The Huntington Disease Health Index (HD-HI): Quantifying Improvements in Disease Burden During Clinical Trials

Chad Heatwole, MD, MS-CI, FAAN
Huntington Study Group
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Dr. Heatwole is the Associate Director of the Center for Health + Technology (CHeT), has provided consultation to the following companies: Cytokinetics, Biogen, Accelis Pharma, Acceleron, Ionis, AMO, Recursion pharmaceuticals, Harmony Biosciences, and aTyr, and holds copyrights for clinical trial instruments.
What is a Patient Reported Outcome Measure?

- A validated outcome designed to evaluate one or several aspects of patient health
- Responses are provided directly by patients without required interpretation or administration by other individuals
- Can measure the severity of a specific symptom, sign, functionality, or overall state of disease
- Can be disease-specific or generic
The Creation of a Network

- NIH Patient-Reported Outcomes Measurement Information System (PROMIS)
- Neuro-Qol
- Epidemiologists
- Biostaticians
- Patient Advocate Groups
- Outcomes researchers
- Psychometricians
- Linguists
- Neurology Patients
Advantages of Disease-Specific vs. Generic Instruments

- Higher relevance and content validity for target population
- Increased sensitivity to detect significant therapeutic change
- Higher precision
- Simpler application
- Lower burden to the patient
- Can emphasize the relevant symptoms and issues of a specific population while excluding non-relevant issues
- Can be scored to prioritize high-impact issues for a specific population

HD-HI

- 127 quick check box questions
- 1 total score (measurement of patient-reported disease burden)
- 13 subscales
- Each subscale (and the total score) range from 0 to 100 with 100 being the greatest disease burden
- State of the art weighting system on a individual question and subscale level based the relative importance of each item
- Subscales can be used individually or as part of the total instrument
- Typically completed in ~15 minutes
HD-HI Subscales

- Mobility
- Involuntary Movements
- Hand and Arm Function
- Emotional Health
- Activity Participation
- Social Performance

- Social Satisfaction
- Fatigue
- Pain
- Cognition
- Communication
- Swallowing Function
- Sleep and Daytime Sleepiness
Important First Question:

What symptoms and issues have the greatest effect on the lives of patients with Huntington Disease?

PRISM-HD Study
Study Design

- **Phase 1:** Qualitative interviews with HD patients
- **Phase 2:** Large Cross Sectional Validation Study with symptomatic HD patients, predromic HD patients, and caregivers with HD
Phase 1:

20 HD patients and 20 caregivers of HD patients
→ Interviewed and asked what aspects of HD have the highest impact on HD patient lives.
Results

- 2082 direct quotes were coded
- 310 potential high-impact HD symptoms were identified
- 17 major themes
- 4 major domains
  - Physical health
  - Mental health
  - Social health
  - HD specific symptoms
Phase 2: Cross Sectional Validation Study

- Individuals were sent survey that inquired about the **216 specific symptoms** identified through the initial interviews.
- For each symptom, participants answered if they had the symptom (and if so, how much impact it had on their life)
Results:

- 389 participated (58.1% response rate)
- Participants included 96 with HD, 60 with prodromal HD, and 233 caregivers
- In total, participants replied to over 84,000 questions regarding the symptomatic burden of HD
U.S. participants were distributed across 11 states in Step 1 (orange) and 46 states in Step 2 (orange and green). International participants in Step 2 hailed from Anguilla, Australia, Brazil, Canada, India, Ireland, Singapore, Spain, and the United Kingdom.
Beta Testing Results (15 patients)

- The instrument was well understood
- The format, scoring, and time frame were acceptable
- One question were reworded due to unclear patient understanding (Daytime Somnolence changed to Daytime Sleepiness)
- Average time to complete instrument: 16.5 minutes (range: 5-30 minutes)
Ongoing Work

- Currently being used as an outcome in a longitudinal pharmaceutical therapeutic trial.
- Pending use in two additional longitudinal trials.
- Correlating scores to other markers of disease burden.
Conclusion

The HD-HI, a multifaceted instrument, is an extensively validated outcome measure that is a viable option to measure small but clinically relevant changes in disease burden during clinical trials.