Face-to-face: Huntington's disease families are heard by the FDA

The HDSA recently coordinated a meeting between Huntington's disease families and the US regulatory agency that approves medicines, to amplify the community's voice and help move us toward treatments.

By Dr Sarah Hernandez | **November 22, 2024** | **Edited by Dr Rachel Harding**

- **TRIGGER WARNING:** *This article contains a frank discussion around the challenges and realities of living with Huntington's disease, as well as caring for those affected by it. Topics include suicidal ideation, threats to family members, financial distress, paranoia, severe anxiety, feelings of hopelessness, and loss of identity. We understand that this may be a difficult article for some to read and caution people about reading this article who may not be in an appropriate headspace to think about such topics. While these types of conversations are difficult, they are necessary to inform those who are unfamiliar with the disease, to help them try to understand the stark realities of living with Huntington's, and the devastation that it causes for those from affected families.*

The regulatory agency in the US that approves all medications, the Food and Drug Administration (FDA), considers disease severity and availability of other treatments throughout the approval process. FDA representatives participate in meetings with those living with the diseases to hear their lived experiences. This can be critical for advancing therapeutics in a timely manner that meet the needs of a patient population. On November 13, 2024, such a meeting took place in College Park, Maryland, bringing people living with Huntington's disease (HD) and their caregivers face-to-face with the FDA.

The opportunity

The Food and Drug Administration, also known as the FDA, is the regulatory agency in the United States with full control over drug approvals, including for Huntington's disease.

Image credit: Image from pharmacydirectgb.co.uk/

The Huntington's Disease Society of America (HDSA) coordinated the Externally-led Patient Focused Drug Development (EL-PFDD) Meeting between HD families and the FDA. HDSA organized a similar meeting in 2015, but **a lot** has changed in the past 9 years – research has taken great strides, we've gone from having one disease-targeting clinical trial to having many, and there are *dozens* of pharmaceutical and biotechnology companies interested in advancing drugs for HD.

The 2024 meeting was described as "a one-time opportunity to provide the FDA and other key stakeholders, including medical product developers, health care providers, and federal partners, your perspectives on the symptoms that matter most to you, impact the disease has on your daily life, and your experiences with currently available treatments". This was a once-in-a-lifetime chance for many to be heard by the agency that has the chance to approve medicines for people living with HD.

The goals

The goals for the meeting were to educate, inform, and advise the FDA and medical product developers on the challenges of living with HD and advocating for disease modifying drugs. The impact of living with HD at pre-symptomatic, early, and mid stages was shared.

The agency was informed about the treatment outcomes that the community prefers and the risks that they're willing to take to get treatments for HD. Advice was given so that the FDA could understand the challenges people with HD face with current clinical trial participation and how it could be improved.

The structure

Following opening remarks and a clinical overview, the day was divided into two panel discussions, one on health effects and daily impacts and another on current approaches to treatments.

People living with pre-symptomatic, early, and mid-stage HD shared their stories and experiences along with caregivers. Together, these perspectives and the information collected in this meeting will be used to "inform FDA's decisions and oversight both during drug development and during the review of a marketing application to treat HD". Put simply, teaching the FDA what it's really like to live with HD could have a big impact on advancing treatments for HD.

After the personal statements, there was a large group facilitated discussion using specific survey questions that were distributed to the HD community by the HDSA ahead of this meeting. This survey, on HD Symptom and Treatment Impact, will be open until December 31, 2024 and the HDSA expects to have results from that survey available in February of 2025. At the event, various HD family members were asked to share their lived experience with the FDA as it related to the question in the survey.

Opening remarks:

> **"Put simply, teaching the FDA what it's really like to live with HD could have a big impact on advancing treatments for HD. "**

Dr. Arik Johnson, Interim CEO and Chief Mission Officer, HDSA

The morning opened with a welcome message from Dr. Arik Johnson, thanking everyone for participating in this important meeting - both those from HD families for sharing their stories and the FDA for listening. There were over 60 people living with HD in the room and over 140 people who registered to attend virtually from across the globe, from 43 US states and 8 countries. The HD community was ready to be heard!

Arik said, "The time is now, for this meeting and for this opportunity". There is more research happening now at earlier disease stages. As trials shift to testing drugs at earlier disease stages, there are different outcomes and risks, of which regulatory agencies and product developers need to be aware.

