



Pope Francis meets 15-year-old Brenda, who has juvenile HD



Brenda and Anyervi, who comes from Lake Maracaibo



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Out of the shadows: Pope Francis embraces the HD community

Laura Spinney

"For too long the fear and difficulties that characterise the lives of Huntington's disease families have led to misunderstanding," Pope Francis told a 1,700-strong gathering of the global HD community at the Vatican on Thursday 18 May. "Today we are here to tell ourselves and the world: hidden no more."

Having delivered his message, the pontiff left the stage of the stunning Sala Nervi and went to greet HD family members who had flown in from far and wide to meet him, and to hear the name of their disease spoken for the first time by a head of state. He took many of them in his arms, kissed them or made the sign of the cross on their foreheads. A large contingent of the privileged guests came from South America, where the prevalence of HD is among the highest in the world. They included families from Lake Maracaibo in Venezuela, previous generations of which contributed to the research that made the identification of the HD gene possible in 1993.

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Photo: Pier Paolo Lisarelli



Members of the HD community gather in St Peter's Square



Charles Sabine and family

Photo: Laura Spinney

That breakthrough led to the development of a diagnostic test that has improved the lives of those at risk of HD significantly. It enables them to make informed reproductive choices, gain access to specialist treatment, take part in clinical research and plan for the future. These possibilities are rarely available to the South American families, however, who often live in poverty and isolation, excluded from mainstream society by fear of a misunderstood and stigmatised disease.

It was to try to correct this injustice that Emmy Award-winning journalist and HD advocate Charles Sabine came up with the idea of bringing some of those families to Rome to meet the Pope, who heads a community of nearly 1.3 billion Catholics worldwide. The initiative, called HDdenmore, was organised with the help of an international team including Italian HD researcher Elena

Cattaneo and CHDI's Ignacio Muñoz-Sanjuán, and funded by Teva Pharmaceuticals and others. And though the focus was on the South American families, the event was attended by HD patients and their relatives and carers from more than 20 countries.

"It's almost miraculous to think that we have an audience with Pope Francis, that he's shining a light on HD," said EHDN's Jamie Levey, whose family is affected by the disease. "We heard how the families from Venezuela lack even the most basic human needs—food, work, housing—so I also see how lucky we are in Europe and North America, to have access to quality care."

"You don't often hear HD and social justice spoken together in the same sentence," said Kenneth Serbin from San Diego, who blogs on HD as Gene Veritas. "With this Pope and this meeting we can now bring

Photo: Laura Spinney



Nancy Wexler (left) and HDdenmore co-organiser Elena Cattaneo



Jamie Levey and her mother (left) meet the pontiff

Photo kindly provided by Jamie Levey



Photo: Laura Spinney

those two things together.” Sabine told the gathering that it was a day to celebrate “a Pope whose mercy embraces the most vulnerable,” while Nancy Wexler—who led the research involving the Venezuelan families, that culminated in the discovery of the location of the HD gene—described the event as “a moving and wonderful tribute to the graceful, elegant families who deserve all of our empathy, compassion and support”.

the care and support offered to those families, and persuade their neighbours to embrace rather than shun them. Within hours of the HDdenmore audience, the outlook was looking promising. Social media was atwitter with news of the historic event, donations had been promised, and medics from around the world were mobilising themselves to provide the much needed aid—with Italian doctors showing a particularly strong early response. This newsletter will keep tabs on the reaction as it develops.



Photo: Laura Spinney

Thirteen-year-old Anyervi, from an HD family in Lake Maracaibo, was presented with a football and a number 11 shirt, as worn by his hero, Neymar of Football Club Barcelona. He then watched in amazement as the Brazilian star paid a personal tribute to him, via a video link. Brenda, who at 15 suffers from the juvenile form of the disease, had her dream come true when she was serenaded by singing sensation Axel

from her home country, Argentina. Axel then accompanied her to present the Pope with a scroll containing a pledge—reproduced in English, Spanish and Italian—that HD should be “HDdenmore”. Guests were entertained by music from American folk rock band Miner and British folk singer Sylvie Lewis, all of whose lives have been affected by HD.



Photos: HDdenmore

To find out more about HDdenmore, and watch a film about the South American families made by Charles Sabine and Brian Moore, please visit the website dedicated to the event: <http://hddenmore.com>

The organisers hope that the Pope’s words will translate into concrete benefits for the HD families in most need. Among other things, they hope his message will stimulate the world’s largest non-governmental healthcare provider—the Catholic Church—to improve





HD Therapeutics 2017: it's more complex than you think

Michael Orth, Central Coordination

The 12th Annual HD Therapeutics Conference highlighted biological complexity. More sophisticated technology empowers the researchers who gathered in St Julian's, Malta from 24 to 27 April, but the insights it generates reveal that the effects of the HD mutation may be less straightforward than was thought.

