sup>1</sup>Intra-class correlation between HD individuals–self-reported (first column) and caregiver-reported (second column) scores.

<sup>2</sup>HD-PRO-TRIAD™ Cognition, Emotional and Behavioral Dyscontrol, and Motor Function scores range from 1–5, with greater scores representing worse functionality. HD-PRO-TRIAD™ Total scores range from 3–15, with greater scores representing worse functionality.

<sup>3</sup>Neuro-QOL scores were converted to T-scores based on a T-score metric, with a mean of 50 and SD of 10. For Neuro-QOL Anxiety and Depression, a greater T-score represents worse functionality, whereas in Neuro-QOL, Lower Extremity Function, Upper Extremity Function and Ability to Participate in Social Roles, a greater T-score represents better functionality.

<sup>4</sup>PROMIS Global Mental Health and Physical Health scores were converted to T-scores based on a T-score metric, with a mean of 50 and SD of 10, with greater T-scores representing better functionality.

<sup>5</sup>SF-12 Mental and Physical score range is 0–100, with greater scores representing better functionality.

<sup>6</sup>EQ-5D score range is 0–1, with greater scores representing better functionality.

<sup>7</sup>UHDRS TFC score range is 0–13, with greater scores representing better functionality.

<sup>8</sup>UHDRS Independence score range is 1–10, with greater scores representing worse functionality.

CI, confidence interval; ICC, intra-class correlation; SD, standard deviation.

**Table 3.** Cronbach's Alpha, Inter-Item, and Item-to-Total Correlations for HD-PRO-TRIAD™ Domain and Total Scores from Individuals with HD and Caregivers

	<b>Cronbach's Alpha</b>	<b>Inter-Item Correlations (Range)</b>	<b>Item-to-Total Correlations (Range)</b>
<b>Patient sample (N=132)</b>			
<b>HD-PRO-TRIAD™ Domain</b>			
Total	0.98	(0.14, 0.88)	(0.54, 0.87)
Cognition	0.97	(0.60, 0.88)	(0.78, 0.90)
Emotional/Behavioral Dyscontrol	0.96	(0.42, 0.87)	(0.66, 0.86)
Motor Function	0.98	(0.40, 0.85)	(0.64, 0.90)
<b>Caregiver sample (N=40)</b>			
<b>HD-PRO-TRIAD™ Domain</b>			
Total	0.98	(-0.14, 0.90)	(0.43, 0.90)
Cognition	0.98	(0.66, 0.89)	(0.84, 0.92)
Emotional/Behavioral Dyscontrol	0.95	(0.24, 0.84)	(0.63, 0.89)
Motor Function	0.98	(0.38, 0.90)	(0.65, 0.94)

individuals in a nursing environment (13%), or friends (8%). Caregivers had known their care recipients for an average of 19.8 years (SD of 13.1), and had been in the role of caregiver for an average of 5.0 years (SD of 5.1).

### Descriptive statistics

The mean HD-PRO-TRIAD™ scores for individuals with HD based on patient and caregiver reports were similar. Based on patient reports, the mean scores for the three Cognition, Emotional and Behavioral Dyscontrol, and Motor Function domains were 3.2 (range, 1.0–5.0; SD, 1.1), 2.7 (range, 1.0–5.0; SD, 1.0), and 2.9 (range, 1.0–4.8; SD, 1.0), respectively. The total mean score for the overall HD-PRO-TRIAD™ instrument was 8.8 (Table 2). Descriptive statistics for the other HRQOL instruments are also presented in Table 2. Scores indicated that individuals with HD reported emotional functioning at degrees comparable to the general population (e.g., Neuro-QOL and PROMIS emotional scores were within 1 SD of the population mean of 50). However, degrees of physical functioning were lower than that of the general population (as indicated by all but one physical functioning score  $\geq 1$  SD below the mean).

### Internal consistency

Internal consistency was excellent for all domains and the overall HD-PRO-TRIAD™ for both individuals with HD and caregivers (all Cronbach's alphas  $>0.95$ ). In addition, item-total correlations ranged

from 0.54 to 0.90 for individuals with HD, and 0.43 to 0.94 for caregivers. Likewise, inter-item correlations ranged from 0.14 to 0.88 for individuals with HD, and  $-0.14$  to 0.90 for caregivers (Table 3).

