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# Rating Scales and Performance-based Measures for Assessment of Functional Ability in Huntington's Disease: Critique and Recommendations

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**Abstract:** Limitation of functional ability is a major feature of Huntington's disease (HD). The International Parkinson and Movement Disorder Society (MDS) commissioned the appraisal of the use and clinimetric properties of clinical measures of functional ability that have been applied in HD studies and trials to date, to make recommendations regarding their use based on standardized criteria. After a systematic literature search, we included a total of 29 clinical measures grouped into two categories: (1) performance-based measures (e.g., balance, walking, and reaching/grasping), and (2) rating scales. Three performance-based measures are rated as "recommended": the Tinetti Mobility Test for screening of fall risk and for severity assessment of mobility in patients with manifest HD (up to stage III); the Berg Balance Scale for severity of balance impairment; and the Six-Minute Walk Test for assessment of walking endurance (severity) in HD subjects with preserved ambulation. No rating scale targeting functional ability reached a "recommended" status either for screening or severity measurement.

The main challenges identified in this review include applying widely accepted conceptual frameworks to the identified measures, the lack of validation of clinical measures to detect change over time, and absence of validated measures for upper limb function. Furthermore, measures of capacity or ability to perform activities of daily living had ceiling effects in people with early and pre-manifest HD. We recommend that the MDS prioritize the development of new scales that capture small, but meaningful changes in function over time for outcome assessment in clinical trials, particularly in earlier stages of HD.

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# Introduction

The ability to perform daily life activities depends on the integration of motor, cognitive, and behavioral functioning. These domains are progressively impaired in Huntington's disease (HD). A measure of functional ability based on key life activities is thus an attractive outcome in clinical studies, namely for treatment trials. A single measure pertinent to patient overall function would be useful to capture changes occurring simultaneously in the different symptom domains in HD. Further, functional ability measures are valued as an outcome for drug development by regulatory agencies.[1]

There is a need to identify and critically appraise the measurement properties of clinical measures currently used to capture functional ability in people with HD to inform optimal application in clinical research. The scope of this review is directed towards physical function and included a wide spectrum of clinical measures from those capturing motor tasks, such as walking and balance ability, to those assessing the ability to perform activities of daily living (ADL).

The current review aims to provide recommendations and identify gaps in the use and validation of these functional measures that have been used in HD studies and trials to date. Such information will inform the field, identifying where additional testing of measurement properties or development of new measures may be required.

# Methods

We followed the methodology proposed by the MDS Committee on Rating Scales Development described elsewhere[2] this includes (1) organization and critique process, (2) selection of scales, (3) inclusion/exclusion for review, and (4) criteria for rating scales recommendation (Table 1). For selection of measures, the keywords selected for this review were "Huntington*" OR "Westphal variant" OR "juvenile Huntington*" and the terms "scale" OR "questionnaire" OR "index" OR "measure" as well as keywords "function", "activit* daily li*", "capacity", "*ability", "impairment". Manuscripts published before October 17, 2016 were retrieved using the above search strategy and thoroughly screened by the chair of the subcommittee (T.A.M.) to ascertain which clinical measure had been used in each study. To aid our categorization of clinical measures in this review, we applied a widely accepted classification of the health components of functioning and disability: The International Classification of Functioning, Disability and Health (ICF).[3] The ICF defines: (1) impairments or problems in body function or structure such as a significant deviation or loss, (2) activity or the execution of a task, and (3) participation or involvement in a life situation.[3] By consensus, we included clinical measures in this review that captured (a) activity or the execution of a task or tasks and (b) participation or involvement in a life situation.

## Identified Clinical Measures and their Utilization in Clinical Research

A total of 47 potentially relevant clinical measures were identified. After screening for exclusion criteria with abstract screening and in-depth review, a total of 29 measures (Table 2) were included and divided in performance-based measures defined as functional assessments based on the live performance of a task (e.g., balance, walking, and reaching/grasping; $n = 17$) and rating scales ($n = 12$) capturing the assessment of various aspects of functional ability based on recall. (See the Supporting Information section for more details.)

## Critique of Measures of Functional Ability

We provide a summary description of the performance-based measures and rating scales classified as "recommended" or "suggested (see Table 3 for an overview of clinimetric properties)." See the Supporting Information section for a full description of all clinical measures included for full review, including those that were included in the "suggested with caveats" or "listed" categories.

