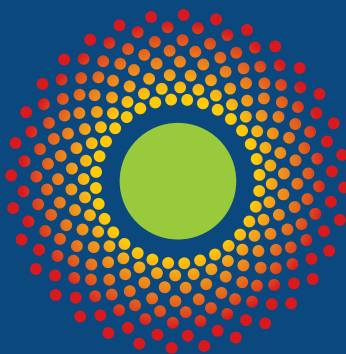


Enroll!

Updates from the Enroll-HD
global community



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SPRING 2016

THE YOUTH CONNECTION

The global young people's organization HDYO grows up

Life for a young person in an HD family can be tough. At home, there may be responsibilities such as helping with household chores or being involved in caregiving. Outside the home, there's the constant feeling of being an outsider. While other teens and young adults focus on studies and fun, youth in HD families have a separate, secret life that they rarely get the chance to talk about with someone who understands. Since the symptoms of HD usually strike adults, children and young people have sometimes been a bit of an afterthought when it comes to services and support.

When they met for the first time at the 2009 HD World Congress in Vancouver, two young people from HD families, 23-year-old American BJ Viau and 21-year-old Englishman Matt Ellison, discovered just how big this problem was. Around a dozen young people in HD families from around the world, including the two of them, had come to the congress on scholarships. As they all got to know each other they soon realized that the lack of information and support for children, teens and young adults was a universal issue. Across the globe young people were often left out of the HD community. "Youth weren't told about HD, they didn't go to fundraisers, young people didn't participate in research," says Viau.

The lack of accurate information was a problem, as was the isolation that can affect young people in HD families. "The impact of having a parent or other family member who has the illness is huge," says Matt. "But youth support is not in the spotlight at all."

If young people became more involved in the HD community, they agreed, everyone would benefit.

A movement is born

Following that meeting Ellison and Viau formed the Huntington's Disease Youth Organization, HDYO. The first priority was to create a website with clear, useful information about HD that made sense for teens and young adults. Launched in 2012, the HDYO website now includes a wealth of features such as a question and answer section, email support, information for parents and friends, a discussion forum, and various sources of information and advice. At least some content is available in nine languages.

"The impact of having a parent or other family member who has the illness is huge."

— Matt Ellison

One striking element of the site is a set of videos of young people from around the world talking about their experiences as caregivers, family members, and people with HD. Many are raw and intense, but some are also funny. Many youth in HD families never get the chance to meet someone else in their situation, says Ellison, so the videos are the next best option: One young person speaking directly about their own worries and experiences and difficulties.



HDYO's first US youth camp in summer 2015



Matt Ellison (l) and BJ Viau founded HDYO to connect young people worldwide.

By 2013, HDYO had raised enough funding to begin paying Ellison as a project director (Viau is the unpaid board chair). The group also organized a week-long youth camp in Spain, bringing together young people from across Europe for that chance to meet face-to-face.

The following year HDYO hired youth worker Chandler Swope, based out of the Washington, D.C. area in the US. She counsels young people one-on-one, works directly with families to find ways to talk about the disease, and connects with other HD families on social media. She also goes to regional events where HDYO hosts families to come out together for rock-climbing or other group activities.

HDYO's next goal was to host a youth camp in North America. "Taking young people out of their environment gives them a whole new way to open up, and a new sense of safety to share what's going on," says Swope. Several such getaways had been held in the UK and Europe but none had yet been organized for the US or Canada. "There aren't many opportunities to meet other young people in the US besides a convention," says Ellison.

Meet you at camp

Late last August the plan became reality, with a weeklong summer youth camp held at a campground in Maryland.

The camp had many different purposes: a chance to learn about HD (and dispel myths), make new friends and have heart-to-hearts. "Within 24 hours the campers were sharing some of

their deepest darkest secrets," says Swope. In some families shame or fear of saying the wrong thing makes it hard to talk about difficult issues. Camp is a chance to talk openly about those problems with peers. It's also an opportunity to have a break from caregiving or potentially stressful family situations and have some fun. "So much of their lives at home are focused on an affected parent, and that's where all the energy and time goes," says Viau. The camp is bordered by a river and a bay, and offers kayaks, standup paddleboards, volleyball nets and a swimming pool, as well as a huge harness swing.

