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**Quality of Life Measures in Huntington’s Disease: Critique and Recommendations**

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Keywords:	patient-centered outcomes, caregiver-centered outcomes, Huntington’s disease, quality of life, rating scales



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3 **Quality of Life in Huntington's Disease: Critique and Recommendations for Measures**  
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5 **Assessing Patient Health-Related Quality of Life and Caregiver Quality of Life**  
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55 caregiver-centered outcomes  
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**Abstract**

The compromise of quality of life (QoL) in Huntington's disease (HD) is a major issue, both for individuals with the disease as well as for their caregivers. The International Parkinson and Movement Disorder Society (MDS) commissioned a review of the use and clinimetric validation status of measures used in HD to assess aspects related with QoL, and to make recommendations on their use following standardized criteria. We included both patient-centered measures (patient Health-related (HR) QoL measures) and caregiver-centered measures (caregiver QoL measures). After conducting a systematic literature search, we included 12 measures of patient HRQoL and 2 measures of caregiver QoL. Regarding patient-centered measures, the Medical Outcomes Study 36-Item Short-Form Health Survey is "recommended" as a generic assessment of HRQoL in patients with HD. The 12-Item Short Form Health Survey, the Sickness Impact Profile, the 12-item World Health Organization Disability Assessment Schedule, and the Huntington's Disease Health-Related Quality of Life questionnaire are "suggested". No caregiver-centered QoL measure obtained a "recommended" status. The Alzheimer's Carer's Quality of Life Inventory and the Huntington's Disease Quality of Life Battery for Carers are "suggested". Recognizing that the assessment of patient HRQoL can be challenging in HD, as patients may lack insight and there is insufficient clinimetric testing of these scales, the committee concluded that further validation of currently available HRQoL measures should be undertaken, namely, those HD-specific HRQoL measures that have recently been reported and used.

## INTRODUCTION

Huntington's disease (HD) is a complex neurodegenerative disorder in which motor, cognitive and behavioral manifestations have a significant impact on health-related quality of life (HRQoL) of patients. The concept of HRQoL has been developed to express the aspects of overall quality of life (QoL) that can be clearly shown to be related to health, be that physical or mental.<sup>1</sup> The World Health Organization (WHO) defines health as "a state of complete physical, mental, and social well-being not merely the absence of disease."<sup>2</sup> The WHO lists the following functioning domains as being part of HRQoL: physical, social, relational, and emotional well-being.<sup>1</sup> Although, the term "QoL" is often used interchangeably with the term "HRQoL", QoL is a much broader multidimensional concept. The WHO defines QoL as "the individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns".<sup>1</sup> Another important concept that is often used in QoL literature is health status (HS). HS is defined as the perceived health in descriptive terms of physical and mental symptoms, disability, and social dysfunction related to the health condition.<sup>3</sup> It is different from HRQoL in that it lacks judgments and reactions.<sup>3</sup> As stated in a similar review for HRQoL measures used in Parkinson's disease, it is reasonable to consider HS as a relevant factor for HRQoL, which is a component of QoL in general.<sup>4</sup>

HRQoL is an important patient-reported outcome that constitutes a core assessment of the efficacy of clinical interventions in HD, as these interventions ideally seek to not only improve patients' symptoms, but ultimately to improve patient QoL. It is therefore important that valid and reliable measures are available that can be used in HD. In addition to measures centered on patients (patient-centered HRQoL measures), ~~the sub-committee the authors decided we also to included~~ measures centered on caregivers and their own QoL (caregiver-centered QoL measures), recognizing that HD impacts the "global" QoL of caregivers and a



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3 potential change in QoL is not necessarily related to health and may include other aspects of  
4  
5 life.<sup>5,6</sup>  
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## 10 **METHODS**

### 13 **Organization and critique process**

16 The Committee on Rating Scales Development of the MDS appointed a team of 10 members  
17 (sub-committee) to review clinical measures used in HD to assess HRQoL measures; these  
18 members included specialists in HD, and an expert in scale development and clinimetrics  
19 (A.M.D.). Two sub-committee members evaluated each measure. If a sub-committee member  
20 was involved in the development of a measure, he/she was not involved in its review. Data  
21 were extracted into a *proforma* provided by the MDS and adapted for the purpose of the  
22 current review. The assessment of the measure included the description of the measure, its  
23 availability, context of use, and reported clinimetric properties in patients with HD. All sub-  
24 committee members jointly assessed the completed reviews of the measures. Any unresolved  
25 issues and limitations of the critiqued measures were identified for discussion and reporting.  
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27 The final recommendations were based on consensus among the sub-committee members and  
28 the liaison member of the Committee on Rating Scales Development of the MDS (E.C.).  
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### 46 **Selection of measures**

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48 The methodology for this review was modeled on a previously used methodology.<sup>7</sup> A  
49 literature search was performed using Medline on PubMed, Web of Science, EMBASE, and  
50 Psychinfo. The keywords used in the search included: "Huntington\*" OR "Westphal variant"  
51 OR "juvenile Huntington\*", and the terms "scale" OR "questionnaire" OR "index" OR  
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53 "measure" as well as the keywords: "Quality of life", "QoL", "health-related quality of life",  
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3 “HRQoL”, “health status”. For each identified clinical measure, a search was conducted for  
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5 the terms “Huntington's disease,” or “Huntington disease” or “Huntington\*” and the name of  
6  
7 the measure. Manuscripts published before October 17, 2016 were retrieved using the above  
8  
9 search strategy and thoroughly screened by the chair of the sub-committee (T.A.M.) to  
10  
11 ascertain which measure had been used in each study.  
12  
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### 14 15 16 17 **Inclusion/exclusion for review**

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19 Measures used at least once in HD populations (patients at risk, presymptomatic gene carriers,  
20  
21 and symptomatic HD patients) were included. Measures were excluded from review if they  
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23 were not available in English, were only mentioned in reviews but not used in an original  
24  
25 study, were created for a specific study without any information about their structure or use,  
26  
27 or if the full-paper was not available (e.g., abstract format only). In terms of construct of  
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29 measures, the sub-committee decided to include all measures proposed by developers to  
30  
31 capture HRQoL, QoL or HS that have been used in HD studies.  
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### 39 **Criteria for rating**

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41 We followed the Classification System for Scale Recommendation used by the MDS that uses  
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43 three criteria: (1) Use in HD populations; (2) Use in HD by groups other than the original  
44  
45 developers and data on its use are available; (3) The available clinimetric/psychometric data  
46  
47 in HD support the goals of measurement of severity (e.g., evaluation of reliability, construct  
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49 validity, and score discrimination across levels of symptom severity). Specific to this review,  
50  
51 while HrQoL is not a symptom *per se*, it reflects the multidimensional construct of the impact  
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53 of a disease/condition on QoL. The ability to differentiate across different levels of severity  
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55 still stands as fundamental for a valid assessment of HrQoL (or caregiver QoL) in  
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3 observational studies or clinical trials. (for further details, see Table 1.)  
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## 8 **RESULTS**

### 9 **Identified Measures and Their Use in Clinical Research**

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11 A total of 19 clinical measures that have been used in HD research studies were identified.

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13 One of these measures was excluded after abstract review due to inadequacy of measure  
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construct (see supplementary material). The remaining 18 clinical measures were included for  
an in-depth review. Four measures were excluded because: 1) their sole use in HD was in case  
series without any clinimetric data available (the Manchester Assessment of Quality of Life,  
the Fatigue Impact scale), 2) it was created solely for a single study (a Non-Standardized QoL  
question), and 3) the proposed construct was inadequate for the current review (the Caregiver  
Burden Inventory). We grouped the 14 remaining measures into patient-centered HRQoL  
measures (n=12) and caregiver-centered QoL measures (n=2).

For patient-centered HRQoL measures, only The Medical Outcomes Study 36-Item Short-  
Form Health Survey was (SF-36) received a classification of “recommended” as a generic  
assessment of health status in manifest HD (severity). The 12-Item Short Form Health Survey  
(SF-12), the Sickness Impact Profile (SIP), the Huntington’s Disease Health-Related Quality  
of Life Questionnaire (HDQoL), and the 12-item World Health Organization Disability  
Assessment Schedule (WHODAS 2.0), were classified as “suggested” (see supplementary  
material for overview of all assessments classified as “suggested with caveats” or “listed”).

For caregiver-centered QoL measures, no measure was “recommended” for any of the  
purposes considered in this review. The Alzheimer’s Carer’s Quality of Life Inventory  
(AQLI), and the Huntington's Disease Quality of Life Battery for Carers (HD-QoL-C) were

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3 classified as “suggested” (see supplementary material for overview of all assessments  
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5 classified as “suggested with caveats” or “listed”).  
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### 10 *Patient-centered HRQoL rating scales*

#### 11 **Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36)**

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18 The SF-36 is an easy-to-administer self-reported set of generic measures of patient health  
19 status developed by the RAND Corporation as part of the Medical Outcomes Study (MOS).  
20  
21 The SF-36 assesses eight functional dimensions: physical functioning, physical role  
22 limitations, mental health, emotional role limitations, social functioning, energy/vitality, pain,  
23 and general health perceptions, which can be summarized into two scores (physical and  
24 mental) and a global utility index.<sup>8</sup> The SF-36 has been widely used in HD<sup>9-12</sup>, and the vast  
25 majority of the data was collected using version 1 of SF-36. The most current SF-36 version 2  
26 has less ambiguous wording, improved layout, enhanced response choices for some items,  
27 and increased cross-cultural validity.  
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31 Internal consistency has been shown for the SF-36 subscales, and domain and component  
32 scores (Cronbach’s alpha  $\geq 0.80$ ).<sup>9-12</sup> The test-retest reliability coefficients, as measured by  
33 Intra-Class Coefficient (ICC), have been reported to be  $> 0.70$  for all domains, apart from the  
34 “emotional role” domain (ICC= 0.63). The Mental Health summary score has been shown to  
35 correlate only with the Beck Depression Inventory (BDI), while the Physical Health summary  
36 score of the SF-36 correlates with the BDI and a patient’s self-rated and clinician’s rating of  
37 patients’ level of functioning/independence level, but no factor analysis has been conducted  
38 for the SF-36 in this population. The SF-36 (total score, Vitality score, and Mental  
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3 Component Score) have been shown to be sensitive to change in manifest HD clinical trials<sup>9</sup>  
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8 **Recommendation:** The SF-36 is “recommended” as a generic assessment of health status in  
9  
10 manifest HD (severity). The physical summary score seems to have better construct validity  
11  
12 in HD. It is not known if the more recent SF-36 Version 2 performs equally well in HD as the  
13  
14 SF-36 Version 1.  
15

### 16 17 18 19 20 **Medical Outcomes Study 12-Item Short-Form Health Survey (SF-12)**

21  
22 The SF-12 is a 12-item shorter version of the SF-36. It covers the same functional dimensions  
23  
24 as the SF-36 but includes fewer items, and thus, is quicker to administer (2 minutes vs. 8-12  
25  
26 minutes for the SF-36).<sup>14</sup> It has been used less extensively in HD than the SF-36.<sup>8</sup> It is  
27  
28 currently being used in Enroll-HD but no data have been reported.<sup>15</sup> Various degrees of  
29  
30 convergent validity have been reported between the SF-12 Physical and Mental Health  
31  
32 components, and the components of the HD-PRO-Triad (SF-12 physical component,  
33  
34 Pearson’s correlations: motor, -0.79; cognition -0.77; emotion/behavioral dyscontrol -0.47;  
35  
36 total score -0.76. SF-12 mental component, cognition -0.61; motor -0.51; total score -0.61),  
37  
38 and emotion/behavioral dyscontrol (Pearson’s correlation: -0.53, all  $p < 0.05$ ).<sup>16</sup> The SF-12  
39  
40 Physical component, but not the Mental Health component, has been shown to be sensitive to  
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42 change following multidisciplinary rehabilitation.<sup>17</sup>  
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47 **Recommendation:** The SF-12 is “suggested” as a generic assessment of health status in  
48  
49 manifest HD (severity), as it lacks test-retest reliability data and internal consistency data.  
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### 51 52 53 54 **Sickness Impact Profile (SIP) 136 items**

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3 The SIP is a generic measure of self-reported health status,<sup>18</sup> consisting of 136 items covering  
4  
5 12 categories grouped into two subscales (physical and psychosocial). Scores are presented as  
6  
7 a percentage of maximal dysfunction ranging from 0 to 100; a higher score indicates a higher  
8  
9 level of dysfunction. The SIP can take up to 30 minutes to complete. The SIP has been used in  
10  
11 two studies in manifest HD,<sup>19, 20</sup> and a modified version using only 3 of the 12 categories was  
12  
13 used in trial for cognition in HD.<sup>21</sup> Internal consistency has been reported to be high  
14  
15 (Cronbach's alpha > 0.80),<sup>19</sup> as has test-retest reliability (ICC > 0.70) for scores of subscales  
16  
17 and all categories, aside from the "emotional behavior" (ICC=0.49) and "work" (ICC=0.68)  
18  
19 categories.<sup>19</sup> The SIP total score has been shown to correlate with both the patient's self-rated  
20  
21 (Spearman's correlation: -0.69) and clinician's rating (Spearman's correlation: -0.64) of  
22  
23 patients' level of functioning/independence (all  $p < 0.01$ ), with the BDI (Spearman's  
24  
25 correlation: 0.47,  $p < 0.01$ ), and with the Unified Huntington's Disease Rating Scale – Total  
26  
27 Motor Score (UHDRS-TMS) (Spearman's correlation: 0.32,  $p < 0.05$ ). The Psychosocial  
28  
29 subscale has been shown to correlate with both the patient's self-rated and the clinician's  
30  
31 rating of patients' level of functioning/independence, while the Physical subscale has been  
32  
33 shown to correlate with both the BDI and the UHDRS-TMS, in addition to both the patient's  
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35 self-rated and the clinician's rating of patients' level of functioning/independence.<sup>19</sup> In a  
36  
37 head-to-head comparison with the SF-36, the SIP was shown to have a worse clinimetric  
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39 performance with less robust construct validity and test–retest reliability. In addition, motor  
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41 symptoms appeared to influence some strictly non-motor dimensions of the SIP.<sup>19</sup>

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47 **Recommendation:** The SIP is "suggested" for assessing health status in manifest HD  
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49 (severity). There are limited clinimetric data on its use in HD, and it performs worse than the  
50  
51 SF-36 in a head-to-head comparison.  
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57 **World Health Organization Disability Assessment Schedule (WHODAS) 2.0 (12-item)**  
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3 The WHODAS 2.0 was developed by the World Health Organization (WHO) is often  
4 considered a generic function-related measure of health status and consequently it was  
5 decided by consensus to include it in this review and not in the review of measures for  
6 assessment of functional ability in HD. The WHODAS 2.0 can be administered as  
7 interviewer-, self-, and proxy-administered forms. The WHODAS 2.0 12-item version, which  
8 is reviewed here, takes 5 minutes to complete and covers 6 domains: cognition, mobility, self-  
9 care, getting along, life activities, and participation. The WHODAS 2.0 12-item has been used  
10 in three studies including both pre-manifest and manifest HD.<sup>22-24</sup> Internal consistency has  
11 been shown with a Cronbach's alpha of 0.94 (95% CI: 0.93 - 0.94).<sup>22</sup> Moderate convergent  
12 validity has been reported between the WHODAS 2.0 and other health-related quality of life  
13 assessments such as the RAND-12 (Pearson correlations ranging from - 0.76 to -0.41), and  
14 the EuroQol Five-dimension questionnaire (EQ-5D; Pearson correlations ranging from = -  
15 0.65 and -0.49).<sup>22</sup> The scores in the WHODAS 2.0 differ significantly across the disease  
16 spectrum from the pre-manifest stage to late HD.<sup>22</sup> In pre-manifest HD, cross-sectional  
17 differences between low-, mid- and high- disease burden groups have been reported.<sup>23</sup> In pre-  
18 manifest HD, only the companion-rated (*proxy*) version of the WHODAS 2.0 has been shown  
19 to be sensitive to change over a period of three years.<sup>23</sup>

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41 **Recommendation:** The WHODAS 2.0 12-item is “suggested” for assessing health status in  
42 HD (severity), as it lacks important clinimetric development in HD, namely, for test-retest  
43 reliability testing and requires more robust construct validity.  
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### 51 **The Huntington's Disease Health-Related Quality of Life Questionnaire (HDQoL)**

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53 The HDQoL is a patient-reported questionnaire that was specifically developed for use in HD  
54 to assess HRQoL.<sup>25</sup> The HDQoL covers three main domains: “primary physical and  
55 cognitive”, “primary emotions and self”, and “primary services”.<sup>25</sup> It takes about 22 minutes  
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3 to complete. The HDQoL has been used in one study by authors<sup>26</sup> other than the group<sup>25, 27</sup>  
4  
5 who originally developed it. The internal consistency of each of the domains has been shown  
6  
7 to vary: “primary services” (Cronbach’s alpha = 0.76), “primary emotions and self”  
8  
9 (Cronbach’s alpha = 0.89), and “primary physical and cognitive” (Cronbach’s alpha = 0.96).  
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11 Test-retest reliability has been reported, but as this was evaluated with Cronbach’s alpha it  
12  
13 does not provide a true adequate measure of concordance.<sup>25</sup> Item ceiling effects range from  
14  
15 12.5% to 50%.<sup>25</sup>  
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17

18 **Recommendation:** The HDQoL is “suggested” for assessment of HRQoL in HD (severity),  
19  
20 as there are limited clinimetric data, namely related with construct validity and test-retest  
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22 reliability.  
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## Caregiver-centered QoL measures

### The Alzheimer's Carer's Quality of Life Inventory (ACQLI)

The ACQLI was developed to assess caregiver QoL in Alzheimer's disease (AD).<sup>28</sup> It is a quick (<5 minutes) questionnaire that consists of 30 items to which the caregiver answers true or not true; 1 point is given for each true answer, giving a possible total score of 30. The ACQLI has been used in a single HD study, in a head-to-head comparison with the HD-QoL-C. The ACQLI<sup>29</sup> showed excellent internal consistency (Cronbach alpha = 0.95).<sup>29</sup>

**Recommendation:** The ACQLI is "suggested" for assessing QoL for HD caregivers (severity), as its use in HD is limited to a single study in HD and clinimetric data in HD are limited to internal consistency.

### Huntington's Disease Quality of Life Battery for Carers (HD-QoL-C)

The HD-QoL-C is a HD-specific, multi-dimensional measure for family or caregivers of patients with HD. It is based upon the domains and facets of the Comprehensive Quality of Life Scale for Adults (ComQoL-A5).<sup>30</sup> Two versions are available: a long-form that consists of 34 items which incorporate measures on "practical aspects of caregiving" (n=9), "satisfaction with life" (n=8) and "feelings about living with HD" (n=17), and a short-form that consists of 20 items (3 items on "satisfaction of life", and 17 items on "feelings about living with HD").<sup>29</sup> The HD-QoL-C has been used in four studies in HD.<sup>9, 29, 31, 32</sup> Internal consistency of the long-form has been shown for the domains "satisfaction with life" (Cronbach's alpha = 0.91) and "feelings about living with HD" (Cronbach's alpha = 0.84), but not for the domain "practical aspects of caregiving" (Cronbach's alpha = 0.62).<sup>29</sup> For the short-form, internal consistency has been shown ("satisfaction with life", 0.92; total score, 0.88).<sup>29</sup> A low correlation has been reported between the HD-QoL-C and the WHO Quality of Life Short Form (WHO-QoL

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3 BREF),<sup>32</sup> and the Huntington Quality of Life Instrument (H-QoL-I; correlations 0.22 to 0.28,  
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5 all  $p < 0.01$ ).<sup>31</sup>  
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7 **Recommendation:** The HD-QoL-C is “suggested” for assessing QoL for HD caregivers  
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9 (severity). It warrants further **additional** clinimetric development, **namely in terms of**  
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11 **validity, reliability and data reproducibility by other groups.**  
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## 14 15 Discussion

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18 We report here the results of an in-depth review of 12 measures used in HD studies to  
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20 evaluate patient-centered HRQoL. The SF-36 is the only measure that can be classified as  
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22 “recommended” to measure patient’s HRQoL in terms of severity. None of the HRQoL  
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24 measures developed specifically for HD have undergone sufficient clinimetric development to  
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26 warrant a similar classification level. There were no HRQoL measures recommended to  
27  
28 measure change of ~~intensity~~ **severity** over time. Regarding patient-centered HRQoL  
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30 measures, the sub-committee identified the following topics that warrant consideration when  
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32 developing these types of measures:  
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- 36  
37 1) The inherent subjective nature of self-reporting HRQoL warrants a special comment  
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39 as HD patients often lack insight regarding the presence or severity of their symptoms.  
40  
41 Along the same lines, the progressive cognitive impairment experienced by HD  
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43 patients is likely to introduce additional difficulties in ensuring the reliability of  
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45 patient-reported HRQoL in HD, namely, at later stages. Proxy reporting was rarely  
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47 included in the measures reviewed here and could be further assessed and considered  
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49 as a strategy to mitigate the above-mentioned limitations of patient-reported outcomes  
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51 in HD.  
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- 53  
54 2) As HD is a rare disease, studies often require a multi-center multi-national design that  
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56 raises the need for validation of HRQoL and QoL measures across different cultures.  
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3 In this review, there were no data available on a formal cross-cultural validation for  
4 any of the included measures when applied to HD populations. Consequently, cross-  
5 cultural validation should be implemented in future development programs of HRQoL  
6 measures in HD.  
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- 10  
11 3) We discussed the need for a generic measure *vs.* a disease-specific measure. Given the  
12 complexity of the clinical presentation of HD, it is likely that a generic scale will not  
13 capture all the disease features that significantly impact on the HRQoL of these  
14 patients, and thus a disease-specific measure may be better positioned to capture  
15 HRQoL in HD in a valid manner. On the other hand, although disease-specific  
16 measures are usually more sensitive, generic measures are able to capture global  
17 aspects of health that may be overlooked by the specific scales. A disease-specific  
18 measure that incorporates items likely found in generic measures is possibly the best  
19 approach.  
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34 The committee also looked at caregiver-centered QoL measures. We recognize that these  
35 measures have their own issues. In this review, we included two caregiver-centered QoL  
36 measures, one developed in Alzheimer's disease and another specifically developed for HD.  
37 Although caregivers play a role in caring for patients with a wide range of neurodegenerative  
38 disorders, and there are many features in common between caring for such patients and caring  
39 for a progressively dependent patient, there are limited data available to determine if  
40 similarities across neurodegenerative disorders are sufficient to warrant a general QoL scale  
41 or whether caregiver QoL needs to be disease-specific. A caregiver-centered measure that  
42 considers both disease-specific items and more generic items would likely be the best  
43 approach.  
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3 In the current review we identified several measures that were 'listed'. In many cases, these  
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5 measures have had limited evaluation of their measurement properties in HD. Still, other  
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7 recently developed HD-specific measures are in the initial stages of comprehensive  
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9 measurement property testing, these include the HDQLIFE, the HDQoL, or HD-PRO-  
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11 TRIAD. Importantly, some of these newer measures incorporate patient stakeholders in their  
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13 development, a contribution deemed essential by regulatory agencies such as the US Food and  
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15 Drug Administration (FDA) for patient-reported outcomes supporting labeling claims.<sup>33</sup>  
16  
17 Further testing of the measurement properties and uptake of these measures by groups other  
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19 than the developers is required to determine their real value in evaluating HRQoL in HD  
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21 patients. The committee concluded that the evaluation of the measurement properties of the  
22  
23 currently available measures that are included in this review, namely those developed  
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25 specifically for HD, is warranted. This should be a priority for HD researchers, considering  
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27 for example the increasing importance of patient-reported outcomes in the development of  
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29 novel therapies and their subsequent approval by regulatory authorities.  
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**Table 1: Classification System for Scale Recommendation**

Category	Criteria
<b>“Recommended”</b>	(1) Scale has been used in HD populations. (2) Use in HD by groups other than the original developers and data on its use were available.* (3) The available clinimetric/psychometric data in HD support the goals of screening (e.g., evaluation of sensitivity/specificity, score cut-off points, and reliability) or measurement of severity (e.g., evaluation of reliability, construct validity, and score discrimination across levels of symptom severity).
<b>“Suggested”</b>	(1) Scale has been used in HD populations. (2) Only one other criteria (2) or (3) from the above recommended category applies.
<b>“Listed”</b>	(1) Scale has been applied to HD populations, but no further criterion met.

