Improving quality of life measures in Huntington disease

Dr Noelle E Carlozzi is an Associate Professor in the Department of Physical Medicine and Rehabilitation at the University of Michigan, as well as Director of the Center for Clinical Outcomes Development and Application (CODA). Her research aims to develop brief, sensitive patient self-report measures that evaluate the impact of a disease on a patient's health-related quality of life.

Huntington disease is an autosomal dominant neurodegenerative disease which affects approximately one in 10,000 individuals in the US. Children of carrier parents have a 50% chance of inheriting the mutation responsible for the disease. Clinical symptoms include motor impairments, as well as behavioural and cognitive abnormalities. Symptoms typically begin around ages 30 to 50. One of the hallmark symptoms of the disease is chorea – irregular, jerky, involuntary movements that are often abrupt and unpredictable. Chorea can affect different parts of the body, inhibiting speech, swallowing, walking and posture. Though clinical progression is different for each patient, Huntington disease is usually fatal within 15 to 20 years following diagnosis. Pneumonia and heart failure are two of the leading causes of death in Huntington disease.

A DISEASE WITHOUT A CURE

Genetic testing for individuals who may be affected is available after the age of 18. In addition, couples who are carriers may undergo pre-implantation genetic diagnostic testing with in vitro fertilisation (IVF) to ensure that fertilised eggs contain no mutation. Beyond preventative measures, there is currently no treatment for Huntington disease. While medications can improve the severity of symptoms, they are often associated with side effects that include somnolence, dysphagia, gait issues and apathy, which can have a serious impact on quality of life. Given the lack of a cure for the disease and that the only treatments are palliative, it is critical to be able to evaluate how health-related quality of life (HRQOL) is affected in these patients. To do this, we need measures that help us understand patient perspectives that are relevant to individuals with Huntington disease.

CHALLENGES IN MEASURING QUALITY OF LIFE

Well-being is a critical aspect in Huntington disease. As such, Dr Carlozzi's research aims to develop new health-related quality of life patient-reported outcome (PRO) measures specifically for individuals with Huntington disease. Existing measures currently used for this are often irrelevant or insensitive to Huntington disease-specific criteria, and can limit the frequency at which meaningful change is observed. Through her work, Dr Carlozzi hopes to change this by creating Huntington disease-sensitive measures

Existing measures currently used are often irrelevant or insensitive to Huntington disease-specific criteria, and can limit the frequency at which meaningful change is observed

that can increase clinical confidence in determining meaningful change in health-related quality of life.

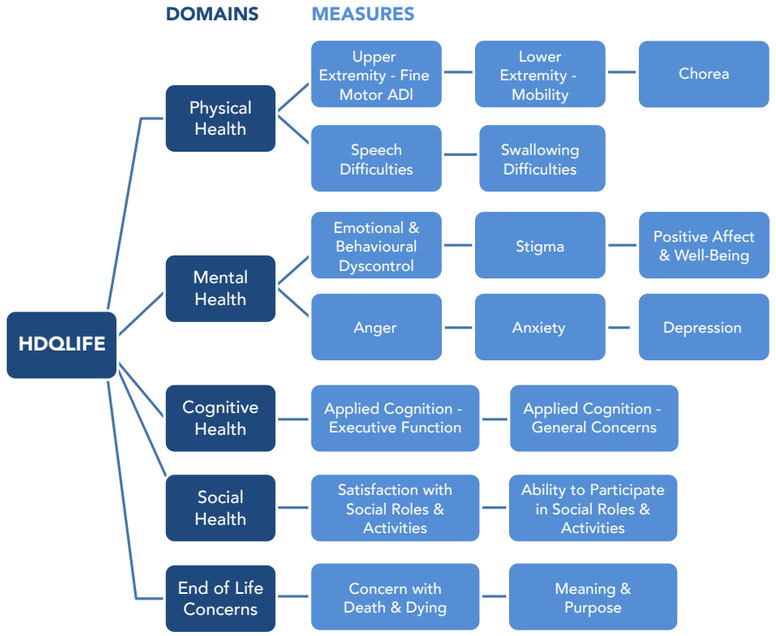
CAT IMPROVES MEASUREMENT OUTCOMES

Recent advances in assessment tools include the Quality of Life for Neurological Disorders (Neuro-QoL) measurement system and the Patient-Reported Outcomes Measurement Information System (PROMIS), which were developed from grants from the National Institutes of Health (NIH). Both measures enable cross-disease comparisons, as well as simplified estimation of scores across systems.