Attendees were between 15 to 23 years old. Most had not yet been tested to see if they have the expanded HD gene, but some knew their status. A few campers were symptomatic.

At last summer's camp, group conversations included weighty subjects like the decision to test, relationships, or grief and loss. But a lot of the time was reserved for swimming or obstacle courses, and opportunities to make new friends.

For 22-year-old Mariah from Michigan, those new friendships were the best part about camp (Mariah was willing to have her full name used in this article but to protect her privacy we have not included it). She'd never met anyone else from an HD family, but even before the bus from the airport arrived at camp she'd already heard three other camper's life stories. "It was really cool," she says. "We

"It was cool to hear different people's stories, and made us all realize that we're all going through the same thing."

— Mariah

were talking about how HD affects you and your friendships and your relationships and family members. It was cool to hear different people's stories, and made us all realize that we're all going through the same thing."

For her, another highlight was hearing Western Washington University researcher Jeff Carroll, who is from an HD family and studies the disease, talk about research progress. "He explained HD from a science point of view, and it was very helpful to hear the facts," says Mariah.

The week would bring a life-changing experience for her. Adopted as a young girl, she'd never met her biological mother and didn't know how to find her. But Mariah did know that HD ran in that family. On the second night at camp the campers gathered around a bonfire, wrote down their biggest fear on a piece of paper, then tossed it in the

fire. Mariah says her fear was that her biological mother might die before she ever got to meet her. She wrote it down and cast it into the flames.

Later, after talking about her situation with new friends at camp, some helped Mariah track down her biological mother—turns out she was living in a nursing home just over an hour away from her own town. She now visits every week.

Finding a friend

The needs of young people in HD families often get short shrift, says Melinda Kavanaugh, a professor of social work at the Helen Bader School of Social Welfare at the University of Wisconsin-Milwaukee. Youth caregiving is even overlooked as a subject of scholarly research: There are 22 studies exploring youth caregiving, in comparison to roughly 2,000 for adults, she says.

Before she was a professor, Kavanaugh was in the HD community for 15 years, and a social worker for six years. She created the group for children and youth to ease their isolation. Rather than sitting in a circle and talking—which many youth might not want to do—it emphasized activities like putt-putt golf or bowling. The idea was to offer a chance to hang out with other young people who know what it's like to have a parent with HD, or be a part-time caregiver.

“A lot of people are scared to have friends over, they don't know how their parent or grandparent is going to act,” agrees Mariah. One true friend who understands can make a huge difference: “If you have that one person you could trust, things might be easier.”

In collaboration with the HDYO board, Kavanaugh has conducted a formal evaluation of the youth camp to identify what worked and what didn't. The complete analysis has not yet been published, but she's already found that even this short experience made a big difference. “Not only is there a clear increase in quality of life and self-esteem and overall social support, but [campers] said things along the lines that they now have friends that understand them and their situation,” she says. Campers felt less embarrassed about HD and more hopeful knowing that other people are in their shoes. Swope has set up a private Facebook group for campers that she also monitors so that friendships forged at camp can continue to develop.

The next chapter

HDYO is still growing. “It's an amazing organization,” says Cath Stanley, chief executive of the Huntington's Disease

Association in the UK. “They've done an incredible job putting together quality information which just wasn't there before.”

Ellison and Viau believe their most important accomplishment is putting the concerns of young people in HD families on the map and demonstrating the need for specialized youth support and services. “Starting out we just hoped someone would like our website,” says Ellison. “And it's grown so much from that.” At the end of 2015 the website added a new component, HDYOLand, to help parents talk to kids between ages 5 and 12 about the disease.

Applications are now closed for 2016 youth camps in both North America and Europe (check the HDYO website, hdyo.org) that will take place in August. The North American camp, planned to be held in the Washington, DC area in partnership with the Huntington's Disease Society of America, will host 50 people between the ages of 15 and 23 from the US and Canada. The European camp will bring roughly 40 people between the ages of 15 and 25 from the United Kingdom, Ireland, Belgium, Germany, Sweden and Norway to a site in southern England. For those accepted there is no charge for transportation, lodging or food.