HD=Huntington’s Disease, \* For rating scales not originally developed for use in HD, criterion 2 was

fulfilled if used in at least one group in HD that reported any kind of clinimetric/psychometric data in HD.

Table 2: Summary of all included scales in HD

Scale/Questionnaire	Developed for use in HD	Scale has been applied to HD populations	Used by other groups beyond the original developing group	Appropriate clinimetric testing in HD	Recommendation level	Comments
<b>PATIENT-CENTERED ASSESSMENTS</b>						
Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36)	No	Yes	Yes	Yes	Recommended as a generic assessment of health status in manifest HD (severity)	Most of the clinimetric data in HD were generated using older Version 1.
Medical Outcomes Study 12-Item Short-Form Health Survey (SF-12)	No	Yes	Yes	No	Suggested as a generic assessment of health status in manifest HD (severity)	
Sickness Impact Profile (SIP)	No	Yes	Yes	No	Suggested for assessing perceived health status in manifest HD (severity)	
12-item World Health Organization Disability Assessment Schedule (WHODAS) 2.0	No	Yes	Yes	No	Suggested for assessing health status in HD (severity)	
The Huntington's Disease health-related Quality of Life questionnaire (HDQoL)	Yes	Yes	Yes	No	Suggested for assessment of health-related QoL in HD (severity)	
EQ-5D	No	Yes	Yes	No	Suggested <i>with caveats</i>	Minimal clinimetric data available
RAND-12 Health Status Inventory (HIS)	No	Yes	Yes	No	Suggested <i>with caveats</i>	Used in a single study
Neuro-Quality of Life	No	Yes	Yes	No	Suggested <i>with caveats</i>	Used in a single

(Neuro-QoL)						study
PROMIS Global Health (PROMIS)	No	Yes	Yes	No	Suggested <i>with caveats</i>	Used in a single study
Huntington Disease Health-Related Quality of Life (HDQLIFE)	Yes	Yes	No	No	Listed	
WHO-Quality of Life-BREF (WHOQOL-BREF)	No	Yes	No	No	Listed	
Quality of Life Index (QoL Index)	No	Yes	No	No	Listed	
Huntington Quality of Life Instrument (H-QoL-I)	Yes	Yes	No	No	Listed	
HD-PRO-TRIAD	Yes	Yes	No	No	Listed	
<b>CAREGIVER-CENTERED ASSESSMENTS</b>						
The Alzheimer's Carer's Quality of Life Inventory (AQLI)	No	Yes	Yes	No	Suggested for assessing quality of life for HD caregivers (severity)	
Huntington's Disease Quality of Life Battery for Carers (HD-QoL-C)	Yes	Yes	Yes	No	Suggested for assessing quality of life for HD caregivers (severity)	

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Table 3. Summary of clinimetric data of all instruments used in HD with a recommendation level of “recommended” or “suggested”

SCALE	INTERNAL CONSISTENCY	TEST-RETEST RELIABILITY	CONSTRUCT VALIDITY	GROUP KNOWN VALIDITY	RESPONSIVENESS	CEILING /FLOOR EFFECT	SENSITIVITY/SPECIFICITY	TRANSLATION STATUS**
<b>PATIENT-CENTERED ASSESSMENTS</b>								
Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36) *	+	+	+	+	+/-	NR	NR	Widespread
Medical Outcomes Study 12-Item Short-Form Health Survey (SF-12)	-	-	+	+	+/-	NR	NR	Widespread
Sickness Impact Profile	+	+/-	+/-	-	NR	NR	NR	English
12-item World Health Organization Disability Assessment Schedule	+	NR	+/-	+	NR	ceiling effect	NR	Widespread

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<p><b>The Huntington's Disease health-related Quality of Life questionnaire</b></p>	+	+	+/-	-	-	ceiling effect	NR	English
<b>CAREGIVER-CENTERED ASSESSMENTS</b>								
<p><b>The Alzheimer's Carer's Quality of Life Inventory</b></p>	+	NR	NR	NR	NR	acceptable floor and ceiling effect	NR	English, French, German, Italian, Spanish.
<p><b>Huntington's Disease Quality of Life Battery for Carers</b></p>	+	+/-	+/- (sparse)	NR	NR	acceptable floor and ceiling effect	NR	English, French Italian

HD –Huntington’s disease. NR – not reported. (+) - good performance, (+/-) contradictory data or very limited data (-) poor performance.

NOTE: data regarding Minimally Clinically Important Difference was not assessed in any of the scales.

\* The SF-36 was the only rating scale “recommended”. Remaining scales were “suggested”. \*\* We list the languages officially recognized as being used for scale translation, widespread = scale translation has been recognized in more than 5 languages

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3 **Quality of Life in Huntington's Disease: Critique and Recommendations for Measures**  
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5 **Assessing Patient Health-Related Quality of Life and Caregiver Quality of Life**  
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46 Potential conflict of interest: Nothing to report

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50 Word count of main text: 3158

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52 Number of tables: 3

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55 **Key words:** Huntington's disease, quality of life, rating scales, patient-centered outcomes,  
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57 caregiver-centered outcomes  
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**Abstract**

The compromise of quality of life (QoL) in Huntington's disease (HD) is a major issue, both for individuals with the disease as well as for their caregivers. The International Parkinson and Movement Disorder Society (MDS) commissioned a review of the use and clinimetric validation status of measures used in HD to assess aspects related with QoL, and to make recommendations on their use following standardized criteria. We included both patient-centered measures (patient **Health-related (HR) Quality of Life (QoL)** measures) and caregiver-centered measures (caregiver QoL measures). After conducting a systematic literature search, we included 12 measures of patient HRQoL and 2 measures of caregiver QoL. Regarding patient-centered measures, the Medical Outcomes Study 36-Item Short-Form Health Survey is "recommended" as a generic assessment of HRQoL in patients with HD. The 12-Item Short Form Health Survey, the Sickness Impact Profile, the 12-item World Health Organization Disability Assessment Schedule, and the Huntington's Disease Health-Related Quality of Life questionnaire are "suggested". No caregiver-centered QoL measure obtained a "recommended" status. The Alzheimer's Carer's Quality of Life Inventory and the Huntington's Disease Quality of Life Battery for Carers are "suggested". Recognizing that the assessment of patient HRQoL can be challenging in HD, as patients may lack insight and there is insufficient clinimetric testing **of these scales**, the committee concluded that further validation of currently available HRQoL measures should be undertaken, namely, those HD-specific HRQoL measures that have recently been reported and used.

## INTRODUCTION

Huntington's disease (HD) is a complex neurodegenerative disorder in which motor, cognitive and behavioral manifestations have a significant impact on health-related quality of life (HRQoL) of patients. The concept of HRQoL has been developed to express the aspects of overall quality of life (QoL) that can be clearly shown to be related to health, be that physical or mental.<sup>1</sup> The World Health Organization (WHO) defines health as "a state of complete physical, mental, and social well-being not merely the absence of disease."<sup>2</sup> The WHO lists the following functioning domains as being part of HRQoL: physical, social, relational, and emotional well-being.<sup>1</sup> Although, the term "QoL" is often used interchangeably with the term "HRQoL", QoL is a much broader multidimensional concept. The WHO defines QoL as "the individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns".<sup>1</sup> Another important concept that is often used in QoL literature is health status (HS). HS is defined as the perceived health in descriptive terms of physical and mental symptoms, disability, and social dysfunction related to the health condition.<sup>3</sup> It is different from HRQoL in that it lacks judgments and reactions.<sup>3</sup> As stated in a similar review for HRQoL measures used in Parkinson's disease, it is reasonable to consider HS as a relevant factor for HRQoL, which is a component of QoL in general.<sup>4</sup>

HRQoL is an important patient-reported outcome that constitutes a core assessment of the efficacy of clinical interventions in HD, as these interventions ideally seek to not only improve patients' symptoms, but ultimately to improve patient QoL. It is therefore important that valid and reliable measures are available that can be used in HD. In addition to measures centered on patients (patient-centered HRQoL measures), ~~the sub-committee the authors decided we also to included~~ measures centered on caregivers and their own QoL (caregiver-centered QoL measures), recognizing that HD impacts the "global" QoL of caregivers and a

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3 potential change in QoL is not necessarily related to health and may include other aspects of  
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5 life.<sup>5,6</sup>  
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## 10 **METHODS**

### 13 **Organization and critique process**

16 The Committee on Rating Scales Development of the MDS appointed a team of 10 members  
17 (sub-committee) to review clinical measures used in HD to assess HRQoL measures; these  
18 members included specialists in HD, and an expert in scale development and clinimetrics  
19 (A.M.D.). Two sub-committee members evaluated each measure. If a sub-committee member  
20 was involved in the development of a measure, he/she was not involved in its review. Data  
21 were extracted into a *proforma* provided by the MDS and adapted for the purpose of the  
22 current review. The assessment of the measure included the description of the measure, its  
23 availability, context of use, and reported clinimetric properties in patients with HD. All sub-  
24 committee members jointly assessed the completed reviews of the measures. Any unresolved  
25 issues and limitations of the critiqued measures were identified for discussion and reporting.  
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27 The final recommendations were based on consensus among the sub-committee members and  
28 the liaison member of the Committee on Rating Scales Development of the MDS (E.C.).  
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### 46 **Selection of measures**

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49 The methodology for this review was modeled on a previously used methodology.<sup>7</sup> A  
50 literature search was performed using Medline on PubMed, Web of Science, EMBASE, and  
51 Psychinfo. The keywords used in the search included: "Huntington\*" OR "Westphal variant"  
52 OR "juvenile Huntington\*", and the terms "scale" OR "questionnaire" OR "index" OR  
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58 "measure" as well as the keywords: "Quality of life", "QoL", "health-related quality of life",  
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3 “HRQoL”, “health status”. For each identified clinical measure, a search was conducted for  
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5 the terms “Huntington's disease,” or “Huntington disease” or “Huntington\*” and the name of  
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7 the measure. Manuscripts published before October 17, 2016 were retrieved using the above  
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9 search strategy and thoroughly screened by the chair of the sub-committee (T.A.M.) to  
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11 ascertain which measure had been used in each study.  
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### 14 15 16 17 **Inclusion/exclusion for review**

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19 Measures used at least once in HD populations (patients at risk, presymptomatic gene carriers,  
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21 and symptomatic HD patients) were included. Measures were excluded from review if they  
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23 were not available in English, were only mentioned in reviews but not used in an original  
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25 study, were created for a specific study without any information about their structure or use,  
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27 or if the full-paper was not available (e.g., abstract format only). In terms of construct of  
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29 measures, the sub-committee decided to include all measures proposed by developers to  
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31 capture HRQoL, QoL or HS that have been used in HD studies.  
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### 40 **Criteria for rating**

41 We followed the Classification System for Scale Recommendation used by the MDS that uses  
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43 three criteria: (1) Use in HD populations; (2) Use in HD by groups other than the original  
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45 developers and data on its use are available; (3) The available clinimetric/psychometric data  
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47 in HD support the goals of measurement of severity (e.g., evaluation of reliability, construct  
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49 validity, and score discrimination across levels of symptom severity). **Specific to this review,**  
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51 **while HrQoL is not a symptom *per se*, it reflects the multidimensional construct of the**  
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53 **impact of a disease/condition on QoL. The ability to differentiate across different levels**  
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55 **of severity still stands as fundamental for a valid assessment of HrQoL (or caregiver**  
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3 **QoL) in observational studies or clinical trials.** (for further details, see Table 1.)  
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6 **RESULTS**  
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8 **Identified Measures and Their Use in Clinical Research**  
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10 A total of 19 clinical measures that have been used in HD research studies were identified.

11 One of these measures was excluded after abstract review due to inadequacy of measure  
12 construct (see supplementary material). The remaining 18 clinical measures were included for  
13 an in-depth review. Four measures were excluded because: 1) their sole use in HD was in case  
14 series without any clinimetric data available (the Manchester Assessment of Quality of Life,  
15 the Fatigue Impact scale), 2) it was created solely for a single study (a Non-Standardized QoL  
16 question), and 3) the proposed construct was inadequate for the current review (the Caregiver  
17 Burden Inventory). We grouped the 14 remaining measures into patient-centered HRQoL  
18 measures (n=12) and caregiver-centered QoL measures (n=2).  
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31 For patient-centered HRQoL measures, only The Medical Outcomes Study 36-Item Short-  
32 Form Health Survey was (SF-36) received a classification of “recommended” as a generic  
33 assessment of health status in manifest HD (severity). The 12-Item Short Form Health Survey  
34 (SF-12), the Sickness Impact Profile (SIP), the Huntington’s Disease Health-Related Quality  
35 of Life Questionnaire (HDQoL), and the 12-item World Health Organization Disability  
36 Assessment Schedule (WHODAS 2.0), were classified as “suggested” (see supplementary  
37 material for overview of all assessments classified as “suggested with caveats” or “listed”).  
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47 For caregiver-centered QoL measures, no measure was “recommended” for any of the  
48 purposes considered in this review. The Alzheimer’s Carer’s Quality of Life Inventory  
49 (AQLI), and the Huntington’s Disease Quality of Life Battery for Carers (HD-QoL-C) were  
50 classified as “suggested” (see supplementary material for overview of all assessments  
51 classified as “suggested with caveats” or “listed”).  
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*Patient-centered HRQoL rating scales*

**Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36)**

The SF-36 is an easy-to-administer self-reported set of generic measures of patient health status developed by the RAND Corporation as part of the Medical Outcomes Study (MOS). The SF-36 assesses eight functional dimensions: physical functioning, physical role limitations, mental health, emotional role limitations, social functioning, energy/vitality, pain, and general health perceptions, which can be summarized into two scores (physical and mental) and a global utility index.<sup>8</sup> The SF-36 has been widely used in HD<sup>9-12</sup>, **and the vast majority of the data was collected using version 1 of SF-36. The most current SF-36 version 2 has less ambiguous wording, improved layout, change in response choices for some items, and increased cross-cultural validity.**

Internal consistency has been shown for the SF-36 subscales, and domain and component scores (Cronbach's alpha  $\geq 0.80$ ).<sup>9-12</sup> The test-retest reliability coefficients, as measured by Intra-Class Coefficient (ICC), have been reported to be  $> 0.70$  for all domains, apart from the "emotional role" domain (ICC= 0.63). The Mental Health summary score has been shown to correlate only with the Beck Depression Inventory (BDI), while the Physical Health summary score of the SF-36 correlates with the BDI and a patient's self-rated and clinician's rating of patients' level of functioning/independence level, but no factor analysis has been conducted for the SF-36 in this population. **The SF-36 (total score, Vitality score, and Mental Component Score) have been shown to be sensitive to change in manifest HD clinical trials<sup>9 11, 13</sup>**

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3 **Recommendation:** The SF-36 is “recommended” as a generic assessment of health status in  
4 manifest HD (severity). The physical summary score seems to have better construct validity  
5 in HD. It is not known if the more recent SF-36 Version 2 performs equally well in HD as the  
6 SF-36 Version 1.  
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### 11 **Medical Outcomes Study 12-Item Short-Form Health Survey (SF-12)**

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15 The SF-12 is a 12-item shorter version of the SF-36. It covers the same functional dimensions  
16 as the SF-36 but includes fewer items, and thus, is quicker to administer (2 minutes vs. 8-12  
17 minutes for the SF-36).<sup>14</sup> It has been used less extensively in HD than the SF-36.<sup>8</sup> It is  
18 currently being used in Enroll-HD but no data have been reported.<sup>15</sup> Various degrees of  
19 convergent validity have been reported between the SF-12 Physical and Mental Health  
20 components, and the components of the HD-PRO-Triad (SF-12 physical component,  
21 Pearson’s correlations: motor, -0.79; cognition -0.77; emotion/behavioral dyscontrol -0.47;  
22 total score -0.76. SF-12 mental component, cognition -0.61; motor -0.51; total score -0.61),  
23 and emotion/behavioral dyscontrol (Pearson’s correlation: -0.53, all  $p < 0.05$ ).<sup>16</sup> The SF-12  
24 Physical component, but not the Mental Health component, has been shown to be sensitive to  
25 change following multidisciplinary rehabilitation.<sup>17</sup>  
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42 **Recommendation:** The SF-12 is “suggested” as a generic assessment of health status in  
43 manifest HD (severity), as it lacks test-retest reliability data and internal consistency data.  
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### 49 **Sickness Impact Profile (SIP) 136 items**

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51 The SIP is a generic measure of self-reported health status,<sup>18</sup> consisting of 136 items covering  
52 12 categories grouped into two subscales (physical and psychosocial). Scores are presented as  
53 a percentage of maximal dysfunction ranging from 0 to 100; a higher score indicates a higher  
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3 level of dysfunction. The SIP can take up to 30 minutes to complete. The SIP has been used in  
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5 two studies in manifest HD,<sup>19,20</sup> and a modified version using only 3 of the 12 categories was  
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7 used in trial for cognition in HD.<sup>21</sup> Internal consistency has been reported to be high  
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9 (Cronbach's alpha > 0.80),<sup>19</sup> as has test-retest reliability (ICC > 0.70) for scores of subscales  
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11 and all categories, aside from the "emotional behavior" (ICC=0.49) and "work" (ICC=0.68)  
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13 categories.<sup>19</sup> The SIP total score has been shown to correlate with both the patient's self-rated  
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15 (Spearman's correlation: -0.69) and clinician's rating (Spearman's correlation: -0.64) of  
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17 patients' level of functioning/independence (all  $p < 0.01$ ), with the BDI (Spearman's  
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19 correlation: 0.47,  $p < 0.01$ ), and with the Unified Huntington's Disease Rating Scale – Total  
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21 Motor Score (UHDRS-TMS) (Spearman's correlation: 0.32,  $p < 0.05$ ). The Psychosocial  
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23 subscale has been shown to correlate with both the patient's self-rated and the clinician's  
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25 rating of patients' level of functioning/independence, while the Physical subscale has been  
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27 shown to correlate with both the BDI and the UHDRS-TMS, in addition to both the patient's  
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29 self-rated and the clinician's rating of patients' level of functioning/independence.<sup>19</sup> In a  
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31 head-to-head comparison with the SF-36, the SIP was shown to have a worse clinimetric  
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33 performance with less robust construct validity and test-retest reliability. In addition, motor  
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35 symptoms appeared to influence some strictly non-motor dimensions of the SIP.<sup>19</sup>

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40 **Recommendation:** The SIP is "suggested" for assessing health status in manifest HD  
41  
42 (severity). There are limited clinimetric data on its use in HD, and it performs worse than the  
43  
44 SF-36 in a head-to-head comparison.  
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### **World Health Organization Disability Assessment Schedule (WHODAS) 2.0 (12-item)**

50  
51 The WHODAS 2.0 was developed by the World Health Organization (WHO) and includes six  
52  
53 domains of functioning. Nevertheless, the WHODAS 2.0 is often considered a generic  
54  
55 function-related measure of health status and consequently it was decided by consensus to  
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2  
3 include it in this review and not in the review of measures for assessment of functional ability  
4  
5 in HD. The WHODAS 2.0 can be administered as interviewer-, self-, and proxy-administered  
6  
7 forms. The WHODAS 2.0 12-item version, which is reviewed here, takes 5 minutes to  
8  
9 complete and covers 6 domains: cognition, mobility, self-care, getting along, life activities,  
10  
11 and participation. The WHODAS 2.0 12-item has been used in three studies including both  
12  
13 pre-manifest and manifest HD.<sup>22-24</sup> Internal consistency has been shown with a Cronbach's  
14  
15 alpha of 0.94 (95% CI: 0.93 - 0.94).<sup>22</sup> Moderate convergent validity has been reported  
16  
17 between the WHODAS 2.0 and other health-related quality of life assessments such as the  
18  
19 RAND-12 (Pearson correlations ranging from - 0.76 to -0.41), and the EuroQol Five-  
20  
21 dimension questionnaire (EQ-5D; Pearson correlations ranging from = - 0.65 and -0.49).<sup>22</sup>  
22  
23 The scores in the WHODAS 2.0 differ significantly across the disease spectrum from the pre-  
24  
25 manifest stage to late HD.<sup>22</sup> In pre-manifest HD, cross-sectional differences between low-,  
26  
27 mid- and high- disease burden groups have been reported.<sup>23</sup> In pre-manifest HD, only the  
28  
29 companion-rated (*proxy*) version of the WHODAS 2.0 has been shown to be sensitive to  
30  
31 change over a period of three years.<sup>23</sup>  
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37 **Recommendation:** The WHODAS 2.0 12-item is “suggested” for assessing health status in  
38  
39 HD (severity), as it lacks important clinimetric development in HD, namely, for test-retest  
40  
41 reliability testing and requires more robust construct validity.  
42  
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#### 46 **The Huntington's Disease Health-Related Quality of Life Questionnaire (HDQoL)**

47  
48 The HDQoL is a patient-reported questionnaire that was specifically developed for use in HD  
49  
50 to assess HRQoL.<sup>25</sup> The HDQoL covers three main domains: “primary physical and  
51  
52 cognitive”, “primary emotions and self”, and “primary services”.<sup>25</sup> It takes about 22 minutes  
53  
54 to complete. The HDQoL has been used in one study by authors<sup>26</sup> other than the group<sup>25,27</sup>  
55  
56 who originally developed it. The internal consistency of each of the domains has been shown  
57  
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3 to vary: “primary services” (Cronbach’s alpha = 0.76), “primary emotions and self”  
4  
5 (Cronbach’s alpha = 0.89), and “primary physical and cognitive” (Cronbach’s alpha = 0.96).  
6  
7 Test-retest reliability has been reported, but as this was evaluated with Cronbach’s alpha it  
8  
9 does not provide a true adequate measure of concordance.<sup>25</sup> Item ceiling effects range from  
10  
11 12.5% to 50%.<sup>25</sup>  
12

13  
14 **Recommendation:** The HDQoL is “suggested” for assessment of HRQoL in HD (severity),  
15  
16 as there are limited clinimetric data, namely related with construct validity and test-retest  
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18 reliability.  
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## Caregiver-centered QoL measures

### The Alzheimer's Carer's Quality of Life Inventory (ACQLI)

The ACQLI was developed to assess caregiver QoL in Alzheimer's disease (AD).<sup>28</sup> It is a quick (<5 minutes) questionnaire that consists of 30 items to which the caregiver answers true or not true; 1 point is given for each true answer, giving a possible total score of 30. The ACQLI has been used in a single HD study, in a head-to-head comparison with the HD-QoL-C. The ACQLI<sup>29</sup> showed excellent internal consistency (Cronbach alpha = 0.95).<sup>29</sup>

**Recommendation:** The ACQLI is "suggested" for assessing QoL for HD caregivers (severity), as its use in HD is limited to a single study in HD and clinimetric data in HD are limited to internal consistency.

