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Identification of Health-Related Quality of Life (HRQOL) Issues Relevant to Individuals with HD

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Abstract

This qualitative study explored health-related quality of life (HRQOL) in individuals with Huntington disease (HD). Sixteen focus groups were conducted (n=6 groups with symptomatic HD individuals; n=5 with individuals who are at-risk or prodromal for HD; n=3 non-clinical HD caregivers; n=2 groups with HD clinicians). Qualitative analysis indicated that 28% of focus group comments were related to emotional health, 27% to social participation, 26% to physical health, 10% to cognitive health, and 9% to end of life issues. Findings highlight the importance of developing HD-targeted items to ensure sensitive assessment of HRQOL in HD research and clinical practice.

Keywords

Outcome Assessment (Health Care); Huntington disease/Huntington's disease; Health-Related Quality of Life; Quality of Life; Patient Reported Outcomes

Huntington disease (HD) is an autosomal dominant neurodegenerative disease affecting approximately 1 in 10,000 individuals in North America (Li, 1999). Every child of a parent who carries the HD gene has a 50% chance of inheritance. HD is both insidious and progressive; an individual who inherits the HD gene will gradually develop motor, cognitive and psychiatric disturbances (Paulsen, 1999), often leading to a diagnosis around age 40 (Ho et al., 2001). Prior to an HD diagnosis (which is based solely on unequivocal, clinically significant motor symptoms), cognitive, behavioral, and motor symptoms can be either non-existent or extremely subtle (referred to from this point forward as prodromal HD). HD is fatal; the average lifespan is 15 – 20 years after symptom onset (Ho, et al., 2001). Despite progressive motor, cognitive, and psychiatric difficulties, some improvement in health-related quality of life (HRQOL) can be achieved over time (D. F. Cella, 1995).

We define HRQOL as a multidimensional construct; it reflects the extent to which one's usual or expected physical, emotional, and social well-being are affected by a medical condition or its treatment (D. F. Cella, 1995). While we define HRQOL as a

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multidimensional construct, this can be contrasted with quality of life (QOL), a less clearly defined unidimensional construct that evaluates general well-being or life satisfaction (Campbell, Converse, & Rodgers, 1976; Patrick & Erikson, 1988). Most individuals use HRQOL and QOL interchangeably, it is important to keep this distinction in mind when evaluating measurement systems designed to evaluate these constructs. Specifically, while a number of measures have been developed to assess QOL, there are far fewer measures designed to assess HRQOL. Further, even measures that target HRQOL specifically lack items that target HD-specific HRQOL. As such, there are no validated HD-specific HRQOL measures. This oversight is particularly important for individuals designing clinical trials. When designing a clinical trial, the FDA requires that researchers include a patient reported outcome (PRO) measure that assesses HRQOL in addition to an outcome measure that evaluates the overall objective effectiveness of the drug/intervention being targeted (Snyder et al., 2007). For instance, a new clinical trial that examines a drug designed to improve cognition in individuals with HD would include both an objective measure of cognitive functioning, as well as a PRO measure of self-reported impressions of the drugs impact on cognitive HRQOL. The lack of such a sensitive targeted measure of HRQOL makes it difficult to detect minor changes in HRQOL in HD (Tabrizi et al., 2011).

Researchers and clinicians tend to examine HRQOL in HD clinical trials in one of three ways: 1) utilize generic measures (that lack items that are HD-specific, but assess HRQOL), 2) utilize a single question to assess general QOL, or 3) focus on a single, limited domain (e.g., motor functioning). Although each of these approaches has merit, they are less ideal for use in a clinical trial, where ability to detect change over time is essential; they each suffer from major limitations that impede our ability to fully capture the multidimensional aspect of HRQOL, as well as their ability to be used as a sensitive assessment of change over time. Specifically, generic measures cannot necessarily detect the subtle differences over time, especially for individuals in the prodromal phases (Solomon et al., 2007) or early phases of the disease (Tabrizi, et al., 2011); single-item ratings of quality of life (Ready, Mathews, Leserman, & Paulsen, 2008; Tibben et al., 1993) lack sensitivity to evaluate change over time (Tibben, et al., 1993); and focus on a single, limited domain (e.g., motor functioning) (de Tommaso et al., 2005; Frank et al., 2004; Hamilton et al., 2003; van Vugt et al., 2001) ignores the multidimensional aspect of HRQOL. Further, the most commonly used measure in HD, the Total Functional Capacity Score (Shoulson & Fahn, 1979) from the Unified Huntington Disease Rating Scale ("Unified Huntington's Disease Rating Scale: reliability and consistency. Huntington Study Group," 1996), is not useful in the prodromal stages of the disease, miscategorizes individuals with psychiatric difficulties, is subject to a floor effect, and is not sensitive to progression in the later stages of the disease (Nance, 2007). For a more detailed discussion of these limitations please see Carlozzi & Ready (2011).