# Performance-based Measures

## Recommended

### Tinetti Mobility Test (TMT)

The TMT is a 16-item clinician-administered performance measure, which consists of balance and gait subscales that measure static and dynamic balance. It was originally developed to measure

**TABLE 1** Classification system for scale recommendation

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

Abbreviations: 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.

balance and screen for risk of falls in the elderly,[4] but has been used in other patient populations.[4] During the 10 to 15 minute test, patients perform a series of balance and walking tasks and are rated on a 0 to 2 scale based on qualitative assessment of performance.[4] The TMT has been used in several studies in HD and demonstrates good test–retest reliability in early, mid, and late-stage HD (ICC = 0.8 to 0.9).[5,6] Higher scores in the TMT correlated positively with spatiotemporal measures of gait (e.g., velocity r = 0.68; stride length r = 0.74), with higher scores of the UHDRS-FAS (r = 0.44) and UHDRS-TFC (r = 0.42) and lower scores of the UHDRS-Total Motor Score (TMS; r = −0.59).[5,7,8] The TMT has demonstrated responsiveness in the context of interventional studies, including an intensive rehabilitation intervention program in patients with HD stages I to III (pre = 15.97, post = 20.79, $p < 0.001$),[9] and off (17.09 ± 4.04) and on tetrabenazine (19.91 ± 3.53, $p < 0.02$) study of manifest HD patients.[10] However, there was no significant change in the TMT following a video-based balance training program.[11] A cut-off score of 21 has 74% sensitivity and 60% specificity in identifying fallers in HD.[5]

**Recommendation**: The TMT is "recommended" for assessment of gait and balance in patients with manifest HD (up to stage III) and "recommended" for screening for risk of falls.

## The Berg Balance Scale (BBS)

The BBS is a performance measure consisting of 14 subtests of various activities related to balance that takes 10 to 15 minutes to complete. These activities include static postures (e.g., sitting, standing), transitions (e.g., sitting-to-standing, transferring between chairs), and challenging positions (e.g., standing with eyes closed). Quality of performance for each item is scored using a 4-point scale, with higher scores indicating better balance, and a possible maximum score of 56. Although originally developed to measure balance in older people, the BBS has been widely used in HD, although it has limited applicability in non-ambulatory HD due to the nature of the activities.[6,12–19] The available clinimetric data show that it has good test–retest reliability in both pre-manifest (ICC = 0.86) and manifest HD (ICC = 0.96).[6] A minimal detectable change (MDC) of five in people with manifest HD has been reported.[6] Convergent validity has been reported between the BBS and the HD-ADL (r = −0.47), UHDRS TFC (r = 0.60[19] and r = 0.43[7]), UHDRS-FAS (r = 0.48)[7], and UHDRS-TMS (r = −0.55).[7] Sensitivity to change following treatment withdrawal (tetrabenazine) was reported in a small open-label cohort.[14] A cut-off score of 40 was used to predict being a "faller" for a plotted probability of 60%.[85]

**Recommendation**: The BBS is "recommended" for assessing severity of balance impairment in ambulatory HD. The BBS is suggested for screening for fall risk, as no sensitivity or specificity data for falls have been reported.

## The Six-Minute Walk Test

The Six-Minute Walk test measures how many meters an individual can walk in 6 minutes.[20,21] Two practice tests are recommended, but not always carried out.[22,23] It has been applied as a measure of endurance in neurological conditions, in contrast to shorter walk tests that generally measure velocity of walking speed.[6] It has been used in patients with pre-manifest and manifest HD, although it cannot be used for those who are non-ambulatory. Excellent test–retest reliability data have been reported in pre-manifest (ICC = 0.98) and manifest HD (IC = 0.94; early and late HD = 0.97, and mid-stage HD = 0.86).[6,24] It is unclear how values discriminate among pre and manifest HD severity levels as there is an overlap of the 95% confidence interval (CI) around mean values in both groups. On the other hand, values may separate pre and early manifest HD from mid to late-stage HD.[6] Low correlations have been reported between the Six-Minute Walk Test and the UHDRS-FAS,[7] but higher correlations are not expected due to the limited overlap of the measure constructs. The MDC has been reported to be 39.2 meters for pre-manifest HD and 86.6 meters for manifest HD (range: 56.6 to 126.1 meters).[6]

**Recommendation**: The Six-Minute Walk test is "recommended" for the assessment of walking endurance (severity) across HD severity.

