Worldwide Clinical Trials

Incorporating the Huntington's Disease Patient Voice

At Worldwide Clinical Trials, the patients, their families, and caregivers are at the heart of what we do. Their collective insights and experiences shape our strategic decisions and trial designs. To support our patient-centric approach to Huntington's disease (HD) research, we conducted numerous qualitative interviews with those affected by HD, and we share some of our findings below.

Participant Demographics

- Eight HD patients & caregivers
- Almost all participated in ENROLL HD[#]
- Symptomatic & asymptomatic
- More than half have experience in clinical trials outside ENROLL HD
- Three to 19 years lived experience with HD
- Average between 39 to 59 CAG repeats[*]
- Seven visit their HD doctor annually,[+] one participant visits every six months

[*] The normal range is 26 or fewer. One patient declined to discover their CAG repeats | [#] The largest observational HD study | [+] Aligns with annual ENROLL HD visit

Symptom Impact

The most common theme amongst the group we interviewed was that while it impacted their life, chorea was not the most bothersome symptom. Consistently, in six out of eight interviews, patients and their caregivers rated the psychological aspects of the diseases as the most impactful; these include cognitive decline, memory loss, and apathy. More than half of the respondents additionally referenced the behavioral changes as having significant impacts on the family living with HD. A presymptomatic patient told us of her struggles to conceive and expressed that both an IVF facility and adoption agency turned her down because of the disease, which in turn led to significant mental health issues.

A wife and caregiver of a man with HD shared her experience of both the early and late stages of the disease. Prediagnosis, this caregiver used to think her husband was secretly drinking, **"Initially going back 10 years, there were times when I thought he was drunk, it would come in short and random periods of time where for 30 minutes he would stumble, I thought he was secretly drinking, his mood changed, accidents started to appear."** Toward the late stage of the disease, she shared the impact of the behavioral symptoms on her and her family, **"He is still verbal but will randomly say inappropriate things in front of the kids. Now, the hardest thing is his defiance for treatment; he doesn't want any help, he is struggling with food and drink but isn't having a PEG [percutaneous endoscopic gastronomy, or feeding tube into the stomach], I have to de-choke him to keep him alive."**

An asymptomatic patient shared how the diagnosis has made her change her perspectives on life events, **"Once I had the result of the test, I was thinking, did I drop the glass because of HD, or did I just drop the glass? Am I overreacting?"**

Another caregiver spoke about both the cognitive decline and also the speech impacts, **"Cognitive decline is really hard; his speech is deteriorating, even I can't understand him. It's upsetting because there is a lack of motivation and apathy."**

Activity Limitations

The themes from activity limitation responses were consistent in that HD has changed their lives completely and has restricted them in some instances entirely to home or a care home. Another theme that appeared was the rapid decline and progression of the disease, leading to patients going from independent and working to no longer working and needing care support in a very short space of time. The survey participants also reported a need for meticulous planning for even the shortest of journeys, which can be burdensome.

An asymptomatic patient spoke to us about how she now changes the way she does things because of her HD diagnosis, **"When I go out into the garden, I always have my phone on me in case I get into trouble or have a fall."**

A caregiver said, **"Holidays are incredibly hard. Anything that requires going away for longer than a day has so much impact. Precision planning, perfect timing, change in environment, food — everything affects him. Getting out is one of the hardest struggles."**

Medications & Side Effects

Consistently, anti-depressants were the most reported medication, in addition to tetrabenazine. Tetrabenazine seemed to cause the most distress to patients and their families as this medication has potentially adverse effects on mental health.

"We weren't originally seeing an HD specialist, just a neurologist. He claimed the only helpful thing was tetrabenazine. From the moment she took it, her chorea calmed down, but her depression, suicidality, irritability, and anger all got worse, and all she could do was sleep. She took herself off it and didn't tell us; she was hiding it behind the microwave — hadn't been taken it for a year before we found all the pills."

"He was put on tetrabenazine, which has had an emotional impact on him, [he] wasn't able to speak and couldn't sleep, so [he] was given sleeping pills, he then made an attempt on his life."

Ideal Treatment

Patients who were symptomatic wanted to increase their quality of life (QoL) while slowing down the progression of the disease. As seen below, the asymptomatic patients wished to stop the symptoms from occurring or to receive treatments that provided a longer window without symptoms.

"[A perfect treatment would] stop me ever getting symptoms, ideally would be an oral medicine which is easy to take but is aware that it may need to be intrathecal to get it where it needs to. If it's something which lowers the protein in the brain, [I] wouldn't care where it was delivered."

"If you asked me now, he is symptomatic, and he wants something that will help him in his current situation, help him to continue to live, with reduced side effects, reduced symptoms, slowing the progression of the illness. I would love to find something that can reverse HD and the damage it causes, but I am pragmatic and know this may not be possible."

An asymptomatic patient expressed her want for any treatments, even saying that they investigated and started the screening process for the UniQure trial AMT-130.

Additionally, patients showed a preference for cognitive medications if no monotherapy is available to them, **"For me, the main area that should be focused on would be neurocognitive symptoms — the areas of the brain shrinking that cause the terrible personality changes. That's what bothers me about my future; I don't want to cause the people I love harm by my behavior or physically like my mum did to me and my dad."**

Clinical Trials Motivation

The main themes that emerged from this were that overwhelmingly, participants stated that their main motivation was altruistic — they wanted to be part of something bigger and to do something for the next generation. Among presymptomatic patients, the theme was centered around stopping their disease from ever manifesting.

