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# EHDN *News*

EUROPEAN **HUNTINGTON'S DISEASE** NETWORK


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## World Congress 2013: highlights from Rio

HDBuzz, edited by Laura Spinney

**In 2013, the World Congress on Huntington's Disease headed to Latin America, a symbolic venue since it was largely thanks to HD families on that continent, and in Venezuela in particular, that the HD gene was identified in 1993. The congress took place in Rio de Janeiro, Brazil, over four days in September. HDBuzz reported from it on a daily basis. Here are some highlights from their roundup Buzzilia...**

An estimated 40,000 Latin Americans suffer from HD, **Rodrigo Osorio**, president of the Chilean patient association and a member of the Latin American Huntington's Network, a new network of HD clinicians, researchers and families, told the conference, while three times that number are affected by the disease. Those people could prove invaluable in clinical trials, but at the moment they are not receiving the same quality of care as their European and North American counterparts.

**Ignacio Muñoz-Sanjuan**, CHDI Foundation's vice president for translational biology, told the conference that CHDI is concentrating a lot of effort on synapses, the chemical junctions between neurons, whose function is damaged in HD. The current goal is to restore that function at different sites in the basal ganglia, brain structures that are affected early in the disease. In collaboration with Pfizer, CHDI hopes to have a clinical trial of a drug

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that inhibits a particular phosphodiesterase enzyme, PDE-10, up-and-running by early 2014. The drug inhibits PDE-10's normal function, which is to remove signalling molecules from synapses. As a result, animal studies have shown, it "calms down" over-excitable medium spiny neurons in the basal ganglia.

**Bernhard Landwehrmeyer** of the University Hospital Ulm, who chairs the EHDN's Executive Committee, pointed out that at least four companies are developing PDE-inhibiting drugs. He suggested that the field has a "high class problem", in having too many promising experimental treatments to choose from when it comes to mounting clinical trials to test them. How should they be prioritised? How much evidence is needed to make such decisions? A debate is needed, but the good news is that it is already feasible to consider running multiple trials in parallel, at experienced study sites on four continents.

Muñoz-Sanjuan also described early results with deep brain stimulation (DBS) of the basal ganglia, which suggest that it can reduce unwanted movements in HD patients. Neurologist **Binit Shah** of the University of Virginia said that a decade of research with DBS for HD had produced variable results overall.

**Andrew Churchyard** of Monash University asked if HD looks the same in genetically diverse countries. There are very few published studies examining its prevalence in Asian countries such as Japan and Taiwan, for example, and the few that do exist suggest that the disease may be much less common in Asia than in North America or Europe. In general, information on prevalence by country is lacking.

Neurogeneticist **Alexandra Dürr** of the Salpêtrière Hospital ran the Paris site of the prospective, observational TRACK-HD study, which was completed this year. She described how this "clinical trial without a drug" had furnished clinical scientists with a toolkit that will enable them to assess how many patients they need to recruit for any future clinical trial.

**Karl Kieburtz** of the University of Rochester told the conference that the medicines-regulating body in the US, the Food and Drug Administration (FDA), had recently indicated that it is now willing to consider biomarkers as primary outcome measures in clinical trials, when it comes to deciding whether to approve a drug for very early brain diseases. Thinking ahead to potential future preventive trials for HD, this represents a relaxation of the FDA's otherwise strict approval criteria based on clinical outcomes.



Representing pharmaceutical company Teva, **Anna Wickenberg** described two drugs the company has in development for HD—an immunomodulator called Laquinimod, and pridopidine (Huntexil, formerly ACR-16), which affects motor symptoms. With its collaborators, Teva is now planning a new trial with pridopidine in HD patients in 2014, to find the optimal dosage.

Landwehrmeyer addressed the issue of coping, since the reported rate of suicide among HD patients is between two and eight times higher than in the general population. A 2012 study by Marloes Hubers of Leiden University in the Netherlands found that 20 per cent of HD mutation carriers had thought of suicide in the previous month, and that depression and suicidal thoughts in patients was something that clinicians needed to attend to. **Ken Serbin**, aka blogger Gene Veritas, and **Charles Sabine**, both gene carriers, talked about their personal coping strategies.