### Huntington's Disease Quality of Life Battery for Carers (HD-QoL-C)

The HD-QoL-C is a HD-specific, multi-dimensional measure for family or caregivers of patients with HD. It is based upon the domains and facets of the Comprehensive Quality of Life Scale for Adults (ComQoL-A5).<sup>30</sup> Two versions are available: a long-form that consists of 34 items which incorporate measures on "practical aspects of caregiving" (n=9), "satisfaction with life" (n=8) and "feelings about living with HD" (n=17), and a short-form that consists of 20 items (3 items on "satisfaction of life", and 17 items on "feelings about living with HD").<sup>29</sup> The HD-QoL-C has been used in four studies in HD.<sup>9, 29, 31, 32</sup> Internal consistency of the long-form has been shown for the domains "satisfaction with life" (Cronbach's alpha = 0.91) and "feelings about living with HD" (Cronbach's alpha = 0.84), but not for the domain "practical aspects of caregiving" (Cronbach's alpha = 0.62).<sup>29</sup> For the short-form, internal consistency has been shown ("satisfaction with life", 0.92; total score, 0.88).<sup>29</sup> A low correlation has been reported between the HD-QoL-C and the WHO Quality of Life Short Form (WHO-QoL

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2  
3 BREF),<sup>32</sup> and the Huntington Quality of Life Instrument (H-QoL-I; correlations 0.22 to 0.28,  
4  
5 all  $p < 0.01$ ).<sup>31</sup>  
6

7 **Recommendation:** The HD-QoL-C is “suggested” for assessing QoL for HD caregivers  
8  
9 (severity). It warrants further **additional** clinimetric development, **namely in terms of**  
10  
11 **validity, reliability and data reproducibility by other groups.**  
12  
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## 14 15 16 Discussion

17  
18 We report here the results of an in-depth review of 12 measures used in HD studies to  
19  
20 evaluate patient-centered HRQoL. The SF-36 is the only measure that can be classified as  
21  
22 “recommended” to measure patient’s HRQoL in terms of severity. None of the HRQoL  
23  
24 measures developed specifically for HD have undergone sufficient clinimetric development to  
25  
26 warrant a similar classification level. There were no HRQoL measures recommended to  
27  
28 measure change of ~~intensity~~ **severity** over time. Regarding patient-centered HRQoL  
29  
30 measures, the sub-committee identified the following topics that warrant consideration when  
31  
32 developing these types of measures:  
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- 36  
37 1) The inherent subjective nature of self-reporting HRQoL warrants a special comment  
38  
39 as HD patients often lack insight regarding the presence or severity of their symptoms.  
40  
41 Along the same lines, the progressive cognitive impairment experienced by HD  
42  
43 patients is likely to introduce additional difficulties in ensuring the reliability of  
44  
45 patient-reported HRQoL in HD, namely, at later stages. Proxy reporting was rarely  
46  
47 included in the measures reviewed here and could be further assessed and considered  
48  
49 as a strategy to mitigate the above-mentioned limitations of patient-reported outcomes  
50  
51 in HD.  
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- 53  
54 2) As HD is a rare disease, studies often require a multi-center multi-national design that  
55  
56 raises the need for validation of HRQoL and QoL measures across different cultures.  
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3 In this review, there were no data available on a formal cross-cultural validation for  
4 any of the included measures when applied to HD populations. Consequently, cross-  
5 cultural validation should be implemented in future development programs of HRQoL  
6 measures in HD.  
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- 10  
11 3) We discussed the need for a generic measure vs. a disease-specific measure. Given the  
12 complexity of the clinical presentation of HD, it is likely that a generic scale will not  
13 capture all the disease features that significantly impact on the HRQoL of these  
14 patients, and thus a disease-specific measure may be better positioned to capture  
15 HRQoL in HD in a valid manner. On the other hand, although disease-specific  
16 measures are usually more sensitive, generic measures are able to capture global  
17 aspects of health that may be overlooked by the specific scales. A disease-specific  
18 measure that incorporates items likely found in generic measures is possibly the best  
19 approach.  
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34 The committee also looked at caregiver-centered QoL measures. We recognize that these  
35 measures have their own issues. In this review, we included two caregiver-centered QoL  
36 measures, one developed in Alzheimer's disease and another specifically developed for HD.  
37 Although caregivers play a role in caring for patients with a wide range of neurodegenerative  
38 disorders, and there are many features in common between caring for such patients and caring  
39 for a progressively dependent patient, there are limited data available to determine if  
40 similarities across neurodegenerative disorders are sufficient to warrant a general QoL scale  
41 or whether caregiver QoL needs to be disease-specific. **A caregiver-centered measure that  
42 considers both disease-specific items and more generic items would likely be the best  
43 approach.**  
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3 In the current review we identified several measures that were 'listed'. In many cases, these  
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5 measures have had limited evaluation of their measurement properties in HD. Still, other  
6  
7 recently developed HD-specific measures are in the initial stages of comprehensive  
8  
9 measurement property testing, these include the HDQLIFE, the HDQoL, or HD-PRO-  
10  
11 TRIAD. Importantly, some of these newer measures incorporate patient stakeholders in their  
12  
13 development, a contribution deemed essential by regulatory agencies such as the US Food and  
14  
15 Drug Administration (FDA) for patient-reported outcomes supporting labeling claims.<sup>33</sup>  
16  
17 Further testing of the measurement properties and uptake of these measures by groups other  
18  
19 than the developers is required to determine their real value in evaluating HRQoL in HD  
20  
21 patients. The committee concluded that the evaluation of the measurement properties of the  
22  
23 currently available measures that are included in this review, namely those developed  
24  
25 specifically for HD, is warranted. This should be a priority for HD researchers, considering  
26  
27 for example the increasing importance of patient-reported outcomes in the development of  
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29 novel therapies and their subsequent approval by regulatory authorities.  
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**EXCLUDED SCALES:**

- **Inadequate construct (n=1)**
  - Family members' perception of community health care services (CHCS) for persons with HD<sup>1</sup>
  - The Caregiver Burden Inventory<sup>2</sup>
  
- **Developed solely for a single study (n=1)**
  - A Non-Standardized QoL question<sup>3</sup>
  
- **Used in a single HD study and no clinimetric data available (n=2)**
  - The Manchester Assessment of Quality of Life<sup>4</sup>
  - The Fatigue Impact scale<sup>5</sup>

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<b>Short-Form 36 Health Survey (SF-36)</b>	
<b>I. Scale description</b>	
<b>Are there several versions of the scale?</b>	Yes. SF-36 v1 and SF-36 v2. RAND 36 includes the same items as SF-36 (from the medical outcome study). <sup>1,2</sup> SF-36 v2 has improved wording and instructions, which are less ambiguous. Layout of questions and answers is also improved; there is also increased comparability (translations and cultural adaptations), five-level response choices in place of dichotomous choices for the seven items in the Role-Physical and Role-Emotional scales, elimination of a response option from the items of the Mental Health and Vitality scales.
<b>If you replied YES, which was assessed?</b>	SF36 v1, as most of the clinimetric evaluation was done using this scale. NOTE: SF-36 v2 was used in Registry 3 and is currently used in Enroll-HD. <sup>3</sup>
<b>Scale construct/ overall structure</b>	The SF-36 a survey of health status developed for use in the Medical Outcomes Study, a multi-year study of patients with chronic conditions.  The SF-36 has 36 items that cover 8 functional dimensions: (physical functioning, physical role limitations, mental health, emotional role limitations, social functioning, energy/vitality, pain, and general health perceptions).  The SF-36 comprises two summary measures: physical component summary and the mental component summary.  Several different scoring methods are available, scoring procedures of the MOS SF-36 are available from the International Resource Center for Health Care Assessment. <sup>1,4</sup> <a href="http://www.rand.org/health/surveys_tools/mos/36-item-short-form/scoring.html">http://www.rand.org/health/surveys_tools/mos/36-item-short-form/scoring.html</a>
<b>a. Question items</b>	
<b>Items of presence of symptom/sign?</b>	Yes.
<b>Items of severity of symptom/sign?</b>	Yes.
<b>b. Response scale</b>	
<b>Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?</b>	Discrete (2, 3, 5 or 6).

<b>c. Is the scale easy to score?</b>	
<b>Approx. time to score patient</b>	8-12 minutes. <sup>5,6</sup>
<b>d. Raters</b>	
<b>Patient, caregiver, or clinician</b>	Patient self-report.
<b>If clinician-rated, is training for application required?</b>	Not applicable.
<b>e. Access to scale</b>	
<b>Copyright or public domain?</b>	The SF-36 v1 is freely available from the RAND corporation ( <a href="http://www.rand.org">www.rand.org</a> ) NOTE: the SF-36 v2 is licensed and has more materials for instruction and evaluation (Optum: <a href="http://www.optum.com">www.optum.com</a> )
<b>How can the scale be obtained (address or website)?</b>	<a href="http://www.rand.org/health/surveys_tools/mos/36-item-short-form.html">http://www.rand.org/health/surveys_tools/mos/36-item-short-form.html</a>
<b>Has the scale been published in other languages?</b>	Yes.
<b>II. Scale properties</b>	
<b>a. Content validity</b>	
<b>Any process for item generation and/or reduction</b>	Yes. The SF-36 was adapted from instruments completed by patients participating in the MOS. <sup>7</sup>
<b>b. Face validity</b>	
<b>Do the items of the scale cover different components of the specific domain?</b>	Yes.
<b>Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?</b>	No.
<b>Does it score current state or is it based on the patient/caregiver recall?</b>	Current state.
<b>What is the time frame (e.g. “during the past week”)?</b>	Mostly past 4 weeks. Some items in comparison with a year ago. <a href="http://www.rand.org/health/surveys_tools/mos/36-item-short-form/survey-instrument.html">http://www.rand.org/health/surveys_tools/mos/36-item-short-form/survey-instrument.html</a>
<b>c. Use</b>	
<b>Purpose: to measure severity, screen or diagnosis of the domain?</b>	Assess health status level (severity).
<b>Is there a cut-off score? (for HD, for non-HD)</b>	There is no cut-off score in HD. Mental health and mental component summary score cut offs have been established for diagnosing depression in various populations. <sup>8,9</sup>



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5	<b>d. Acceptability</b>	
6	<b>Is the length of the scale appropriate?</b>	Yes (judgment of the task force).
7	<b>Are there ambiguities in instructions to patient/rater (as applicable)?</b>	No (judgment of the task force).
8	<b>Are there ambiguities in rating anchors?</b>	No (judgment of the task force).
9	<b>Are the questions appropriate for use in an HD population?</b>	Yes, but they are not complete (judgment of the task force).
10	<b>Is the scale applicable across HD disease stages?</b>	Advanced HD patients will not be able to fill in the questionnaire by themselves (judgment of the task force).
11	<b>Are there HD stages in which the scale is not applicable?</b>	
12	<b>e. Has this scale been specifically developed for use in HD (yes/no)?</b>	No.
13	<b>e1. If yes to the above, has the scale been deployed in HD by groups other than the developers?</b>	Not applicable.
14	<b>III. Clinimetric/psychometric properties</b>	
15	<b>Are there clini- or psychometric properties in HD ?</b>	Yes.
16	<b>a. Reliability</b>	
17	<b>Assessed – not assessed</b>	Assessed in HD.
18	<b>Internal consistency</b>	<b>Manifest HD, n=48.</b> Cronbach's alpha $\geq 0.80$ . <sup>3</sup>
19	<b>Test-retest reliability</b>	<b>Manifest HD, n=48.</b> ICC > 0.70 for the SF-36 dimensions and aggregate scales, with exception of the “emotional role limitation” subscale for patients (ICC=0.64). <sup>3</sup>
20	<b>Inter-rater reliability</b>	—
21	<b>b. Validity in HD</b>	
22	<b>Assessed vs. not assessed</b>	Assessed in HD. <sup>3</sup>
23		There is no gold standard.
24	<b>Criterion validity (any comparison with gold-standard)</b>	<b>Note:</b> In a head-to-head comparison with the SIP, performed better, with more robust construct validity and test-retest reliability; in addition, motor symptoms appeared to influence some strictly non-motor dimensions of the SIP. <sup>3</sup>
25	<b>Construct validity</b>	
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<p><b>Factor analysis</b></p>	<p>Not assessed in HD. Assessed in non-HD populations during initial scale development.<sup>7</sup></p>
<p><b>Convergent validity</b></p>	<p><b>Manifest HD, n=48.</b> <i>Correlation of SF-36 v1 components with BDI, UHDRS Total Motor Section, clinician's self-rated score on the patient's level of functioning and patient's self-rated score on the patient's level of functioning</i></p> <ol style="list-style-type: none"> <li>1. <u>BDI</u>: correlation with all components and summary scores of the SF-36 (except for physical functioning). Correlation coefficient range: 0.35 – 0.66, all p&lt; 0.05. NOTE: higher correlations with non-physical components.<sup>3</sup></li> <li>2. <u>UHDRS Total Motor Section</u>: correlation with only <u>Mental health component</u> (Spearman's correlation, 0.27) and <u>Physical functioning</u> (Spearman's correlation, 0.54, all p&lt; 0.05)<sup>3</sup></li> <li>3. <u>Clinician's self-rated score on the patient's level of functioning</u>: correlation with the physical functioning component (Spearman's 0.70), physical role limitations (Spearman's 0.45), energy/vitality (Spearman's 0.35), general health perceptions (Spearman's 0.46), physical summary (Spearman's 0.59) and the SF-36 Utility Index (Spearman's 0.54; all p&lt; 0.05).<sup>3</sup></li> <li>4. <u>Patient's self-rated score on their level of functioning</u>: correlation with the physical functioning (Spearman's 0.64), physical role limitations (Spearman's 0.42), general health perceptions (Spearman's 0.44), physical summary (Spearman's 0.57) and the SF-36 Utility Index (Spearman's 0.51) all significantly correlate with the (p&lt; 0.05).<sup>3</sup></li> <li>5. <u>Telephone Interview of Cognitive Status</u>: correlation with the physical functioning (Spearman's 0.51), physical summary (Spearman's 0.36) and SF-36 Utility Index (Spearman's 0.32, all p&lt;0.05).</li> </ol> <p><b>Manifest HD, n=70.</b><sup>10</sup> <u>Physical summary score</u> correlated with UHDRS-TMS (r= -0.41), BDI (r= -0.51), verbal fluency (r= 0.21), symbol digit modality test (r= 0.29), and UHDRS-TFC (r= -0.51, all p&lt;0.05). <u>Mental summary score</u> correlated only with BDI (r= -0.72) and UHDRS-TFC (r=0.42)</p> <p><b>Manifest HD, n=80</b><sup>11</sup> SF-36 mental summary correlated with depressive mood (Hamilton Rating Scale), but not with motor or cognition scales.</p>

	<p><b>Manifest HD, n=252, app. 2 year of symptom duration</b><sup>12</sup>  H-QoL-I vs. SF-36:</p> <ul style="list-style-type: none"> <li>SF-36 physical summary vs.: H-QoL-I motor functioning (<math>r=0.74</math>), psychology (<math>r=0.59</math>), socializing (<math>r=0.55</math>) and total (<math>r=0.75</math>, all <math>p&lt;0.01</math>).</li> <li>SF-36 mental summary vs.: H-QoL-I motor functioning (0.44), psychology (0.58) and socializing (0.52) and total (<math>r=0.65</math>, all <math>p&lt;0.01</math>).</li> </ul> <p><b>Non-HD populations:</b> (please see Brazier 1992)<sup>13</sup></p>
<b>Divergent validity</b>	-
<b>Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)</b>	There is some good data to support this measure. It has a reasonable psychometric data and it performed better than the SIP (judgment of the task force)
<b>Generalizability</b>	
<b>Shown to be valid at any stage of HD?</b>	Yes, used in several HD populations. <sup>14</sup>
<b>Shown to be valid in any population with dementia or significant cognitive impairment?</b>	Questionable as it is a patient self-report (judgment of the task force).
<b>Responsiveness (detect change over time in the construct)</b>	
<b>Demonstrated to be sensitive to change (change over time or to treatment)?</b>	<p>The SF-36 has been shown to be sensitive to change following multidisciplinary rehabilitation in early-to-mid HD.<sup>15</sup>  No change reported in quality of life as measured with the SF-36 following a structured home-based exercise program in mid-stage HD.<sup>16</sup></p> <p>The SF-36 Vitality score significantly improved in HD (stages 2-3) following a 4 week treatment trial with (-)-OSU6162.<sup>17</sup>  The SF-36 Mental Component Score significantly improved following a 12-week community-based exercise program (<math>p&lt;0.05</math>).<sup>18</sup></p>
<b>Interpretability</b>	
<b>Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?</b>	No.
<b>Floor and ceiling effects</b>	Not assessed in HD.
<b>Score distributions</b>	<p><b>Manifest HD, n=70.</b><sup>10</sup></p> <ul style="list-style-type: none"> <li>Physical functioning: 66.80 (34.11)</li> </ul>

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	<ul style="list-style-type: none"> <li>• Role functioning—physical: 50.60 (44.58)</li> <li>• Bodily pain: 84.45 (22.97)</li> <li>• General health: 57.43 (23.69)</li> <li>• Vitality: 59.21 (23.69)</li> <li>• Social functioning: 61.75 (22.13)</li> <li>• Role functioning emotional: 57.62 (48.13)</li> <li>• Mental health: 71.70 (19.58)</li> <li>• Physical summary score: 26.43 (39.11)</li> <li>• Mental summary score: 19.35 (41.60)</li> </ul> <p><b>NOTE:</b> The SF-36 (<b>Version 2</b>) total score has been shown to differentiate between HD and controls (<math>p &lt; 0.0001</math>), between pre-manifest HD and HD (<math>p = 0.0004</math>), and between HD stage 2 and HD stage 1 (<math>p &lt; 0.0001</math>), but not between pre-manifest HD vs. controls (<math>p = 0.21</math>).<sup>14</sup></p>
<b>IV. Overall impression</b>	
<b>Advantages</b>	Generic instrument. This is a generic instrument, which enables comparison between diseases. Relevant, depending on question at hand.
<b>Disadvantages</b>	Does not differentiate emotion and mental aspects
<b>V. Recommendation</b>	<b>Recommended as a generic assessment of health status in HD (severity)</b>

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RAND > RAND Health > Surveys > RAND Medical Outcomes Study > 36-Item Short Form Survey (SF-36) >

## 36-Item Short Form Survey Instrument (SF-36)

### RAND 36-Item Health Survey 1.0 Questionnaire Items

Choose one option for each questionnaire item.

1. In general, would you say your health is:

- 1 - Excellent
- 2 - Very good
- 3 - Good
- 4 - Fair
- 5 - Poor

2. Compared to one year ago, how would you rate your health in general now?

- 1 - Much better now than one year ago
- 2 - Somewhat better now than one year ago
- 3 - About the same
- 4 - Somewhat worse now than one year ago
- 5 - Much worse now than one year ago

The following items are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
3. <b>Vigorous activities</b> , such as running, lifting heavy objects, participating in strenuous sports	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
4. <b>Moderate activities</b> , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
5. Lifting or carrying groceries	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
6. Climbing <b>several</b> flights of stairs	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
7. Climbing <b>one</b> flight of stairs	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
8. Bending, kneeling, or stooping	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
9. Walking <b>more than a mile</b>	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
10. Walking <b>several blocks</b>	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
11. Walking <b>one block</b>	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3
12. Bathing or dressing yourself	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3

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During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health?**

- |   | Yes                     | No                      |
|---|-------------------------|-------------------------|
| 13. Cut down the <b>amount of time</b> you spent on work or other activities                          | <input type="radio"/> 1 | <input type="radio"/> 2 |
| 14. <b>Accomplished less</b> than you would like  | <input type="radio"/> 1 | <input type="radio"/> 2 |
| 15. Were limited in the <b>kind</b> of work or other activities                                       | <input type="radio"/> 1 | <input type="radio"/> 2 |
| 16. Had <b>difficulty</b> performing the work or other activities (for example, it took extra effort) | <input type="radio"/> 1 | <input type="radio"/> 2 |

During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

- |  | Yes                     | No                      |
|--|-------------------------|-------------------------|
| 17. Cut down the <b>amount of time</b> you spent on work or other activities | <input type="radio"/> 1 | <input type="radio"/> 2 |
| 18. <b>Accomplished less</b> than you would like                             | <input type="radio"/> 1 | <input type="radio"/> 2 |
| 19. Didn't do work or other activities as <b>carefully</b> as usual          | <input type="radio"/> 1 | <input type="radio"/> 2 |

20. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?

- 1 - Not at all
- 2 - Slightly
- 3 - Moderately
- 4 - Quite a bit
- 5 - Extremely

21. How much **bodily** pain have you had during the **past 4 weeks?**

- 1 - None
- 2 - Very mild
- 3 - Mild
- 4 - Moderate
- 5 - Severe
- 6 - Very severe

22. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?