A wife and caregiver of a male patient with HD told us, **"[My] husband has a really good mindset; once he realized he had the disease, he said it's his responsibility to change their future; he said he always wanted to be a part of [clinical trials] because, 'if it accidentally killed me, it would mean it wouldn't kill my kids.'"**

A presymptomatic patient said, **"My primary motivation would be to delay the onset of my symptoms or help my life or future in some way."**

Invasive Procedures

Most patients commented about some level of anxiety or fear when going to a lumbar puncture. A number commented about both positive and negative experiences with lumbar punctures and emphasized the person conducting the lumbar puncture and the aftercare provided. While participants told us about their fear and anxiety, most agreed that this is a part of research in HD and doing it is part of a "lesser evil" in the end.

"When I had a lumbar puncture, I was really well looked after; I had acupuncture to help with relaxation and recovery, had music in my ears, and was talked through the procedure. Afterwards, I was given a number you could ring if there were any concerns after the procedure; I felt supported and cared for."

"During my last visit, I had a new doctor perform the test, and it wasn't so smooth; it took two days for me to fully recover with severe headaches and leakage of CSF."

Other Assessments

Almost all participants told us that they were not concerned with completing multiple MRIs or questionnaires as part of a clinical trial. However, they shared with us the need for sedation during the MRI and their frustration with the length and repetitiveness of the questionnaires.

"I personally hate MRI machines. I am claustrophobic so I can't stay in there long. I may need to be sedated, but sometimes it becomes a lot."

"MRIs were difficult before he was taking lorazepam."

"Anything longer than 30 minutes, and I would expect something in return — having a way which you could do the questionnaire in stages throughout the day would be helpful."

Travel for Clinical Trials

On average, most patients would be willing to travel regularly for two to three hours. Travel emerged as a key theme that needed support, and any out-of-pocket expenses, including stipends for lost work, were critical in their decision-making process.

A caregiver commented, **"We don't mind traveling but I am [on a] one-person income with four people to feed."** Additionally, she commented about parking at the hospitals, **"I need to get close for parking with a campervan; the hospital is a nightmare to get to, I need to drop him off, put the hazards on, get the wheelchair, and get him inside, then come back and try and park — they should provide dedicated trial parking spaces."**

Others who have been part of trials and used concierge services showed overwhelming praise for this: **"We needed to stay close to the hospital for 10 days but wanted to bring our dogs. The company made this no issue and was even going to let us book an Airbnb, which they would pay for."**

Support from Drug Developers & CROs

There were several varied responses that motivate patients and caregivers to enroll in a clinical trial, including:

- More frequent and transparent communication, especially post-trial outcomes and information
- Clear guidance on eligibility criteria
- Emotional and psychological support, travel reimbursement, and financial incentives

"[I need] lots of information and clear information. What's going to be involved and how long it is, care packages and finances. Finding out what would make a difference and having flexibility. The patients need to feel like whatever they need can be provided for them."

"As long as there are clear [eligibility] criteria, I took an afternoon of work, took him to the hospital, got the bus because they were so stressed out about parking, had to factor that in. When we got there, they identified he wasn't able to take part."

"Reimbursement for food at the restaurant, transport to the hospital would be much easier; parking at the hospital was a nightmare."

Optimizing HD Clinical Trials, "No Research About Us Without Us!"

The perspectives of patients and caregivers in HD clinical trials are crucial for advancing research and improving the lives of those affected. The psychological and behavioral impacts of HD, such as cognitive decline and memory loss, are often the most challenging aspects of the disease, significantly affecting daily activities and QoL. Despite these challenges, patients and caregivers are motivated by a strong sense of altruism, driven to participate in clinical trials to help future generations.

To make HD clinical trials more aligned with the needs and hopes of patients and caregivers, trial design can take several key actions:

1. **Clear and Frequent Communication:** Ensure participants fully understand the trial process, eligibility criteria, and potential outcomes. Transparent communication builds trust and reduces anxiety.
2. **Emotional and Psychological Support:** Provide comprehensive support to address the emotional and psychological burdens of HD. This can include counseling services, support groups, and regular check-ins.
3. **Practical Support:** Offer assistance such as travel reimbursement, parking assistance, and accommodation for family members. These measures can alleviate financial and logistical burdens.
4. **Flexible Trial Design:** To enhance patient comfort and participation, trials should be designed with flexibility in mind, allowing questionnaires to be completed in stages and providing sedation for procedures like MRIs.

By prioritizing these perspectives and needs, we can create a more supportive and considerate environment for participants. This approach improves the QoL for those involved while fostering community and shared purpose. The commitment and resilience of patients and caregivers in the face of HD are a testament to their support and trust in our capabilities, and by working together, we can make significant strides in the fight against this disease.

About Worldwide Clinical Trials

Worldwide Clinical Trials (Worldwide) is a leading full-service global contract research organization (CRO) that works in partnership with biotechnology and pharmaceutical companies to create customized solutions that advance new medications – from discovery to reality.

Anchored in our company's scientific heritage, we are therapeutically focused on cardiovascular, metabolic, neuroscience, oncology, and rare diseases. Our deep therapeutic knowledge enables us to develop flexible plans and quickly solve problems for our customers.

For more information on Worldwide, visit www.worldwide.com or connect with us on LinkedIn.