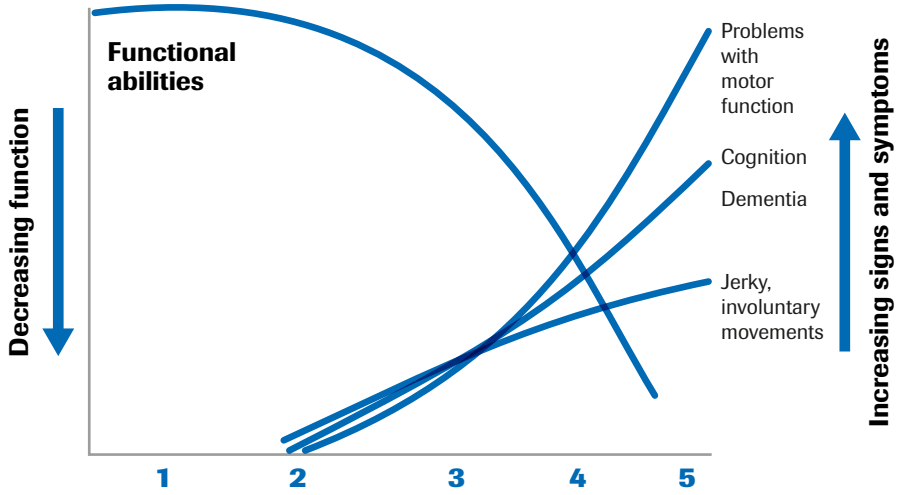
How can progression of Huntington's disease (HD) be measured?

HD is a multidimensional disease, with patients experiencing a wide range of symptoms that negatively impact their overall quality of life. Subtle symptoms can be present for many years before a diagnosis of HD is made[1–3]

Stages of HD[3]:



1. Pre-symptomatic
HD is a genetic (inherited) disease, but patients don't initially experience symptoms.
The mean age of onset for diagnosis of motor symptoms (affecting movement) is 45 years[1,2]

2. Prodromal
Gradual appearance of subtle signs and symptoms of HD[1–3]

3. Early
Increased symptoms begin to affect ability to carry out daily tasks, motor diagnosis received[1,2]

4. Moderate
Worsening of symptoms leading to a dramatic reduction in quality of life[1,2]

5. Advanced
Very severe impairment of movement and profound physical disability[1,2]
Dementia-like symptoms[1,2]

Symptoms usually affect three main areas or domains: movement, cognitive (difficulties with memory, thinking and planning) and psychiatric (changes in behaviour and personality)[4,5]

Cognition
- Ability to think clearly and quickly
- Attention
- Perception of time
- Difficulty learning new tasks

Motor function
- Jerky, involuntary movements
- Balance issues
- Fine motor issues
- Speech and swallowing issues

Behaviour
- Depression
- Apathy
- Irritability and angry outbursts
- Anxiety

Other/impacts
- Sleep problems
- Inability to work
- Isolation
- Pain

In patient registries (e.g. Enroll-HD) and clinical trials, doctors and scientists use assessment scales to diagnose and monitor the progression of these symptoms[6]

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Rating scales for HD typically measure individual clinical domains or they summarise a number of assessments, which may have limited sensitivity for measuring changes associated with disease progression[6,7]

The Unified Huntington's Disease Rating Scale (UHDRS) is a collection of assessments of clinical HD features, including motor function, cognition, behaviour, and overall function[8]

Motor assessment

Cognitive assessment

Behavioural assessment

Independence scale

Functional assessment

Total Functional Capacity

There is a need for valid HD assessments that can reliably measure meaningful changes in disease progression, to enhance the potential to detect effects of investigational medicines[6]

One example of a holistic approach to measure patient experience is the composite Unified Huntington's Disease Ratings Scale (cUHDRS)[7,9]

The cUHDRS combines a subset of UHDRS scales (TFC, TMS, SDMT and SWR; sum of z-scores) that have been shown to reliably detect clinically meaningful changes associated with disease progression in patients with HD[9]

Overall function
Total Functional Capacity (TFC) scale

Motor function
Total Motor Score (TMS)

Cognitive function
Symbol Digit Modalities Test (SDMT)
Stroop Word Reading (SWR)

Studies using patient registry data (TRACK-HD, CARE-HD, COHORT, 2CARE) show that the cUHDRS provides an improved measure of clinical progression relative to individual motor, cognitive and functional outcome measures, in terms of both sensitivity and association with measures of brain atrophy[7]

The cUHDRS is valid, reliable, able to detect change, and associated with clinically meaningful differences (both cross-sectional and longitudinal) in function and independence across the spectrum of patients with early-manifest HD[9]

1. Reilmann R, et al. Mov Disord 2014;29:1335–41; 2. Bates GP, et al. Nat Rev Dis Primers 2015;1:15005; 3. Ross CA, et al. Nat Rev Neurol 2014;10:204–16;
4. Simpson JA, et al. J Huntingtons Dis 2016;5:395–403; 5. US Food and Drug Administration (FDA). The Voice of the Patient. Huntington's Disease Public Meeting Report. March 2016;
6. Arney K. Nature 2018;557:S46–7; 7. Schobel SA, et al. Neurology 2017;89:2495–502; 8. Huntington Study Group. Mov Disord 1996;11:136–42;
9. Trundell D, et al. European Huntington's Disease Network (EHDN) Plenary Meeting, Vienna, Austria. 14–16 September 2018.

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