# Suggested

## Timed "Up and Go" Test (TUG)

The TUG is a simple and quick (< 3 minutes) to use test that assesses mobility, balance, and risk of falls. Although not specifically developed for use in HD, it has been used in pre-manifest and manifest HD to measure severity and screen for risk of falls.[13,25] The TUG measures the time it takes for a patient to rise from a chair, walk three meters, turn around, walk back to the chair, and sit down. One practice test is recommended before scoring the test.[25] Mean scores for patients with manifest HD range from 9 to 17 seconds[6,19] and a cut-off score of 14 seconds has been reported to predict being a "faller" for a plotted probability of 60%.[13] Test–retest reliability in HD has been shown to be excellent (ICC = 0.93 [pre-manifest HD], 0.96 [manifest HD]) and the MDC has been reported to be 1.34 seconds in pre-manifest HD and 2.98 seconds in manifest HD.[6] The TUG was not statistically significantly correlated with the UHDRS-TMS or the UHDRS-TFC and correlated weakly with the UHDRS-FAS ($r = -0.33$, $p < 0.01$).[7] Pre–post scores improved by an average of 1.3 seconds following training in a noncontrolled study, that follow within the MDC.[26] The TUG can be used in early to mid-stages of HD, but not in pre-manifest or late stage HD, and it appears to be sensitive to disease progression, but does not discriminate between disease subtypes.[6,19,27]

**Recommendation**: The TUG is suggested for assessing severity of balance and mobility, and suggested for screening for fall risk. There are no sensitivity or specificity data for the reported cut-off point. Construct validity needs further assessment.

## The Ten-Meter Walk Test

The Ten-Meter Walk test is a quick and easy performance-based measure that assesses walking speed. The score is based on the mean of two tests. The test has been used in pre-manifest and manifest HD with varying walking speeds: self-paced[6,7,24] and

**TABLE 2** Summary of all included scales or instruments 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 |
|---|---|---|---|---|---|---|
| PERFORMANCE-BASED MEASURES | | | | | | |
| Tinetti mobility test | No | Yes | Yes | Yes | Recommended for assessment of gait and balance problems in patients with manifest HD (up to stage III)<br>Recommended for screening for risk of falls | |
| The Berg Balance Scale | No | Yes | Yes | Yes[1]/No[2] | [1] Recommended for assessing severity of balance impairment in HD with preserved ambulation<br>[2] Suggested for screening risk of falls | |
| 6-Minute Walk Test | No | Yes | Yes | Yes | Recommended for assessing walking endurance (severity) in HD with preserved ambulation | |
| Timed 'up and go' Test | No | Yes | Yes | No | Suggested for assessing balance and mobility (severity)<br>Suggested for screening for risk of falls | |
| 10 Meter walk Test | No | Yes | Yes | No | Suggested for assessing walking speed in manifest HD | |
| 4 Square step test (FSST) | No | Yes | Yes | No | Suggested for assessing dynamic balance in HD | |
| Mini-BESTest | No | Yes | Yes | No | Suggested for assessing severity of balance impairment in HD | |
| Physical Performance Test (PPT) | No | Yes | Yes | No | Suggested for assessing severity of impairment of physical function (activities of daily living) | |
| Six-condition Romberg test | No | Yes | Yes | No | Suggested for assessing severity of balance impairment in HD | |
| Functional reach test | No | Yes | Yes | No | Suggested *with caveats* | Very limited data by a single group in HD |
| 5 Times Sit to Stand Test | No | Yes | Yes | No | Suggested *with caveats* | Very limited data in a single trial in HD |
| 30 Second Chair Stand | No | Yes | Yes | No | Suggested *with caveats* | Very limited data in a single trial in HD |
| Dynamic gait index | No | Yes | *Yes* | No | Suggested *with caveats* | Very limited data in a single trial in HD |
| Walking while talking test | No | Yes | *Yes* | No | Suggested *with caveats* | Very limited data in a single study in HD |
| Timed 25 Foot Walk Test | No | Yes | No | No | Listed | |
| 12 meter walking, hand tapping in 30s, and time to drink 120 ml | No | Yes | No | No | Listed | |
| Jebsen-Taylor Hand Function Test | No | Yes | No | No | Listed | |