### Convergent and divergent validity

Strong evidence supports both convergent and divergent validity for the three domains, as well as the overall HD-PRO-TRIAD™ instrument. In general, correlations were moderate to strong in the HD patient sample (Table 4). The magnitudes of most correlation coefficients for the relationships between HD-PRO-TRIAD™ scores and other HRQOL instruments were greater than 0.70. Moreover, consistent with our hypotheses, correlations for HD-PRO-TRIAD™ Emotional/Behavioral Dysfunction were greatest with other measures of emotion, while correlations between HD-PRO-TRIAD™ Motor Function and other indices of physical function were substantial. For Cognition, correlations with other general HRQOL and disease severity indices were moderate to strong.

### Consistency between caregiver proxy and HD patient self-report measures

Analysis of the data collected from the 29 HD patient-caregiver dyads indicates substantial consistency between caregiver proxy and HD patient self-reports. All intra-class correlations for the three domains and the overall HD-PRO-TRIAD™ instrument were  $>0.90$ .

**Table 4.** Pearson's Correlations Between HD-PRO-TRIAD™ and Other Instruments in Patient Sample (N=132)<sup>1</sup>

Metric	HD-PRO-TRIAD™			
	Total	Cognition	Emotional/Behavioral Dyscontrol	Motor Function
<b>Mental Health</b>				
Neuro-QOL Anxiety	0.70	0.62	0.75	0.51
Neuro-QOL Depression	0.71	0.61	0.75	0.54
PROMIS Global Mental Health <sup>2</sup>	0.77	0.72	0.73	0.62
SF-12 Mental Component <sup>2</sup>	0.61	0.61	0.53	0.51
<b>Physical Health</b>				
Neuro-QOL Lower Extremity Function <sup>2</sup>	0.73	0.74	0.45	0.77
Neuro-QOL Upper Extremity Function <sup>2</sup>	0.74	0.73	0.44	0.81
PROMIS Global Physical Health <sup>2</sup>	0.82	0.83	0.57	0.80
SF-12 Physical Component <sup>2</sup>	0.76	0.77	0.47	0.79
<b>Social Health</b>				
Neuro-QOL Ability to Participate in Social Roles <sup>2</sup>	0.55	0.61	0.27	0.58
<b>Overall HRQOL</b>				
EQ-5D <sup>2</sup>	0.75	0.77	0.49	0.75
<b>Index of HD severity</b>				
UHDRS TFC <sup>2</sup>	0.72	0.77	0.40	0.76
UHDRS Independence	0.59	0.58	0.35	0.66

All  $p < 0.05$ .

<sup>1</sup>For HD-PRO-TRIAD™ (Total, Cognition, Emotional and Behavioral Dyscontrol and Motor Function), Neuro-QOL (Anxiety and Depression), and UHDRS Independence, greater scores represent worse functionality. For all other metrics (i.e., Neuro-QOL Lower Extremity Function, Upper Extremity Function, and Ability to Participate in Social Roles, PROMIS Global Mental Health and Physical Health, EQ-5D, SF-12, and UHDRS TFC), greater scores represent better functionality.

<sup>2</sup>Correlations were negative between the two instruments assessed. In all cases, negative signs were expected because of differences in scoring methodology between the two instruments. Negative signs were removed for consistent presentation purpose and to emphasize magnitude of correlations.

## Discussion

Understanding HRQOL in HD is a necessary component of evaluating the effectiveness of clinical interventions. Furthermore, the Food and Drug Administration requires a clinical outcome assessment (COA) qualification for trials that demonstrate treatment benefit in addition to clinical effectiveness. A COA qualification identifies drugs with clear treatment benefits through both objective findings and subjectively reported improvements. The lack of an HD-specific self-report instrument with evidence of sensitive assessment over time has made it difficult to evaluate the self-reported effectiveness of clinical treatments. This study details the use, validity, and reliability of the HD-PRO-TRIAD™, a new HD-specific instrument of HRQOL for use in clinical research and in optimizing treatment in clinical practice.

This new instrument includes several items from pre-existing validated measures (e.g., Neuro-QOL and HDQLIFE).

HD-PRO-TRIAD™ is both reliable (internally consistent) and valid, demonstrating convergent and divergent validity with other HRQOL instruments. In particular, overall HD-PRO-TRIAD™ scores demonstrated strong relationships with all other HRQOL instruments for both HD patient and caregiver proxy reports. Similarly, the patterns among triad domains were as anticipated, with the strongest relationships between corresponding measures (e.g., correlations between HD-PRO-TRIAD™ Emotional and Behavioral Dysfunction were greatest with other measures of emotion), and weaker relationships between each of the areas of the triad.