- 1 - Not at all
- 2 - A little bit
- 3 - Moderately
- 4 - Quite a bit
- 5 - Extremely

These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the **past 4 weeks**...

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
23. Did you feel full of pep?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	<input type="radio"/> 6
24. Have you been a very nervous person?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	<input type="radio"/> 6
25. Have you felt so down in the dumps that nothing could cheer you up?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	<input type="radio"/> 6
26. Have you felt calm and peaceful?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	<input type="radio"/> 6
27. Did you have a lot of energy?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	<input type="radio"/> 6
28. Have you felt downhearted and blue?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	<input type="radio"/> 6
29. Did you feel worn out?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	<input type="radio"/> 6
30. Have you been a happy person?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	<input type="radio"/> 6
31. Did you feel tired?	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5	<input type="radio"/> 6

32. During the **past 4 weeks**, how much of the time has **your physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?

- 1 - All of the time
- 2 - Most of the time
- 3 - Some of the time
- 4 - A little of the time
- 5 - None of the time

How TRUE or FALSE is **each** of the following statements for you.

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
33. I seem to get sick a little easier than other people	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5
34. I am as healthy as anybody I know	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5
35. I expect my health to get worse	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5
36. My health is excellent	<input type="radio"/> 1	<input type="radio"/> 2	<input type="radio"/> 3	<input type="radio"/> 4	<input type="radio"/> 5

**ABOUT**

The RAND Corporation is a research organization that develops solutions to public policy challenges to help make communities throughout the world safer and more secure, healthier and more prosperous. RAND is nonprofit, nonpartisan, and committed to the public interest.

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<b>Short-Form 12 Health Survey (SF-12)</b>	
<b>I. Scale description</b>	
<b>Are there several versions of the scale?</b>	Yes. SF-12 v1, SF-12 v2. <sup>1</sup>
<b>If you replied YES, which was assessed?</b>	Both versions.
<b>Scale construct/ overall structure</b>	The SF-12 is based in the SF-36, but has fewer items (12 vs. 36).  As the SF-36, the SF-12 is a patient-reported survey of patient health that covers 8 functional dimensions: physical functioning, physical role limitations, mental health, emotional role limitations, social functioning, energy/vitality, pain, and general health perceptions.
<b>a. Question items</b>	
<b>Items of presence of symptom/sign?</b>	Yes.
<b>Items of severity of symptom/sign?</b>	Yes.
<b>b. Response scale</b>	
<b>Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?</b>	Discrete steps (3 or 5).
<b>c. Is the scale easy to score?</b>	
<b>Approx. time to score patient</b>	SF-12, < 2 minutes. <sup>2</sup>
<b>d. Raters</b>	
<b>Patient, caregiver, or clinician</b>	Patient self-report.
<b>If clinician-rated, is training for application required?</b>	Not applicable.
<b>e. Access to scale</b>	
<b>Copyright or public domain?</b>	Copyright.
<b>How can the scale be obtained (address or website)?</b>	QualityMetric @ <a href="https://www.optum.com/campaign/lis/outcomes-survey-request.html">https://www.optum.com/campaign/lis/outcomes-survey-request.html</a>
<b>Has the scale been published in other languages?</b>	Yes.
<b>II. Scale properties</b>	
<b>a. Content validity</b>	
<b>Any process for item generation and/or reduction</b>	Yes. The SF-12 represents an item reduction effort from SF-36.  The following criteria were followed for item reduction: <sup>3</sup> 1) Could be scored to explain at least 90% of the variance in SF-36 physical and mental health summary measures; 2) Would reproduce the average scores for the summary measures and eight-scale

	profile with a high degree of comparability; 3) Could be printed on one to two pages of a self-administered questionnaire or administered by an interviewer in less than 2 minutes, on average.
<b>b. Face validity</b>	
<b>Do the items of the scale cover different components of the specific domain?</b>	Yes (judgment of the task force).
<b>Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?</b>	No (judgment of the task force).
<b>Does it score current state or is it based on the patient/caregiver recall?</b>	Current state and patient recall.
<b>What is the time frame (e.g. “during the past week”)?</b>	Past 4 weeks, but some items refer to one year ago.
<b>c. Use</b>	
<b>Purpose: to measure severity, screen or diagnosis of the domain?</b>	Assess health status level (severity).
<b>Is there a cut-off score? (for HD, for non-HD)</b>	No.
<b>d. Acceptability</b>	
<b>Is the length of the scale appropriate?</b>	Yes (judgment of the task force).
<b>Are there ambiguities in instructions to patient/rater (as applicable)?</b>	No (judgment of the task force).
<b>Are there ambiguities in rating anchors?</b>	No (judgment of the task force).
<b>Are the questions appropriate for use in an HD population?</b>	Yes (judgment of the task force).
<b>Is the scale applicable across HD disease stages?</b>	Not suitable in advanced stages (judgment of the task force).
<b>Are there HD stages in which the scale is not applicable?</b>	
<b>e. Has this scale been specifically developed for use in HD (yes/no)?</b>	No.
<b>e1. If yes to the above, has the scale been deployed in HD by groups other than the developers?</b>	Not applicable.
<b>III. Clinimetric/psychometric properties</b>	
<b>Are there clini- or psychometric properties in HD ?</b>	Yes.
<b>a. Reliability</b>	
<b>Assessed – not assessed</b>	Assessed in HD.

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5	<b>Internal consistency</b>	Not assessed in HD.
6	<b>Test-retest reliability</b>	Not assessed in HD.
7	<b>Inter-rater reliability</b>	<b>Manifest HD, n=132; HD caregivers, n=40</b> SF-12 Physical component: HD individuals self-reported vs. caregiver-reported scores: ICC = 0.94 (CI 95%: 0.88, 0.97). <sup>4</sup> SF-12 Mental health component: HD individuals self-reported vs. caregiver-reported scores: ICC = 0.83 (95% CI: 0.68, 0.91). <sup>4</sup>
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12	<b>b. Validity in HD</b>	
13	<b>Assessed vs. not assessed</b>	Partially in the development of new scales.
14	<b>Criterion validity (any comparison with gold-standard)</b>	-
15	<b>Construct validity</b>	
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17	<b>Factor analysis</b>	Not assessed in HD.
18	<b>Convergent validity</b>	<b>Manifest HD, n=152.<sup>5</sup></b> SF-12v2 physical component: Correlation coefficients: Physical and Cognitive (0.8) of the Primary scales, and the Physical and Functional (0.8) of the Six Specific Scales of the HDQoL. SF-12v2 mental component: Correlation coefficients: emotions and self (0.8) of the Primary scales, and Mood state (0.7), Self and Vitality (0.7) of the Six Specific Scales of the HDQoL. <b>NOTE: P values not reported.</b>  <b>Manifest HD, n=132,<sup>4</sup></b> Correlation between the SF-12v2 components of HD-PRO-Triad: SF-12 physical component correlated with motor (Pearson's correlation: -0.79), cognition (Pearson's correlation: -0.77), total score (Pearson's correlation: -0.76) and emotion/behavioral dyscontrol (Pearson's correlation: (-0.47). SF-12 mental component correlated with cognition (Pearson's correlation: -0.61), total score (Pearson's correlation: -0.61), motor (Pearson's correlation: -0.51), and emotion/behavioral dyscontrol (Pearson's correlation: -0.53). NOTE: p<0.05. <sup>4</sup>
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34	<b>Divergent validity</b>	<b>Manifest HD, n=152.<sup>5</sup></b> SF-12v2 physical component: Correlation coefficients: emotions and self (0.4), of the Primary scales, and the Mood state (0.3), Self and Vitality (0.5) of the Six Specific Scales of the HDQoL. SF-12v2 mental component: Correlation coefficients: Physical and Cognitive (0.5) of the Primary scales, and Physical and Functional (0.4) of the Six Specific Scales of the HDQoL, <b>NOTE: P values not reported.</b>
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Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)	Good evidence of construct validity. No reliability data.
<b>Generalizability</b>	
Shown to be valid at any stage of HD?	No.
Shown to be valid in any population with dementia or significant cognitive impairment?	No. Questionable as self-report by patient
<b>Responsiveness (detect change over time in the construct)</b>	
Demonstrated to be sensitive to change (change over time or to treatment)?	The SF-12 physical component, but not the mental component, has been shown to be sensitive to change following a multidisciplinary rehabilitation. <sup>6</sup>
<b>Interpretability</b>	
Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?	No.
Floor and ceiling effects	Not reported.
Score distributions	<p><b>Manifest HD, n=105.<sup>7</sup></b>                      SF-12v2 Physical Component Score: 41.52 ± 12.78                      SF-12v2 Mental Component Score: 39.95 ± 11.50</p> <p><b>Manifest HD, n=132<sup>4</sup></b>                      SF-12v2 Physical Component Score: 37.7 ± 10.8                      SF-12v2 Mental Component Score: 41.3 ± 10.5</p>
<b>IV. Overall impression</b>	
Advantages	This is a generic instrument, which enables comparison between diseases. Does not differentiate emotional aspects. Good for physical health related items. Relevant, depending on question at hand. Heavily used in HD (Registry, Enroll-HD). Relevant depending on research question, purpose of use.
Disadvantages	Does not differentiate emotion, mental Physical component is acceptable.
<b>V. Recommendation</b>	<b>Suggested as a generic assessment of health status in manifest HD (severity)</b>

## References

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<b>Sickness Impact Profile (SIP)</b>	
<b>I. Scale description</b>	
<b>Are there several versions of the scale?</b>	Yes. Original of 136 items. In 1994, a shorter version of the SIP, the SIP-68, was created and evaluated; this version contains 68 items in six areas of activity: somatic autonomy; mobility control; psychological autonomy and communication; social behavior; emotional stability; and mobility range. <sup>1</sup> Cubo et al. used a modified version that included only 3 out of 12 categories of the SIP. <sup>2</sup>
<b>If you replied YES, which was assessed?</b>	The original, 136 items
<b>Scale construct/ overall structure</b>	It is a generic measure of perceived health status. <sup>3</sup>  It consists of 136 items; 2 subscales physical and psychosocial; 12 categories (sleep and rest, eating, work, home management, recreation and pastimes, ambulation, mobility, body care and movement, social interaction, alertness behavior, emotional behavior, communication).  An overall SIP percent score may be obtained by summing the scale values of all items endorsed in the entire SIP, dividing that sum by the sum of the values of all the items in the SIP and multiplying the obtained quotient by 100. Scores for each category are calculated in a like manner.  Scores on the SIP are presented as a percentages of maximal dysfunction ranging from 0 to 100, <u>higher scores on the SIP indicate a higher level of dysfunction</u> : SIP scores < 6 indicate no impairment, scores between 6 and 10 are indicative of mild impairment, scores between 15 and 20 indicate moderate to severe impairment, and scores > 20 are indicative of severe illness-related impairment. <sup>3</sup>
<b>a. Question items</b>	
<b>Items of presence of symptom/sign?</b>	Yes.
<b>Items of severity of symptom/sign?</b>	No.
<b>b. Response scale</b>	
<b>Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?</b>	The SIP is a checklist, whereby items that apply on a given day are ticked.
<b>c. Is the scale easy to score?</b>	

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5	<b>Approx. time to score patient</b>	30 minutes (judgment of the task force).
6	<b>d. Raters</b>	
7	<b>Patient, caregiver, or clinician</b>	Patient self-report or interview.
8	<b>If clinician-rated, is training for application required?</b>	No.
9	<b>e. Access to scale</b>	
10	<b>Copyright or public domain?</b>	Copyright.
11	<b>How can the scale be obtained (address or website)?</b>	E-mail Mapi Research Trust @ <a href="mailto:trust@mapi.fr">trust@mapi.fr</a>
12	<b>Has the scale been published in other languages?</b>	None currently authorized by the copyright holder. Guidelines for translation are available through the <a href="#">Medical Outcomes Trust</a> or through <a href="#">Johns Hopkins University</a> . (Judgment of the task force).
13	<b>II. Scale properties</b>	
14	<b>a. Content validity</b>	
15		Initial work began in 1972 with the development of procedures to collect and evaluate statements describing sickness-related behavioral dysfunction from patients, individuals caring for patients, and apparently healthy health care professionals.
16		These statements were subjected to standard grouping and sorting techniques yielding 312 unique items (reduced to 136 in the final form) each describing a sickness-related behavioral change.
17	<b>Any process for item generation and/or reduction</b>	The 312 items were grouped into areas of activity or categories and then included in a prototype Sickness Impact Profile. This questionnaire, together with its applications, reliability testing, validation and revisions was the subject of the field trials to be described.
18		The strategy chosen for developing, assessing and revising the SIP was based on methodological principles that emphasized the evaluation of reliability and validity in a variety of settings, the determination of the relationship of the SIP to other measures currently in use and the evaluation of its unique contribution as an outcome measure of health status. This strategy was operationalized and implemented through a series of field trials, each designed to address specific issues in the developmental process. The sequential properties of the overall research design were particularly valuable. <sup>3</sup>
19	<b>b. Face validity</b>	
20	<b>Do the items of the scale cover different components of the specific domain?</b>	Yes.
21	<b>Is the scale heavily weighted towards one aspect of the</b>	-
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1	domain it measures and which components of the domain	
2	are not covered?	
3	Does it score current state or is it based on the	Current time.
4	patient/caregiver recall?	
5	What is the time frame (e.g. “during the past week”)?	“Today”
6	c. Use	
7	Purpose: to measure severity, screen or diagnosis of the	Assess perceived health status (severity).
8	domain?	
9	Is there a cut-off score? (for HD, for non-HD)	No
10	d. Acceptability	
11	Is the length of the scale appropriate?	Too long (judgment of the task force).
12	Are there ambiguities in instructions to patient/rater (as	No (judgment of the task force).
13	applicable)?	
14	Are there ambiguities in rating anchors?	No (judgment of the task force).
15	Are the questions appropriate for use in an HD	Not enough data to determine.
16	population?	
17	Is the scale applicable across HD disease stages?	Not enough data to determine.
18	Are there HD stages in which the scale is not applicable?	
19	e. Has this scale been specifically developed for use in HD	No.
20	(yes/no)?	
21	e1. If yes to the above, has the scale been deployed in HD	Not applicable.
22	by groups other than the developers?	
23	<b>III. Clinimetric/psychometric properties</b>	
24	Are there clini- or psychometric properties in HD ?	Yes. <sup>4</sup>
25	a. Reliability	
26	Assessed – not assessed	Assessed in HD.
27	Internal consistency	<b>Manifest HD, n=48.</b> <sup>4</sup> Cronbach’s alpha: > 0.80 at time 1 and time 2 (exact value not provided).
28	Test-retest reliability	<b>Manifest HD, n=48.</b> <sup>4</sup> All ICC's above 0.7 (including total score), except emotional behavior and work.
29	Inter-rater reliability	-
30	b. Validity in HD	



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5	<b>Assessed vs. not assessed</b>	Assessed in HD.
6	<b>Overall impression: good – not good</b>	Very limited data for an impression to be given.
7	<b>Criterion validity (any comparison with gold-standard)</b>	-
8	<b>Construct validity</b>	
9	<b>Factor analysis</b>	Not assessed in HD.
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11	<b>Convergent validity</b>	<b>Manifest HD, n=48.</b> <i>Correlation of SIP components with BDI, UHDRS Total Motor Section, clinician's self-rated score on the patient's level of functioning and patient's self-rated score on the patient's level of functioning.</i> <sup>4</sup>
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13		<u>Physical dimension:</u> correlation with BDI (r=0.29), UHDRS Total Motor Section (r=0.42), Clinician's self-rated score on the patient's level of functioning (r=-0.72), Patient's self-rated score on their level of functioning (r=-0.72), and Telephone Interview of Cognitive Status (r=-0.29).
14		<u>Psychosocial dimension:</u> correlation with Clinician's self-rated score on the patient's level of functioning (r=-0.40), and Patient's self-rated score on their level of functioning (r=-0.51), and BDI (r= 0.60).
15		<u>Total SIP score:</u> correlation with BDI (r=0.47), UHDRS Total Motor Section (r=0.32), Clinician's self-rated score on the patient's level of functioning (r=-0.64), Patient's self-rated score on their level of functioning (r=-0.69), and Telephone Interview of Cognitive Status (r=-0.33)
16		NOTE: all p<0.05.
17	<b>Divergent validity</b>	See above in “ <b>Convergent validity</b> ”
18	<b>Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)</b>	Spearman's correlations support convergent/divergent validity but very variable. Too long. (Judgment of the task force).
19	<b>Generalizability</b>	
20	<b>Shown to be valid at any stage of HD?</b>	Only assessed in manifest HD. <sup>4,5</sup>
21	<b>Shown to be valid in any population with dementia or significant cognitive impairment?</b>	Yes. (Judgment of the task force).
22	<b>Responsiveness (detect change over time in the construct)</b>	
23	<b>Demonstrated to be sensitive to change (change over time or to treatment)?</b>	Unknown. NOTE: Cubo et al. used a modified version, reported no change but the trial was negative. <sup>2</sup>
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<b>Interpretability</b>	
<b>Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?</b>	No
<b>Floor and ceiling effects</b>	Not reported.
<b>Score distributions</b>	Not reported. References in HD only show graphs with scores.
<b>IV. Overall impression</b>	
<b>Advantages</b>	Some psychometric data in HD.
<b>Disadvantages</b>	Too long. Performed worse in a head-to-head comparison with SF-36.
<b>V. Recommendation</b>	
<b>Suggested for assessing perceived health status in manifest HD (severity)</b>	

## References

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- Cubo E, Shannon KM, Tracy D, Jaglin JA, Bernard BA, Wu J, *et al.* Effect of donepezil on motor and cognitive function in Huntington disease. *Neurology* 2006;67:1268-71.
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<b>12-item World Health Organization Disability Assessment Schedule (WHODAS) 2.0</b>	
<b>I. Scale description</b>	
<b>Are there several versions of the scale?</b>	Yes. There are 12-item and 36-item versions available. The 36-item version can be scored simply or via an item response theory (IRT)-based scoring algorithm. The WHODAS is available as interviewer-, self-, and proxy-administered forms. <a href="http://www.who.int/classifications/icf/more_whodas/en/">http://www.who.int/classifications/icf/more_whodas/en/</a>
<b>If you replied YES, which was assessed?</b>	WHODAS 2.0, 12-item version (more frequently used in HD).
<b>Scale construct/ overall structure</b>	The WHODAS II assesses health status, disability, and functioning, linked to concepts from the International Classification of Functioning, Disability and Health (ICF) framework.  For the 12-item version, there are 2 items in six areas of day-to-day functioning: <ol style="list-style-type: none"> <li>1. Cognition</li> <li>2. Mobility</li> <li>3. Self-care</li> <li>4. Getting along</li> <li>5. Life activities</li> <li>6. Participation</li> </ol> Total score computed as the sum of the 12 items, with higher scores indicating worse functioning.
<b>a. Question items</b>	
<b>Items of presence of symptom/sign?</b>	Yes.
<b>Items of severity of symptom/sign?</b>	Yes.
<b>b. Response scale</b>	
<b>Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?</b>	Five response categories for each item (none=1; mild=2; moderate=3; severe=4; extreme/cannot do=5). <a href="http://www.who.int/classifications/icf/more_whodas/en/">http://www.who.int/classifications/icf/more_whodas/en/</a>
<b>c. Is the scale easy to score?</b>	
<b>Approx. time to score patient</b>	5 minutes. <a href="http://www.who.int/classifications/icf/more_whodas/en/">http://www.who.int/classifications/icf/more_whodas/en/</a>

<i>d. Raters</i>	
<b>Patient, caregiver, or clinician</b>	<b>VARIABLE:</b> Self-administration of a paper-and-pencil version. Interview administered in person or over the telephone. Proxy i.e. to obtain a third-party view of functioning such as; family members, caretakers or other observers.
<b>If clinician-rated, is training for application required?</b>	
<i>e. Access to scale</i>	
<b>Copyright or public domain?</b>	Public domain.
<b>How can the scale be obtained (address or website)?</b>	<a href="http://www.who.int/classifications/icf/more_whodas/en/">http://www.who.int/classifications/icf/more_whodas/en/</a>
<b>Has the scale been published in other languages?</b>	Yes.
<b>II. Scale properties</b>	
<b>a. Content validity</b>	
<b>Any process for item generation and/or reduction</b>	—
<b>b. Face validity</b>	
<b>Do the items of the scale cover different components of the specific domain?</b>	It covers multiple domains: examines activity limitations and restrictions for six different tasks: (1) understanding and communication; (2) self-care; (3) mobility (getting around); (4) interpersonal relationships (getting along with others); (5) work and household roles (life activities); and (6) community and civic roles (participation);
<b>Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?</b>	1-2 items domain so relatively well balanced (judgment of the task force).
<b>Does it score current state or is it based on the patient/caregiver recall?</b>	Patient/caregiver recall.
<b>What is the time frame (e.g. “during the past week”)?</b>	The past 30 days.
<b>c. Use</b>	
<b>Purpose: to measure severity, screen or diagnosis of the domain?</b>	Assess health status (severity).
<b>Is there a cut-off score? (for HD, for non-HD)</b>	No.
<b>d. Acceptability</b>	
<b>Is the length of the scale appropriate?</b>	Yes (judgment of the task force).
<b>Are there ambiguities in instructions to patient/rater (as applicable)?</b>	No (judgment of the task force)

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5	<b>Are there ambiguities in rating anchors?</b>	No (judgment of the task force).
6	<b>Are the questions appropriate for use in an HD population?</b>	The questions are somewhat general. (Judgment of the task force).
7	<b>Is the scale applicable across HD disease stages?</b>	Limited information on applicability in very late stage HD, and also in the context of cognitive
8	<b>Are there HD stages in which the scale is not applicable?</b>	impairment. (Judgment of the task force).
9	<b>e. Has this scale been specifically developed for use in HD (yes/no)?</b>	No.
10	<b>e1. If yes to the above, has the scale been deployed in HD by groups other than the developers?</b>	Not applicable.
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13	<b>III. Clinimetric/psychometric properties</b>	
14	<b>Are there clini- or psychometric properties in HD ?</b>	Yes. <sup>1,2</sup>
15	<b>a. Reliability</b>	
16	<b>Assessed – not assessed</b>	Assessed in HD
17	<b>Internal consistency</b>	<b>Prodromal and/or manifest HD (n=477)<sup>1</sup></b> a) Overall Cronbach's alpha = 0.94 (95% CI: 0.93-0.94). b) For the six subdomains, Cronbach's alpha was 0.90 for self-care (95% CI: 0.88–0.91), 0.89 for mobility (95% CI: 0.87–0.91), 0.83 for life activities (95% CI: 0.80–0.86), 0.82 for cognition (95% CI: 0.78–0.85), 0.74 for getting along (95% CI: 0.69–0.78), and 0.74 for participation (95% CI: 0.69–0.78).
18	<b>Test-retest reliability</b>	-
19	<b>Inter-rater reliability</b>	-
20	<b>b. Validity in HD</b>	
21	<b>Assessed vs. not assessed</b>	Assessed in HD.
22	<b>Criterion validity (any comparison with gold-standard)</b>	-
23	<b>Construct validity</b>	
24	<b>Factor analysis</b>	<b>Prodromal and/or manifest HD (n=477)<sup>1</sup></b> 6 factor structure replicated in HD sample, CFI = 0.99, TLI = 0.99, and RMSEA = 0.02.
25	<b>Convergent validity</b>	<b>Prodromal and/or manifest HD (n=477)<sup>1</sup></b> Moderate to significant correlations with other general measures of HRQOL (i.e., EQ5D and RAND-12); correlations ranged from -0.41 to -0.76 (RAND-12 Physical [-0.76], EQ-5D index [-0.65], EQ-5D health scale [-0.49], and the RAND-12 Mental [-0.41], all p<0.0001. <sup>1</sup>
26	<b>Divergent validity</b>	-
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Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)	
<b>Generalizability</b>	
Shown to be valid at any stage of HD?	<b>Prodromal and/or manifest HD (n=477)<sup>1</sup></b> Analysis showed that late HD participants have poorer scores than early HD, who had lower scores than pre-manifest HD participants. <b>Pre-manifest HD, n=726; companions, n= 630<sup>2,3</sup></b> In pre-manifest HD, cross-sectional differences between low-, mid- and high- disease burden groups have been reported.
Shown to be valid in any population with dementia or significant cognitive impairment?	No. (judgment of the task force)
<b>Responsiveness (detect change over time in the construct)</b>	
Demonstrated to be sensitive to change (change over time or to treatment)?	No. <b>NOTE:</b> in Kim et al, <u>Pre-manifest HD, n=726; companions, n= 630</u> , data suggests sensitivity over a three-year duration only for the proxy-rated version. <sup>2,3</sup>
<b>Interpretability</b>	
Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?	Not reported.
Floor and ceiling effects	<b>Prodromal and/or manifest HD (n=477)<sup>1</sup></b> Ceiling effect (19.5%). <sup>1</sup>
Score distributions	-
<b>IV. Overall impression</b>	
Advantages	The WHODAS 12-item version is brief and has validation data in both pre-manifest and manifest HD.
Disadvantages	Limited uptake.
<b>V. Recommendation</b>	<b>Suggested for assessing health status in HD (severity)</b>

References

1. Carlozzi NE, Kratz AL, Downing NR, Goodnight S, Miner JA, Migliore N, *et al.* Validity of the 12-item World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) in individuals with Huntington disease (HD). *Qual Life Res* 2015;24:1963-71.