Importantly, these systems include computerised adaptive test (CAT) technology, which aims to deliver a "personalised" questionnaire, where only the most relevant questions are administered to an individual. Everyone answering the questionnaire receives the same first question, but subsequent questions are delivered based on the response to the previous questions. This technology has been shown to offer improved precision compared to fixed length questionnaires. It also enables clinicians and researchers to determine a patient's health status in a shorter amount of time without jeopardising test sensitivity. In addition, CAT has been shown to be able to detect more subtle changes than other measures. Because of the improved sensitivity and specificity of the CAT measures, as well as the need for fewer assessment items, disease-specific CATs can help minimise test administration burden, optimise clinical trials and ultimately improve patient care.

PATIENT-REPORTED OUTCOMES TO ASSESS CONCERNS AND SYMPTOMS

Patient-reported outcome measures (PROs) are designed to improve patient-centred care, providing Huntington disease patients with a voice to discuss their disease, its symptoms, and associated quality of life, with physicians and other providers. PROs aim to incorporate the patient's perspective about his/her health care to ensure that he/she receives the best level of treatment possible.



PROs also prove valuable in defining the influence of chorea on health-related quality of life in Huntington disease. In a recent study led by Dr Carlozzi, a new HDQLIFE Chorea item bank was developed using CAT technology. The HDQLIFE Chorea item bank is comprised of 34 questions that assess the impact of chorea on health-related quality of life in Huntington disease patients; most patients will typically complete 6–8 items before receiving a score. As such, clinicians can use the information provided by this questionnaire to identify individuals whose quality of life is negatively impacted by chorea, and direct them to appropriate treatments/referrals.

Similarly, Dr Carlozzi has developed two PROs to evaluate end-of-life concerns in Huntington disease. One PRO focuses on meaning and purpose, and the second relates to concerns about death and dying. End-of-life discussions are difficult for most people, but are common concerns for those affected by an incurable disease. Therefore, the 'HDQLIFE Concern with Death and Dying CAT' and 'HDQLIFE Meaning and Purpose scale' are important tools to assess changing patient opinions on death-related concerns. This consequently ensures that healthcare providers can adequately cater to end-of-life needs.

Though much less discussed, dysarthria and dysphagia are common symptoms of Huntington disease which result in slowed or irregular speech rates and swallowing difficulties. Such complications can have a profound impact on the quality of life of patients and, until recently, no Huntington disease-specific PRO existed to measure them. As part of the HDQLIFE assessment system, Dr Carlozzi helped to develop measurements for both speech and swallowing difficulties (HDQLIFE Speech Difficulties and HDQLIFE Swallowing Difficulties). Though originally developed with Huntington patients, these measures may be useful in assessing speech and swallowing issues in other clinical populations.

Dr Carlozzi's work has shown that health-related quality of life patient-reported outcome measures provide much better information in a more efficient way in Huntington disease patients

Dr Carlozzi's work has shown that health-related quality of life PROs including those developed specifically for Huntington Disease (Chorea, Difficulties with Speech, Difficulties with Swallowing, Concern with Death and Dying, and Meaning and Purpose), as well as PROMIS and Neuro-QoL, provide much better information in a more efficient way in Huntington disease patients. Because they have improved sensitivity and specificity in this population, they can likely detect smaller changes than more generic PROs. Given that Huntington disease is rare, such measurements are likely to improve clinical trials by reducing the total number of participants required to discover significant deviations in function. By enhancing clinical trials, researchers are hoping to speed up the process of finding a viable treatment for Huntington disease.