There are often discrepancies between what individuals with HD and their caregivers report to treating physicians. However, the HD-PRO-TRIAD™ proxy report and HD patient report were found to be highly consistent, in sharp contrast with other HD research of caregiver dyads that failed to find such a relationship.<sup>10</sup> The consistency between individuals with HD and their caregivers in our study suggests that HD-PRO-TRIAD™ may have utility in evaluating HRQOL for individuals with HD that may be unable to complete these measures themselves.

The HD-PRO-TRIAD™ includes 47 items (14 Cognition, 14 Emotional and Behavioral Dyscontrol, 19 Motor Function) and was developed to be easily administered and scored in both clinical and research settings. The intent of the authors is to have this instrument publically available for use to clinicians and researchers via an online domain. This measure is designed to capture PROs for individuals with HD. However, there is much discussion in the HD community about an individual's ability to provide reliable self-report data during the later phases of the disease, when both cognitive problems and anosognosia are common.<sup>33-35</sup> To this end, the general consensus is that self-report measures, by themselves, only capture one component of the clinical picture. Input from providers, caregivers, family members, and patients themselves is needed to provide a full clinical picture. Therefore, while PROs are an essential component of the clinical picture, they should be used in conjunction with both clinician and family-rated measures to build a complete clinical picture. Taken together, the HD-PRO-TRIAD™ captures the triad of symptoms characteristic of HD.

While these findings highlight the initial reliability and validity of HD-PRO-TRIAD™, future work in other HD patient samples is needed to fully understand both the sensitivity and the strengths and weaknesses of this instrument. Future work is needed to examine the relationship of these items to objective assessments of emotional, motor, and cognitive function and further refine this instrument by selecting the most sensitive items, allowing quick administration of HD-PRO-TRIAD™. In addition, the use of the instrument in the context of an interventional trial still needs to be completed.

We acknowledge the limitations of this study. First, data were collected via an online panel. Therefore, patient clinical characteristics, including diagnoses, gene testing, years since diagnosis, and years with symptoms, were self-reported and were not independently verified. Indeed, this was a convenience sample rather than a clinical study sample of HD patients. Second, we were only able to solicit self-reported estimates of disease stage, functional ability, and independence (rather than more typically used clinician-rated scales). Future work is required to evaluate the relationship between the self-report and clinician-rated versions of these scales. Third, while internal consistency was excellent, as indicated by Cronbach's alpha values greater than 0.95, we note that excessively high internal consistency may suggest item redundancy.<sup>36,37</sup> That is, the items' content may be too narrow, with some not necessarily contributing incremental additional information. While there are no standard cutoffs for optimal internal consistency, it has been suggested that coefficient

alphas of at least 0.80 are considered sufficient, and limiting items to no more than 35 for broad constructs (e.g., cognition, emotional/behavioral dysfunction, and motor function) could reduce the risk of redundancy.<sup>37</sup> Nonetheless, item factor analysis should be explored in future analyses to assess the need for further item reduction.

Both HD individuals and caregivers were instructed to take the online instruments separately, on their own. During the recruitment of participants at the HDSA meeting, HD individuals and caregivers were also reminded orally that the survey needed to be filled out separately and that HD individuals needed to be capable of filling out the forms without assistance, as noted in the eligibility criteria. However, we were not able to assess the extent to which such instructions were followed, and that HD individuals and caregivers did not share information. This is a fourth limitation of the study.

A final limitation is that the current study enrolled individuals with HD who were able to independently complete online panel testing. Therefore, application of the results may be limited to a greater-functioning HD patient sample. Indeed, our patient sample was a very well-educated group of fairly high-functioning individuals. This limits the generalizability of our results at this time. In the future, this instrument will also be evaluated for more moderate and more severe individuals with HD who require 24-hour supervision. This instrument, as with other HRQOL measures, is not appropriate for non-verbal individuals. The validity of this instrument in individuals with significant psychiatric issues, behavioral dyscontrol, or advanced dementia will also need to be determined.

Since we found that the caregiver proxy measures are well-correlated with the HD patient measures, the HD-PRO-TRIAD™ instrument may have the potential to be used for more severe individuals with HD. Further prospective validation based on a larger patient sample over multiple time points would confirm the dynamic validity of this instrument. In addition, further validation of HD-PRO-TRIAD™ may be achieved when consecutive individuals are recruited in the clinical setting, with their HD histories recorded by neurologists through the assistance of patients and caregivers; with full examinations undertaken by neurologists; and with cognitive testing administered.