Dr. Teresa Buracchio, Director, Office of Neuroscience, Center for Drug Evaluation and Research, FDA

Dr. Teresa Buracchio's job at the FDA is to oversee drugs in development for a variety of neurological conditions, including HD. She assured the crowd that many people across the FDA are listening, and that the FDA takes these meetings very seriously. She noted that the people living with HD and their caregivers are the experts, and the FDA is eager to listen to their stories. Teresa said, "the voice of the patient is very important to us", and the FDA references these reports when working to advance drugs for diseases.

It is the job of the FDA to ensure that the benefits oftherapeutics outweigh the risks. So understanding how patients view the risks and benefits of treatments will help them advance treatments that will have a positive impact on people with HD. Teresa noted the

exciting advancements that have been made for Alzheimer's disease and genetic forms of ALS and she said they're excited to incorporate similar advances to the field of HD.

Dr. Victor Sung, Professor of Neurology, Division of Movement Disorders and Director of the HDSA HD Center of Excellence, University of Alabama

Dr. Victor Sung gave a clinical overview of HD, sharing details about the natural history and progression of HD. He noted that HD is considered a rare disease and is less well known than other diseases. Even still, the prevalence of HD is actually similar to ALS, which gets a lot more "press time" and is more recognizable by name.

Even as a less well-known rare disease, HD has had massive importance in the landscape of genetics - the discovery of the gene that causes HD, led by Dr. Nancy Wexler with the help of families from Venezuela, directly led to the Human Genome Project.

Dr. Arik Johnson, Interim CEO and Chief Mission Officer of the Huntington's Disease Society of America, shared opening remarks, thanking everyone for participating in this important event that brought 200 people affected by HD into a direct conversation with the United States Food and Drug Administration.

Victor detailed the genetics of the disease; that it is caused by the repetition of a C-A-G letter code in the huntingtin gene that's on the 4th chromosome. But he also highlighted the socioeconomic burdens of HD and how it differs from other diseases. HD impacts wage earnings from people affected by the diseases as well as caregivers, generation after generation. It also differs from other brain diseases that are sporadic, like ALS, in that it can impact many people within a family, sometimes entire generations. The details that Victor shared demonstrated to the FDA that the tragedy of HD is truly unparalleled.

He then showed data that suggests there are changes occurring before people start to show symptoms of HD, like behavioral and cognitive changes associated with thinking, learning, and memory. This suggests developing early treatments for HD is potentially feasible.

He ended by saying that we have no disease modifying treatments for HD right now, but we are pushing into that realm. "The future is bright. There are lots of things happening in the disease-modifying space for HD. But we can only do this together, and we **will** do this together."

Panel 1: Health effects and daily impacts

The first panel began with representatives at the pre-symptomatic, early, and mid stages, as well as a family member. They shared their stories about living with HD at each of these stages, highlighting how the disease, or knowledge that they'll develop the disease without some sort of intervention, has affected their lives.

Speakers underscored the impact that HD has had, influencing the decision to have biological children, creating early conversations around life insurance and retirement planning, and becoming a caregiver to parents who represent a constant reminder of what the future holds unless we figure out a way to slow or stop HD.

Speakers detailed the changes they've experienced because of HD, such as a reduced ability to think through problems, multitask, and organize their lives, which has led to a loss of jobs, the ability to drive, and independence, causing an overall feeling of a loss of identity. Physical exercise and outdoor walks that used to be the highlight of a day now brought feelings of dread because of balance issues that have caused falls, leading to cuts so severe they require stitches. The emotional changes that HD brings were also discussed, with the onset of depression, anxiety, and panic disorder.

Loss and grief were common themes. Along with the emotional ups and downs of HD, hope itself has become an emotional rollercoaster for those affected by HD, with the highs many experienced during the start of the GENERATION-HD1 trial, and the lows from the halting of that same trial in March of 2021.

Panel 1: Group discussion around health effects and daily impacts

> **"There were over 60 people living with HD in the room and over 140 people who registered to attend virtually from across the globe, from 43 US states and 8 countries. The HD community was ready to be heard! "**

Questions that were discussed with the group from the HD Symptom and Treatment Impact survey around the health effects and daily impacts of living with HD were:

- Of all the symptoms that you have experienced because of your condition, which 1-3 have had the most significant impact on your life?
- Are there specific activities that are important to you, but that you cannot do at all or as fully as you would like because of your condition?
- As it relates to your condition, what does a good day / bad day look like?
- How has your condition changed over time?
- What worries you most about your condition?

Pre-symptomatic

People living with pre-symptomatic HD said that cognitive and psychiatric symptoms are the primary issues, citing anxiety, depression, emotional outbursts, mind fog, and difficulty concentrating.