Future goals include establishing more youth workers around the world through partnerships with local organizations. Viau and Ellison hope to change the role of young people in the HD community. They believe that helping young people cope with HD will pay back dividends over the long term. “If we can support people when they're young and educate them, they'll be more likely to be motivated to get involved in studies like Enroll-HD, or fundraising or advocacy,” says Viau. “We're empowering them to fight back and do whatever they feel comfortable. The earlier we can reach them for support, the better.”

10,000!!!

On April 8 2016, Enroll-HD reached a milestone as the 10,000th person signed up to be part of the study. That person joined 9,999 others in the worldwide collaborative effort to understand more about HD and provide an infrastructure for more and better research and provide an infrastructure for more and better research, including clinical trials of potential new drugs. Enroll-HD is now growing at full speed, adding about 1,000 people every quarter of the year. For current numbers, check the website at www.enroll-hd.org.

A FIRST FOR IRELAND

Enroll-HD now underway in Dublin

Enroll-HD is now up and running in Ireland, the first time the country has joined a large-scale international study of the disease in people. The launch was the combined effort of the Huntington's Disease Association of Ireland (HDAI) and neuropsychologist Niall Pender, who together put resources in place to launch the study. "There's a great interest in the HD community," says Pender, who is principal clinical neuro-psychologist at Beaumont Hospital in Dublin, where the study site is located. "The patients and families are behind us, they're really keen, because there's no other major research project in the country." The first participant in Ireland officially joined the study in November 2015.

"We wanted to make sure that Irish people had the same opportunity to engage in research," says Patricia Towey, information and services coordinator for the HDAI.

"We're hoping that having Enroll-HD in Ireland will create more awareness among health professionals as well. It will encourage professionals to get involved in research if they see that Irish people are interested in contributing to research."

Prior to Enroll-HD some clinicians in Ireland had been involved in smaller research projects but the infrastructure wasn't yet in place to join a study like REGISTRY, the European observational study that came before Enroll-HD. Such studies usually have specific requirements about how various tests should be conducted and how data is collected and maintained. In order to join, a site needs staff who can be trained up in the specific methods for the study, as well as facilities to conduct the tests.

HDAI helped get this process off the ground with an initial grant. Pender then needed to arrange for the space to see study participants, and for staff who could handle the administrative aspects of it such as documentation and systems. "You need

somebody dedicated, to make sure that's up and running and to answer queries," he says.

Pender aims to recruit about 100 people in Enroll-HD. "I can't see that as being too challenging, given the popularity and interest in the HD community at the moment," he says.

New hopes for HD help

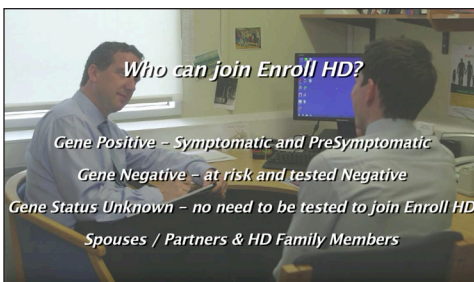
Beginning last spring the HDAI began introducing the study to people in the community at support meetings and seminars. HDAI volunteer Brian Moore, a professional cameraman, produced a short video featuring presenter Charles Sabine that briefly explains the study. "It demystifies it for people," says Towey.

In mid-June the study was featured on a national TV program called Nationwide. "Because it's a large-scale international study, it gets attention in its own right," says Pender. "That gets the message out there." Raising awareness in this way makes it easier to argue for more public funding for HD services, he says.

Currently Ireland has few specialized services for HD: There's only one genetic counselor knowledgeable about the disease, and there's no multidisciplinary clinic that can address the diverse medical needs that the disease often involves. Instead it's up to a patchwork of experts. "We're poorly serviced at the moment for HD," says Pender. "That was the real importance of getting Enroll-HD here." He and a colleague, a neurologist in Galway, are exploring the possibility of setting up three specialist sites across the country with multidisciplinary teams familiar with HD care.

In the meantime Pender welcomes the launch of Enroll-HD. "We're incredibly excited to be a part of it, it's a big step in terms of getting the services for HD," he says. "I've been amazed by the positivity of the patients. I know that research can be scary for people, but the HD community has been excited about it."

"Research can be scary for people, but the HD community has been excited."
— Niall Pender



A short video introduces Enroll-HD to the Irish community, explaining what the study is for and what it involves.