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2. Downing NR, Kim JI, Williams JK, Long JD, Mills JA, Paulsen JS. WHODAS 2.0 in prodromal Huntington disease: measures of functioning in neuropsychiatric disease. *Eur J Hum Genet* 2014;22:958-63.

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For Peer Review

<b>Huntington's Disease Health-related Quality of Life questionnaire (HDQoL)</b>	
<b>I. Scale description</b>	
<b>Are there several versions of the scale?</b>	No.
<b>If you replied YES, which was been assessed?</b>	Not applicable.
<b>Scale construct/ overall structure</b>	HDQoL is a 40-item scale with three primary subscales (Primary Physical and Cognitive (PPC), (ii) Primary Emotions and Self (PES), and (iii) Primary Services (PSR) and Six Specific Scales (Cognitive, Hopes and Worries, Services, Physical and Functional, Mood State, Self and Vitality). <sup>1</sup>
<b>a. Question items</b>	
<b>Items of presence of symptom/sign?</b>	Yes
<b>Items of severity of symptom/sign?</b>	No
<b>b. Response scale</b>	
<b>Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?</b>	Discrete: Never, Very rarely, Infrequently, Sometimes, Often, Most of the time, All Of the time
<b>c. Is the scale easy to score?</b>	
<b>Approx. time to score patient</b>	22 minutes (administration time). <sup>1</sup>
<b>d. Raters</b>	
<b>Patient, caregiver, or clinician</b>	Patient NOTE: the patient can invite a proxy to complete a form based on how the proxy felt the patient would answer. <sup>1</sup> Agreement between patient-Proxy forms agreement was substantial to excellent for the Summary Scale score of the HDQoL, and also for most of its Specific Scales. <sup>2</sup> There was a tendency for proxies to over-estimate internal emotional aspects of patients' health-related quality of life as better than patients' own ratings, while on more external physical and cognitive aspects the reverse was true. <sup>3</sup>
<b>If clinician-rated, is training for application required?</b>	Not applicable
<b>e. Access to scale</b>	
<b>Copyright or public domain?</b>	Copyright
<b>How can the scale be obtained (address or website)?</b>	<a href="http://www.hdqol.info">http://www.hdqol.info</a>



1 2 3 4 5 6 7 8 9	<b>Has the scale been published in other languages?</b>	Unknown. NOTE: during development of item structure: <i>Where necessary, these items were translated by two appropriately bilingual members of the European Huntington's Disease Network Quality of Life Working Group and/or their associates.</i> <sup>1</sup>
10	<b>II. Scale properties</b>	
11	<b>a. Content validity</b>	
12 13 14 15 16 17 18 19 20 21 22 23	<b>Any process for item generation and/or reduction</b>	In Hocaoglu 2012 et al: <sup>1</sup> 1) <u>Item generation from qualitative interviews</u> Semi-structured interviews were conducted with the full spectrum of people living with HD, to form a pool of items, which were then examined in a larger sample prior to data-driven item reduction. 2) <u>Item selection and questionnaire refinement</u> Feedback on these initial items was sought from a wider pool of people living with HD to aid data-driven item selection. Items with low importance scores, high omission rates or ambiguous content were eliminated. 3) <u>Pre-testing of HDQoL</u>
24	<b>b. Face validity</b>	
25	<b>Do the items of the scale cover different components of the specific domain?</b>	Yes
26	<b>Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?</b>	Apparently no.
27	<b>Does it score current state or is it based on the patient/caregiver recall?</b>	Patient recall
28	<b>What is the time frame (e.g. "during the past week")?</b>	"Past month"
29	<b>c. Use</b>	
30	<b>Purpose: to measure severity, screen or diagnosis of the domain?</b>	degree of HrQoL (Severity).
31	<b>Is there a cut-off score? (for HD, for non-HD)</b>	No.
32	<b>d. Acceptability</b>	
33	<b>Is the length of the scale appropriate?</b>	NOTE: Unable to review items, but presumably yes. It is very long, which suggests that the items are overly complex. <sup>1</sup>
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Are there ambiguities in instructions to patient/rater (as applicable)?	Minimal instructions.
Are there ambiguities in rating anchors?	Somehow. Difficult to differentiate between response options for frequency of symptoms.
Are the questions appropriate for use in an HD population?	Yes
Is the scale applicable across HD disease stages? Are there HD stages in which the scale is not applicable?	Yes. <sup>1</sup>
e. Has this scale been specifically developed for use in HD (yes/no)?	Yes. <sup>1</sup>
e1. If yes to the above, has the scale been deployed in HD by groups other than the developers?	Yes. <sup>4</sup>
<b>III. Clinimetric/psychometric properties</b>	
Are there clini- or psychometric properties in HD ?	Yes.
<b>a. Reliability</b>	
Assessed – not assessed	Assessed
Internal consistency	<b>Pre-manifest, at risk and manifest HD, n=152<sup>1</sup></b> Cronbach's alpha $\geq 0.7$ for three primary scales and Sum score: "Primary physical and cognitive" = 0.96, "Primary Emotions and Self" = 0.89; "Primary Services" = 0.76
Test-retest reliability	<b>Pre-manifest, at risk and manifest HD, n=152<sup>1</sup></b> Sum score=0.7. All sub scales $\geq 0.7$ . $p < 0.0001$ . <sup>1</sup> NOTE: Cronbach was used – not appropriate measure to report test-retest reliability
Inter-rater reliability	Not applicable.
<b>b. Validity in HD</b>	
Assessed vs. not assessed	Assessed in HD.
Criterion validity (any comparison with gold-standard)	No.
<b>Construct validity</b>	
Factor analysis	<b>Pre-manifest, at risk and manifest HD, n=152<sup>1</sup></b> Three-factor (Primary scales) solution was found: (i) Primary Physical and Cognitive (PPC), (ii) Primary Emotions and Self (PES), and (iii) Primary Services (PSR). <sup>1</sup> 6 factor (specific scales) solution was also presented: (i) Specific Cognitive (SCG), (ii) Specific Hopes and Worries (SHW), (iii) Specific Services (SSR), (iv) Specific Physical and Functional (SPF), (v) Specific Mood State (SMS), and (vi) Specific Self and Vitality (SSV).

	Submitted to RASCH analysis. Retained items did not show differential item functioning for gender, although differential item functioning analyses cannot be run for this few participants (generally 200 people per group are required, and therefore this analysis is not deemed accurate).
<b>Convergent validity</b>	<b>Pre-manifest, at risk and manifest HD, n=152<sup>1</sup></b> Correlation between the sum score and the SF-12 (physical: 0.6 mental:0.7). Correlation between the sum score and the EQ5D (range for subscales: -0.4 to -0.7).  <b>Comment:</b> Method unknown. P values not given
<b>Divergent validity</b>	-
<b>Known groups validity</b>	Ratings become progressively poorer across the three groups. <sup>3</sup> Comment: data for the moderate HD group are not as expected—data for early and advanced HD are as expected. <sup>1</sup>
<b>Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)</b>	In general, there are some positives, but it is long, the psychometrics are adequate to good. This measure has not gained traction, likely due to the length and some of the less impressive psychometric properties (judgment of the task force).
<b>Generalizability</b>	
<b>Shown to be valid at any stage of HD?</b>	Not evaluated.
<b>Shown to be valid in any population with dementia or significant cognitive impairment?</b>	Not evaluated.
<b>Responsiveness (detect change over time in the construct)</b>	
<b>Demonstrated to be sensitive to change (change over time or to treatment)?</b>	<b>Mid-stage HD, n=30</b> In a Randomized Controlled Feasibility Trial for Task-Specific Training in HD: at 8 weeks: -3.7 (95% CI: -9.0, 1.6), at 12 weeks: 3.9 (95% CI: -4.1, 11.9), all n.s. <b>Comment:</b> methodology to calculate effect size is not clear – “Effect sizes are calculated from the adjusted treatment effect”. <sup>4</sup>
<b>Interpretability</b>	
<b>Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?</b>	No
<b>Floor and ceiling effects</b>	<b>Pre-manifest, at risk and manifest HD, n=152<sup>1</sup></b> Floor effects < 12.5 for all scales and sum score (good). Ceiling effect: sum score =16.4 (< 10 excellent and < 20 acceptable). Item ceiling effects ranged from 12.5 to 50; the following scale exceeds what is acceptable: Physical/cognitive

	(30.9), services (50.0), cognitive (27), services (50), physical and functional (36.2) <sup>1</sup>
<b>Score distributions</b>	<b>Pre-manifest, at risk and manifest HD, n=152<sup>1</sup></b> Skewness is acceptable.
<b>IV. Overall impression</b>	
<b>Advantages</b>	Psychometric data is generally adequate to good
<b>Disadvantages</b>	Long administration time (judgment of the task force) Unclear if it is sensitive to change over time. Only one group, other than the developers have used this measure. User access is restricted.
<b>V. Recommendation</b>	
	<b>Suggested for assessment of health-related QoL in HD (severity)</b>

## References

1. Hocaoglu MB, Gaffan EA, Ho AK. The Huntington's Disease health-related Quality of Life questionnaire (HDQoL): a disease-specific measure of health-related quality of life. *Clin Genet* 2012;81:117-22.
2. Ho AK, Hocaoglu MB, Gaffan EA. L09 The Huntington's Disease health-related Quality of Life questionnaire (HDQoL): validation of a disease-specific measure of health-related quality of life. *Journal of Neurology, Neurosurgery & Psychiatry* 2012;83:A46.1-A46.
3. Hocaoglu MB, Gaffan EA, Ho AK. Health-related quality of life in Huntington's disease patients: a comparison of proxy assessment and patient self-rating using the disease-specific Huntington's disease health-related quality of life questionnaire (HDQoL). *J Neurol* 2012;259:1793-800.
4. Quinn L, Debono K, Dawes H, Rosser AE, Nemeth AH, Rickards H, *et al.* Task-specific training in Huntington disease: a randomized controlled feasibility trial. *Phys Ther* 2014;94:1555-68.

<b>EQ-5D</b>	
<b>I. Scale description</b>	
<b>Are there several versions of the scale?</b>	Yes. EQ-5D-3L, EQ-5D-5L and EQ-5D-Y (EQ-5D Youth version), an EQ-5D-3L self-complete version for children and adolescents aged 8-15. <a href="http://www.euroqol.org/eq-5d-products.html">http://www.euroqol.org/eq-5d-products.html</a>
<b>If you replied YES, which was been assessed?</b>	EQ-5D-3L, EQ-5D-5L
<b>Scale construct/ overall structure</b>	The EQ-5D is a standardized non-disease-specific instrument for describing and evaluating health-related quality of life. <sup>1</sup> Nevertheless, the EQ-5D asks about health state to respondents. <a href="http://www.euroqol.org/eq-5d-products/how-to-obtain-eq-5d.html">http://www.euroqol.org/eq-5d-products/how-to-obtain-eq-5d.html</a>  The EQ-5D consists of a 5-question multi-attribute questionnaire and a visual analogue self-rating scale. The 5 questions are titled in the following domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.  The EQ5D Health Scale scores range from 0 (low health) to 100 (highest level of health), while the EQ5D Index Value scores range from 0 (low health) to 1 (highest level of health).
<b>a. Question items</b>	
<b>Items of presence of symptom/sign?</b>	Yes.
<b>Items of severity of symptom/sign?</b>	Yes.
<b>b. Response scale</b>	
<b>Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?</b>	Discrete steps (3L version - no problems/some or moderate problems/extreme problems; 5L - no problems/slight problems/moderate problems/severe problems/extreme problems) and a VAS.
<b>c. Is the scale easy to score?</b>	
<b>Approx. time to score patient</b>	5 minutes.
<b>d. Raters</b>	
<b>Patient, caregiver, or clinician</b>	Patient.
<b>If clinician-rated, is training for application required?</b>	Not applicable.
<b>e. Access to scale</b>	

1 2 3 4 5 6 7 8	<b>Copyright or public domain?</b>	Copyright. NOTE: If non-commercial parties intend to use EQ-5D for research purposes, no license fee is charged. <a href="http://www.euroqol.org/eq-5d-products/how-to-obtain-eq-5d.html">http://www.euroqol.org/eq-5d-products/how-to-obtain-eq-5d.html</a>
9 10 11	<b>How can the scale be obtained (address or website)?</b>	EuroQol Research Foundation. <a href="http://www.euroqol.org/eq-5d-products/how-to-obtain-eq-5d.html">http://www.euroqol.org/eq-5d-products/how-to-obtain-eq-5d.html</a>
12	<b>Has the scale been published in other languages?</b>	Yes.
13	<b>II. Scale properties</b>	
14	<b>a. Content validity</b>	
15	<b>Any process for item generation and/or reduction</b>	--
16	<b>b. Face validity</b>	
17	<b>Do the items of the scale cover different components of the specific domain?</b>	Yes.
18	<b>Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?</b>	No.
19	<b>Does it score current state or is it based on the patient/caregiver recall?</b>	Current state.
20	<b>What is the time frame (e.g. "during the past week")?</b>	Today.
21	<b>c. Use</b>	
22	<b>Purpose: to measure severity, screen or diagnosis of the domain?</b>	To measure severity.
23	<b>Is there a cut-off score? (for HD, for non-HD)</b>	No.
24	<b>d. Acceptability</b>	
25	<b>Is the length of the scale appropriate?</b>	Yes (judgment of the task force).
26	<b>Are there ambiguities in instructions to patient/rater (as applicable)?</b>	No (judgment of the task force).
27	<b>Are there ambiguities in rating anchors?</b>	No (judgment of the task force).
28	<b>Are the questions appropriate for use in an HD population?</b>	Yes, partially (judgment of the task force).
29	<b>Is the scale applicable across HD disease stages?</b>	No (judgment of the task force).
30	<b>Are there HD stages in which the scale is not applicable?</b>	No (judgment of the task force).
31	<b>e. Has this scale been specifically developed for use in HD</b>	No.

(yes/no)?	
e1. If yes to the above, has the scale been deployed in HD by groups other than the developers?	Not applicable.
<b>III. Clinimetric/psychometric properties</b>	
Are there clini- or psychometric properties in HD ?	Only minimal clinimetric testing. The EQ-5D has been used as a comparator in validation studies, and as a composite in new scales (H-QoL, I HD-PRO-TRIAD).
<b>a. Reliability</b>	
Assessed – not assessed	Not assessed in HD.
Internal consistency	Not assessed in HD.
Test-retest reliability	Not assessed in HD.
Inter-rater reliability	Not assessed in HD.
<b>b. Validity in HD</b>	
Assessed vs. not assessed	Only used as a comparator.
Criterion validity (any comparison with gold-standard)	Not assessed in HD.
<b>Construct validity</b>	
Factor analysis	Not assessed in HD.
Convergent validity	<b>Pre-manifest, at risk and manifest HD, n=152.<sup>2</sup></b> Correlation between the EQ5D Index Score and the HDQoL sum score: 0.8.  <b>Prodromal and/or manifest HD, n=477.<sup>3</sup></b> Moderate to significant correlations with WHODAS 2.0: EQ-5D index [-0.65], EQ-5D health scale [-0.49], all p<0.0001.
Divergent validity	
Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)	Limited information for a substantive impression.
<b>Generalizability</b>	
Shown to be valid at any stage of HD?	Used in several studies.
Shown to be valid in any population with dementia or significant cognitive impairment?	Likely not (judgment of the task force).
<b>Responsiveness (detect change over time in the construct)</b>	

Demonstrated to be sensitive to change (change over time or to treatment)?	Not in HD.
<b>Interpretability</b>	
Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?	No.
Floor and ceiling effects	<b>Prodromal and/or manifest HD, n=477.<sup>3</sup></b> 23.9 % for the EQ5D index scale; and 8.9 % for the EQ5D health scale).
Score distributions	<b>Pre-manifest, at risk and manifest HD, n=105.<sup>4</sup></b> EQ-5D Index Score - $0.56 \pm 0.35$  Prodromal HD, n=190, $0.89 \pm 0.12$ . <sup>3</sup> Early HD, n=196, $0.80 \pm 0.14$ . <sup>3</sup> Late HD, n=89, $0.71 \pm 0.16$ . <sup>3</sup>
<b>IV. Overall impression</b>	
Advantages	Widely used, but limited use in HD. Simple, generic (comparison with other neurological diseases).
Disadvantages	Ceiling effects. Limited validation in HD.
<b>V. Recommendation</b>	
<b>Suggested with caveats</b>	

## References

- Brooks R. EuroQol: the current state of play. *Health Policy* 1996;37:53-72.
- Hocaoglu MB, Gaffan EA, Ho AK. The Huntington's Disease health-related Quality of Life questionnaire (HDQoL): a disease-specific measure of health-related quality of life. *Clin Genet* 2012;81:117-22.
- Carlozzi NE, Kratz AL, Downing NR, Goodnight S, Miner JA, Migliore N, *et al.* Validity of the 12-item World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) in individuals with Huntington disease (HD). *Qual Life Res* 2015;24:1963-71.
- Hocaoglu MB, Gaffan EA, Ho AK. Health-related quality of life in Huntington's disease patients: a comparison of proxy assessment and patient self-rating using the disease-specific Huntington's disease health-related quality of life questionnaire (HDQoL). *J Neurol* 2012;259:1793-800.



<b>RAND-12 Health Status Inventory (HIS)</b>	
<b>I. Scale description</b>	
<b>Are there several versions of the scale?</b>	Yes. 12-, 20- and 36-item versions.
<b>If you replied YES, which was assessed?</b>	The 12-item version.
<b>Scale construct/ overall structure</b>	<p>General health status. The RAND 12 is based on the SF-12 which summarizes four of the Medical Outcomes Study 36 Item Short-Form Health Survey (SF-36) eight health dimensions (physical functioning, role-physical, role-emotional, and mental health) using two items each. The remaining four health dimensions (pain, vitality, social functioning, and general health) are each represented by a single item.</p> <p>The RAND 12 comprises the same 12 items as the SF12 but uses scaling based on Item Response Theory.</p> <p>It also includes two extra items on change in physical and emotional health over the past year. <a href="http://www.rand.org/health/surveys_tools/mos/12-item-short-form.html">http://www.rand.org/health/surveys_tools/mos/12-item-short-form.html</a></p>
<b>a. Question items</b>	
<b>Items of presence of symptom/sign?</b>	Yes.
<b>Items of severity of symptom/sign?</b>	Yes.
<b>b. Response scale</b>	
<b>Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?</b>	Discrete steps, 6 for most of the items.
<b>c. Is the scale easy to score?</b>	
<b>Approx. time to score patient</b>	Scoring algorithm required.
<b>d. Raters</b>	
<b>Patient, caregiver, or clinician</b>	Patient.
<b>If clinician-rated, is training for application required?</b>	Not applicable.
<b>e. Access to scale</b>	
<b>Copyright or public domain?</b>	Public domain.
<b>How can the scale be obtained (address or website)?</b>	Freely available from the principal developers e.g. Dr. Lewis Kazis at lek@bu.edu
<b>Has the scale been published in other languages?</b>	Yes.

<b>II. Scale properties</b>	
<b>a. Content validity</b>	
Any process for item generation and/or reduction	See SF12.
<b>b. Face validity</b>	
Do the items of the scale cover different components of the specific domain?	See SF12.
Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?	See SF12.
Does it score current state or is it based on the patient/caregiver recall?	Mostly patient recall.
What is the time frame (e.g. “during the past week”)?	Past 4 weeks.
<b>c. Use</b>	
Purpose: to measure severity, screen or diagnosis of the domain?	Mainly to measure severity.
Is there a cut-off score? (for HD, for non-HD)	No.
<b>d. Acceptability</b>	
Is the length of the scale appropriate?	Yes (judgment of the task force).
Are there ambiguities in instructions to patient/rater (as applicable)?	Yes (judgment of the task force).
Are there ambiguities in rating anchors?	No (judgment of the task force).
Are the questions appropriate for use in an HD population?	The scale is somewhat general (judgment of the task force).
Is the scale applicable across HD disease stages? Are there HD stages in which the scale is not applicable?	Limited information on applicability in very late stage disease and also in the context of cognitive impairment (judgment of the task force).
e. Has this scale been specifically developed for use in HD (yes/no)?	No.
e1. If yes to the above, has the scale been deployed in HD by groups other than the developers?	Not applicable.
<b>III. Clinimetric/psychometric properties</b>	
Are there clini- or psychometric properties in HD ?	Yes.
<b>a. Reliability</b>	
Assessed – not assessed	Not assessed in HD.