Despite these limitations, HD-PRO-TRIAD™ provides an advantage over more generic instruments of HRQOL that do not fully capture the behavioral characteristics of this triad disorder. In addition, the HD-PRO-TRIAD™ does not have some of the limitations of previous PRO measures developed for HD. The HD-QOL-I<sup>17</sup> is available in French and Italian, but not English. The HD-QoL<sup>18</sup> did not assess accepted norms for minimum sample patient sizes for the analyses it employed.<sup>38</sup> Moreover, the HD-PRO-TRIAD™ has demonstrated excellent reliability, as well as convergent and divergent validity. The HD-PRO-TRIAD™ is the first brief, validated HRQOL instrument to assess the full triad of symptoms associated with HD. Importantly, it is Neuro-QOL, HDQLIFE, and PROMIS compatible. HD-PRO-TRIAD™ should prove to be a useful instrument for evaluating the effectiveness of clinical interventions designed to improve the lives of individuals with HD.

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**Appendix 1.**

**Unified Huntington’s Disease Rating Scale (UHDRS)  
Modified Independence Scale**

Please indicate the answer choice that **best** describes your current independence level. Please choose only one response.

- a) No special care is needed.
- b) No physical care is needed if I avoid difficult tasks.

- c) I have experienced changes in employment or have stopped working. I am unable to perform household chores like I could before my experience with Huntington’s Disease. I may need help with finances.
- d) I am able to bathe myself but I have limited household duties (cooking and use of knives). I am unable to drive or manage finances.
- e) I require minor assistance in dressing, toileting, or bathing. Food must be cut for me.
- f) I require 24-hour supervision and assistance for bathing, eating, and toileting.
- g) I require services from a chronic care facility. I am limited in feeding myself. I require a liquefied diet.
- h) I provide minimal assistance in my own feeding, bathing, and toileting.
- i) I am unable to speak and must be fed.
- j) I am tube fed and require total bed care.

**Appendix 2.**

**Unified Huntington’s Disease Rating Scale\_Total  
Functional Capacity Scale, modified for assessment  
center (caregiver version)**

The following are questions on levels of functioning in the domains of occupation, finances, domestic chores, activities of daily living, and requirements for unskilled or skilled care. For each question, please indicate the answer choice that best describes the ability of the person with Huntington’s disease whom you care for (i.e., as the care receiver) to accomplish the tasks described given his/her current Huntington’s disease condition. In situations where the care receiver has not performed a certain task to allow for your observation, please estimate his/her ability to conduct such a task.

[UHDRS\_occupation] Is the care receiver able to work?

- 0=No, he/she is unable to work
- 1=Yes, but he/she can only work part-time doing tasks that are less complicated than his/her usual work
- 2=Yes, but he/she needs special accommodations to get his/her work done
- 3=Yes, he/she can work normally with no accommodations needed

[UHDRS\_finances] Is the care receiver able to manage his/her own finances?

- 0=No, he/she is unable to manage his/her own finances independently
- 1=Yes, but with major assistance from another person/people
- 2=Yes, but with slight assistance from another person/people
- 3=Yes, he/she can to manage finances independently without assistance

[UHDRS\_chores] Is the care receiver able to complete household chores independently?

- 0=No, he/she is unable to complete household chores independently
- 1=Yes, he/she can complete some, but not all, chores independently
- 2=Yes, he/she can complete all chores independently

[UHDRS\_ADL] Is the care receiver able to accomplish daily living tasks, such as bathing, dressing, and meal preparation independently?

- 0=No, he/she is unable to accomplish daily living tasks independently
- 1=Yes, he/she can accomplish some, but not all, daily living tasks independently
- 2=Yes, he/she can accomplish many, but not all, daily living tasks independently
- 3=Yes, he/she can accomplish all daily living tasks independently without assistance

[UHDRS\_CareLevel] What type of care does the care receiver receive?

- 0= he/she has full-time nursing care
- 1= he/she has part-time nursing help
- 2= he/she lives independently

### **Unified Huntington's Disease Rating Scale\_Total Functional Capacity Scale, modified for assessment center (patient version)**

The following are questions on levels of functioning in the domains of occupation, finances, domestic chores, activities of daily living, and requirements for unskilled or skilled care. For each question, please indicate the answer choice that best describes your ability to accomplish the tasks described given your current Huntington's disease condition.