**James Gusella** of Massachusetts General Hospital and Harvard University, one of those who led the hunt for the HD gene, described his current research looking in large numbers of patients for variants of *non-huntingtin* genes that might influence the onset of the disease.

**Neil Aronin** of the University of Massachusetts, who has been testing RNA interference (RNAi) gene silencing therapy in mice, has now shifted his efforts to the larger sheep brain in order to determine the optimal viral vector and dose. The results of small safety trials have been encouraging, so the group will now head to Australia to conduct a larger safety trial in 60 sheep.

**Doug Macdonald**, CHDI's director of drug discovery and development, described a clinical trial planned for late 2014 by pharmaceutical companies Isis and Roche, of another approach to silencing the HD gene: antisense oligonucleotides (ASOs). ASOs are infused into the spinal fluid rather than injected directly into the brain, like RNAi, and Aronin and Macdonald agreed that a combination of the two could potentially be even more effective at silencing the HD gene than either one alone. Another approach to gene silencing, DNA editing, is also showing promise. Meanwhile, a method is being developed that allows for the HD gene product to be measured in spinal fluid, meaning that the efficacy of these techniques could soon be quantifiable.

***Rodrigo Osorio (left) and other organisers at the WCHD***


***The HDBuzz team, Jeff Carroll (left) and Ed Wild***

# Barriers to predictive testing: a European perspective

Marina Frontali, Co-Lead Facilitator, Genetic Testing and Counselling Working Group

**Predictive testing for HD brings with it a number of ethical, psychological and social challenges that should be taken into consideration in pre- and post-test counselling of at-risk individuals.**

Guidelines exist that help healthcare professionals address these issues, and in centres that offer predictive testing, a multidisciplinary team of experts generally adopts a standardised protocol based on these guidelines. Because the protocol is relatively complex, and the multidisciplinarity of the team is a requirement of the guidelines, there tend to be relatively few centres offering HD predictive testing in each country, creating a problem of accessibility. Could this be one reason for the relatively low uptake of predictive testing among those at risk of the disease?

Recently, Alice Hawkins, Susan Creighton and Michael Hayden explored obstacles to predictive testing in Canada by interviewing 33 at-risk individuals who had requested the test at a clinic in Vancouver. The distance they had to travel to reach the clinic emerged as a major barrier to getting tested. A second obstacle was related to the inflexibility of the testing process itself, which those interviewed felt did not take into account their individual needs and circumstances. They complained about the lengthiness of the process, the high number of visits involved, and the paternalistic attitude of the experts they encountered, for example.

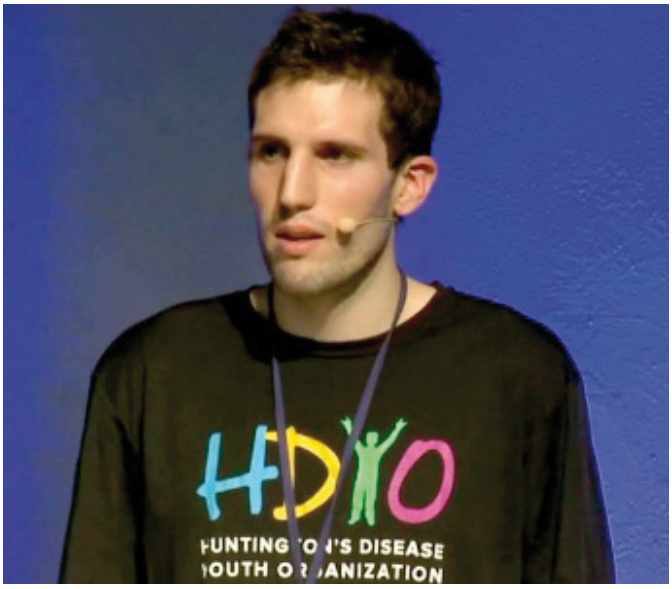
Removing these obstacles would clearly increase accessibility to genetic services, and also help improve at-risk individuals' sense of autonomy when it comes to making decisions about their health. The Canadian researchers propose several ways of achieving this, including tailoring the testing process to individual circumstances, and adopting novel telecommunication methods such as videoconferencing, to overcome the distance problem. They have reported positive results in tests of the latter solution, notably with the development and implementation of a dedicated, patient-friendly, educational predictive testing website, complete with interactive diagrams, video documentaries and personal stories of others who had considered testing.