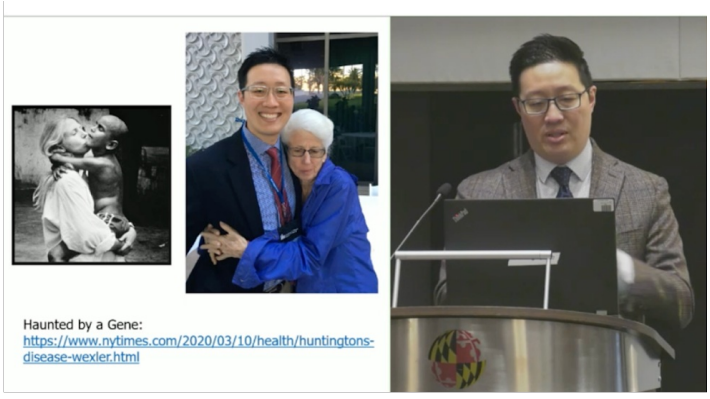
People shared that even at this stage they began to feel a loss of identity. Some people with high-level jobs, such as those working in finance on Wall Street, were fired because of changes experienced due to HD even 5 to 10 years before anyone on the outside would say they had symptoms.

The group noted that even though they are typically considered pre-symptomatic until HD-associated movement symptoms begin, there are real problems that begin to present in this stage. People overall felt like they were being forced to live their lives in a holding pattern, unable to receive treatment because they didn't yet have symptoms, but also unable to receive treatment for the symptoms they were experiencing because they were being told they aren't severe enough.

Early-stage

People living with early-stage HD cited some of the same issues as the pre-symptomatic group, highlighting problems with anxiety, depression, difficulty concentrating, and memory lapses. While the overarching issues were the same, the tone captured the more advanced state of these issues.

Overall, people cited that at the early-stage HD has caused them significant worry about the future. They fear becoming a burden to their loved ones and the impact that HD will have on their children. The thinking problems that increase during this stage cause people to make poor financial decisions and prevent them from being able to pay their own bills.



Dr. Victor Sung, a Professor of Neurology from the University of Alabama, gave a clinical overview of Huntington's disease, detailing the work done by Dr. Nancy Wexler to find the genetic cause of Huntington's disease.

Participants stated that the early-stage brings changes related to independence – those who were once fully independent transition to being fully reliant on others for many basic functions, which is devastating, particularly for those who don't have a support system. And for those seeking intimate relationships, HD has made dating "impossible". An audience

member with early-stage HD shared that they're afraid to hold their grandchildren because of balance issues. Others shared that they avoid family functions because they don't want to go in public or be seen for fear that people will think they're drunk or on drugs.

This group also said emotional outbursts were a serious concern, becoming dangerous at times with the fear of law enforcement involvement. Others detailed the increase in paranoia at this stage, causing one person to hold a shotgun up against their own child because they didn't know who they were or why they were there. Situations with law enforcement and nursing staff can easily become reactive because of such paranoia.

Mid-stage

People living with mid-stage HD shared that they're unable to do work that they've done in the past or have been trained for, that they've lost independence, that they're no longer able to drive, and that they're financially unstable. The massive financial burden that HD causes was noted, both from the loss of income for the person living with HD as well as the loss of income from the caregiver rerouting their time to take care of the person with HD.

At the mid-stage, components of a good day related to things many of us often take for granted – a good night's sleep, forgiving yourself for missteps and realizing it's okay to not be perfect, and not having urinary incontinence. Those in this group cited bad days as those fraught with obsession over death and suicidal ideations.

For people in the mid-stage of HD, participants cited that symptoms around clumsiness, movements, anxiety, and difficulty concentrating have had the biggest impact on their lives. They shared that their ability to walk and speak has degraded to the point of constantly stumbling and having slurred speech, which causes them to feel uncomfortable in social situations and lose social connections and peer support. Gastrointestinal issues, which are a known problem for many people living with HD, were brought up for the first time in this group.

For people in mid-stage HD, many were most worried about the capacities they're losing, or will lose next. They shared grief over loved ones constantly losing pieces of themselves. Caregivers expressed worry over what will happen when loved ones need more consistent full-time care and the financial impact that will have on their families.

Panel 2: Current approaches to treatment

The second panel centered around current approaches to treatment, bringing in a different group of panelists, one each with pre-symptomatic, early, and mid-stage HD, along with a family member of a person living with pre-symptomatic HD.

Panelists shared that the psychological and physical toll of HD is grueling. People with pre-symptomatic HD want to participate in trials to prevent the onset of the most severe symptoms but are told their disease hasn't progressed enough to be considered for trials.