Table 2: *Continued*

| 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 |
|---|---|---|---|---|---|---|
| RATING SCALES | | | | | | |
| The Unified Huntington's Disease Rating Scale (UHDRS) Total Functional Capacity | Yes | Yes | Yes | No | Suggested for assessing severity of limitation in functional capacity in HD | |
| UHDRS - Functional Assessment Scale | Yes | Yes | Yes | No | Suggested for assessing severity of limitation in functional capacity in HD | |
| UHDRS - Independence Scale | Yes | Yes | Yes | No | Suggested for assessing severity of limitation in functional ability in HD | |
| HD Activities of Daily Living | Yes | Yes | Yes | No | Suggested for assessing severity of limitation in ADLs in HD | |
| Activity-specific balance scale | No | Yes | Yes | No | Suggested for assessing level of self-reported balance confidence in HD | Questionable use, since lack of insight is a feature in HD |
| Rivermead Mobility Index | No | Yes | Yes | No | Suggested for assessing severity of mobility restriction (as a generic measure) | |
| Barthel Index of ADL | No | Yes | *Yes* | No | Suggested *with caveats* | Very limited clinimetric data |
| Modified Self-Assessment PD Disability Scale | No | Yes | *Yes* | No | Suggested *with caveats* | Very limited clinimetric data |
| Self-report HD Work function | Yes | Yes | No | No | Listed | |
| Behavior Observation Scale Huntington - ADL subscale | Yes | Yes | No | No | Listed | |
| Alzheimer's Disease Cooperative Study Activities of Daily Living Scale | No | Yes | No | No | Listed | |
| Quick DASH | No | Yes | No | No | Listed | |

**TABLE 3** Summary of clinimetric data of all instruments used in HD with a recommendation level of "suggested" or "recommended"

| Scale | Internal Consistency | Test-Retest Reliability | Inter-Rater Reliability | Construct Validity | Discrimination Across Disease Stages/Severity | Responsiveness | Ceiling/Floor Effect | Sensitivity/ Specificity (E/S) |
|---|---|---|---|---|---|---|---|---|
| **PERFORMANCE-BASED MEASURES** | | | | | | | | |
| Tinetti Mobility test | NR | + | NR | + | +/− | +/− (in non-RCTs) | Ceiling and floor effects | + |
| The Berg Balance Scale | NR | + | NR | + | + (Stage I *vs.* II/III) | +/− (in non-RCT trials) | Ceiling and floor effects | +/− (no E/S data for cut-off for risk of falls) |
| Six Minute Walk Test | N/A | + | NR | + | +/− | - (data from RCTs) | NR | NR |
| Timed 'up and go' Test | N/A | + | NR | +/− (no correlation with UHDRS-TMS) | +/− | +/− (data from trials) | Ceiling and floor effects | +/− (no E/S data for cut-off for risk falls) |
| Ten Meter Walk Test | N/A | + | NR | + | +/− (non-linear with disease stages) | +/− (in rehabilitation trials) | None | NR |
| Four square step test | N/A | + | NR | + | - (poor discrimination) | NR | NR | NR |
| Mini-BESTest | NR | NR | NR | + | +/− | NR | Floor effect | NR |
| Physical Performance Test | NR | + | NR | + | +/− (separates pre/mild vs/ middle/late) | +/− | Ceiling effect | NR |
| Six-condition Romberg test | NR | + | NR | NR | +/− (premanifest vs. manifest) | - (data from 1 trial) | NR | NR |
| **RATING SCALES** | | | | | | | | |
| UHDRS - Total Functional Capacity | NR | NR | +/− | + | + | + | Ceiling and floor effects | NR |
| UHDRS - Functional Assessment Scale | + | NR | NR | + | + | + | Ceiling effects | NR |
| UHDRS - Independence Scale | NR | NR | +/− | + | + | + | Ceiling effects | NR |
| HD Activities of Daily Living | + | NR | NR | +/− | +/− | +/− (data from RCTs) | Floor effect | NR |
| Activity-specific balance scale | NR | + | NR | +/− | NR | +/− (data from 1 trial) | NR | +/− (no E/S data for cut-off for fallers) |
| Rivermead Mobility Index | NR | + | NR | NR | +/− | NR | Ceiling effect | NR |