The reasons for choosing to undergo—or not—a predictive test are very personal. The removal of barriers to accessibility is not meant to put pressure on individuals to take the test, but rather to facilitate their decision once they have made it. Investigating these barriers is important everywhere, not just in very large countries or regions such as British Columbia (with an area of around one million square kilometres) where the distance problem may be insurmountable.

Different countries have different obstacles and different potential solutions to removing them. In the Netherlands, for example, with an area of 41,000km$^2$ and a very good public transport system, distance may be not be the main obstacle. In Italy and other southern European countries where distance is a problem, on the other hand, telehealth may not be the solution, since Internet access is not available to many people in rural areas. In such places, the role of general practitioners in disseminating information about HD and predictive testing remains critical, at least for the time being.

The flexibility of the predictive testing process is another universal issue. It is very important that each step of pretest counselling is tailored to the individual's specific needs, rather than imposed as standard. Understanding those needs requires patience, discussion and a high level of professional skill, something that isn't always recognised by national health services, or given adequate financial support. But being flexible doesn't mean taking shortcuts. It is important that the person requesting the test understands that the process is complex for a reason: to protect them from any psychological, ethical or social problems the results of the test may raise.

It is essential that all over the world the guidelines are viewed, not as norms or laws to be followed to the letter, but as helpful indicators to how to avoid a test result having lifelong harmful consequences. "First do no harm" remains the first obligation of any health professional, and in this context, fulfilling it may require the flexible application of the predictive testing protocol.




# Changing attitudes: the power of documentary

Matt Ellison, Founder, Huntington's Disease Youth Organization

**Increasingly, young people are making their own documentaries as a way of sharing their experiences of HD. These films have the potential to drive positive change.**

Technology, especially the Internet, has enabled people to tell their story from their own living rooms. Blogs, pictures, forums, videos, documentaries—you name it, people are using it to get their experiences seen and heard. Technology has become a powerful tool in overcoming the stigma associated with HD—stigma that prevented previous generations of young people from speaking out.

It's not just technology that is driving change. Many in the HD community are working hard to tackle the stigma head-on, and perhaps the best weapon against fear is knowledge—knowledge of the disease itself, and knowledge of how to treat it. However, technology has an important role in making the conversation global, rather than local. And together these forces mean that barriers are tumbling and young people affected by the disease are feeling less isolated. They are realising that there is a community around them, of people who have been through what they have, who understand them and who are there to help them cope.

Generally, sharing experiences about HD is a good thing, and documentaries are one of the most powerful ways of telling a story. That's why those who make them need to be aware of the impact they can have, and sensitive to the image of HD they are projecting. One produced by the group We Have a Face had mixed reviews after the trailer was released. It portrays HD as a "monster" and has been described by some in the community as "too dark" and "scary". Others aim to show HD as something real and normal, and to provide hope and inspiration—Do you Really Want to Know? being an example.

A different style of documentary has emerged recently, however, in which young people affected by HD recount their personal journeys. Twitch by Kristen Powers and Father Spirit by Jonathan Dickinson are two notable examples. Twitch tells the story of Kristen's experiences of living in a family with HD, and being tested for the disease herself. Father Spirit follows Jonathan and his symptomatic father as they take one last journey together through the Himalayas on a motorbike. These films inspire by their positive energy and their can-do attitude, and have become empowering examples to others.

Such documentaries, often made in the film-makers' own homes, touch others in theirs, offering them a different, more hopeful image of HD. They reach people who may not have thought they needed to be reached. And while they are certainly not the only means we have for destigmatising a disease that consumes so many lives, they may be among the most effective.