The frustration around wanting to try but not being able to is defeating. One panelist stated, “We know what happens when we do nothing. We just want a chance to fight.”

> **“People were most interested in medications that could potentially treat thinking changes brought about by HD, which could help them keep their jobs for longer to offset the financial burden associated with HD. ”**

Those with multi-generational experience with HD shared stories of watching their parents use treatments for their movements, only to have their engagement with the world slowed. Panelists shared their experiences participating in clinical trials that were ultimately halted, saying that even though they felt they were benefiting they no longer had access to that medication. They also detailed the heart wrenching conversation with their children, having to explain the lack of access to a drug they thought helped.

A heartfelt plea was made to the FDA for a special designation for unproven and unapproved treatments that make people feel better regardless of trial outcome, to help develop better determinants for trial endpoints, to move trials into pre-symptomatic groups, to focus on cognitive, psychiatric, and behavioral symptoms, and to help increase funding for HD research.

Panel 2: Group discussion around current approaches to treatment

Questions that were discussed with the group from the HD Symptom and Treatment Impact survey around the current approaches to treatment for HD were:

- What are you currently doing to help treat your HD symptoms?
- How has your treatment regimen changed over time and why?
- How well does your current treatment regimen treat the most significant symptoms of HD that you experience? How well do your treatments improve your ability to do specific activities?
- How well have these treatments worked for you as your condition has changed over time?
- What are the most significant downsides to your current treatments and how do they affect your daily life?
- Short of a complete cure, what specific things are most important to you around delaying the progression of HD?
- If you could have a reduction in symptoms, what would make the most positive change in your life?
- Do you have any concerns around participating in aclinical trial?

Pre-symptomatic

At the pre-symptomatic stage, many people indicated that they're taking medication for anxiety and depression. Tellingly, caregivers also stated they're on similar medications along with blood pressure medication, suggestive of the ripple effect that HD has through families. Participants also cited non-medical treatments that have been suggested to slow disease onset, such as exercise, good sleep, a healthy diet, and a positive mindset.

By and large the most significant downside noted from the pre-symptomatic group was their inability to qualify for clinical trials. While they see massive changes in themselves that they believe are from HD, they're constantly told they don't have symptoms and thus don't qualify for trials.

For people with pre-symptomatic HD, they expressed a strong desire to try anything in trials that could slow disease progression or delay onset. They noted that a treatment wouldn't have to even hold the promise of a cure, and that delaying onset would be enough. People were most interested in medications that could potentially treat thinking changes brought about by HD, which could help them keep their jobs for longer to offset the financial burden associated with HD.

A representative from the FDA shared that they're having a virtual patient listening event on December 4th to hear from the community on what they think about enrolling in a clinical trial at pre and early symptomatic stages. She encouraged everyone from the Huntington's disease community to register, listen, then add their thoughts into the meeting notes. After the meeting they're going to develop a summary to help inform the FDA and stakeholders in drug development. Registration for this event will close December 3, 2024.

Early-stage

Along with anxiety and depression medication mentioned by the previous group, people living with early-stage HD stated that they're prioritizing exercise, getting outside more, and participating in music therapy. People also said that they're challenging themselves intellectually, by going back to school and playing brain games.

In the early-stage HD group, some felt that medications used to control movement symptoms have been critical. However, some of these medications don't work for everyone, so trying several regulatory approved medications allowed them to find one that helped

control their movements while also decreasing negative mental side effects that caused suicidal ideations. Others found that ADHD medication has helped with thinking and memory problems. One participant stated that medication that she takes for anger outbursts has allowed her to keep her job and has helped keep her family together. Several in this group cited medical marijuana as being a “game changer”, although laws vary state-by-state in the US, which some noted as being an issue for access and regulation.

Many people in the early-stage group noted challenges around trial participation related to traveling far distances and logistical difficulties for caregivers who often coordinate care and trial participation. Others detailed challenges with navigating the US healthcare system. Some HDSA Centers of Excellence don’t accept some insurance plans and some medications prescribed by physicians for HD symptoms aren’t covered by insurance.

As in the previous group, people living with early-stage HD stated that they want medications that could help with cognitive effects and thinking problems. This could help with time management issues, help people keep their jobs for longer, and defray financial concerns by extended wage-earning years. Improving cognition could also help people communicate better and maintain independence for as long as possible.

One person from the early-stage HD group cited that they just wanted to retain their dignity. Being able to go to the bathroom and take a shower on their own would have the most positive change in their life.