Abbreviations: N/A, not applicable; NR, not reported; UHDRS, The Unified Huntington's Disease Rating Scale; TMS, Total Motor Score; RCTs, randomized controlled trial; HD, Huntington's disease.
(+) good performance, (+/−) contradictory data or very limited data, (-) poor performance.
NOTE: data regarding Minimally Clinically Important Difference were only assessed for Tinetti Mobility Test.

fast-paced.[6,17,24] Test-retest reliability has been shown to be good in both pre-manifest and manifest HD for the self-paced version.[6] For the self-paced version there was no correlation with the UHDRS-TMS, a weak correlation was reported with the UHDRS-FAS ($r = 0.35$, $p < 0.01$) and none with the UHDRS-TFC.[7] The fast-paced version of the test has been shown to be sensitive to change following a rehabilitation program intervention in mild to moderate manifest HD (improvement of 0.27 m/s).[17] Following a 12-week community-based exercise program there was no significant change for either the self- or fast-paced versions.[24]

**Recommendation**: The Ten-Meter walk test is suggested for assessing walking speed in manifest HD. The vast majority of the clinimetric data sustaining this recommendation was obtained using the self-paced version.

### Four Square Step Test (FSST)

The FSST is a 5 to 10 minute test of dynamic balance. The FSST clinically assesses a patient's ability to step over canes positioned in a cross shape in three directions in a set sequence: forward, sideways, and backwards. The test was not specifically developed for use in HD, but has been used in three studies in HD and some clinimetric data are available in pre-manifest and manifest HD.[6,8,11] Test-retest reliability has been reported to be excellent in pre-manifest HD (ICC = 0.91) and good in manifest HD (ICC = 0.78).[6] The MDC is higher in manifest HD (15.2) than in pre-manifest HD (1.9).[6] Moderate to high correlation has been shown between the FSST and the ABC (Pearson correlations: $-0.57$; $p < 0.05$); the Tinetti Mobility Test (Pearson correlations: $-0.67$, $p < 0.01$), and gait velocity (Pearson correlations: -0.69, $p < 0.01$).[8] The FSST has not been shown to be sensitive to change in one exercise study.[11]

**Recommendation**: The FSST is suggested for assessing dynamic balance in HD.

### Mini Balance Evaluation Systems Test (Mini-BESTest)

The Mini-BESTest is a 14-item measure of dynamic balance. Derived from the Balance Evaluation Systems Test (BESTest), factor analysis was used for item reduction to include dynamic balance only and to improve clinical utilization.[28] Administered in 10–15 minutes, the Mini-BESTest evaluates domains of postural control. Each question is rated from normal to severe and scored between 0 and 2, for a maximum total score of 28 points. The test was not specifically developed for HD and has not been assessed comprehensively across stages of HD. The test is not applicable to non-ambulatory patients.[29] Convergent validity has been shown between the Mini-BESTest and the ABC ($r^2 = 0.45$), UHDRS-TFC ($r^2 = 0.75$) and UHDRS-TMS ($r^2 = 0.68$).[29]

**Recommendation**: The Mini-BESTest is suggested for assessing severity of balance impairment in HD, as it has been used in only one study with a very small sample size across HD severity with a partial clinimetric assessment.

### Physical Performance Test (PPT)

The PPT is a ten-minute test, which assesses multiple domains of physical function using observed performance of tasks that simulate activities of daily living (ADL) of various degrees of difficulty (writing, eating, dressing, walking, and climbing stairs).[30] Each activity is timed and rated from 0–4, a higher score indicating better physical performance. The test was not specifically developed for use in HD, but some of its clinimetric properties have been assessed in both pre-manifest and manifest HD. Good test–retest reliability has been recorded in pre-manifest HD (ICC = 0.76) and excellent reliability in manifest HD (ICC = 0.95). The MDC was 3 points for pre-manifest HD and 5 points for manifest HD, respectively.[6] Convergent validity has been reported in manifest HD between the PPT and the UHDRS-TMS ($r = -0.41$ $n = 63$, $p < 0.01$), the UHDRS-FAS ($r = 0.59$, $p < 0.01$); and the UHDRS-TFC ($r = 0.48$, $p < 0.05$).[7] A ceiling effect has been reported in pre-manifest HD.[6] It has also been shown to be valid in patients with cognitive impairment.[31]

**Recommendation**: The PPT is suggested for assessing severity of impairment of physical function in performance of tasks that simulate activities of daily living.