# On Twitch

Kristen Powers

**Huntington's disease has always been a dominant factor in my life. My mum was diagnosed with the disease when I was nine, moved to a nursing home when I was 11, and died from complications due to pneumonia when I was 17.**

Her deterioration was quick and brutal. Unfortunately, many of my childhood memories are composed of broken noses, nasty falls, emotional outbursts and long, blank stares, especially after she lost the ability to speak. Thankfully, during this dark time, I managed to remain a very optimistic, happy teenager, determined to make sure this never happened to anyone else I loved.

Fast forward to 2013. I am a student at Stanford University in California, and like any other student, trying to find the time to hang out with friends, write 15-page papers, and stay in touch with family back on the East Coast. I'm also making a documentary following my genetic testing for the very disease that took over my mum's life.

Two years ago, shortly after her passing, I found myself torn between false freedoms. I no longer had to endure the painful, quiet visits to the nursing home where I watched her suffer, but I was increasingly aware that I was at risk for the disease myself. Despite all that I witnessed in the seven years from my mum's diagnosis to her death, I wanted to know my fate. Being the overly ambitious kid that I am, I also wanted to capture my own journey using the power of film. I was tired of the world not knowing about this disease. I was tired of people not understanding why genetic testing was such a life-changing process. I wanted them to understand what living in the world of HD was like.

In January 2012, I launched my first online fundraiser at indiegogo. My goal was to raise $10,000 in order to hire a professional film crew to film the process of my undergoing the test, which would happen the following May. This was one of the scariest moments of my life. I was 18 and the most I had ever raised was $200, yet I hit my goal in only nine days—on the first anniversary of my mother's passing.

The next few months passed in a crazy whirl. My indiegogo campaign continued to be a success, generating $18,000 in total. With those funds, I was able to film my entire documentary between April and August 2012. USA Today covered my story, giving me a front page spot for its first article, and one on the third page for its second.

twitch

On 31 May 2012, I received my genetic testing results. A week later, I graduated from high school. I spent that summer filming, the winter fundraising (indiegogo helped me raise another $15,000 in a second campaign) and the following spring editing the first cut. CBS News, Stanford University's news network, and many local media outlets have covered my story. I've spoken at conferences, classes and board meetings on the topic of genetic testing. Fundraising continues, and I hope to be able to release my film in January 2014.

I've experienced a lot in the past 19 years, especially after receiving my test results. I discovered how many people cared about me. The world showed its support and I appreciate that support beyond measure. I feel more passionate than ever about making sure no-one else has to undergo what I did. I've experienced many identity changes and challenging moments, but in the end, I realised something important that was true even before I received my test results:

> *"I am going to be OK."*

This documentary has been a challenge to make. However, it has also helped me grow as a business-woman, educator and compassionate person. I will do everything in my power to make sure it has as much of an impact on the world as it has had on my own life. Together, both this film and I will fight for the day when genetic testing for HD will not be a death sentence, but rather a step in the treatment plan towards ridding an individual of the disease. I believe that day isn't far away.

We've raised over $30,000 to make my documentary Twitch happen, but film-making is expensive. If you're dying to learn what happened during my testing process, please help us reach our fundraising goal faster so we can show it to you! You can also find us on Facebook.

# Horizon 2020: get set...

Fionnuala Margreiter, Grant Manager

**With a budget of around €70 billion, Horizon 2020, the European Union's new funding programme for research and innovation covering the period 2014 – 2020, is a key element in its drive to foster growth and jobs across Europe.**

Horizon 2020 combines three previously separate initiatives: the Seventh Framework Programme (FP7), the innovation-related activities of the Competitiveness and Innovation Framework Programme (CIP), and the EU's contribution to the European Institute of Innovation and Technology (EIT). Horizon 2020 will place greater emphasis on innovation and close-to-market activities than FP7. It is also intended to be simpler, operating according to a single set of rules. It comprises three main themes, or "pillars":

1. **Excellent science** – funding the best science through open competition. This will work through four programmes: the European Research Council; Research Infrastructures; Future and Emerging Technologies; and the Marie Skłodowska-Curie research grant scheme.

2. **Industrial leadership** – including a programme to support innovative small and medium enterprises; financial instruments to fund innovation; and a programme to encourage the development of enabling and industrial technologies.