Mid-stage

From the mid-stage group, some cited that they’re taking sleep medication. One said that sleep apnea machines have helped with getting better rest. Others said they’re working to improve the small things that affect health, like dental, vision, and hearing problems, that can add up over time.

Others mentioned small lifestyle changes that have made a difference, such as always using a straw and moving to a single level house so that falls down stairs are less likely. Those in the mid-stage group stated they’re working to make accommodations for what they or their loved ones are experiencing, which can be as simple as putting a tablecloth down instead of trying to get someone to eat more neatly. Astutely, one participant noted that you have to think outside the box for HD to find things that will work at each stage.

> **“Many experiences were punctuated with statements around wanting to not just survive but to live, wanting to participate in trials, wanting to be a part of the science that will get us a treatment for HD. ”**

One participant said that her life changed when her husband went on antipsychotics, which helped control abusive and paranoid behavior.

As for the previous groups, trial location was a concern. One participant from the mid-stage group said, “I will do anything if it means helping my husband and helping my kids”. HD is a family disease, evidenced by the caregivers that stood up, literally and figuratively, at the recent FDA meeting for their loved ones with HD. Another woman said she would give her life in a trial if she thought that meant it would secure the future for her daughter and granddaughter. A sentiment she said that she hopes doesn’t fall on deaf ears.

The conversation will continue

A representative from the FDA shared that they’re having a virtual patient listening event on December 4th to hear from the community on what they think about enrolling in a trial at pre and early symptomatic stages. She encouraged everyone to register, listen, then add their thoughts into the meeting notes. After the meeting they’re going to develop a summary to help inform the FDA and stakeholders in drug development. Registration for this event will close December 3, 2024.

Arik delivered closing remarks, thanking everyone who participated, both in person and online. He noted that we have a lot of work left to do and this is just the first step in the process. There is still a lot that wasn’t said, but the work will continue to ensure that everyone is heard. Every lived experience with HD, in every stage of HD, is impactful and matters, and will be used in future decision making.

Arik noted that there are things that can be done right now, such as participating in observational studies like ENROLL-HD, POWER-HD, and MyHDStory. He noted that it’s important for everyone to take care of themselves and reach out to people if you need help.

The takeaways

The discussions with the pre-symptomatic group highlights that the term “symptomatic” needs to be reconsidered, as the time when many are considered to be without symptoms is filled with behavioral and psychological changes. For them, the pre-symptomatic stage doesn’t mean they don’t have symptoms. People reported feeling frustrated that they see that they’re changing, with anxiety, depression, or executive functioning, but people don’t see that on the outside and doctors will tell them to come back in 5 or 10 years when they start to show symptoms.

At points, an FDA representative took the microphone to directly ask the audience what types of medications would be most useful for them. Almost everyone agreed that having something that works to improve cognition would be their number one choice. This could improve their thinking so that they could keep their jobs longer, defray the financial burden of HD, and help them communicate better with loved ones.

The direct exchange between the FDA and HD families underscored what this meeting was all about – a two-way conversation to help the FDA understand the needs of HD families to get this community treatment options as soon as possible to improve their lives. The HD

families were heard.

Thank you!

Any meeting to educate the uninformed about HD will be emotional. There's no way to describe HD without stirring feelings of loss, grief, and despair. Even through that though, a strong, bright thread remained – that of resilience, that of hope, that of determination.

Many experiences were punctuated with statements around wanting to not just survive but to live, wanting to participate in trials, wanting to be a part of the science that will get us a treatment for HD. Along with the heartache that HD brings, there's no doubt that the FDA also heard the underlying message of strength within this community.

To everyone from the community who participated, attended, and shared your stories - *thank you*. Thank you for your willingness to be vulnerable. Thank you for your honesty. Thank you for standing up to change how the FDA views HD. You represented every HD family member who couldn't be in that room, and you did it gracefully. Because of you, the needle was moved today. Because of you, we're one step closer. Because of you, the HD community stood face-to-face with the change makers and was heard. *Thank you.*

The authors have no conflicts of interest to declare.For more information about our disclosure policy see our FAQ...

GLOSSARY

Food and Drug Administration The government regulatory authority in the US responsible for approving new drugs

clinical trial Very carefully planned experiments designed to answer specific questions about how a drug affects human beings

observational A study in which measurements are made in human volunteers but no experimental drug or treatment is given

therapeutics treatments

prevalence A figure estimating how many people there are in a particular population who have a certain medical condition.

genome the name given to all the genes that contain the complete instructions for making a person or other organism