The National Institutes of Health and the National Institute of Neurological Disorders and Stroke (NINDS) have recognized the lack of disease-specific measurement tools as a recurring weakness across a number of clinical populations. As such, they have prioritized research to improve HRQOL patient reported outcome (PRO) measurement through research endeavors such as the Patient Reported Outcomes Measurement Information System (PROMIS) and the Quality of Life for Neurological Disorders (Neuro-QOL). PROMIS has built a comprehensive system of generic item banks to assess PROs across chronic disease conditions (D Cella et al., 2010). Specifically, PROMIS measures currently exist across several domains of self-reported health including Physical Health (Physical Functioning, Fatigue, Pain Behavior, Pain Interference, Sleep Disturbance, and Sexual Function), Mental Health (Depression, Anxiety, Anger, Illness Impact, and Applied Cognition), and Social Health (Satisfaction with Social Roles, Satisfaction with

Discretionary Social Activities, Ability to Participate in Roles & Activities, Companionship, Emotional Support, Instrumental Support, and Social Isolation).

Neuro-QOL complements this work with the development of similar item banks with clinical relevance to stroke, Parkinson's disease, multiple sclerosis, child and adult epilepsy, amyotrophic lateral sclerosis, and muscular dystrophy (D. Cella et al., 2011). Neuro-QOL includes measures that evaluate Physical Health (Lower Extremity Function-Mobility, Upper Extremity Function-Fine Motor and ADL, Fatigue, and Sleep Disturbance), Emotional Health (Depression, Anxiety, Anger, Stigma, Positive Affect and Well-Being, and Emotional and Behavioural Dyscontrol), Social Health (Ability to Participate in Social Roles and Activities, and Satisfaction with Social Roles and Activities), and Cognitive Health (Applied Cognition-General Concerns, Applied Cognition-Executive Functions, and Communication).

The PROMIS and Neuro-QOL frameworks allow for cross-disease comparison (generic item banks) and disease-specific sensitivity (disease-specific item banks). Many identical items (i.e., common data elements; CDEs) are used on both PROMIS and Neuro-QOL to allow "linking" between measures, such that a score on one measure (e.g., PROMIS) can be used to estimate a score on another (e.g., Neuro-QOL). Similarly, other federal agencies have made investments to extend these initiatives to include spinal cord injury and traumatic brain injury (Carlozzi, Tulsky, & Kisala, (Supplement) In press; Slavin, Kisala, Jette, & Tulsky, 2010; Tulsky et al., (Supplement) Under Review). These PRO initiatives have gone a long way towards improving the sensitivity and specificity of health outcomes measurement assessment. Unfortunately, individuals with HD were not originally included in the conceptualization or development of either of these systems.

Recently, the NINDS funded the development of the HD-QOL to extend PROMIS and Neuro-QOL to HD. Thus, this study was designed to identify domains of functioning (i.e., within an emotional, physical, social, and cognitive health framework) that capture the multifaceted nature of HRQOL in HD. Further this study was also designed to identify pre-existing measures of HRQOL from PROMIS and Neuro-QOL that are relevant to HD. This new PRO measurement system should be appropriate for use across all stages of HD (from prodromal through the later stage disease process) and represent the multifaceted issues that are specific to HD, as well as more generic HRQOL issues that will allow for direct comparison with other clinical populations. Further, this new system should have clinical utility and be brief enough to be administered in a waiting room or on a smart device (in real time). Scores ultimately should help clinicians target specific areas of clinical treatment, as well as track improvements related to clinical interventions.

Method

This study was designed to replicate the methodology used to develop the PROMIS and Neuro-QOL measurement systems to allow for extensions of these systems to individuals with HD. Therefore, we conducted sixteen focus groups with key HD stakeholders. Six groups were conducted with individuals with symptomatic HD (n=24 clinically diagnosed patients with symptoms across the HD spectrum), five groups of n=16 individuals either at-risk (i.e., have a parent with HD diagnosis but have not been tested themselves) or prodromal for HD (i.e., had a positive gene test, but no current clinical symptoms), three groups with non-clinical HD caregivers (n=17) and two groups with HD clinicians (n=25). Focus groups provide a good forum for discussion of issues related to quality of life, while simultaneously allowing access a relatively large number of participants (maximizing time and other resources). Further, such groups allowed for discussion of both generic, as well as disease-specific issues related to HRQOL, which was consistent with PROMIS and Neuro-

QOL methodology. Data were collected across different groups to ensure that the complete, multidimensional HRQOL framework was represented. Specifically, HD participants were selected to represent the full spectrum of HD symptomatology, caregivers were included to ensure that HRQOL issues were included for things that the patients themselves might not recognize (due to the cognitive decline associated with the disease process), and clinicians were included to ensure that HRQOL domains would represent areas all areas appropriate for clinical intervention. All data were collected in accordance with local institutional review boards, and participants provided informed consent prior to participation.