Q&A

Are there other clinical areas of interest your research could be applied to?

This type of work is relevant and can potentially be applied to many different patient populations. My own work also includes improving measurement of health-related quality of life (HRQOL) and neuropsychological (i.e. cognitive) assessments for individuals with traumatic brain injury and their caregivers; individuals with spinal cord injury; individuals with stroke; and children and adults with nephrotic syndrome. But the list is endless. Improving HRQOL, or specifically in the case of my own work, the assessment of HRQOL, is critical to improving patient-centered care and outcomes.

As part of the limitations in some of these studies, you mention a lack of caregiver perspectives. Will these be implemented in future QoL assessments?

Caregivers are often an overlooked and understudied population. With advances in medicine, family members are often forced to assume the role of a caregiver and are given increasingly complex responsibilities for helping to monitor the care and status of an individual with a chronic condition. We have been conducting some preliminary research in caregivers of individuals in Huntington disease, and I also have another NIH-funded study that examines caregivers of individuals with traumatic brain injury. Thus, it is my hope to continue to build upon this work to better address HRQOL for caregivers in Huntington disease and other clinical populations. This work is especially important given that caregiver quality of life is strongly linked to patient-reported quality of life, such that caregivers with better HRQOL have care-recipients that have better HRQOL.

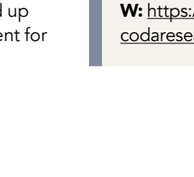
What aspects are you most excited about when it comes to your research?

I have always been most excited about the research process rather than in any 'destination', so to speak. That being said, I want to make sure what I'm doing is relevant and efficient. As such, talking to individuals with Huntington disease and their families and understanding their stories is really important to ensuring that the work that I do has meaning.

What other future challenges are there in addressing quality of life in Huntington disease?

So, my role in the research is really just a small cog in the larger wheel of improving health-related quality of life. I want to improve measurement so that we can do things more efficiently and be confident that a treatment is either working or not. Yet, in the larger scheme of things, finding treatments that delay the clinical onset of the disease and ultimately finding a cure is the biggest challenge we currently have in the field. Until then, if my work can help us better understand how to maximise quality living, I will count my work as a success.

Detail



RESEARCH OBJECTIVES

Dr Carlozzi's research focuses on developing brief, individually tailored measures that can be used by providers to evaluate patient-reported symptoms and health-related quality of life for individuals with Huntington disease. She uses state-of-the art survey design and statistical techniques, allowing her to greatly shorten the length of the assessment while also improving the sensitivity. This results in decreased patient burden and improved efficiency in clinical trials.

FUNDING

- National Institutes of Health (NIH)
- National Institute of Neurological Disorders and Stroke (NINDS) R01NS077946

COLLABORATORS

Praveen Dayalu, Anna Kratz, Stephen Schilling, Jane Paulsen, Nancy Downing, Kimberly Quaid, Christopher Ross, Susan Perlman, Michael McCormack, Humberto Marin, Joel Perlmutter, Martha Nance, Stephen Rao, Anwar Ahmed, Michael Geschwind, Elizabeth Hahn, David Cella, Richard Gershon, Jin-Shei Lai, Samuel Frank, Rebecca Ready, Ira Shoulson, Julie Stout

BIO

Dr Carlozzi is the Director of CODA at the University of Michigan. She is an expert in health-related quality of life computer adaptive test development, and measurement validation. She is a previous recipient of the prestigious Rosenthal Early Career Award courtesy from the American Psychological Association.

CONTACT

Noelle E Carlozzi, PhD
Center of Clinical Outcomes Development and Application (CODA)
Department of Phys. Medicine & Rehab.
University of Michigan
North Campus Research Complex
2800 Plymouth Road
Building NCRC B14, Room G216
Ann Arbor, MI 48109-2800, USA
E: carlozzi@med.umich.edu
T: +1 (734) 763 8917
W: https://sites.google.com/site/codaresearch/