### Six-Condition Romberg Test

The six-condition Romberg test is a five-minute easy to administer performance-based measure of balance developed in the context of myelopathies and neuropathies with an associated sensory dysfunction. The amount of time the patient maintains the position without loss of balance for six standard conditions is recorded for a maximum score of 180 seconds. Higher scores indicate better balance. The test has been used in some HD studies[6,10] and the clinimetric data available document good test–retest reliability in both pre-manifest (ICC = 0.73) and manifest HD (ICC = 0.89).[6] The six-condition Romberg test is a valid tool that can be used across all stages of HD provided that the patient is ambulatory as it is likely to have floor effects in non-ambulatory patients.[6] It has not been shown to be sensitive to change in treatment.[10] People with pre-manifest HD (158.8 ± 22.2) have higher scores (better performance) than those with manifest HD (70.0 ± 41.1).[6]

**Recommendation**: The six-condition Romberg test is suggested for assessing severity of balance impairment in HD.

# Rating Scales

## Suggested

### The Unified Huntington's Disease Rating Scale (UHDRS)-Total Functional Capacity (TFC)

The UHDRS-TFC is part of a multi-component rating scale originally designed to prospectively evaluate all patients with HD and individuals at risk for HD.[34] It assesses capacity as opposed to actual performance and consists of a 5-item interview between a clinician, and the patient and a person familiar with the patient's

functioning. It takes < 5 minutes to complete and covers basic activities of living: occupation, handling finances, and domestic responsibilities and ADLs such as eating, dressing, bathing, and level of care (home or facility). A higher score indicates better functional capacity. The UHDRS-TFC has been used in pre-manifest and manifest HD populations in multiple observational studies and randomized controlled trials.[34–51] The TFC total score can be categorized into Shoulson and Fahn HD stages.[35] There is evidence of excellent inter-rater reliability, but only for a modified version of the UHDRS-TFC that is filled by patient or the caregiver (ICC = 0.96, 95% CI: 0.92, 0.98).[52] Data from multiple studies suggest good convergent validity with other components of the UHDRS assessing the functional domain and quality of life, and good divergent validity with motor disability, cognitive deficits, and behavioral problems.[19,29,34,53–60] Extensive data from multiple observational studies and clinical trials suggest sensitivity to change over time.[34–51,61–69] There appears to be a ceiling effect for early stage HD and a floor effect for late stage HD.[41]

**Recommendation**: The UHDRS-TFC is suggested for assessing severity of limitation in functional capacity in HD, because it lacks core clinimetric data, namely, test–retest reliability and internal consistency to reach a "recommended" status.

## The UHDRS-Functional Assessment Scale (FAS)

The UHDRS-FAS is an extensively used checklist that is also part of the UHDRS. It is a clinician-administered questionnaire with 25 items, which screen an individual's capacity to complete specific tasks, enables the clinician to assess severity, and make longitudinal assessments. The questionnaire takes 5–10 minutes to complete. It is considered an extension of the TFC and is more detailed in certain tasks.[34] A total score is obtained by giving one point to all "yes" replies, and a higher score indicates better functioning.[34] It has been used in multiple observational studies and randomized controlled trials in manifest HD populations.[34,39,43,48,49,61–63,67,69–71] The UHDRS-FAS has been shown to have high internal consistency (Cronbach's $\alpha = 0.95$).[34] There are no available data on test–retest reliability or inter-rater reliability. Good convergent validity with other components of the UHDRS has been shown, as well as with motor disability, cognitive, and behavioral deficits.[34,54,58,72,73] The UHDRS-FAS has been shown to be sensitive to change over time in several studies.[34,39,42,43,48,49,61–63,67,69,70,74]

**Recommendation**: The UHDRS-FAS is suggested for assessing severity of limitation in functional capacity in HD, because it lacks core clinimetric data, namely, test–retest or inter-rater reliability data.