[UHDRS\_occupation] Are you able to work?

- 0=No, I am unable to work

- 1=Yes, but I can only work part-time doing tasks that are less complicated than my usual work
- 2=Yes, but I need special accommodations to get my work done
- 3=Yes, I can work normally with no accommodations needed

[UHDRS\_finances] Are you able to manage your own finances?

- 0=No, I am unable to manage my own finances independently
- 1=Yes, but with major assistance from another person/people
- 2=Yes, but with slight assistance from another person/people
- 3=Yes, I can manage finances independently without assistance

[UHDRS\_chores] Are you able to complete household chores independently?

- 0=No, I am unable to complete household chores independently
- 1=Yes, I can complete some, but not all, chores independently
- 2=Yes, I can complete all chores independently

[UHDRS\_ADL] Are you able to accomplish daily living tasks, such as bathing, dressing, and meal preparation independently?

- 0=No, I am unable to accomplish daily living tasks independently
- 1=Yes, I can accomplish some, but not all, daily living tasks independently
- 2=Yes, I can accomplish many, but not all, daily living tasks independently
- 3=Yes, I can accomplish all daily living tasks independently without assistance

[UHDRS\_CareLevel] What type of care do you receive?

- 0=I have full-time nursing care
- 1=I have part-time nursing help
- 2=I live independently

**Appendix 3.**  
**HD-PRO-TRIAD™ Version 1**

HD-PRO-TRIAD™ v.1.0						Official Use Only
<b>Cognition</b>						
Please respond to each question or statement by marking one box per row.						<i>Please fill in the score for each question in the boxes below.</i>
In the past 7 days...	Very often (several times a day)	Often (once a day)	Sometimes (2-3 times)	Rarely (once)	Never	
1. I had trouble keeping track of what I was doing if I was interrupted.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
2. I had trouble concentrating.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
3. I had difficulty doing more than one thing at a time.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
4. I had trouble planning out steps of a task.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
5. I had trouble remembering new information, like phone numbers or simple instructions.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
How much DIFFICULTY do you currently have...	Cannot do	A lot	Somewhat	A little	None	
6. getting things organized?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
7. keeping important personal papers such as bills, insurance documents and tax forms organized?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
8. learning new tasks or instructions?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
9. remembering a list of 4 or 5 errands without writing it down?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
In the past 7 days...	Very often (several times a day)	Often (once a day)	Sometimes (2-3 times)	Rarely (once)	Never	
10. I had trouble remembering things.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
11. My inability to solve problems limited my ability to work.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>

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Figure 2. HD-PRO-TRIAD(tm) Domains (pages 1–5)

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In the past 7 days...							
		Cannot do	A lot	Somewhat	A little	None	
12.	How much DIFFICULTY do you currently have...adapting to a new situation?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/>
13.	How much DIFFICULTY do you currently have...being flexible in a new situation?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/>
14.	How much DIFFICULTY do you currently have...thinking about two tasks at the same time?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/>

Page 2

Figure 2. Continued

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<b>Emotional and Behavioral Dyscontrol</b>							
Please respond to each question or statement by marking one box per row.							
In the past 7 days...		Never	Rarely	Sometimes	Often	Always	
1.	It was hard to control my behavior.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
2.	I was irritable around other people.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
3.	I was bothered by little things.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
4.	I became easily upset.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
5.	I said or did things without thinking.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
6.	I got impatient with other people.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
7.	I felt angry.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
8.	I felt impulsive.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
9.	It was hard to adjust to unexpected changes.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
10.	It was hard to keep up enthusiasm to get things done.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
11.	I was in conflict with others.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
12.	I said or did things that other people probably thought were inappropriate.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
13.	I threatened violence toward people or property.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
14.	I had trouble controlling my temper.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>

