Case study

Driving innovation in Huntington's Disease by tracking progression through at-home digital measurements

About F. Hoffmann-La Roche Ltd.

Founded in 1896, Roche is a leading biotechnology company and top provider of in-vitro diagnostics. Combining pharma and diagnostics, Roche advances research to enhance disease understanding and develop innovative diagnostics, medicines, and digital solutions. Through global partnerships, it pushes scientific boundaries to transform healthcare and improve lives with groundbreaking research and personalized care.

The opportunity

- At-home digital measurement of motor ability enables a sensitive assessment of the progression of the motor manifestation of Huntington's disease (HD). This allows the identification of treatment benefits with smaller sample sizes, particularly early in the disease course.
- At-home digital measurements improve sensitivity by three mechanisms: collecting data across multiple days allows reducing day-to-day measurement variability through averaging, assessing motor ability without a human rater in the loop removes a potential source of variability, and measurement on a continuous, not inherently bounded scale increases the sensitivity and avoids ceiling effects.

The challenge

- Huntington's disease (HD) is a rare neurodegenerative disease with slow progression, and the standard clinical endpoints have limited sensitivity. This leads to the need for large and lengthy trials.
- With no disease-modifying treatments available for HD, there is a substantial unmet need. Fortunately, there is a growing number of clinical programs to identify therapeutic targets that can benefit people with HD. However, with a limited number of people meeting inclusion criteria, recruitment is becoming challenging.
- Furthermore, the field is moving to treat people earlier in their disease course, before the disease has strongly impacted function. This further decreases the sensitivity of accepted functional outcomes accepted by health authorities, like the Total Functional Capacity score, making clinical development even more difficult.

The approach

- Work with people living with Huntington's and expert neurologists to develop assessments for use at home with a mobile phone.
- Deploy the technology in clinical trials in HD as exploratory measures to refine the assessments and operations and create a data set for developing endpoints.
- Develop a digital motor score that sensitively tracks disease progression using data pooled across three observational and early-phase studies and evaluate it on data from a separate late-phase study to increase generalizability.
- Derive potential sample size reduction by using the same formalism used to calculate sample size for HD studies and substituting the expected change and variability of the clinical measures for those of the digital measures.

The impact

- ✔ Sample size estimations suggest that the HD digital motor score is sensitive enough to potentially detect a treatment signal with substantially fewer study participants.
- ✔ Comparison between interventional and observational data suggests that the HD digital motor score exhibits no discernible placebo effect, which may enable external reference arms, particularly for early-phase trials.
- ✔ For people with HD early in their disease course, where standard clinical measures do not detect clear 12-month progression yet, the HD digital motor score can identify significant progression from baseline, suggesting its possible usefulness in trials in earlier stages of the disease.

> "More sensitive measures for disease progression, especially in early stages of HD, hold the promise of shorter smaller trials, which is particularly important in rare diseases."

— Peter McColgan, MD PhD

Senior Medical Director and Global Development Leader, Roche

This case study was adapted from the paper "**A digital motor score for sensitive detection of progression in Huntington's disease**" by Louis-Solal Giboin, Cedric Simillion, Johannes Rennig, Atieh Bamdadian, Fiona C. Kinsella, Anne V. Smith, Peter McColgan, Michael Lindemann, Florian Lipsmeier, Edward J. Wild, and Jonas Dorn (2025), recently accepted into *Brain*.