A NEW APPROACH IN CHILE

The study expands to a clinic with a mission

Many Enroll-HD sites are located at academic medical centers—institutions with medical schools and teaching hospitals, and often physically linked to elite universities. But the first study site to open in Chile is quite different. It is located at CETRAM, a unique patient-centered clinic in a working-class neighborhood in Santiago, the country's biggest city. Since it launched at the end of 2013 it's become the largest site in Latin America, with 80 people participating in Enroll-HD.

"Enroll is very important to us—it's a new thing to offer," says Daniela Albuquerque, executive director at CETRAM (Centro de trastornos del movimiento, or "Movement Disorders Center" in English). Participants "have the possibility of being part of something bigger that has benefits for all. It's not only for you, for your family, but for all."

This community approach is part of the philosophy of CETRAM, a movement disorders clinic founded about 15 years ago with the aim of encouraging more collaborative relationships between medical professionals and families dealing with disease. (They don't use the term "patient," and refer instead to "users" or just "people".) The idea is to replace the traditional hierarchical relationships of medicine with a more grassroots approach in which health professionals and people seeking treatment are all part of a team.

The clinic was founded with the help of the University of Santiago, which offered space in an old hospital. In the



Osorio, CETRAM president Pedro Chana and neurologist Claudia Perandones



CETRAM's Daniela Albuquerque and businessman Rodrigo Osorio

beginning only four people were involved—including Albuquerque and neurologist Pedro Chana, now CETRAM president (they are husband and wife). They worked closely with movement disorders patients' organizations to shape the vision of this new style of clinic. "People with disabilities are the most important part of the process," says Albuquerque (she spoke on behalf of herself and Chana during an interview in English). "They have developed the process of rehabilitation and medical support from a family and community point of view."

*"People with disabilities are the most important part of the process."
— Daniela Albuquerque*

The philosophy leans on the idea of "transknowledge," the idea that health professionals and

families collaborate to learn from one another and improve health. "People go to the doctor believing that doctors know more," she says. "That's not true. We are professionals, but at the same time people know about their own disease, their suffering." The goal is to empower people to talk about their own experience and share their knowledge to improve health care.

Some doctors may think the idea of sharing power with the patient is naïve or misguided, says Albuquerque, but she and Chana note that the authoritarian approach used by some old-fashioned practitioners rarely works very well. "When a user comes out of your office, they do whatever they want or need"—not necessarily what the doctor orders.

The team approach

Today CETRAM has grown to a staff of 50 medical professionals and more than 3,000 users each year, about 200 of

whom have HD. The clinic has a close relationship with the university: Most of the CETRAM staff also have titles at the university, and medical students, movement disorders fellows and rehabilitation medicine students all come to the clinic to learn. Albuquerque, an occupational therapist, is also the coordinator of the occupational therapy degree program at the Medicine Science Faculty at the university. In addition the CETRAM website hosts an open-access library of research and coursework in movement disorders, and many clinicians are also involved in research.

A person treated at the center for the first time will meet with a group of experts; a neurologist or movement disorder specialist, a rehabilitation specialist, usually a patient advocate from a disease association, and perhaps a student as well. Family members are encouraged to be part of this meeting.

The goal is a comprehensive assessment of all the needs in a person's life, to invite a broad discussion about values rather than focusing on one specific physical symptom, says Albuquerque. "The disease is only part of the problem," she says. "Someone might say, 'I have this tremor,' and we'd say, 'Who do you live with, and where do you live? Do you have problems with money, with education?' You get the big picture of the quality of life, the real problems."

Following the assessment the team may suggest speech therapy, physical therapy, and even community-based rehabilitation, in which the specialists and physicians support people at home.

Help for HD

For people with HD there is now another resource: A day care center where people with diagnosed disease can be looked after, meet other HD families, and participate in therapy. The center was the inspiration of Rodrigo Osorio, the president of the Agrupación Chilena de Huntington, a nonprofit disease association. His intention was to help people with HD who have little other support. "The dream was to do something for people who have HD, especially people who are in a very bad situation not only because of the disease, but have no network or family—because the family was destroyed by the disease," says Osorio.