The average age was 39 years (SD = 12.2) for the individuals at-risk or prodromal for HD and 49 years (SD = 11.3) for the symptomatic groups; 40% of these participants were male, and 90% were Caucasian. The caregiver groups were comprised of 53% spouses, 23% children, 12% siblings, one close friend and one parent of someone with HD. Finally, the clinician groups included physicians (24%), nurses (16%), certified nursing assistants (16%), psychologists/neuropsychologists (8%), social workers (8%), physical therapists (8%), recreational therapists (8%), speech therapists (8%), and one dietician.

Focus Group Guides

Semi-structured focus group guides were developed to assess participants' HRQOL experiences. Guides began with broad, open-ended questions (e.g., defining HRQOL) and then progressed to questions regarding specific HRQOL domains (i.e., physical, emotional, cognitive, and social functioning; thereby mirroring the structure of the Neuro-QOL). Caregivers were instructed to respond from the perspective of their care recipient and clinicians were instructed to focus on their HD patients.

Data Analysis

Audio recordings of the focus groups were transcribed and deidentified. Members of the research team read all transcripts and imported the data into NVivo 8.0, a qualitative data analysis and management software package.

Codebook Development—Two independent investigators identified major content areas and developed an initial list of subdomains through transcript review. The initial structure for identifying themes was derived from the multidimensional HRQOL theoretical framework developed by the World Health Organization (WHO; (World Health Organization, 1946)) which includes physical, social, and emotional well-being. PROMIS and Neuro-QOL expanded upon this framework to also include cognitive health (as a subcomponent of emotional health). Transcripts of all patient, caregiver, and clinician groups were reviewed, and an inductive process was utilized to expand this framework to include HD-specific domains/subdomains, thus creating a "codebook" for each domain. A literature review and a review of current instruments further informed codebook development. Codebook structures were refined and expanded to reflect the emerging themes. Project team members with expertise in either HD or PRO measurement development independently reviewed and confirmed the emerging domain framework. Finally, codebooks were expanded to include code definitions and inclusion/exclusion rules.

Selective Coding and Descriptive Analysis—Two independent raters "selectively" coded all transcripts; that is, they exhaustively coded each segment of text to a specific code in the codebook (Kisala & Tulsky, 2010). This approach was designed specifically for use in participatory action research designed to inform patient reported outcomes measurement development. It expands upon more traditionally based grounded theory approaches to qualitative analysis (Glaser & Strauss, 1967; Strauss & Corbin, 1998) and provides a practical approach to quantifying qualitative data; it utilizes the development of a domain

framework (described above), open and axial coding, selective coding, and descriptive analysis. Specifically, for each domain, a third expert was utilized to conceptually anchor responses on the inter-rater reliability exercise. This exercise, designed to ensure consistent interpretation of codes, consisted of 25 verbatim statements. The three raters had to achieve at least 80% overall agreement to progress to the next step. If raters did not achieve over 80% on the first exercise, codebook definitions were expanded to enhance clarity and a second exercise was completed, with agreement reaching satisfactory levels. For each domain, two individuals applied the codebook to the thirteen focus group transcripts using the coding blueprint laid out in Kisala and Tulsky (Kisala & Tulsky, 2010). To ensure inter-rater reliability, the two raters coded the first transcript together, then, independently coded each subsequent transcript. As the independent rating of each transcript was completed, raters reconciled (with a third party when necessary) all instances of disagreement. This process served to continually align the raters' interpretation and application of the codebook ultimately resulting in 100% agreement through detailed reconciliation. This approach replicated methodology utilized by projects designed to extend the PROMIS and Neuro-QOL frameworks to both traumatic brain injury (Carlozzi, Tulsky, & Kisala, 2011) and spinal cord injury (Tulsky et al., 2011).

