Dear Editors,

As of now, the clinical diagnosis of HD is predominantly made on the basis of characteristic motor signs resulting in a diagnostic confidence level of 4 in the UHDRS TMS, meaning the rater is > 99% certain that motor abnormalities are caused by HD. In 2020, Oosterloo et al. (DOI: 10.1002/mdc3.13148) showed that the diagnostic confidence level DCL is not an accurate instrument to determine phenoconversion and the need to develop more reliable diagnostic criteria.

Many researchers have convincingly argued that non-motor symptoms should be included in the diagnosis of HD: Mark Guttman (2012), Kevin M. Biglan et al. (2013), Clement T Loy and Elizabeth A McCusker (2013), Ralf Reilmann et al. (2014), Christopher A. Ross et al. (2019). The PREDICT-HD, PHAROS, and TRACK-HD studies, including combined >1,400 premanifest participants, identified non-motor symptoms >10 years ahead of clinical motor diagnosis.

The group of McAllister et al.* analyzed clinical features of 6,316 patients with HD followed in REGISTRY. They found that "42.4% of HD patients reported at least one psychiatric or cognitive symptom before motor symptoms, with depression most common. Each non-motor symptom was associated with significantly reduced total functional capacity scores." Despite these reliable findings, their conclusion is wrong: "… because it is impossible to distinguish confidently between nonmotor symptoms arising from HD and primary psychiatric disorders, particularly in younger premanifest patients, nonmotor symptoms should not be used to make a clinical diagnosis of HD."

This prevalent convention for diagnosis could lead to harm. Patients who suffer disability as a result of HD may not be able to access services or disability rights because they aren't "diagnosed". Additionally, changes in behavior (such as impulsivity or irritability) may be falsely attributed to other causes because the patient has not reached the diagnostic threshold.

Beyond doubt, HD is not just a movement disorder, it is a neurodegenerative disease with motor, cognitive, psychiatric, vegetative, and metabolic symptoms, appearing in a high variable way and sequence. Non-motor symptoms are often the first to emerge, and usually influence quality of life more than motor symptoms.

Non-motor symptoms (cognitive, behavioural, and psychiatric) can be the presenting and most prominent aspects of HD and should be a crucial part of the diagnostic evaluation. If diagnosis can only be made using a motor score with a cut-off with 99% level of confidence, many people affected by HD around the world will be denied the expert healthcare that they need.

Families affected by HD have long known that the true burden of Huntington's disease starts earlier and is more complex that medical literature describes, To further illustrate this, nearly 4,000 HD community participants signed a global petition (www.WeHaveAFace.org/results) advocating for the clinical diagnosis to better capture the non-motor symptoms.

In support of their voice and journey, we urge a path for HD diagnosis that is not dependent solely on motor symptoms.

Sincerely,

Vita Aguiar de Oliveira, Associação Brasil Huntington
Debbi Fox-Davis, HD Reach
Carol Kennedy, WeHaveAFace England & Wales
Herwig Lange, MD, WeHaveAFace Germany
Cindy Moore, WeHaveAFace Canada
Frances Saldaña, HD-CARE
Cath Stanley, Huntington Disease Association (UK)
Donaji Toledo, Asociación Mexicana de la Enfermedad de Huntington
James Valvano, WeHaveAFace
Louise Vetter, Huntington's Disease Society of America

* McAllister Paper: "Timing and Impact of Psychiatric, Cognitive, and Motor Abnormalities in Huntington Disease" Neurology® 2021;96:e2395-e2406. doi:10.1212/WNL.0000000000011893
https://pubmed.ncbi.nlm.nih.gov/33766994/

HD Diagnosis - Moving from an Event to a Spectrum
Mark Guttman (2012) CHDI 7th Annual HD Therapeutics Conference
https://chdifoundation.org/2012-conference-2/#guttman

Refining the diagnosis of Huntington disease: the PREDICT-HD study
Kevin M. Biglan et al. (2013) doi: 10.3389/fnagi.2013.00012

Is a Motor Criterion Essential for the Diagnosis of Clinical Huntington Disease?
Clement T Loy and Elizabeth A McCusker (2013)
doi: 10.1371/currents.hd.f4c66bd51e8db11f55e1701af937a419:
"New, broader, criteria for the diagnosis of clinical HD would be helpful in many ways. However its formulation will need to flexible rather than prescriptive, and will require extensive consultation with clinicians and families with HD."

Diagnostic Criteria for Huntington's Disease Based on Natural History
Ralf Reilmann et al. (2014) DOI: 10.1002/mds.26011

Movement Disorder Society Task Force Viewpoint: Huntington's Disease Diagnostic Categories
Christopher A. Ross et al. (2019) doi: 10.1002/mdc3.12808

Disease Onset in Huntington's Disease: When Is the Conversion?
Mayke Oosterloo et al. (2021) doi: 10.1002/mdc3.13148