Setting up a day care center wouldn't only improve the quality of life for people dealing with HD. It would also provide education, helping family understand the disease, and allow family members to work rather than be full-time caregivers.

The people at CETRAM were interested in Osorio's idea. With support from officials in the Chilean government and a contribution from the Swiss embassy, Lugar Pura Vida ("Space for pure living" is a rough English translation) was launched in 2013 in a cottage right next door to CETRAM. (Osorio, a businessman, describes it as a "joint venture.") Now, about 15 people come each day, ferried from all over the city by the center's van. They're given lunch—essential

for some people who may not have enough to eat at home—and engage in activities like gardening and music.

It's the first such center in Chile, says Osorio, and he hopes that the model can be expanded to other sites and even other nations.

The collaboration between the Chilean HD organization and

CETRAM also opened up the possibility of hosting an Enroll-HD site. The structure of the Enroll-HD platform, where de-identified data is made freely available to any legitimate researcher, fits well with their philosophy. Osorio says that the Agrupación has been introducing the study to the HD community, to explain how it works and why people might want to join. "Users and family know this is important, not only for them but for all the community with HD," says Albuquerque. "It really is possible to do academic research and work with people in equality and in a respectful relationship."

*"It really is possible to do academic research and work with people in equality and in a respectful relationship."
— Albuquerque*

WANT TO KNOW MORE ABOUT THE DISCOVERIES THAT ENROLL-HD DATA IS MAKING POSSIBLE?

There are now descriptions of 35 research studies that dip into the data being collected across the world. Read more about this science at <https://www.enroll-hd.org/for-researchers/current-enroll-hd-data-projects/>.

BRINGING IT TOGETHER

Site investigator meetings keep Enroll-HD running smoothly

By 2015 Enroll-HD was underway on four continents, in some sites for as long as three years. With so many sites in so many nations it was time for the core personnel to meet up again for an investigator meeting. Getting everyone together ensures that every site is up to date and that each is conducting the study the same way. The meetings act like glue to hold this very large study together.

But since Enroll-HD takes place all over the world, it isn't practical to convene everyone at one meeting. Instead five separate site investigator meetings were held in 2015; one each for Australia/New Zealand, North America, the UK (including Scandinavia), Western Europe and Southern Europe. (There wasn't one in Latin America because only a few study sites are up and running.) Between a few dozen and more than 100 people involved in running Enroll-HD attended each two-day meeting; the largest was in Madrid, with 138 people. Attendees included the principal investigator and study coordinator from each site, as well as staff who work with study participants.

The meetings included updates on the progress of the study, new and refresher training, and reviews of protocols. Talks focused on the idea of Enroll-HD as a platform and how it can speed recruitment for future clinical trials. At the European meetings, teams described research projects that tap into the data now available from the study.

The North American meeting was held in Tampa, Florida in the US in collaboration with the annual Huntington Study Group (HSG) meeting. The two meetings are a natural fit, says Liz McCarthy, director of special programs at HSG, because both bring together similar networks of investigators and site staff to share updates and participate in education and training. "It makes sense, because 80 to 90 percent of Enroll-HD sites in North America are also HSG sites," she says. "It's mutually beneficial for both groups to have that meeting together."

At the Tampa meeting, presentations included a panel session of the North American members of the Enroll-HD steering committee, including Martha Nance, MD, director of the HDSA center of excellence at Hennepin County Medical Center Minneapolis, and neurologists Jody Corey-Bloom, MD, PhD, of the University of California, San Diego, and Mark Guttman, MD, FRCPC, of the Centre for Movement Disorders in Toronto. They discussed participant recruitment and what motivates people to get involved in Enroll-HD.

The HSG is a nonprofit research organization that facilitates clinical research studies and trials for HD, with a network of about 400 investigators, coordinators and clinicians across the world, primarily in North America. The group supports research, education and training for its own membership and for the larger HD professional community. Its annual meeting includes HSG members, advocacy groups, industry representatives, and HD family members. This year brought its largest registration so far, with 380 people over the course of 4 days.

The next set of Enroll-HD investigator meetings will take place in two to three years.



RESEARCH UPDATE FROM PALM SPRINGS

This year, CHDI's annual Huntington's Disease Therapeutics Conference (HDTTC) in Palm Springs, California brought something new and an indication of where HD research is now heading: a session packed with updates from clinical trials.