3. **Societal challenges** – supporting research in areas such as health, climate, food, security, transport and energy.

Kick-off events for Horizon 2020 are being organised in all participating countries, and more information about these is available from national contact points.

The draft work programme for the first two years, 2014 - 2015, is now available for the societal challenge called "Health, demographic change, and wellbeing". Horizon 2020 starts on 1 January 2014... are we ready?

*For further information or advice on how to make the most of the funding opportunities offered under Horizon 2020, please contact Fionnuala directly: fionnuala.margreiter@euro-hd.net*

# Update: Enroll-HD

Olivia Handley, Global Project Manager, Enroll-HD

**Enroll-HD has chalked up a couple of milestones lately. The first Australasian participant was recruited on 26 July at the University of Otago, New Zealand, and less than a month later the 1000th participant was recruited at Columbia University in New York City.**

The study continues to thrive, with at least 100 new participants joining each month. As of 20 September, the tally is 1,145 participants, 53 sites, four countries, three continents.

In Europe, the transition from Registry to Enroll-HD is fast approaching, with the first Registry site scheduled to join Enroll-HD in November. Preparations to ensure the transition is smooth have been underway for over a year. It will take place on a site-by-site basis, and the same procedure will be repeated for each of the 150 Registry sites. Before a site can register its first participant in Enroll-HD, the following steps must be completed:

1. Site receives Enroll-HD starter pack
2. Site obtains regulatory (if applicable) and ethical/institutional approvals, along with data protection notifications/approvals
3. Enroll-HD site contract is executed between site and CHDI
4. Final Registry monitoring visit is completed
5. Site initiation visit is completed (including motor certification and PBA-s training)
6. Data migration from Registry to Enroll-HD is completed

The transition process requires significant collaboration and communication between the study site staff, language coordinators and EHDN Central Coordination, CHDI, the clinical research organisation Quintiles Outcome, the biorepository company BioRep and the software company 2mt. For this reason, a substantial amount of time has been dedicated to working out a transition process that enables us to track timelines, complete critical steps, and make sure that the target dates for transition are realistic. Key to this process has been the prioritisation of countries and sites, which has enabled the team to accurately predict and manage each site's transition.

While activities connected to the launch of Enroll-HD in Europe are expected to last approximately 18 months, the study will continue to expand into more countries in Latin America. It will also complete its site initiation activities in North America and Australasia during the remainder of 2013 and early 2014.

*For further information, please contact EnrollHD@quintiles.com or visit the Enroll-HD website.*

# Destination Europe

Tim McLean, Clinical Operations Manager

**About four years ago, I was looking for a change. For 25 years I had worked in drug development for a succession of large pharmaceutical, small biotech and contract research companies, in a wide range of therapeutic areas, and I was contemplating turning freelance. I just needed the right incentive. Agencies called, and one of them finally caught my attention. The challenge they presented was clinical operations management for a European network in HD.**

I had become aware of HD a few years earlier while researching Parkinson's disease, another devastating neurodegenerative disease from which my mother had suffered for 15 years. At the time, however, I had neither the reason nor the opportunity to investigate it further. Now I did. I was at a point in my career where I wanted to change direction, and I was attracted by the refreshing variety that this new role offered.

> *"Many questions were asked around the McLean family dinner table in the summer of 2009, not least, 'Where's Ulm?'"*

—the German city being in effect the nerve centre of the EHDN. I would be working from home in Edinburgh, but travelling a lot more too. I'm not sure which appealed to my family the most, but eventually the plan received their approval and I took up my new post that September.

Within a few weeks I had the great fortune to attend the World Congress on HD in Vancouver. In marked contrast to all previous therapeutic conferences I had attended, this international gathering struck me by its compactness, the open willingness of its members to share data and observations, and the relatively high attendance of HD patients and family members. Above all, I discovered a strong desire for collaboration and support across the global HD community. It was an immensely powerful introduction, and I have since been lucky enough to meet and work with leading researchers and clinicians in the field, from both Europe and the Americas. I have also been privileged enough to hear firsthand about the experiences of patients and their families on both sides of the Atlantic.