## The UHDRS-Independence Scale (IS)

The UHDRS-IS is a clinician-rated tool, which assesses the actual reduction of functional ability.[75] It is rated from 100 (no special care needed) to 0 (tube-fed, total bed care) and takes approximately 5 minutes to complete. It has been used in many observational and randomized controlled trials in manifest HD populations.[34,41–44,46,48–50,61–63,67,69] The clinimetric data available show that the UHDRS-IS has moderate inter-rater reliability but in a modified version that compares caregiver report with patient self-report (ICC = 0.71, 95% CI: 0.48, 0.85).[59] Good correlation with other components of the UHDRS, as well as motor disability, cognitive and behavioral deficits has been shown in various studies.[34,54,58,59,72,75–78] Data from clinical trials suggest sensitivity of the UHDRS-IS to change over time and across disease stages.[35,41]

**Recommendation**: The UHDRS-IS is suggested for assessing severity of limitation in functional ability in HD, because reliability data are missing, including test–retest, inter-rater (for clinicians) and internal consistency.

## HD Activities of Daily Living (HD-ADL) 17-item

The HD-ADL Scale, which was developed to be used specifically in HD, was modeled after the Scale for Instrumental Activities of Daily Living.[79] It is a 17-item informant-completed instrument on which the informant rates the HD patient's ability to perform specific activities, covering the domains of personal care, household care, work and money, social relationships, and communication. For each item, the patient is rated on a 4-point scale, from normal to severely limited. The total score of the HD-ADL scale ranges from 0 (normal) to 51 (maximal limitation).[53] With exception of one study,[19] the scale has not been used outside the John Hopkins group who developed it. Clinimetric testing show that the HD-ADL has good internal consistency ($\alpha = 0.91$ to 0.96).[53] Principal Component Analysis showed that four factors account for 72 to 74% of the total variance.[53] Convergent validity has been shown between the total score of the HD-ADL and the UHDRS-TFC ($r = -0.89$, $p < 0.001$), as well as all factors except for the domain "family relationships."[53] Multiple correlations have been reported with measures of cognitive impairment or disease duration.[53,80,81] The HD-ADL failed to show differences in treatment compared to placebo.[82,83]

**Recommendation**: The HD-ADL is suggested for assessing severity of limitation in ADL, because studies of the scale's clinimetric properties are lacking, namely for any type of reliability.

## Activity-specific Balance Scale (ABC)

The ABC is a patient-completed scale that measures balance confidence and fear of falling. The ABC can take anywhere between 6 and 30 minutes to complete depending on the patient. Although it is a self-administered scale, a face-to-face interview is recommended.[84] Patients rate their balance confidence on a visual analogue scale ranging from 0 to 100 for each of 16 tasks, with higher scores indicating greater confidence and lower fall risk. The ABC has been widely used in HD,[8,17,29] including a modified ABC-UK version adapted for British culture,[85] but normative cut-off scores have not been established. The clinimetric data available show that the ABC has good test–retest reliability (ICC = 0.74 95% CI: 0.58, 1.0),[8] the MDC has been reported to be 27.33.[8] There is good convergent validity with the Mini-

BESTest,[29] and the modified ABC-UK can distinguish between non-fallers and fallers in HD (mean score: 77.5 vs. 47.9).[85] While the ABC has been shown to be sensitive to change in one study (after a 9-month multidisciplinary rehabilitation program),[86] no change was reported in two other studies.[8,17]

**Recommendation**: The ABC is suggested for assessing level of self-reported balance confidence in HD. The use of the ABC is challenged since the lack of insight is a feature of HD.

### Rivermead Mobility Index (RMI)

The RMI is an extension of the Rivermead Motor Assessment Gross Function Scale that assesses functional mobility and was initially developed for stroke. The RMI consists of 14 questions about a patient's ability to perform a wide range of activities, from turning over in bed to running, and one observation (standing for 10 seconds without any aid). Questions are answered as "able" (1 point) or "unable" (0 points) and summed to produce a total score, with a higher score reflecting better mobility.[87] Test–retest reliability has been reported in HD (ICC in pre-manifest HD = 0.81; ICC in manifest HD = 0.94).[6] A MDC of 2 points has been reported in manifest HD; ceiling effects are present in pre-manifest HD.[6] There are no cut-off scores established in HD, which limits its use as a screening tool in HD.