Internal consistency	-
Test-retest reliability	-
Inter-rater reliability	-
<b>b. Validity in HD</b>	
Assessed vs. not assessed	Assessed in HD.
Criterion validity (any comparison with gold-standard)	-
Construct validity	
Factor analysis	
Convergent validity	<b>Prodromal and/or manifest HD, n=477</b> Moderate to significant correlations with WHODAS 2.0: RAND-12 Physical [-0.76] and the RAND-12 Mental [-0.41], all $p < 0.0001$ . <sup>1</sup>
Divergent validity	-
Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)	Very limited information.
Generalizability	
Shown to be valid at any stage of HD?	Limited in HD. Physical Health composite score is poorer for late HD compared to early HD, which was lower than for pre-manifest HD. For the Mental Health composite score there were no differences between late, early and prodromal HD. <sup>1</sup>
Shown to be valid in any population with dementia or significant cognitive impairment?	Limited information on applicability in very late stage disease and also in the context of cognitive impairment (judgment of the task force).
<b>Responsiveness (detect change over time in the construct)</b>	
Demonstrated to be sensitive to change (change over time or to treatment)?	No.
<b>Interpretability</b>	
Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?	No.
Floor and ceiling effects	<b>Prodromal and/or manifest HD, n=477.</b> <sup>1</sup> No floor or ceiling effects.
Score distributions	RAND-12. <sup>1</sup>

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	<u>Physical Health</u> Prodromal HD, n=190, 53.87 ± 5.58 Early HD, n=196, 46.88 ± 9.18 Late HD, n=87, 38.17 ± 9.09 <u>Mental Health</u> Prodromal HD, n=190, 49.87 ± 9.32 Early HD, n=196, 47.60 ± 10.99 Late HD, n=87, 49.60 ± 11.42
<b>IV. Overall impression</b>	
<b>Advantages</b>	Brief.
<b>Disadvantages</b>	Not specifically for HD. Mental health composite score same for all HD (pre-manifest, early and late HD). Very limited validation in HD.
<b>V. Recommendation</b>	<b>Suggested with caveats</b>

References

1. Carlozzi NE, Kratz AL, Downing NR, Goodnight S, Miner JA, Migliore N, *et al.* Validity of the 12-item World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) in individuals with Huntington disease (HD). *Qual Life Res* 2015;24:1963-71.

<b>Neuro-QoL (Quality of Life in Neurological Disorders)</b>	
<b>I. Scale description</b>	
<b>Are there several versions of the scale?</b>	Yes, different item banks within Neuro-QoL. <a href="http://www.healthmeasures.net/explore-measurement-systems/neuro-qol">http://www.healthmeasures.net/explore-measurement-systems/neuro-qol</a>
<b>If you replied YES, which was been assessed?</b>	In HD, a self-report version with a fixed-length short forms of the following item banks has been used: 1) Anxiety, 2) Depression, 3) Social Roles, 4) Lower extremity function, 5) Upper extremity function. <sup>1</sup> More recently, the item banks of the domains Stigma, Emotional and Behavioral Dyscontrol, Positive Affect and Well-Being, Ability to Participate in Social Roles and Activities, Satisfaction with Social Roles and Activities, Lower Extremity-Function/Mobility, Upper Extremity-Function/ADLs, Applied Cognition-Executive Functioning, Applied Cognition-General Concerns have also been used. <sup>2</sup>
<b>Scale construct/ overall structure</b>	Neuro-QoL instruments were developed through a collaborative, multi-site research initiative to construct psychometrically-sound and clinically-relevant health-related quality of life (HRQOL) measurement tools for individuals with neurological conditions or disorders such as stroke, multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), Parkinson's disease (PD), epilepsy, and muscular dystrophy (MD).  Each item bank consists of 8 to 9 items.  <a href="http://www.healthmeasures.net/explore-measurement-systems/neuro-qol/measure-development-research">http://www.healthmeasures.net/explore-measurement-systems/neuro-qol/measure-development-research</a>
<b>a. Question items</b>	
<b>Items of presence of symptom/sign?</b>	Yes.
<b>Items of severity of symptom/sign?</b>	Yes.
<b>b. Response scale</b>	
<b>Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?</b>	Five response options.
<b>c. Is the scale easy to score?</b>	
<b>Approx. time to score patient</b>	Scoring algorithm is required.
<b>d. Raters</b>	
<b>Patient, caregiver, or clinician</b>	Patient.

<b>If clinician-rated, is training for application required?</b>	Not applicable.
<i>e. Access to scale</i>	
<b>Copyright or public domain?</b>	Copyright, but all English and Spanish version of Neuro-QoL are publicly available for use in one's individual research, clinical practice, educational assessment, or other application without licensing or royalty fees.
<b>How can the scale be obtained (address or website)?</b>	From the NINDS. <a href="http://www.healthmeasures.net/explore-measurement-systems/neuro-qol">http://www.healthmeasures.net/explore-measurement-systems/neuro-qol</a>
<b>Has the scale been published in other languages?</b>	Yes.
<b>II. Scale properties</b>	
<b>a. Content validity</b>	
<b>Any process for item generation and/or reduction</b>	<a href="http://www.healthmeasures.net/explore-measurement-systems/neuro-qol">http://www.healthmeasures.net/explore-measurement-systems/neuro-qol</a>
<b>b. Face validity</b>	
<b>Do the items of the scale cover different components of the specific domain?</b>	Yes (judgment of the task force)/
<b>Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?</b>	<b>NOTE:</b> by design, each measure is focused on a single aspect of HRQoL, thus they are intentionally developed to be unidimensional measures.
<b>Does it score current state or is it based on the patient/caregiver recall?</b>	Based on patient recall.
<b>What is the time frame (e.g. "during the past week")?</b>	Past 7 days.
<b>c. Use</b>	
<b>Purpose: to measure severity, screen or diagnosis of the domain?</b>	Measures severity.
<b>Is there a cut-off score? (for HD, for non-HD)</b>	No.
<b>d. Acceptability</b>	
<b>Is the length of the scale appropriate?</b>	Yes (judgment of the task force).
<b>Are there ambiguities in instructions to patient/rater (as applicable)?</b>	No (judgment of the task force).
<b>Are there ambiguities in rating anchors?</b>	No (judgment of the task force).
<b>Are the questions appropriate for use in an HD population?</b>	Yes, but somewhat general (judgment of the task force).

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5	<b>Is the scale applicable across HD disease stages?</b>	Limited information on applicability in very late stage disease and also in the context of
6	<b>Are there HD stages in which the scale is not applicable?</b>	cognitive impairment (judgment of the task force).
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8	<b>e. Has this scale been specifically developed for use in HD (yes/no)?</b>	No.
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10	<b>e1. If yes to the above, has the scale been deployed in HD by groups other than the developers?</b>	Not applicable.
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12	<b>III. Clinimetric/psychometric properties</b>	
13	<b>Are there clini- or psychometric properties in HD ?</b>	No.
14	<b>a. Reliability</b>	
15	<b>Assessed – not assessed</b>	Not assessed in HD.
16	<b>Internal consistency</b>	-
17	<b>Test-retest reliability</b>	-
18	<b>Inter-rater reliability</b>	-
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20	<b>b. Validity in HD</b>	
21	<b>Assessed vs. not assessed</b>	Not assessed in HD.
22	<b>Criterion validity (any comparison with gold-standard)</b>	-
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24	<b>Construct validity</b>	
25	<b>Factor analysis</b>	Not assessed in HD.
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27	<b>Convergent validity</b>	<b>Manifest HD, n=132.</b> <sup>3</sup> Correlation between the different NEURO-QOL components and total score of HD-PRO-Triad: Anxiety (Pearson's correlation: 0.70), Depression (Pearson's correlation: 0.71), Social Roles (Pearson's correlation: 0.55), Lower extremity function (Pearson's correlation: 0.73), Higher extremity function (Pearson's correlation: 0.74). NOTE: p<0.05  Neuro-QoL had moderate relationships with WHODAS 2.0 and EQ-5D (correlation coefficients ranged: 0.34 – 0.74, p < 0.0001). <sup>2</sup>
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35	<b>Divergent validity</b>	Not assessed in HD.
36	<b>Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)</b>	Very limited information on which to base an impression.
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38	<b>Generalizability</b>	
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40	<b>Shown to be valid at any stage of HD?</b>	<b>Pre-manifest and manifest HD, n=536</b>
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	Pre-manifest HD performed better than early-HD and late-HD, and early-HD performed better than late-HD. (P values not provided) <sup>2</sup>
<b>Shown to be valid in any population with dementia or significant cognitive impairment?</b>	Likely not (judgment of the task force).
<b>Responsiveness (detect change over time in the construct)</b>	
<b>Demonstrated to be sensitive to change (change over time or to treatment)?</b>	No.
<b>Interpretability</b>	
<b>Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?</b>	No.
<b>Floor and ceiling effects</b>	Unknown.
<b>Score distributions</b>	<b>Manifest HD, n=132.<sup>3</sup></b> Anxiety - 57.5 (8.0). Depression - 54.1 (8.2). Social Roles - 42.2 (7.4). Lower extremity function - 38.3 (10.9). Higher extremity function - 33.0 (11.6).
<b>IV. Overall impression</b>	
<b>Advantages</b>	Single domain short forms are brief.
<b>Disadvantages</b>	Multiple short forms might be needed and assessment is longer. Very limited use and validation in HD
<b>V. Recommendation</b>	
<b>Suggested with caveats</b>	

References

1. Carlozzi NE, Victorson D, Sung V, Beaumont JL, Cheng W, Gorin B, *et al.* HD-PRO-TRIAD Validation: A Patient-reported Instrument for the Symptom Triad of Huntington's Disease. *Tremor Other Hyperkinet Mov (N Y)* 2014;4:223.
2. Carlozzi NE, Schilling SG, Lai JS, Paulsen JS, Hahn EA, Perlmutter JS, *et al.* HDQLIFE: development and assessment of health-related quality of life in Huntington disease (HD). *Quality of Life Research* 2016;25:2441-55.
3. Carlozzi NE, Kratz AL, Downing NR, Goodnight S, Miner JA, Migliore N, *et al.* Validity of the 12-item World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0) in individuals with Huntington disease (HD). *Qual Life Res* 2015;24:1963-71.



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<b>PROMIS Global Health (PROMIS)</b>	
<b>I. Scale description</b>	
<b>Are there several versions of the scale?</b>	Yes. The 10-item version. The 29-item version. <a href="http://www.healthmeasures.net/explore-measurement-systems/promis">http://www.healthmeasures.net/explore-measurement-systems/promis</a>
<b>If you replied YES, which was assessed?</b>	The 10-item version.
<b>Scale construct/ overall structure</b>	The PROMIS assesses global health perception, and consists of 10 items, with each item having 5 response options apart from pain where 10 options are presented.  The 10-item PROMIS Global Health instrument yields two summary scores — Physical Health and Mental Health.  <a href="http://www.healthmeasures.net/explore-measurement-systems/promis">http://www.healthmeasures.net/explore-measurement-systems/promis</a>
<b>a. Question items</b>	
<b>Items of presence of symptom/sign?</b>	Yes.
<b>Items of severity of symptom/sign?</b>	Yes.
<b>b. Response scale</b>	
<b>Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?</b>	Discrete step: 5 (Variable anchors), except for pain where there are 10 (from “No pain” to “Worst Imaginable Pain”).
<b>c. Is the scale easy to score?</b>	
<b>Approx. time to score patient</b>	Scoring algorithm is required.
<b>d. Raters</b>	
<b>Patient, caregiver, or clinician</b>	Patient.
<b>If clinician-rated, is training for application required?</b>	Not applicable
<b>e. Access to scale</b>	
<b>Copyright or public domain?</b>	Copyright. NOTE: publicly available for use without licensing or royalty fees for individual research or individual clinical use, meaning solely for user’s research, clinical, educational, or other application. <a href="http://www.healthmeasures.net/explore-measurement-systems/promis/obtain-administer-">http://www.healthmeasures.net/explore-measurement-systems/promis/obtain-administer-</a>

	<a href="#">measures</a>
<b>How can the scale be obtained (address or website)?</b>	From PROMIS. <a href="http://www.healthmeasures.net/explore-measurement-systems/promis/obtain-administer-measures">http://www.healthmeasures.net/explore-measurement-systems/promis/obtain-administer-measures</a>
<b>Has the scale been published in other languages?</b>	Danish, Dutch, English, French, German, Italian, Portuguese, Simplified Chinese (Mandarin), Spanish <a href="http://www.healthmeasures.net/search-view-measures?task=Search.search">http://www.healthmeasures.net/search-view-measures?task=Search.search</a>
<b>II. Scale properties</b>	
<b>a. Content validity</b>	
<b>Any process for item generation and/or reduction</b>	
<b>b. Face validity</b>	
<b>Do the items of the scale cover different components of the specific domain?</b>	Yes (judgment of the task force).
<b>Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?</b>	<b>NOTE:</b> by design, each measure is focused on a single aspect of HRQoL, and are thus intentionally developed to be unidimensional measures.
<b>Does it score current state or is it based on the patient/caregiver recall?</b>	Patient recall.
<b>What is the time frame (e.g. “during the past week”)?</b>	Past 7 days (three last questions) or “in general”.
<b>c. Use</b>	
<b>Purpose: to measure severity, screen or diagnosis of the domain?</b>	Measure severity.
<b>Is there a cut-off score? (for HD, for non-HD)</b>	
<b>d. Acceptability</b>	
<b>Is the length of the scale appropriate?</b>	Yes (judgment of the task force).
<b>Are there ambiguities in instructions to patient/rater (as applicable)?</b>	No (judgment of the task force).
<b>Are there ambiguities in rating anchors?</b>	No (judgment of the task force).
<b>Are the questions appropriate for use in an HD population?</b>	Yes, although they do not specifically address HD issues (judgment of the task force).
<b>Is the scale applicable across HD disease stages?</b>	Limited information on applicability in very late stage disease and also in the context of cognitive impairment <sup>1</sup> (judgment of the task force).
<b>Are there HD stages in which the scale is not applicable?</b>	
<b>e. Has this scale been specifically developed for use in HD</b>	No.

(yes/no)?	
e1. If yes to the above, has the scale been deployed in HD by groups other than the developers?	Not applicable.
<b>III. Clinimetric/psychometric properties</b>	
Are there clini- or psychometric properties in HD ?	Some.
<b>a. Reliability</b>	
Assessed – not assessed	Not assessed in HD.
Internal consistency	-
Test-retest reliability	-
Inter-rater reliability	-
<b>b. Validity in HD</b>	
Assessed vs. not assessed	Assessed in HD.
Criterion validity (any comparison with gold-standard)	Not assessed in HD.
Construct validity	
Factor analysis	
Convergent validity	<b>Manifest HD, n=132.</b> <sup>1</sup> Correlation between the different PROMIS Global Physical measures and different score of the HD-PRO-Triad: PROMIS Global Physical Health vs. HD-PRO-TRIAD Total (0.82), Cognition (0.83), Motor Function (0.80) and Emotional/Behavioral Dyscontrol (0.57). PROMIS Global Mental Health vs. HD-PRO-TRIAD Total (0.77), Cognition (0.72), Motor Function (0.62) and Emotional/Behavioral Dyscontrol (0.73). <sup>1</sup>
Divergent validity	-
Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)	Very limited information.
Generalizability	
Shown to be valid at any stage of HD?	No.
Shown to be valid in any population with dementia or significant cognitive impairment?	Limited information on applicability in very late stage disease and also in the context of cognitive impairment.
<b>Responsiveness (detect change over time in the construct)</b>	
Demonstrated to be sensitive to change (change over time	No.

or to treatment)?	
<b>Interpretability</b>	
Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?	No.
Floor and ceiling effects	
Score distributions	Manifest HD, n=132. <sup>1</sup> PROMIS Global Physical Health 42.6 (9.7) PROMIS Global Mental Health 39.0 (10.5)
<b>IV. Overall impression</b>	
Advantages	
Disadvantages	Online study and questionnaire completion.
<b>V. Recommendation</b>	<b>Suggested with caveats</b>

## References

1. Carlozzi NE, Victorson D, Sung V, Beaumont JL, Cheng W, Gorin B, *et al.* HD-PRO-TRIAD Validation: A Patient-reported Instrument for the Symptom Triad of Huntington's Disease. *Tremor Other Hyperkinet Mov (N Y)* 2014;4:223.

Huntington Disease Health-Related Quality of Life (HDQLIFE)	
<b>I. Scale description</b>	
Are there several versions of the scale?	No.
If you replied YES, which was been assessed?	Not applicable.
Scale construct/ overall structure	HDQLIFE is a patient-reported outcome measurement system that was developed to capture both the generic and more unique aspects of HRQOL in HD. <sup>1</sup> It includes 12 validated Neuro-QoL/PROMIS measures in HD, as well as five new HD-specific measures, including speech and swallowing dysfunction, <sup>2</sup> chorea, <sup>3</sup> and end of life issues including concerns with death and dying, and meaning and purpose. <sup>4</sup>
<b>a. Question items</b>	
Items of presence of symptom/sign?	
Items of severity of symptom/sign?	Yes. <sup>2-4</sup>
<b>b. Response scale</b>	
Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?	The HDQLIFE uses computer adaptive tests (CATs) where each individual item is selected based on the response to the previous item. The HDQLIFE can also use Static Short forms (which are 6-items) depending on the administrator's preference. <sup>1</sup>
<b>c. Is the scale easy to score?</b>	
Approx. time to score patient	Administration of each HDQLIFE measure is < 1 minute. <sup>1</sup>
<b>d. Raters</b>	
Patient, caregiver, or clinician	Clinician.
If clinician-rated, is training for application required?	Unknown.
<b>e. Access to scale</b>	
Copyright or public domain?	Public domain.
How can the scale be obtained (address or website)?	<a href="http://www.assessmentcenter.net">www.assessmentcenter.net</a> , free of charge.
Has the scale been published in other languages?	-
<b>II. Scale properties</b>	
<b>a. Content validity</b>	
Any process for item generation and/or reduction	HDQLIFE validates 12 PROMIS/NEURO-QoL domains to capture generic, relevant aspects of health-related QoL in patients with HD. <sup>1</sup> 1. Item development: a. The relevant domains, subdomains, and items to assess HRQOL in HD were

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	<p>identified through literature review and qualitative focus groups including at-risk, pre-manifest, manifest HD individuals, non-clinical caregivers, and HD clinicians.<sup>5</sup> While several PROMIS/Neuro-QoL measures were identified as relevant in HD, a number of HD-specific HRQOL issues were found not to be captured by these measures.<sup>1,5</sup></p> <p>b. Preliminary item pools were created to examine chorea, speech and swallowing difficulties, and end of life issues. Each item pool went through several iterations following expert review, cognitive debriefing interviews with people with HD, literacy and translatability review: the initial HDQLIFE Chorea item pool consisted of 141 items, later reduced to 64; the Speech and Swallowing pool initially consisted of 102 items, later revised to 47 items; the End of Life Concerns item pool initially consisted of 69 later reduced to 45 items.<sup>1</sup></p> <p>2. Quantitative study.</p> <p>3. All items were field tested in 536 patients with pre- and manifest HD.</p> <p>4. Computer adaptive tests (CATs) were developed for each of the domains:</p> <p>a. Exploratory and confirmatory factor analyses were used to identify unidimensional item pools (speech difficulties (27 items) and swallowing difficulties (16 items)<sup>2</sup>, and item response theory was used to calibrate the final measures.</p> <p>b. Items were calibrated separately for the two item pools resulting in measures that can be administered as computer adaptive tests and/or 6-item static short forms.</p>
<b>b. Face validity</b>	
<b>Do the items of the scale cover different components of the specific domain?</b>	Yes.
<b>Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?</b>	-
<b>Does it score current state or is it based on the patient/caregiver recall?</b>	Patient recall.
<b>What is the time frame (e.g. “during the past week”)?</b>	Past 7 days. <sup>2-4</sup>
<b>c. Use</b>	
<b>Purpose: to measure severity, screen or diagnosis of the domain?</b>	To measure severity. <sup>2-4</sup>