Results

Emotional Health

Emotional Health refers to feelings of emotional distress (e.g., anxiety, depression, anger, etc.), as well as positive emotional experiences (e.g., happiness, resilience to life challenges, gratitude). Findings from our focus groups indicated that Emotional Health was extremely relevant for all groups (see Table 1). Focus group discussion included anxiety, depression, anger, positive psychological function, and stigma, as well as behavioral change/psychiatric functioning, resilience, emotional roadblocks and grief/loss (see Table 2).

When discussing Emotional Health, focus group participants highlighted the significance of anxiety/fear citing specific worries related to being at-risk for HD ("I don't share my fears about being at risk"), as well as general anxiety ("I just feel anxious"). Additionally, there was a pervasive theme of anxiety related to whether or not subtle symptoms were indicative of disease onset ("Is this a bad day, or is this the beginning of something really, that's maybe a real problem"). Caregivers and clinicians also frequently discussed obsessive-compulsive symptoms ("they'll obsess on a pattern or a schedule").

Issues related to behavioral changes or psychiatric symptoms were also frequently discussed across all groups with the exception of the symptomatic groups; this is not surprising given that anosagnosia is common in HD (Deckel & Morrison, 1996). Concerns related to lack of insight ("poor safety awareness"), disinhibition ("there is no gatekeeper anymore--there's no filter"), and apathy ("the things that were important to him are no longer important, and the things that he wanted to do before he doesn't do") were discussed.

Stigma was also frequently cited. Individuals discussed the secrecy surrounding this disease ("when I was growing up we didn't talk about it. I mean, it was not talked about. We were not supposed to tell anybody"). Groups also discussed the lack of awareness and understanding that others had for HD ("we just need more awareness and more publicity"), as well as the misconception that symptoms were a sign of drug or alcohol use ("a lot of people think I'm drunk or on drugs"). Anger was also mentioned across all focus groups including general anger ("I have anger problems"), specific instances of anger ("home repair projects became tough because if the slightest little thing went wrong then suddenly there was a hole in the drywall") and anger related to having HD ("I was pretty angry when I first heard, I wanted to throw things").

Aspects of general positive psychological functioning were also discussed including hope ("you can always live on hope"), happiness ("I have to do what I need to do now to be happy"), gratitude ("I appreciate life right now") and sense of purpose ("it gives you a reason to keep going"). In addition, groups emphasized the concept of resilience ("being able to take where you are and make the best of that particular time"), reflecting the ability to rise to the challenge of living with a terminal diagnosis, focusing on the present ("live day-to-day") and thriving in the face of ongoing limitations (Luthar, Cicchetti, & Becker, 2000).

Focus groups also discussed emotional roadblocks (e.g., behaviors related to poor adjustment such as emotional avoidance) and behaviors that prevent healthy living. Caregivers often talked about denial ("she's kind of in denial") or invention of excuses for behavior ("there's always an excuse for everything"). Individuals with HD also talked frequently about emotional avoidance ("I tend to push everything just kind of away, and try and act like it's not there").

There was also discussion regarding feelings of sadness and depression including feelings of hopelessness ("there's no hope"), and loneliness ("I'm still lonely"); many individuals reported either knowing someone with HD who had attempted suicide or contemplating it themselves ("I might as well do away with myself"). In addition, individuals discussed feelings of guilt related to the possibility of passing on the gene to their children ("you feel guilty about maybe you just passed it on"), as well as feelings of guilt related to having to depend on loved ones for care ("the rest of my life I'm not gonna put a burden on my caretaker"). While some level of sadness or depression was universally reported, themes related to grief/loss (of abilities and lifestyle) were less prominent. Finally, self-esteem, defined as a form of self-evaluation, was not commonly endorsed.

Taken together, emotional health is an important HRQOL topic for individuals with HD. Further, many emotional subdomains from other PRO's initiatives appear to be relevant for this population. Qualitative analysis supported the expectation that anxiety, stigma, anger, depression, behavioral change, and positive psychological functioning are important in HD (see Table 3).

Social Health

Focus groups findings indicated that Social Health was also an extremely relevant HRQOL domain (see Table 1). Participants frequently discussed social relationships, social participation, leisure activities, and independence/autonomy (see Table 2).

Participants in all groups reported that HD had a significant impact on social relationships and social participation. The most frequently discussed subtopic was interpersonal relationships, which was comprised of general ("it's good to have friends out there") and specific interpersonal interactions ("to have a disease where you really need the support of your spouse""), relationships ("you kind of find out who some of your true friends are, and surprisingly they weren't who I thought they were gonna be"), and change in social roles ("I'm a parent, not a wife").