One of my early tasks was to review the structure of the EHDN. It quickly became clear that one of its strengths was the versatility of core team members and their willingness to do whatever was required, regardless of their formally designated roles. This gave the network the flexibility it needed to adapt to evolving demands. As organisations grow, their structure must evolve too, and in the EHDN's case this required the definition of four functional groups: Clinical Operations, Science, Administration/Human Resources and Communication. While the principal activities of the core EHDN team fall within these four groups, there is also a degree of cross-functional activity that allows for continued flexibility and willingness to adapt. Many of the Central Coordination (CC) team, including myself, were attracted to the network by the variety of tasks it offers within most roles, and the benefits of that variety have been retained as the structure has evolved.

My own role is mainly concerned with overseeing clinical operations, including coordinating and supporting the development and implementation of study-specific procedures by the teams running and

monitoring Registry, which is currently being prepared for transition into Enroll-HD. Similarly, I oversee and assist in the development of the operational support the network provides to facilitate clinical trials it has endorsed.

In addition, I overlap with the Science functional group in my work with CC team members Juliana Bronzova and Michael Orth, in the implementation of the EHDN Scientific Strategic Plan. This includes assisting in the review of, and support for, EHDN Working Groups, as well as in the development of the Clinical Trial Task Force. I also work closely with Jamie Levey of CC to support the team's human resource function, assisting in the assessment and selection of candidates as required, and coordinating the annual self-assessment of staff members.

As we are a pan-European team spread across 17 countries, it is not surprising that there is a relatively heavy emphasis on frequent conference calls, occasional webinars and periodic face-to-face meetings. Regular calls demand a commitment of time and effort, but we find that the investment is generously repaid in terms of progress. There are inevitably glitches, but by maintaining an open, forward-looking working culture, we usually manage to overcome them.

Looking back over the past four years, I consider myself very lucky to be surrounded by a team of highly capable and conscientious individuals, and to be part of this ongoing, collective effort to improve the lives of HD patients and their families—an effort whose ultimate goal is to find a cure. As for my family, it turns out not to be such a big deal when I am away travelling from one week to the next, and they seem to tolerate my working from home as well. So I have approval for a few more years if required.

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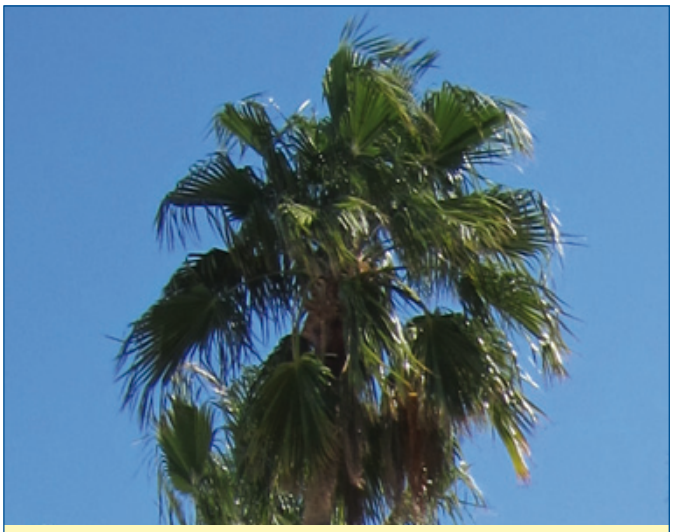

Photo kindly provided by Gill Bates

## Dates for your diary

Save the dates for

- The 2nd Conference on Large Animal Models in Neurodegenerative Diseases in Chateau Liblice, Czech Republic, 17-20 November 2013
- CHDI's 9th annual HD Therapeutics Conference in Palm Springs, USA, 24-27 February 2014
- The European Conference on Rare Diseases & Orphan Products in Berlin, Germany, 8-10 May 2014
- 18th International Congress of Parkinson's Disease and Movement Disorders in Stockholm, Sweden, 8-12 June 2014
- EHDN2014 in Barcelona, Spain, 19-21 September 2014