Speakers at the three-day conference, which includes researchers and clinicians from universities and pharmaceutical/biotech companies, recapped some of the year's big findings, such as the study that identified genes in humans that modify HD—that is to say, genes that delay the start of symptoms.

Other talks covered efforts to visualize the 3-D structure of huntingtin, the HD protein; research on the role of the

normal, non-mutant huntingtin protein; identifying the brain circuitry involved in emotional problems in HD, and finding new and better ways to measure symptoms.

And there are now enough clinical trials of experimental HD drugs to justify a "Clinical Trial Update Blitz". This session included four short presentations with updates on the current status of trials such as Pfizer's PDE-10 inhibitor study and the Roche/Ionis (formerly Isis) study of the antisense oligonucleotide (see interview with Sarah Tabrizi on p. 8 for more details). For more coverage of the HDTTC see the Postcard from Palm Springs and the Clinical Trial Update Blitz on the CHDI website (www.chdifoundation.org) or HD Buzz (hdbuzz.net)



RESEARCH UPDATE

Q&A with Sarah Tabrizi



Sarah Tabrizi

Tabrizi is involved in HD at almost every level. She's professor of clinical neurology at the National Hospital for Neurology and Neurosurgery and director of the Huntington's Disease Center at University College London and the National Hospital for Neurology and Neurosurgery, Queen Square, which serves more than 800 families. She leads a large and busy clinical research lab. And she's also the global head investigator for the new huntingtin-lowering trial from Ionis Pharmaceuticals and Roche, as well as an investigator on two other ongoing drug trials: Pfizer's PDE-10 inhibitor and Teva Pharmaceutical's LEGATO-HD.

How did you get involved in HD?

I started my PhD in 1996, working with [Anthony] Schapira at UCL. Tony took me to a nursing home just outside London where I got to know HD patients. I realized that this was a terrible disease, and also a disease I wanted to get involved in doing something for.

Tell us about the Ionis trial, which enrolled its first patient last October.

The Ionis-HTT-Rx study is something I'm thrilled to be leading. I think it's hugely important.

The drug is a chemically modified piece of DNA that sticks to the huntingtin messenger molecules, and reduces the amount of the toxic huntingtin protein made. People sometimes call it gene silencing, and that drug is known as an anti-sense oligonucleotide (ASO).

Work in animal models showed that reducing mutant huntingtin slows the disease and in some cases allows brain recovery. This trial aims to test the safety of huntingtin-lowering in patients.

What can we expect?

In this study, the numbers will be too small to figure out whether the drug has a beneficial effect on the disease. Because it's a first-into-man ascending-dose study, the trial will last until late 2017. If it is safe and tolerated, then it will move forward into larger trial in which we will then test whether it's modifying the disease and having beneficial effects in patients.

What other projects are underway?

I'm still involved in trying to understand how the brain breaks down in HD. I have a big project looking at how the brain compensates for the effects of the mutant HD protein.

On the lab side, we're looking at the innate immune system, testing potential therapies in mouse models, and also working with cell models and human iPS stem cells to model aspects of the disease and test possible therapies in the cell dish. I'm also involved in looking at genetic modifiers of HD.

Much of your research has focused on biomarkers—why?

We want to be able to develop and test new therapies for HD. If we can't measure the disease really accurately in early-stage participants, it's going to be difficult to test new drugs. We need to have biomarkers of disease progression to know if the drug is hitting its target correctly, and whether the drug is modifying disease progression or pathogenesis.

How optimistic are you?

I think we still have a long way to go. But to me this is one of the most exciting times in HD. The Ionis trial is a milestone that families have been waiting for for decades. Many other things are coming through the pipeline.

Eventually, over the next 10 to 15 years, I want us to be able to do trials toward preventing the disease completely in people who have inherited the HD mutation. These things will all take time—but it's an important time we're in.

Enroll! is a publication of CHDI Foundation, Inc., a non-profit biomedical research organization that is exclusively dedicated to rapidly and collaboratively developing therapies that slow the progression of Huntington's disease (HD). As part of that mission, CHDI Foundation sponsors and manages Enroll-HD. More information can be found at: www.chdifoundation.org

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