Leisure activities were also discussed including community life ("I got to know a little more people in the community, I guess, the HD community"), home life ("I can't cook anymore 'cause I can't follow the directions"), recreation ("they have good activities here"), driving ("I'm still driving…I don't drive far"), and communication ("I get the e-mail from them and they send me updates and trials, meds that are comin' out, things like that").

Participants also discussed vocation which included employment ("I just couldn't do the job anymore"), volunteering ("I volunteered at the hoop-a-thon") and education ("Or maybe it's [HD] just an excuse to not have to go to grad school"), although this was less relevant as per the caregivers. There was also much discussion on navigating social systems and policies in reference to medical and disability insurance as individuals discontinued employment ("I have a problem with Social Security and Medicare").

In addition to the social factors mentioned above, many comments were related to issues of independence/autonomy ("it's hard for me to do things on my own now"), and dependence ("you've got to have somebody you depend on, somebody that's gonna make the right decisions, at least in your heart"), although this was less relevant for individuals at-risk or prodromal for HD.

When examining the relationship between HD-related Social Health concepts and those of other new PRO initiatives, we found that all HD-QOL Social Health issues overlapped with previously existing item banks (see Table 3).

Physical Health

Physical Health issues were the most common topic of discussion within the HD clinician groups, and were among the most commonly discussed topics for other groups (see Table 1). Focus group participants discussed a number of physical subdomains including gene testing, speech and swallowing difficulties, medications, mobility/ambulation, involuntary movements or chorea, health promotion, activities of daily living (ADLs), upper extremities, weight loss, and to a lesser extent pain, fatigue and sexual functioning (see Table 2).

One of the most frequently endorsed topics related to physical functioning was gene testing, especially for individuals at-risk or prodromal for HD. Participants discussed deciding whether or not to get tested ("if I got tested now, what good would that do? Like what mentally I can't handle it and it would just change things"), and the things that lead them to get tested ("discussing when to get tested if we're gonna have kids"). They also discussed the impact that the gene test will have on their own children ("maybe it's better not to know so that they don't ever have to be at risk if I'm not at risk") and their relationships ("knowing that you might have it and might be positive and sort of negotiating where at that point in that relationship where do you bring it up").

Groups also spent a substantial portion of physical health discussion on motor functioning. While all groups spent time discussing speech and swallowing difficulties, clinicians spent more time on this than the others. Clinicians discussed difficulties with dysarthria ("notable dysarthria") and dysphasia ("their dysphasia is out of control"), as well as the quality of their vocalizations ("they have slurred speech"). They also discussed both general swallowing concerns ("the main problem is… the swallowing dysfunction") and specific concerns raised by both patients ("yeah, I choke every time I eat") and their families ("I gave the Heimlich maneuver three times this week"). Further there was discussion related to palliative care and feeding tubes ("these people just get put on puree, and they're left for dead, and that's it, and then they get the G tube, and then that's the end of the story").

All groups spent a lot of time discussing motor functioning issues related to chorea, the "signature" symptom of HD (Roos, 2010). Description of these movements ranged from "a lot of subtle twitching," to "it almost looks like a seizure going on at all times." In addition, there was discussion about how chorea was often most distressing for other people ("I'm concerned about the movements 'cause I've already – they, they upset people") but not the patient themselves ("the chorea… it's usually the family who complains, because they see somebody shaking, and you ask the patients, and they're like, 'I'm fine'"). In addition, all

groups talked about how chorea impacts mobility/ambulation ("he can't walk straight"), and often requires the use of assistive devices ("for their safety they have to be in a chair"). Balance issues ("balance is an issue") and subsequent falls ("I fell couple days ago") were commonplace. Less frequently endorsed were motor functioning difficulties with upper extremities ("he can't hold his hands still enough to do it"), difficulties with ADLs ("unable to keep up the house"), and difficulties maintaining weight due to constant movements ("she just couldn't keep the weight on no matter how much she ate").

Finally, groups spent time discussing the importance of medication management ("I mean we've certainly been through a number of medications") and their side effects ("he had something called tardive dyskinesia"), as well as lengthy discussions regarding health promotion including preventative care ("I'm doing what I can to stay happy and healthy and stay in shape") and being actively engaged in different rehabilitation therapies ("we see the nutritionist, the occupational therapist, the physical therapist").

We found that our HD concepts of mobility/ambulation, ADLs, and upper extremities were congruent with pre-existing item banks. However, the pre-existing item banks did not cover HD-specific issues of gene testing, involuntary movements/chorea, speech/swallowing difficulties, weight loss, medication, and health promotion. Further, groups only spent minimal time discussing pain, fatigue, suggesting that these might be less important to assess in HD. In addition, sexual functioning was also not commonly discussed, although this is likely a reflection of the mode of evaluation (i.e., people were likely uncomfortable discussing this topic in a group setting) (see Table 3).