Page 3

Figure 2. Continued

HD-PRO-TRIAD™ v.1.0						Official Use Only  <i>Please fill in the score for each question in the boxes below.</i>	
<b>Motor Function</b>							
Please respond to each question or statement by marking one box per row.							
<b>Section A</b>							
<b>In the past 7 days...</b>		<b>Never</b>	<b>Rarely</b>	<b>Sometimes</b>	<b>Often</b>	<b>Always</b>	
1.	How often did you feel unsteady when you were standing?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
2.	How often did you have movements?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
3.	How often were you unable to stay still?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
4.	How often did your chorea impact your ability to hold things, like a glass or fork?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
5.	How often did you experience severe chorea?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
6.	How often did you limit your physical activities because of your chorea?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
7.	How often did you limit your social activities because of your chorea?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
8.	How often did your chorea impact your ability to enjoy life?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
9.	How often did your chorea interfere with your ability to get dressed?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
10.	How often did your chorea interfere with your ability to walk?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
11.	How often did your chorea interfere with your social activities?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
12.	How often did your chorea limit you at work (include work at home)?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="text"/>
Page 4							

Figure 2. Continued



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13.	How often did you experience severe movements?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/>
14.	How often did you have shakiness?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/>
<b>In the past 7 days...</b>		<b>Not at all</b>	<b>A little bit</b>	<b>Somewhat</b>	<b>Quite a bit</b>	<b>Very much</b>	
15.	I needed help doing my usual activities.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/>
Section B							
<b>In the past 7 days...</b>		<b>Not at all</b>	<b>A little bit</b>	<b>Somewhat</b>	<b>Quite a bit</b>	<b>Very much</b>	
16.	I am able to communicate with others.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/>
17.	I can swallow naturally and easily.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/>
<b>In the past 7 days...</b>		<b>Very often (several times a day)</b>	<b>Often (about once a day)</b>	<b>Sometimes (2-3 times)</b>	<b>Rarely (once)</b>	<b>Never</b>	
18.	My speech was difficult for others to understand.	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/>
<b>How much DIFFICULTY do you currently have ...</b>		<b>Cannot do</b>	<b>A lot</b>	<b>Somewhat</b>	<b>A little</b>	<b>None</b>	
19.	speaking clearly enough to use the telephone?	<input type="checkbox"/> 1	<input type="checkbox"/> 2	<input type="checkbox"/> 3	<input type="checkbox"/> 4	<input type="checkbox"/> 5	<input type="checkbox"/>

Figure 2. Continued

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### Cognition Scoring Instructions

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1. Are answers provided for at least 8 questions? If **no**, this survey does not provide enough information to be analyzed. If **yes**, continue to step 2.
2. Please sum the scores for all questions in the Cognition domain to obtain the Raw Score.

*Raw Score*

---

3. Please compute the **Cognition Score** using the equation below:

$$\text{Cognition Score} = \frac{(\text{\# of questions answered} \times 6) - \text{Raw Score}}{\text{\# of questions answered}} = \text{Final Score}$$

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Figure 3. HD-PRO-TRIAD™ Instrument and Scoring Instructions (page 6–9)

**Emotional and Behavioral Dyscontrol Scoring Instructions**

1. Are answers provided for at least 8 questions? If **no**, this survey does not provide enough information to be analyzed. If **yes**, continue to step 2.
2. Please sum the scores for all questions in the Emotional and Behavioral Dyscontrol domain to obtain the Raw Score.

*Raw Score*

3. Please compute the **Emotional and Behavioral Dyscontrol Score** using the equation below:

**Emotional and Behavioral  
Dyscontrol Score =**

*Raw Score*

=

*# of questions  
answered*

*Final Score*

Figure 3. Continued

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### Motor Function Scoring Instructions

1. Are answers provided for at least 10 questions in Section A and Section B combined? If **yes**, proceed to step 2. If **no**, this survey does not provide enough information to be analyzed.
2. Please sum the scores for all questions in Section A of the Motor Function domain to obtain Raw Score A.

**Raw Score A**

3. Please compute Raw Score B using the equation below.

$$\left( \begin{array}{c} \square \\ \text{\# of questions answered} \\ \text{in Section B} \end{array} \times 6 \right) - \begin{array}{c} \square \\ \text{Sum of provided} \\ \text{answers in Section B} \end{array} = \begin{array}{c} \square \\ \text{Raw Score B} \end{array}$$

Figure 3. Continued

4. Please compute the **Motor Function Score** using the equation below:

$$\text{Motor Function Score} = \frac{\text{Raw Score A} + \text{Raw Score B}}{\text{\# of questions answered in Sections A and B combined}} = \text{Final Score}$$


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**Total Scoring Instructions**

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1. Please compute the **Total Score** by solving the following equation:

$$\text{Total Score} = \text{Cognition Score} + \text{Emotional and Behavioral Dyscontrol Score} + \text{Motor Function Score} = \text{Total Score}$$


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Figure 3. Continued