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5	<b>Is there a cut-off score? (for HD, for non-HD)</b>	No.
6	<b>d. Acceptability</b>	
7	<b>Is the length of the scale appropriate?</b>	Yes.
8	<b>Are there ambiguities in instructions to patient/rater (as applicable)?</b>	No (judgment of the task force).
9	<b>Are there ambiguities in rating anchors?</b>	No (judgment of the task force).
10	<b>Are the questions appropriate for use in an HD population?</b>	Yes.
11	<b>Is the scale applicable across HD disease stages?</b>	Yes.
12	<b>Are there HD stages in which the scale is not applicable?</b>	Yes.
13	<b>e. Has this scale been specifically developed for use in HD (yes/no)?</b>	Yes.
14	<b>e1. If yes to the above, has the scale been deployed in HD by groups other than the developers?</b>	No.
15	<b>III. Clinimetric/psychometric properties</b>	
16	<b>Are there clini- or psychometric properties in HD ?</b>	Yes.
17	<b>a. Reliability</b>	
18	<b>Assessed – not assessed</b>	Assessed in HD.
19	<b>Internal consistency</b>	<b>Pre-manifest and manifest HD, n=536</b> Chorea scale, Cronbach's alpha 0.98, and all item-total correlations were $> 0.7$ . <sup>3</sup> . Meaning and purpose, Cronbach's alpha 0.84. item-total correlations $> 0.4$ . <sup>4</sup> Death and dying scale, Cronbach's alpha 0.94. All item-total correlations $> 0.4$ . <sup>4</sup> Speech Difficulties, Cronbach's alpha 0.98 and all item-total correlations $> 0.4$ .
20	<b>Test-retest reliability</b>	Unknown.
21	<b>Inter-rater reliability</b>	Not applicable.
22	<b>b. Validity in HD</b>	
23	<b>Assessed vs. not assessed</b>	Assessed.
24	<b>Criterion validity (any comparison with gold-standard)</b>	-
25	<b>Construct validity</b>	
26	<b>Factor analysis</b>	Exploratory and confirmatory factor analyses were used to identify unidimensional item pools, which were analyzed separately. Once unidimensional item sets were identified, an IRT graded response model was implemented.
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	<p><b>Chorea:</b> five factors were originally identified, and 40 items were retained for confirmatory factor analyses which revealed 6 items to have residual correlations, these were removed leaving 34 items; comparative fit index (CFI) = 0.98; TLI=0.98; root mean square error of approximation (RMSEA)=0.07, all <math>r^2&gt;0.03</math>.</p> <p><b>Meaning and purpose,</b> reduced from 14 to 7 items. CFI = 0.99, TLI = 0.98, RMSEA = 0.11, all <math>r^2&gt;0.03</math>.<sup>4</sup></p> <p><b>Death and dying, reduced from</b> 16 items to 13. CFI = 0.97, TLI = 0.96, RMSEA = 0.15, all <math>r^2&gt;0.03</math>.<sup>4</sup></p> <p>EFA and CFA identified two separate unidimensional sets of items:  <b>Speech difficulties</b> (27 items) and <b>Swallowing difficulties</b> (16 items), both of which were developed further into 6-item short-forms and CATS. For Speech difficulties (Factor 1 in EFA results), acceptable fit indices were found in CFA results: CFI = 0.98, TLI = 0.98, RMSEA = 0.09, all <math>r^2&gt;0.3</math>.  <b>Swallowing Difficulties</b> (Factor 2 in EFA results), acceptable fit indices were found in CFA results: CFI = 0.98, TLI = 0.98, RMSEA = 0.11, all <math>r^2&gt;0.3</math>.</p>
<b>Convergent validity</b>	Significant positive correlation between HDQLIFE Chorea and the UHDRS TMS ( $r = 0.64$ , $p<0.0001$ ). <sup>3</sup>
<b>Divergent validity</b>	-
<b>Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)</b>	
<b>Generalizability</b>	
<b>Shown to be valid at any stage of HD?</b>	Yes.
<b>Shown to be valid in any population with dementia or significant cognitive impairment?</b>	Unknown.
<b>Responsiveness (detect change over time in the construct)</b>	
<b>Demonstrated to be sensitive to change (change over time or to treatment)?</b>	Not assessed.
<b>Interpretability</b>	
<b>Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?</b>	No
<b>Floor and ceiling effects</b>	-
<b>Score distributions</b>	-



<b>IV. Overall impression</b>	
<b>Advantages</b>	HDQLIFE includes new HD-specific items as well as generic items from PROMIS and Neuro-QoL, which enable comparisons across different medical populations.
<b>Disadvantages</b>	Requires further clinimetric development and use by other groups than developers.
<b>V. Recommendation</b>	<b>Listed</b> <b>NOTE: Only used by one group and further clinimetric testing is required.</b>

## References

1. Carlozzi NE, Schilling SG, Lai JS, Paulsen JS, Hahn EA, Perlmutter JS, *et al.* HDQLIFE: development and assessment of health-related quality of life in Huntington disease (HD). *Quality of Life Research* 2016;25:2441-55.
2. Carlozzi NE, Schilling SG, Lai JS, Perlmutter JS, Nance MA, Waljee JF, *et al.* HDQLIFE: the development of two new computer adaptive tests for use in Huntington disease, Speech Difficulties, and Swallowing Difficulties. *Quality of Life Research* 2016;25:2417-27.
3. Carlozzi NE, Downing NR, Schilling SG, Lai JS, Goodnight SM, Miner JA, *et al.* The development of a new computer adaptive test to evaluate chorea in Huntington disease: HDQLIFE Chorea. *Quality of Life Research* 2016;25:2429-39.
4. Carlozzi NE, Downing NR, McCormack MK, Schilling SG, Perlmutter JS, Hahn EA, *et al.* New measures to capture end of life concerns in Huntington disease: Meaning and Purpose and Concern with Death and Dying from HDQLIFE (a patient-reported outcomes measurement system). *Quality of Life Research* 2016;25:2403-15.
5. Carlozzi NE, Tulskey DS. Identification of health-related quality of life (HRQOL) issues relevant to individuals with Huntington disease. *J Health Psychol* 2013;18:212-25.

WHO-Quality of Life-BREF (WHOQOL-BREF)	
<b>I. Scale description</b>	
Are there several versions of the scale?	No.
If you replied YES, which was been assessed?	Not applicable.
Scale construct/ overall structure	Generic quality of life instrument developed by the World Health Organization (WHO). This is a shorter version with broad representations of the WHOQOL100. It consists of 26 items scored on a five-point Likert scale (from 1 = very dissatisfied to 5 = very satisfied). <sup>1</sup> It includes items for physical health, psychological, social relationships and environment. The WHOQOL-BREF is a cross-cultural assessment of well-being.
<i>a. Question items</i>	
Items of presence of symptom/sign?	
Items of severity of symptom/sign?	Yes.
<i>b. Response scale</i>	
Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?	Likert scale items. <i>Scoring instructions provided in manual</i> <a href="http://www.who.int/mental_health/media/en/76.pdf">http://www.who.int/mental_health/media/en/76.pdf</a>
<i>c. Is the scale easy to score?</i>	
Approx. time to score patient	
<i>d. Raters</i>	
Patient, caregiver, or clinician	Patient self-report.
If clinician-rated, is training for application required?	
<i>e. Access to scale</i>	
Copyright or public domain?	Copyright.
How can the scale be obtained (address or website)?	World Health Organization. WHOQOL@who.int
Has the scale been published in other languages?	Yes. <sup>1</sup>
<b>II. Scale properties</b>	
<i>a. Content validity</i>	
Any process for item generation and/or reduction	WHOQOL-100 was developed through the collaboration of 15 international sites in their own language. <sup>1</sup> Pooled data from the WHOQOL-100 was used to select items for the WHOQOL-BREF, resulting in four domains of QoL: physical, psychological, social and environment. <sup>1</sup>
<i>b. Face validity</i>	

1 2 3 4 5 6	<b>Do the items of the scale cover different components of the specific domain?</b>	Includes items for physical health, psychological, social relationships and environment.
7 8 9	<b>Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?</b>	Only 3 items for domain 3 (social relationships). The other domains have 6, 7, & 8 items. Unbalanced (judgment of the task force).
10 11 12	<b>Does it score current state or is it based on the patient/caregiver recall?</b>	Based on patient-recall.
13 14 15 16 17 18	<b>What is the time frame (e.g. “during the past week”)?</b>	A time frame of two weeks is indicated in the assessment. It is recognized that different time frames may be necessary for particular uses of the instrument in subsequent stages of work. For example, in the assessment of QoL in chronic conditions, such as arthritis, a longer time frame such as four weeks may be preferable. Furthermore, the perception of time is different within different cultural settings and therefore changing the time scale may be appropriate (judgment of the task force).
19	<b>c. Use</b>	
20	<b>Purpose: to measure severity, screen or diagnosis of the domain?</b>	Assess well-being.
21	<b>Is there a cut-off score? (for HD, for non-HD)</b>	Not in HD.
22	<b>d. Acceptability</b>	
23	<b>Is the length of the scale appropriate?</b>	A little long (judgment of the task force).
24	<b>Are there ambiguities in instructions to patient/rater (as applicable)?</b>	No (judgment of the task force).
25	<b>Are there ambiguities in rating anchors?</b>	No (judgment of the task force).
26	<b>Are the questions appropriate for use in an HD population?</b>	Yes (judgment of the task force).
27	<b>Is the scale applicable across HD disease stages? Are there HD stages in which the scale is not applicable?</b>	Unknown in HD.
28	<b>e. Has this scale been specifically developed for use in HD (yes/no)?</b>	No.
29	<b>e1. If yes to the above, has the scale been deployed in HD by groups other than the developers?</b>	Not applicable.
30	<b>III. Clinimetric/psychometric properties</b>	
31	<b>Are there clini- or psychometric properties in HD ?</b>	No.
32	<b>a. Reliability</b>	

Assessed – not assessed	Not assessed in HD.
<b>Internal consistency</b>	<b>Non-HD populations:</b> Cronbach's alpha for the total population, >0.7). <sup>1</sup> Cronbach's alpha for domains 1, 2 and 4 i.e. physical health=0.82, psychological=0.81, environment=0.80, social relationships=0.68. <sup>1</sup>
<b>Test-retest reliability</b>	Not assessed in HD.
<b>Inter-rater reliability</b>	Not assessed in HD.
<b>b. Validity in HD</b>	
Assessed vs. not assessed	Not assessed in HD.
<b>Criterion validity (any comparison with gold-standard)</b>	-
<b>Construct validity</b>	
<b>Factor analysis</b>	Not assessed in HD. NOTE: The WHOQOL-100 was based on six theoretical domains that were reorganized into four domains during the development of the WHOQOL-BREF. Analysis of the total population data showed four factors (eigenvalues >1.0) that explained 53% of the variance in the data. <sup>1</sup>
<b>Convergent validity</b>	Not assessed in HD. NOTE: Construct validity was partly assessed by correlating the domain scores with each general item: overall assessment of QoL was most strongly associated with the psychological (standardized beta=0.290) and environment domains (standardized beta=0.252), and the overall assessment of health with the physical domain (standardized beta=0.428). <sup>1</sup>
<b>Divergent validity</b>	Not assessed in HD. NOTE: t-tests of domain scores for illness vs. well samples: Physical=39.2, psychological=19.9, social=13, environment=7.6, (all p<0.01). <sup>1</sup>
<b>Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)</b>	
<b>Generalizability</b>	
<b>Shown to be valid at any stage of HD?</b>	Not assessed in HD.
<b>Shown to be valid in any population with dementia or significant cognitive impairment?</b>	-

<b>Responsiveness (detect change over time in the construct)</b>	
<b>Demonstrated to be sensitive to change (change over time or to treatment)?</b>	There were no significant treatment effects observed for WHOQOL-BREF between the Dance Dance Revolution and handheld video game interventions, and no significant differential treatment effects by disease severity. NOTE: values not given <sup>2</sup>
<b>Interpretability</b>	
<b>Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?</b>	No.
<b>Floor and ceiling effects</b>	Unknown.
<b>Score distributions</b>	Unknown.
<b>IV. Overall impression</b>	
<b>Advantages</b>	-
<b>Disadvantages</b>	This scale has been used in HD but no data are available regarding the scale from this trial. As such, it would be similar to employing the WHOAOL 100 or any other generic quality of life scale in HD without any supportive data in this population. <sup>2</sup> Not suited to HD, a more suitable generic measure of QoL would be the WHODAS or PROMIS/Neuro-QoL, which are much better alternatives (judgment of the task force).
<b>V. Recommendation</b>	<b>Listed</b>

#### References

1. Skevington SM, Lotfy M, O'Connell KA. The World Health Organization's WHOQOL-BREF quality of life assessment: psychometric properties and results of the international field trial. A report from the WHOQOL group. *Qual Life Res* 2004;13:299-310.
2. Kloos AD, Fritz NE, Kostyk SK, Young GS, Kegelmeyer DA. Video game play (Dance Dance Revolution) as a potential exercise therapy in Huntington's disease: a controlled clinical trial. *Clinical rehabilitation* 2013;27:972-82.

<b>Quality of Life Index (QIL Index)</b>	
<b>I. Scale description</b>	
<b>Are there several versions of the scale?</b>	Yes. There is a general form and many forms adapted for different condition.
<b>If you replied YES, which was been assessed?</b>	Unknown. <sup>1,2</sup>
<b>Scale construct/ overall structure</b>	See in: <a href="https://qli.org.uic.edu">https://qli.org.uic.edu</a>  The QLI was developed by Carol Estwing Ferrans and Marjorie Powers in 1984 to measure quality of life in terms of satisfaction with life. The QLI measures both satisfaction and importance regarding various aspects of life.  The QLI produces five scores: quality of life overall and in four domains (health and functioning, psychological/spiritual domain, social and economic domain, and family).  It has 33 items asked in two framework: on “how satisfied you are” and “how important is”?
<b>a. Question items</b>	
<b>Items of presence of symptom/sign?</b>	No.
<b>Items of severity of symptom/sign?</b>	Yes.
<b>b. Response scale</b>	
<b>Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?</b>	Discrete from 1 to 6. Different formulations in the two section.
<b>c. Is the scale easy to score?</b>	
<b>Approx. time to score patient</b>	
<b>d. Raters</b>	
<b>Patient, caregiver, or clinician</b>	Patient.
<b>If clinician-rated, is training for application required?</b>	Not applicable.
<b>e. Access to scale</b>	
<b>Copyright or public domain?</b>	Copyright.
<b>How can the scale be obtained (address or website)?</b>	See in: <a href="https://qli.org.uic.edu">https://qli.org.uic.edu</a> The QLI is made available through this website for use in non-profit research and non-profit clinical practice.
<b>Has the scale been published in other languages?</b>	

<b>II. Scale properties</b>	
<b>a. Content validity</b>	
Any process for item generation and/or reduction	Unknown.
<b>b. Face validity</b>	
Do the items of the scale cover different components of the specific domain?	Yes (judgment of the task force).
Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?	No (judgment of the task force).
Does it score current state or is it based on the patient/caregiver recall?	
What is the time frame (e.g. “during the past week”)?	
<b>c. Use</b>	
Purpose: to measure severity, screen or diagnosis of the domain?	Measure severity
Is there a cut-off score? (for HD, for non-HD)	No
<b>d. Acceptability</b>	
Is the length of the scale appropriate?	A little long (judgment of the task force).
Are there ambiguities in instructions to patient/rater (as applicable)?	No (judgment of the task force).
Are there ambiguities in rating anchors?	No (judgment of the task force).
Are the questions appropriate for use in an HD population?	Yes (judgment of the task force).
Is the scale applicable across HD disease stages? Are there HD stages in which the scale is not applicable?	Unknown
e. Has this scale been specifically developed for use in HD (yes/no)?	It is a generic scale.
e1. If yes to the above, has the scale been deployed in HD by groups other than the developers?	No.
<b>III. Clinimetric/psychometric properties</b>	
Are there clini- or psychometric properties in HD ?	No.
<b>a. Reliability</b>	
Assessed – not assessed	Not assessed

Internal consistency	-
Test-retest reliability	-
Inter-rater reliability	-
<b>b. Validity in HD</b>	
Assessed vs. not assessed	Not assessed.
Criterion validity (any comparison with gold-standard)	-
Construct validity	
Factor analysis	Not assessed in HD.
Convergent validity	Not assessed in HD.
Divergent validity	Not assessed in HD.
Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)	No information.
Generalizability	
Shown to be valid at any stage of HD?	Largest between-group differences were evident between spouses and their partners with early stage disease; and different QoL domains were impacted in the different participant groups. The data presented shows the QoL domains affected in each group; and the impact of specific neuropsychiatric, cognitive and motor symptoms on spouse partners. Identification of the specific domains impacted in spouse/partners at an early stage of disease is crucial for establishing appropriate and long-term support. <sup>1,2</sup>
Shown to be valid in any population with dementia or significant cognitive impairment?	Likely limited.
<b>Responsiveness (detect change over time in the construct)</b>	
Demonstrated to be sensitive to change (change over time or to treatment)?	It is not sensitive to change over time after 12 months (TRACK-HD Study). <sup>1,2</sup>
<b>Interpretability</b>	
Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?	No
Floor and ceiling effects	Unknown
Score distributions	Unknown.
<b>IV. Overall impression</b>	
Advantages	-



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<b>Disadvantages</b>	There are virtually no data on this scale other than it has been used in a large HD study with some descriptive results.
<b>V. Recommendation</b>	<b>Listed</b>

References

1. Tabrizi SJ, Langbehn DR, Leavitt BR, Roos RA, Durr A, Craufurd D, *et al.* Biological and clinical manifestations of Huntington's disease in the longitudinal TRACK-HD study: cross-sectional analysis of baseline data. *Lancet Neurol* 2009;8:791-801.
2. Tabrizi SJ, Scahill RI, Durr A, Roos RA, Leavitt BR, Jones R, *et al.* Biological and clinical changes in premanifest and early stage Huntington's disease in the TRACK-HD study: the 12-month longitudinal analysis. *Lancet Neurol* 2011;10:31-42.

<b>Huntington Quality of Life Instrument (H-QoL-I)<sup>1</sup></b>	
<b>I. Scale description</b>	
<b>Are there several versions of the scale?</b>	No.
<b>If you replied YES, which was been assessed?</b>	Not applicable.
<b>Scale construct/ overall structure</b>	The H-QoL-I is a specific HRQoL tool. It consists of 11 items, which are divided into three dimensions rated from 0 - 100: motor functioning (four items), psychology (four items) and socializing (three items). <sup>1</sup>
<b>a. Question items</b>	
<b>Items of presence of symptom/sign?</b>	Yes. <sup>1</sup>
<b>Items of severity of symptom/sign?</b>	Yes. <sup>1</sup>
<b>b. Response scale</b>	
<b>Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?</b>	Discrete steps (5, from never to always). <sup>1</sup>
<b>c. Is the scale easy to score?</b>	
<b>Approx. time to score patient</b>	< 5 minutes.
<b>d. Raters</b>	
<b>Patient, caregiver, or clinician</b>	Patient.
<b>If clinician-rated, is training for application required?</b>	Not applicable
<b>e. Access to scale</b>	
<b>Copyright or public domain?</b>	Unclear.
<b>How can the scale be obtained (address or website)?</b>	From the original reporting paper. <sup>1</sup>
<b>Has the scale been published in other languages?</b>	French and Italian. <sup>1</sup>
<b>II. Scale properties</b>	
<b>a. Content validity</b>	
<b>Any process for item generation and/or reduction</b>	Yes. <ol style="list-style-type: none"> <li>1. A literature review identified the main relevant domains to be explored.</li> <li>2. A concept list was created in French after semi-structured interviews with patients, caregivers and HD healthcare professionals.</li> <li>3. A HD patient focus group came to a consensus on the aspects that impact the HRQoL of HD patients affected by HD.</li> </ol>

	<p>4. Three domains were identified as crucial: motor functioning, psychology, and socializing.</p> <p>5. The questionnaire was developed in French, resulting in a long self-reported questionnaire.</p> <p>6. The most relevant items were kept.</p> <p>7. The final pre-version of the H-QoL-I included 42 Likert-type items and was translated into Italian using a forward–backward translation method.<sup>1</sup></p> <p>8. ITEM REDUCTION: “<i>Before any item was excluded, its metrological properties and impact on the final instrument’s content were carefully considered.</i>”</p>
<b>b. Face validity</b>	
<b>Do the items of the scale cover different components of the specific domain?</b>	Yes. <sup>1</sup>
<b>Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?</b>	No. <sup>1</sup>
<b>Does it score current state or is it based on the patient/caregiver recall?</b>	Within the last two weeks. <sup>1</sup>
<b>What is the time frame (e.g. “during the past week”)?</b>	Last two weeks. <sup>1</sup>
<b>c. Use</b>	
<b>Purpose: to measure severity, screen or diagnosis of the domain?</b>	Severity. <sup>1</sup>
<b>Is there a cut-off score? (for HD, for non-HD)</b>	No.
<b>d. Acceptability</b>	
<b>Is the length of the scale appropriate?</b>	Yes (judgment of the task force).
<b>Are there ambiguities in instructions to patient/rater (as applicable)?</b>	No judgment of the task force).
<b>Are there ambiguities in rating anchors?</b>	No (judgment of the task force).
<b>Are the questions appropriate for use in an HD population?</b>	Yes (judgment of the task force).
<b>Is the scale applicable across HD disease stages? Are there HD stages in which the scale is not applicable?</b>	Yes. <sup>1</sup>
<b>e. Has this scale been specifically developed for use in HD (yes/no)?</b>	Yes. <sup>1</sup>
<b>e1. If yes to the above, has the scale been deployed in HD</b>	No.

by groups other than the developers?	
<b>III. Clinimetric/psychometric properties</b>	
Are there clini- or psychometric properties in HD ?	Yes. <sup>1</sup>
<b>a. Reliability</b>	
Assessed – not assessed	Assessed in HD. <sup>1</sup>
Internal consistency	<b>Manifest HD, n=252</b> Motor functioning - Cronbach's alpha: 0.9. Psychology - Cronbach's alpha: 0.84. Socializing - Cronbach's alpha: 0.86.
Test-retest reliability	Not reported.
Inter-rater reliability	Not applicable.
<b>b. Validity in HD</b>	
Assessed vs. not assessed	Not reported.
Overall impression: good – not good	Limited information for an impression.
Criterion validity (any comparison with gold-standard)	
Construct validity	
Factor analysis	<b>Manifest HD, n=252</b> Factor analysis with varimax rotation. The items within factors with loadings of at least 0.50 were considered to be significantly related to the factor. A three-factor solution accounted for 75% of total variance with varimax rotation (22.4-27.9%%). <sup>1</sup>
Convergent validity	<b>Manifest HD, n=252</b> Correlations of 0.5-0.7 with a variety of other quality of life instruments. <sup>1</sup>
Divergent validity	-
Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)	Not good (judgment of the task force).
Generalizability	
Shown to be valid at any stage of HD?	Not reported.
Shown to be valid in any population with dementia or significant cognitive impairment?	Not assessed.
<b>Responsiveness (detect change over time in the construct)</b>	
Demonstrated to be sensitive to change (change over time	Not assessed.

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or to treatment)?	
<b>Interpretability</b>	
Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?	No.
Floor and ceiling effects	<b>Manifest HD, n=252<sup>1</sup></b> Socializing = floor effect of 32%. Motor function = Ceiling effect of 16.6 %.
Score distributions	Acceptable. <sup>1</sup>
<b>IV. Overall impression</b>	
Advantages	Very simple to use.
Disadvantages	Language issues (developed in French and Italian translated into English) and limited data available at this time.
<b>V. Recommendation</b>	
<b>Listed</b>	

References

1. Clay E, De Nicola A, Dorey J, Squitieri F, Aballea S, Martino T, *et al.* Validation of the first quality-of-life measurement for patients with Huntington's disease: the Huntington Quality of Life Instrument. *Int Clin Psychopharmacol* 2012;27:208-14.