Cognitive Health

Cognitive Health was also endorsed, but generally less so than Emotional or Social Health (see Table 1). Groups discussed cognitive health subdomains of executive functioning, learning and memory, communication/comprehension, attention/concentration and compensatory techniques (see Table 2).

In general, the largest portions of the cognitive discussion were spent on difficulties with executive function including decision-making ("you know making poor decisions"), problem-solving ("he lost that problem solving ability"), planning/organizing/sequencing ("I have the sequencing problem"), slowed processing speed ("I'm still pretty slow up here"), perseveration ("my brain does that hamster wheel thing"), and multitasking ("I could never give him more than one task").

Cognitive functioning discussion included learning ("trouble getting the information in, in the first place") and memory difficulties ("it's hard to remember things"), as well as the impact that HD has on communication and comprehension ("before I was able to hold a whole conversation, and now just to talk amongst us is hard for me to do"). To a lesser extent, groups also discussed problems with attention/concentration ("I can't even like really concentrate") and the importance of utilizing compensatory techniques ("I started doing crosswords so I know more words").

When examining the relationship between HD-related Cognitive Health concepts and those of other existing PROs, we found that all HD-QOL Cognitive Health issues overlapped with previously existing item banks (see Table 3).

End of Life Issues

Finally, the other area of functioning that consistently arose in all of our focus groups was end of life issues (see Table 1 and Table 2). As one participant expressed, "it's not how you're gonna die. It's just how you're living or how you're gonna live." Over 50% of

discussion regarding end of life issues revolved around planning ("she went and got long term life insurance, nursing care, all that stuff"). In particular, participants discussed family planning ("do I have kids"), financial planning ("I feel like more pressure to plan financially for the future"), and palliative care ("I don't want my sons to see me on feeding tubes"). Participants also discussed how HD impacts their entire family ("being at risk for HD or having a family that's affected by HD, you just don't want it to completely make your life abnormal") and the difficulties related to making forward comparisons after watching family members with disease ("they do a look back in which a mother or a father that they inherited that disease from, and they now see themselves fast forward into that time space").

When examining the relationship between end of life issues reported in focus groups and preexisting item banks, none of this content area has been covered in any of the other new PRO measurement systems (see Table 3).

Discussion

This study identifies a number of significant issues that confront individuals who are at risk for or diagnosed with HD, including emotional, social, physical, cognitive, and end of life issues. Endorsement rates for emotional, social and physical HRQOL were highest regardless of group type (e.g. at risk, caregiver); ratings for each of these domains comprised 20–30% of the overall group discussions (all of these domains, regardless of group type were within 10% of one another) indicating similar levels of importance for each construct. Emotional HRQOL was endorsed most highly by at-risk/prodromal HD groups and caregiver groups. As these groups are dealing with both their own emotional health issues as well as secondary emotional health issues related to the health decline of their family member with HD symptom progressions, this may reflect these compounded emotional health issues. Further, the symptomatic HD groups endorsed social health HRQOL most highly, possibly reflecting the fact that these individuals all lived in nursing homes where such issues appeared to be a primary focus of daily life. Clinicians were the only group to endorse physical functioning HRQOL above the other HRQOL domains; we speculate that this reflects the clinical focus of available palliative care, which most often targets motor symptoms and emotional HRQOL.

Findings from this study also support the premise that a targeted, sensitive measure of HRQOL is needed for this population. First, many of the constructs measured by the new PROs measurement initiatives (e.g., PROMIS and Neuro-QOL) are relevant and important in this population. Specifically, many of the emotional, social and cognitive HRQOL subdomains that are examined by existing PROs appear to represent HRQOL issues that are relevant and important in HD. This overlap likely reflects types of palliative care designed to target HD symptoms that overlap with other disease symptoms/interventions (i.e., medications/interventions designed to enhance mood or slow cognitive decline).

Regardless of this overlap, there were a number of physical HRQOL subdomains that are relevant and important for HD, but that are not fully captured by these ongoing initiatives. Specifically, HRQOL issues of chorea, weight loss, medication, and health promotion were described as important in the HD groups but are not currently evaluated by other PROs initiatives and as such may warrant additional HRQOL item development. Further, clinicians highlighted the importance of speech and swallowing issues, especially during the later stages of the disease. Notably, chorea, weight management, and speech and swallowing issues are often the focus of HD palliative care efforts, making them ideal endpoints in HD-specific clinical trials.