**Recommendation**: The RMI is suggested for the assessment of severity of restriction of mobility

## Discussion

The current critique focuses on performance-based measures and rating scales assessing functional ability in HD. In the process of developing the protocol for the review, we found a variety of scale constructs and other instruments that could be associated with various aspects of functional ability. We used the ICF[3] as a conceptual framework related with function to guide us in the inclusion or exclusion of rating scales based on the adequacy of their constructs. Nevertheless, we realize that the measures included in this review represent a wide variety of concepts that apply across the components of the ICF. Many of these measures included multiple ICF components, raising challenges for conceptual clarity and subsequent evaluation of validity. For example, balance can be seen as a sheer impairment but it can overlap with activity/function, depending on how it is captured in a given clinical measure. Considering these aspects, we decided to be inclusive and included balance measures in this review. Ultimately, there is a need for clear definitions for future measures to better enable validation and application in HD populations.

We identified and included a range of performance-based measures. We provide a "recommended" level of recommendation for both screening purposes related to balance, gait and/or risk of falling, and measurement of severity of impairment of specific motor tasks. There were, however, no "recommended" performance-based measures covering upper limb function. It is also important to emphasize that the majority of these performance measures were only used in ambulatory HD populations.

We did not identify a rating scale that met the criteria for "recommended". If further testing of the measurement properties is conducted, we agreed that UHDRS sub-scales related with function (TFC, FAS, and IS) are in a good position to reach the higher level of recommendation in the future due to their widespread use, specific development in HD and known initial clinimetric development. For each one of these scales important shortcomings in terms of clinimetric development were identified, namely incomplete reliability testing, which precluded a "recommended" level of recommendation. In addition, these scales have limiting ceiling effects that make them unattractive for use in earlier stages of HD. For example, the use of these UHDRS subscales in a clinical trial conducted with the purpose of capturing a disease-modifying effect in an ideal HD subgroup of individuals with a high level of functional ability would be performed at the cost of a prohibitively long trial duration to capture a meaningful change. Rating scales such as the Functional Rating Scale Task force for pre-Huntington Disease 2 (FuRST-pHD)[88,89] are currently being developed and are expected to fill this gap in the future.

The assessment of functional ability as a clinical outcome is deemed essential for therapeutic approval by regulatory agencies such as the FDA.[1] In this regulatory context, it is important to emphasize that there was no recommendation for the purpose of measuring change over time in individuals or groups of subjects in either a pure observational study or in an interventional context. In fact, formal testing for responsiveness was missing in all the included rating scales, and important measures of reliability such as test–retest had not been evaluated in many cases. Along the same lines, there is a need to assess the validity of each rating scale in different subgroups of patients with HD, as these data are presently lacking for most of the measures. The knowledge about responsiveness and its variation in important patient subgroups can determine sample size requirements and help with the interpretation of clinical trial results, respectively.[1]

Looking towards the future, the committee concludes that there are well-validated performance-based measures that capture motor tasks such as walking or balance, but further clinimetric development is required for performance-based measures that capture other aspects of physical function such as upper limb function. For rating scales, including those evaluating activities of daily living, we cannot endorse an existing scale at a "recommended" level and encourage the MDS to prioritize the development of such instruments for clinical care and research purposes. Further validation of HD-specific scales such as the UHDRS-TFC are warranted, as is the development of new scales designed to have greater sensitivity in capturing function in HD subgroups who have a relatively well-preserved functional ability as measured by currently available rating scales.

## Author Roles

1. Research Project: A. Conception, B. Organization, C. Execution; 2. Statistical Analysis: A. Design, B. Execution, C. Review

and Critique; 3. Manuscript Preparation: A. Writing the First Draft, B. Review and Critique.

T.A.M.: 1A, 1B, 1C, 3A, 3B
M.B.: 1A, 1B, 1C, 3B
A.M.D.: 1A, 1C, 3B
L.Q.: 1A, 1C, 3B
F.B.R.: 1A, 1C, 3B
J-M.B.: 1A, 1C, 3B
N.C.: 1A, 1C, 3B
F.W.: 1A, 1C, 3B
A.H.: 1A, 1C, 3B
C.S.: 1A, 1C, 3B
C.G.G.: 1A, 3B
E.C.: 1B, 3B
P.M-M.: 1A, 3B
G.T.S.: 1A, 3B

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# Supporting Information

Supporting information may be found in the online version of this article.

**Supplementary Material S1**. Full description of all clinical measures included for full review, including those that were included in the "suggested with caveats" or "listed" categories.