<b>HD-Pro-TRIAD</b>	
<b>I. Scale description</b>	
<b>Are there several versions of the scale?</b>	No
<b>If you replied YES, which was been assessed?</b>	-
<b>Scale construct/ overall structure</b>	47 items comprising 14 for cognition, 14 for emotional and behavioral dyscontrol and 19 for motor function. These 47 items are drawn from other instruments i.e., Neuro-QOL, Traumatic Brain Injury - QoL, HDQLIFE, FACIT. <sup>1</sup>
<b>a. Question items</b>	
<b>Items of presence of symptom/sign?</b>	Yes.
<b>Items of severity of symptom/sign?</b>	Yes.
<b>b. Response scale</b>	
<b>Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?</b>	5 discrete steps.
<b>c. Is the scale easy to score?</b>	
<b>Approx. time to score patient</b>	5 minutes.
<b>d. Raters</b>	
<b>Patient, caregiver, or clinician</b>	Patient, caregiver.
<b>If clinician-rated, is training for application required?</b>	Not applicable
<b>e. Access to scale</b>	
<b>Copyright or public domain?</b>	Public domain.
<b>How can the scale be obtained (address or website)?</b>	From the original article. <sup>1</sup>
<b>Has the scale been published in other languages?</b>	Constituent items are from scales with language translations.
<b>II. Scale properties</b>	
<b>a. Content validity</b>	
<b>Any process for item generation and/or reduction</b>	<ol style="list-style-type: none"> <li>1. A literature review was performed to define the triad of symptoms relevant to a HD-specific health-related QoL instrument.</li> <li>2. Phone interviews with HD patients and caregivers.</li> <li>3. An expert survey was conducted to identify HRQOL issues important to individuals with HD and develop items for a preliminary version of HD-PRO-TRIAD.</li> <li>4. Relevant items from the Neuro-QOL, the Traumatic Brain Injury-QOL, the HDQLIFE</li> </ol>

	and the Functional Assessment of Chronic Illness Therapy (FACIT) were included. 5. Content was matched with patient, caregiver, and provider perspectives. 6. A preliminary instrument was cognitively tested in 10 individuals with HD. <sup>1,2</sup>
<b>b. Face validity</b>	
<b>Do the items of the scale cover different components of the specific domain?</b>	Yes (judgment of the task force).
<b>Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?</b>	No (judgment of the task force).
<b>Does it score current state or is it based on the patient/caregiver recall?</b>	Patient and caregiver recall. <sup>1,2</sup>
<b>What is the time frame (e.g. “during the past week”)?</b>	Past 7 days.
<b>c. Use</b>	
<b>Purpose: to measure severity, screen or diagnosis of the domain?</b>	Measure severity.
<b>Is there a cut-off score? (for HD, for non-HD)</b>	No.
<b>d. Acceptability</b>	
<b>Is the length of the scale appropriate?</b>	It is long (47 questions). (Judgment of the task force)
<b>Are there ambiguities in instructions to patient/rater (as applicable)?</b>	Yes (judgment of the task force).
<b>Are there ambiguities in rating anchors?</b>	Yes (judgment of the task force).
<b>Are the questions appropriate for use in an HD population?</b>	No (judgment of the task force).
<b>Is the scale applicable across HD disease stages? Are there HD stages in which the scale is not applicable?</b>	Limited information is available about the online self-report (judgment of the task force).
<b>e. Has this scale been specifically developed for use in HD (yes/no)?</b>	Yes.
<b>e1. If yes to the above, has the scale been deployed in HD by groups other than the developers?</b>	No.
<b>III. Clinimetric/psychometric properties</b>	
<b>Are there clini- or psychometric properties in HD ?</b>	Limited.
<b>a. Reliability</b>	
<b>Assessed – not assessed</b>	Assessed in HD.

<p><b>Internal consistency</b></p>	<p><b>Manifest HD, n=132.<sup>1</sup></b>                      HD-PRO-TRIAD TOTAL - Cronbach's alpha 0.98;                      HD-PRO-TRIAD Cognition - Cronbach's alpha 0.97;                      HD-PRO-TRIAD Emotional/Behavioral - Cronbach's alpha 0.96;                      HD-PRO-TRIAD Motor Function - Cronbach's alpha 0.98;</p> <p>NOTE: item-total correlations from 0.54 to 0.84.<sup>1</sup></p>
<p><b>Test-retest reliability</b></p>	<p>No</p>
<p><b>Inter-rater reliability</b></p>	<p>Not applicable.</p>
<p><b>b. Validity in HD</b></p>	
<p><b>Assessed vs. not assessed</b></p>	<p>Assessed.</p>
<p><b>Criterion validity (any comparison with gold-standard)</b></p>	<p>-</p>
<p><b>Construct validity</b></p>	
<p><b>Factor analysis</b></p>	<p>No.</p>
<p><b>Convergent validity</b></p>	<p><b>Manifest HD, n=132.<sup>1</sup></b>                      Motor - SOME EVIDENCE: 0.77 with Neuro-QoL lower extremity, 0.81 with Neuro-QoL upper extremity, 0.83 with PROMIS global physical health, 0.77 with SF-Physical, 0.77 with EQ-5D, 0.77 with TFC, 0.58 with IS; and 0.62. 0.61. 0.55 with NeuroQoL Anxiety, Depression &amp; Social roles, 0.72 with PROMIS global mental health, 0.61 with SF Mental)</p> <p>Emotional/behavioral dyscontrol domains (0.75. 0.75, 0.27 with NeuroQoL Anxiety, Depression &amp; Social Roles - SOME EVIDENCE: 0.73 with PROMIS global mental health, 0.53 with SF Mental; and 0.45 with Neuro-QoL lower extremity, 0.44 with Neuro-QoL upper extremity, 0.57 with PROMIS global physical health, 0.47 with SF-Physical, 0.49 with EQ-5D, 0.40 with TFC, 0.35 with IS).</p> <p>Cognition – LIMITED (no cognitive measures and highest correlations were for NeuroQoL upper extremity (0.81) and PROMIS global physical health (0.80)).<sup>1</sup></p>
<p><b>Divergent validity</b></p>	<p>-</p>
<p><b>Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)</b></p>	<p>Limited data.</p>
<p><b>Generalizability</b></p>	
<p><b>Shown to be valid at any stage of HD?</b></p>	<p>No.</p>



Shown to be valid in any population with dementia or significant cognitive impairment?	No.
<b>Responsiveness (detect change over time in the construct)</b>	
Demonstrated to be sensitive to change (change over time or to treatment)?	No.
<b>Interpretability</b>	
Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?	No.
Floor and ceiling effects	Unknown.
Score distributions	<b>Manifest HD, n=132.<sup>1</sup></b> HD-PRO-TRIAD Cognition - 3.2 (1.1). HD-PRO-TRIAD Emotional/Behavioral - 2.7 (1.0). HD-PRO-TRIAD Motor Function - 2.9 (1.0).
<b>IV. Overall impression</b>	
Advantages	Inclusion of generic and HD-specific contents.
Disadvantages	Online study with unverified self-reported clinical characteristics. Cognition scale not examined against cognitive assessments for concurrent validity. More data are needed for convergent and discriminant validity.
<b>V. Recommendation</b>	
Listed	

## References

- Carlozzi NE, Victorson D, Sung V, Beaumont JL, Cheng W, Gorin B, *et al.* HD-PRO-TRIAD Validation: A Patient-reported Instrument for the Symptom Triad of Huntington's Disease. *Tremor Other Hyperkinet Mov (N Y)* 2014;4:223.
- Victorson D, Carlozzi NE, Frank S, Beaumont JL, Cheng W, Gorin B, *et al.* Identifying Motor, Emotional-Behavioral, and Cognitive Deficits that Comprise the Triad of HD Symptoms from Patient, Caregiver, and Provider Perspectives. *Tremor Other Hyperkinet Mov (N Y)* 2014;4:224.

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HD-PRO-TRIAD™ v.1.0

**Cognition**

Please respond to each question or statement by marking one box per row.

In the past 7 days...	Very often (several times a day)	Often (once a day)	Sometimes (2-3 times)	Rarely (once)	Never	Official Use Only
1. I had trouble keeping track of what I was doing if I was interrupted.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
2. I had trouble concentrating.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
3. I had difficulty doing more than one thing at a time.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
4. I had trouble planning out steps of a task.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
5. I had trouble remembering new information, like phone numbers or simple instructions.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>

**How much DIFFICULTY do you currently have...**

	Cannot do	A lot	Somewhat	A little	None	Official Use Only
6. getting things organized?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
7. keeping important personal papers such as bills, insurance documents and tax forms organized?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
8. learning new tasks or instructions?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
9. remembering a list of 4 or 5 errands without writing it down?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<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	Official Use Only
10. I had trouble remembering things.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
11. My inability to solve problems limited my ability to work.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>

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HD-PRO-TRIAD™ v.1.0

For Official Use Only

**Cognition 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 Cognition domain to obtain the Raw Score.

**Raw Score**

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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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Carlozzi NE, Victorson D, Sung V, Beaumont JL, Cheng W, Gorin B, et al. HD-PRO-TRIAD Validation: A Patient-reported Instrument for the Symptom Triad of Huntington's Disease. *Tremor Other Hyperkinet Mov (N Y)* 2014;4:223.

## CAREGIVER FOCUSED

The Alzheimer's Carer's Quality of Life Inventory (ACQLI)	
<b>I. Scale description</b>	
Are there several versions of the scale?	No. <sup>1</sup>
If you replied YES, which was been assessed?	Not applicable.
Scale construct/ overall structure	Assesses quality of life (QoL) of Alzheimer's disease (AD) caregivers; needs-based QoL model; assessed by AD caregivers from 5 countries. <sup>1</sup> 30 items are scored 0/1 (not true/true); summed into a total score with a 0–30 range. <sup>1</sup> <a href="http://www.galen-research.com/content/measures/ACQLI%20UK%2030%20Male%20Patient%20-%20First%20page%20sample.pdf">http://www.galen-research.com/content/measures/ACQLI%20UK%2030%20Male%20Patient%20-%20First%20page%20sample.pdf</a>
<b>a. Question items</b>	
Items of presence of symptom/sign?	Presence or absence of symptoms.
Items of severity of symptom/sign?	Unknown.
<b>b. Response scale</b>	
Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?	Binary: yes or no.
<b>c. Is the scale easy to score?</b>	
Approx. time to score patient	5 minutes (judgment of the task force).
<b>d. Raters</b>	
Patient, caregiver, or clinician	Patient.
If clinician-rated, is training for application required?	Not applicable.
<b>e. Access to scale</b>	
Copyright or public domain?	Copyright, Galen Research and Glaxo SmithKline.
How can the scale be obtained (address or website)?	From Mapi: <a href="https://eprovide.mapi-trust.org/index.php/instruments/alzheimer-s-carer-s-quality-of-life-instrument">https://eprovide.mapi-trust.org/index.php/instruments/alzheimer-s-carer-s-quality-of-life-instrument</a>
Has the scale been published in other languages?	9 translations <a href="https://eprovide.mapi-trust.org/index.php/instruments/alzheimer-s-carer-s-quality-of-life-instrument">https://eprovide.mapi-trust.org/index.php/instruments/alzheimer-s-carer-s-quality-of-life-instrument</a> Includes English, French, German, Italian and Spanish. <sup>2</sup>
<b>II. Scale properties</b>	
<b>a. Content validity</b>	

<b>Any process for item generation and/or reduction</b>	In-depth qualitative interviews conducted with 40 carers in the UK. <sup>2</sup> Items were translated for use in each of the languages with emphasis on producing conceptual equivalence. Field-testing of the measure in each country indicated that the respondents found it acceptable, relevant and easy to complete.
<b>b. Face validity</b>	
<b>Do the items of the scale cover different components of the specific domain?</b>	Yes (judgment of the task force). <sup>1</sup>
<b>Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?</b>	No (judgment of the task force). <sup>1</sup>
<b>Does it score current state or is it based on the patient/caregiver recall?</b>	Current state.
<b>What is the time frame (e.g. “during the past week”)?</b>	Current time.
<b>c. Use</b>	
<b>Purpose: to measure severity, screen or diagnosis of the domain?</b>	Assess severity of caregiver burden. <sup>1</sup>
<b>Is there a cut-off score? (for HD, for non-HD)</b>	No.
<b>d. Acceptability</b>	
<b>Is the length of the scale appropriate?</b>	Yes. <sup>1</sup>
<b>Are there ambiguities in instructions to patient/rater (as applicable)?</b>	Note: the task force was unable to procure a copy of the scale.
<b>Are there ambiguities in rating anchors?</b>	Not applicable.
<b>Are the questions appropriate for use in an HD population?</b>	Appropriate for HD caregivers. <sup>1</sup>
<b>Is the scale applicable across HD disease stages? Are there HD stages in which the scale is not applicable?</b>	Applicable for caregivers of all HD stages (judgment of the task force).
<b>e. Has this scale been specifically developed for use in HD (yes/no)?</b>	No. <sup>1</sup>
<b>e1. If yes to the above, has the scale been deployed in HD by groups other than the developers?</b>	Not applicable.
<b>III. Clinimetric/psychometric properties</b>	
<b>Are there clini- or psychometric properties in HD ?</b>	Yes.

<b>a. Reliability</b>	
Assessed – not assessed	Assessed in HD.
Internal consistency	<b>61 HD Caregivers:</b> Coefficient alpha = 0.95. <sup>1</sup>
Test-retest reliability	Not assessed in HD.
Inter-rater reliability	Not assessed in HD.
<b>b. Validity in HD</b>	
Assessed vs. not assessed	Not assessed in HD.
Overall impression: good – not good	<b>Limited information</b>
Criterion validity (any comparison with gold-standard)	
Construct validity	
Factor analysis	N/A, unidimensional scale. <sup>1</sup>
Convergent validity	Not assessed in HD.
Divergent validity	Not assessed in HD.
Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)	Not good (judgment of the task force).
Generalizability	
Shown to be valid at any stage of HD?	Not applicable
Shown to be valid in any population with dementia or significant cognitive impairment?	Not applicable
<b>Responsiveness (detect change over time in the construct)</b>	
Demonstrated to be sensitive to change (change over time or to treatment)?	Not assessed in HD.
<b>Interpretability</b>	
Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?	No.
Floor and ceiling effects	<b>61 HD Caregivers:</b> Acceptable: 9.8% floor effect, 1.6% ceiling effect. <sup>1</sup>
Score distributions	<b>61 HD Caregivers:</b> 42 (29.5) <sup>1</sup>
<b>IV. Overall impression</b>	

<b>Advantages</b>	Quick, easy to use assessment.
<b>Disadvantages</b>	Further clinimetric testing is required.
<b><i>V. Recommendation</i></b>	<b>Suggested for assessing quality of life for HD caregivers (severity)</b>

#### References

1. Hagell P, Smith S. A psychometric comparison of two carer quality of life questionnaires in Huntington's disease: implications for neurodegenerative disorders. *J Huntingtons Dis* 2013;2:315-22.
2. Doward LC. The Development of the Alzheimer's Carers' Quality of Life Instrument *Quality of Life Research* 1997;6:639.

<b>Huntington's disease quality of life battery for carers (HD-QoL C)</b>	
<b>I. Scale description</b>	
<b>Are there several versions of the scale?</b>	Yes, short (20-item) and long (34-item) forms are available. <sup>1</sup>
<b>If you replied YES, which was assessed?</b>	Both.
<b>Scale construct/ overall structure</b>	<p>The HDQoL-C is a HD-specific, multi-dimensional and validated tool for measuring quality of life (QoL) in family caregivers of patients with HD.</p> <p>It is based upon the domains and facets of the Comprehensive Quality of Life scale for adults (ComQoL-A5).<sup>2</sup></p> <p>The 34-item version covers three domains: “practical aspects of caregiving” (n=9), “satisfaction with life” (n=8) and “feelings about living with HD” (n=17).</p> <p>The 20-item version comprises: 3-items on “satisfaction of life” and all items from “feelings about living with HD” (n=17).</p> <p>Long-form: 11-grade (0–10) numerical rating scale, summed and transformed into a 0–100 range, (100 = better QoL); total score = is computed as the overall sum, transformed into a 0–100 range (100 = better QoL).</p> <p>Short-form: item scores are summed and transformed into a 0–100 range (100 = better QoL) for each suggested subscale.</p>
<b>a. Question items</b>	
<b>Items of presence of symptom/sign?</b>	Yes. <sup>3</sup>
<b>Items of severity of symptom/sign?</b>	Frequency is assessed, as well as satisfaction, but not severity. <sup>3</sup>
<b>b. Response scale</b>	
<b>Are the items of the scale scored in discrete steps (specify number) or in a visual analogue scale?</b>	Discrete steps: 11. <sup>3</sup>
<b>c. Is the scale easy to score?</b>	
<b>Approx. time to score patient</b>	Total time (scoring and administration time): 27 minutes. Instructions exist on how to set up a syntax, which would make it quicker to score. <sup>3</sup>
<b>d. Raters</b>	

Patient, caregiver, or clinician	Caregiver. <sup>3</sup>
If clinician-rated, is training for application required?	Not applicable
<i>e. Access to scale</i>	
Copyright or public domain?	Copyright.
How can the scale be obtained (address or website)?	From the original author: Aimee Aubeeluck. <sup>3</sup>
Has the scale been published in other languages?	Yes, 3 languages. <sup>3</sup>
<b>II. Scale properties</b>	
<b>a. Content validity</b>	
Any process for item generation and/or reduction	1) The HDQoL-C was developed using the data gathered from our three preliminary investigations and the existing domains and facets of the COMQOL-A5. <sup>3</sup> 2) A number of items were revised or removed from the scale as they were not deemed as pertinent to the HD spousal caregivers QoL. 3) From the 63 items in the pilot version of the HDQoL-C, 27 items were accepted, four items were revised, one item was rewritten and 31 were discarded. Two qualitative questions were also added to the HDQoL-C in line with comments from experts and carers.
<b>b. Face validity</b>	
Do the items of the scale cover different components of the specific domain?	Yes.
Is the scale heavily weighted towards one aspect of the domain it measures and which components of the domain are not covered?	There are more items on feelings about life (17); satisfaction with life has 8 questions, aspects of caring 9 questions. <sup>3</sup>
Does it score current state or is it based on the patient/caregiver recall?	Current state. <sup>3</sup>
What is the time frame (e.g. “during the past week”)?	Not specified. <sup>3</sup>
<b>c. Use</b>	
<b>Purpose: to measure severity, screen or diagnosis of the domain?</b>	
Is there a cut-off score? (for HD, for non-HD)	No.  NOTE: there are instructions on interpreting the scores: <sup>3</sup>  “A high score (119 or more) would suggest how you feel is having very little impact on your quality of life.”



	A middle score (between 69 and 118) would suggest how you feel is having a moderate impact on your quality of life.
	A low score (68 or less) would suggest how you feel is having a big impact on your quality of life.”
<b>d. Acceptability</b>	
<b>Is the length of the scale appropriate?</b>	A little long, but not excessively (judgment of the task force). <sup>3</sup>
<b>Are there ambiguities in instructions to patient/rater (as applicable)?</b>	No. <sup>3</sup>
<b>Are there ambiguities in rating anchors?</b>	Not applicable.
<b>Are the questions appropriate for use in an HD population?</b>	For HD caregivers, yes. <sup>3</sup>
<b>Is the scale applicable across HD disease stages?</b>	Caregiver scale. <sup>3</sup>
<b>Are there HD stages in which the scale is not applicable?</b>	
<b>e. Has this scale been specifically developed for use in HD (yes/no)?</b>	Yes. <sup>3</sup>
<b>e1. If yes to the above, has the scale been deployed in HD by groups other than the developers?</b>	Yes.
<b>III. Clinimetric/psychometric properties</b>	
<b>Are there clini- or psychometric properties in HD ?</b>	Yes.
<b>a. Reliability</b>	
<b>Assessed – not assessed</b>	Assessed in HD caregivers.
<b>Internal consistency</b>	<u>Long-form:</u> Cronbach’s alpha “Practical aspects of caregiving”: 0.62; “Satisfaction with life”: 0.91; “Feelings about living with HD”, 0.84. <sup>4</sup> Cronbach’s alpha: Component 2, 0.801; Component 3, 0.844; Component 4, 0.885. Total, 0.92. <sup>3</sup> <u>Short-form:</u> Cronbach’s alpha, Satisfaction with life, 0.92; total, 0.88. <sup>4</sup>
<b>Test-retest reliability</b>	10 carers completed the HDQoL-C two weeks after first administration. Both questionnaire scores were subsequently correlated using Pearson’s correlation coefficient: component 2, r=0.86; component 3, r=0.90; component 4, r=0.92. <sup>3</sup>
<b>Inter-rater reliability</b>	-
<b>b. Validity in HD</b>	
<b>Assessed vs. not assessed</b>	Assessed in HD caregivers.

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5	<b>Criterion validity (any comparison with gold-standard)</b>	-
6	<b>Construct validity</b>	
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8	<b>Factor analysis</b>	Principal components analysis (PCA) <sup>3</sup> PCA revealed the presence of seven subscales subsumed within the three components of practical aspects of care-giving <sup>3</sup> , satisfaction with life <sup>3</sup> and feelings about living with HD. <sup>3</sup>
9		
10	<b>Convergent validity</b>	<b>Correlations with WHO-QoL BREF.<sup>3</sup></b> Pearson’s correlation coefficient of 0,0.58, p<0.01 for component (practical aspects of caregiving), of 0.64, p<0.01 for component (satisfaction with life) and of 0.76, p<0.01 for component (feelings about living with HD). <b>Correlations of 0.22 to 0.28 with H-QoL-I.<sup>5</sup></b>
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12	<b>Divergent validity</b>	
13	<b>Overall impression: good – not good (based on references preferably, judgment of the task force can be stated)</b>	OK, and can be considered if performing a study on caregivers, but more established measures from other caregiving populations may be considered. (Judgment of the task force).
14	<b>Generalizability</b>	
15	<b>Shown to be valid at any stage of HD?</b>	Not applicable.
16	<b>Shown to be valid in any population with dementia or significant cognitive impairment?</b>	Not applicable
17	<b>Responsiveness (detect change over time in the construct)</b>	
18	<b>Demonstrated to be sensitive to change (change over time or to treatment)?</b>	No.
19	<b>Interpretability</b>	
20	<b>Has the minimal clinically important change and minimal clinically relevant incremental difference been assessed?</b>	No.
21	<b>Floor and ceiling effects</b>	<u>Long-form:</u> “Practical aspects of caregiving”: 0/0; “Satisfaction with life”: 3.3/0; “Feelings about living with HD”: 0/0 Total 0/0 (all okay 15-205 set as maximum). <sup>4</sup> <u>Short-form:</u> “Satisfaction with life”: 6.6/1.6 and total 0/0 (both okay). <sup>4</sup>
22	<b>Score distributions</b>	<u>Long-form:</u> 49.6 (16.8). <sup>4</sup> <u>Short-form:</u> 49.5 (18.2). <sup>4</sup>
23	<b>IV. Overall impression</b>	
24	<b>Advantages</b>	Specific for HD.
25	<b>Disadvantages</b>	Reduced uptake.
26	<b>V. Recommendation</b>	<b>Suggested for assessing quality of life for HD caregivers (severity)</b>
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For Peer Review