Finally, end of life issues arose as an important HRQOL topic in HD that is not currently examined by any of the other PRO initiatives. Issues related to family planning, financial planning and palliative care were frequently discussed. Further, the impact of HD on the family and the difficulties related to making forward comparisons (seeing someone with HD symptoms and knowing that you will also experience these symptoms) were also prevalent.

Expanding the PROMIS and Neuro-QOL content areas with domains relevant to persons with HD will enhance overall HRQOL measurement in clinical trials. Incorporating items from these PRO measurement initiatives into the HD-QOL will allow for comparisons across studies and patient populations. The HD-QOL will be applicable for a range of clinical trials, screening tools for clinical practice, and as a brief and efficient way to assess change over time in any given HRQOL domain.

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Table 1

Health-Related Quality of Life (HRQOL) Domains Generated Among Focus Groups

HRQOL Domain	Overall Thematic Breakdown				
	At-Risk/ Prodromal HD Focus Groups	Symptomatic HD Focus Groups	Caregiver Focus Groups	Clinician Focus Groups	Total Across All Groups
EMOTIONAL HEALTH	30.1%	22.8%	28.0%	28.1%	27.6%
SOCIAL PARTICIPATION	27.5%	30.9%	27.0%	19.8%	27.4%
PHYSICAL HEALTH	24.2%	24.1%	27.0%	33.7%	26.0%
COGNITIVE HEALTH	7.1%	13.8%	10.7%	12.1%	10.4%
END OF LIFE ISSUES	10.3%	8.4%	7.7%	6.3%	8.7%

Numbers reflect the overall percentage of comments related to this specific domain for each set of focus groups.

Table 2

Thematic breakdown of focus group data across all focus groups

HRQOL Domain and Subdomains	Example Quotation	Overall Thematic Breakdown				
		At-Risk/ Prodromal Focus Groups	Symptomatic Focus Groups	Caregiver Focus Groups	Clinician Focus Groups	Total Across All Groups
EMOTIONAL HEALTH		30.1	22.8	28.0	28.1	27.6
Anxiety/Fear	I just feel anxious	17.4	15.2	4.8	14.6	13.7
Stigma	We were not supposed to tell anybody, ‘cause my dad was afraid he was gonna lose his job because of insurance and everything	11.8	11.1	19.6	6.3	12.7
Anger	I have anger problems	10.5	11.1	13.6	12.6	11.6
Psychiatric/Behavioral changes	there is no gatekeeper anymore--there’s no filter	10.4	3.7	20.7	28.9	13.6
Positive Psychological Function	to appreciate each day that you have	10.3	16.7	7.4	11.3	11.3
Resilience	it’s just trying to live every day, you know as best you can	10.0	9.8	4.8	1.7	7.7
Depression	I’ve been crying about this a lot lately	7.2	11.3	10.5	9.0	9.1
Emotional Roadblocks	there’s always an excuse for everything	6.6	4.1	7.6	5.3	6.0
Grief/Loss	I used to have a life before this	4.8	8.9	1.4	2.7	4.7
Self-Evaluation	I wasn’t good enough	1.1	0.9	3.1	0.7	1.4
SOCIAL PARTICIPATION		27.5	30.9	27.0	19.8	27.4
Interpersonal Relationships	I should be able to just to enjoy my family	54.0	43.6	54.0	42.0	49.5
Leisure	we play cards	25.5	32.7	34.1	36.3	30.7
Vocation	she couldn’t hold a job	16.1	14.6	2.0	10.4	12.0

HRQOL Domain and Subdomains	Example Quotation	Overall Thematic Breakdown				
		At-Risk/ Prodromal Focus Groups	Symptomatic Focus Groups	Caregiver Focus Groups	Clinician Focus Groups	Total Across All Groups
Independence/Autonomy	it's hard for me to do things on my own now	3.4	7.3	7.4	8.5	5.9
PHYSICAL HEALTH		24.2	24.1	27.0	33.7	26.0
Gene Testing	from the beginning when they tested for the marker I was against it, dead set because there's nothing that they could do for you	25.6	9.6	11.5	7.5	15.1
Involuntary Movements/Chorea	she used to try and shave her legs and she'd end up with cuts on her face	9.6	8.9	6.0	11.4	8.9
Mobility/Ambulation	I have problems walking	9.2	10.0	11.1	13.3	10.5
Speech/Swallowing Difficulties	choked early on, on things	8.6	9.8	12.5	21.6	12.0
Medications	now I'm on medicine and it really helps me	7.9	14.2	13.3	6.4	10.6
Health Promotion	I'm doing what I can to stay happy and healthy and stay in shape	7.7	9.6	6.2	6.4	7.6
ADLS	I know he has a hard time dressing	5.7	7.0	7.0	9.4	7.0
Upper Extremities	she may not be able to unscrew this bottle of water anymore	5.1	8.2	6.0	5.3	6.2
Weight Loss	she had trouble keeping the weight on through the whole fidgeting and everything	4.7	5.1	4.2	2.8	4.4
Pain	my hands hurt	0.8	0.2	1.4	1.1	0.8
Fatigue	they feel more exhausted at the end of the day	0.3	1.2	0.0	0.8	0.6
Sexual Functioning	being able to have a fulfilling sex life	0.1	1.8	2.4	1.7	1.3
COGNITIVE HEALTH		7.1	13.8	10.7	12.1	10.4
Learning/Memory	he lost that problem solving ability	23.7	19.3	10.5	11.6	17.3
Executive Function	memory, you know, like I'll put the keys somewhere	21.9	37.7	44.5	40.3	35.7

HRQOL Domain and Subdomains	Example Quotation	Overall Thematic Breakdown				
		At-Risk/ Prodromal Focus Groups	Symptomatic Focus Groups	Caregiver Focus Groups	Clinician Focus Groups	Total Across All Groups
	and forget where I put it					
Communication/ Comprehension	I couldn't finish a conversation	14.4	10.1	7.9	16.3	11.6
Attention/Concentration	I'll lose my train of thought	9.8	5.8	1.0	2.3	5.2
Compensatory Techniques	just trying to keep my brain active	6.5	8.6	2.1	2.3	5.7
END OF LIFE ISSUES		10.3	8.4	7.7	6.3	8.7
Planning	I went out and got long-term care insurance at the ripe old age of 32	53.7	52.0	47.9	29.9	49.9
Interactions with others With HD	it's different when it's personal, a person in your family	34.1	33.3	29.6	10.4	30.8
Forward Comparison	knowing that this is gonna be me	5.5	6.1	4.9	11.9	6.1

Percentages for Domains reflect the total percentage of comments related to this specific domain (Domain percentages should sum to 100 with rounding); percentages within each subdomain reflect the percentage of comments within each Domain (should sum to ~100).

Table 3

Thematic overlap among patient reported outcome measurement initiatives

Domain and Subdomains	Overlap with Neuro-QOL	Overlap with PROMIS	Overlap with TBI-QOL	Overlap with SCI-QOL/ SCI-CAT	Possible Inclusion on HD-QOL (>5% endorsement)
EMOTIONAL HEALTH					
Anxiety/Fear	X	X	X	X	X
Stigma	X		X	X	X
Anger		X	X		X
Psychiatric/Behavioral Changes	X		X		X
Positive Psychological Function	X		X	X	X
Resilience			X	X	X
Depression	X	X	X	X	X
Emotional Roadblocks					**X**
Grief/Loss			X	X	X
Self-Evaluation			X	X	
SOCIAL PARTICIPATION					
Interpersonal Relationships	X	X	X	X	X
Leisure	X	X	X	X	X
Vocation	X	X	X	X	X
Independence/Autonomy			X	X	X
PHYSICAL HEALTH					
Gene Testing					**X**
Involuntary Movements/Chorea					**X**
Mobility/Ambulation	X	X	X	X	X
Speech/Swallowing Difficulties					**X**
Medications					**X**
Health Promotion					**X**
ADLS	X	X	X	X	X
Upper Extremities	X	X	X	X	X

Domain and Subdomains	Overlap with Neuro-QOL	Overlap with PROMIS	Overlap with TBI-QOL	Overlap with SCI-QOL/ SCI-CAT	Possible Inclusion on HD-QOL (>5% endorsement)
Weight Loss					
Pain		X	X	X	
Fatigue	X	X	X		
Sexual Functioning		X	X	X	
COGNITIVE HEALTH					
Learning/Memory	X	X	X		X
Executive Function	X	X	X		X
Communication/Comprehension	X	X	X		X
Attention/Concentration	X	X	X		X
Compensatory Techniques					
END OF LIFE ISSUES					
Planning					**X**
Interactions with others with HD					**X**
Forward Comparison					**X**

TBI-QOL = traumatic brain injury patient reported outcome measurement initiative

SCI-QOL/SCI-CAT = spinal cord injury patient reported outcome measurement initiative

Bolded items are subdomains that may warrant additional item development for use in clinical trials

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