The Genetic Modifiers of Huntington's Disease (GeM-HD) consortium applies unbiased approaches at the genome level, using samples donated by thousands of Registry



Lesley Jones

and Enroll-HD participants, to understand how the HD mutation interacts with other biological processes. As GeM-HD member Lesley Jones (Cardiff University) reported, the consortium's efforts have highlighted a possible role for DNA quality control. Given that the HD mutation is a glitch in DNA, it makes intuitive sense that the efficacy of repair mechanisms should influence how much damage and stress that glitch causes.

Biological complexity reveals itself beyond DNA too, in the proteins that it encodes. Methods for probing that complexity are improving all the time, and Matthias Mann (University of Copenhagen) described a method employing proteomics that his group has refined for accurately quantifying thousands of proteins at the same time. Christian Néri (Inserm/University Pierre and Marie Curie) gave another example of



Christian Néri

an unbiased approach based on bioinformatics, that his group has used to investigate how thousands of molecules—including RNA and proteins—interact in the context of the HD mutation.



Darren Monckton

Darren Monckton (University of Glasgow) talked about how the CAG repeat length can differ significantly between cell types in a single individual. In striatal neurons, for example, the number of repeats can be more than a hundred times that found in blood cells. Kevin Weeks (University of North Carolina) presented the three-dimensional structure of RNA and suggested that there might be more to it—functionally speaking—than just a “go-between” in the translation of DNA into protein. If the HTT gene contains a mutation, for example, his methods predict an additional protrusion from the RNA molecule that is likely to affect its function—although it is not yet clear how.

Despite all this newly revealed complexity, reducing levels of huntingtin is still regarded as a promising therapeutic avenue, and it is encouraging that at each annual HD Therapeutics meeting, new approaches for achieving this are unveiled. One, IONIS-HTT_{Rx}, is already in clinical trials, and it is hoped that others coming down the pipeline will soon be too. Preparing for such trials therefore remains a pressing task.

One important element of that task is measuring the effects of huntingtin-lowering approaches. Good progress has been made in the accurate detection and quantification of the huntingtin protein *in vivo*, reported Edward Wild (University College London). Biomarkers are also being explored that reflect the amount of damage done to the brain, with promising results. It is possible that many outcome measures will need to be analysed simultaneously, to capture all the effects of huntingtin-lowering treatments. Since the complexity of the relevant biological systems may be too great for the human brain to grasp, said Jim Koslowski (IBM), researchers may benefit from the additional data-crunching power of high-performance computers.



Edward Wild

Finally, important lessons can be learned from failure, and in his keynote lecture, Stephen Paul (Voyager Therapeutics) suggested reasons for the failure of recent clinical trials of treatments for Alzheimer's disease (AD)—a neurodegenerative disease that shares some features with HD. They may include an inability of the compound to engage with its target, and dosing issues. Moreover, among those diagnosed with AD,

there is significant variability in both the clinical presentation and the progression of the disease—something that is also true of HD. Going forward, it will be very important to develop more sensitive measures of target engagement and treatment effects. The goal, ultimately, must be to treat the right group of patients with the right agent at the right dose at the right time.

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HD Clinical Trial Site Certification off to a good start

Jenny Townhill and Tim McLean, Central Coordination

The HD Clinical Trial Site Certification scheme has seen an enthusiastic response in the first month of its existence, with applications coming in from HD clinical trial sites all over the world.

The goal of the scheme, an initiative of the HD Clinical Trials Task Force ([HD-CTTF](#)), is to improve the visibility of such sites to approved sponsors, and to facilitate clinical trials in HD by reducing the administrative burden associated with trial set-up, providing access to a large cohort of trial participants, and speeding up feasibility assessment and site identification. With several clinical trials in the pipeline, the HD-CTTF is keen to establish a comprehensive database of certified sites, and all HD clinical sites are encouraged to apply for the scheme. Certified sites have a significantly improved chance of being considered for participation in clinical trials, and a higher profile among patients, healthcare providers, clinicians, industry and academic partners, not to mention institutional and external funding partners.

Details of how to apply can be found [here](#). A prerequisite for application is completion of the HD Global Site & Investigator Database (GSID-HD), which stores

information about site feasibility, training and qualifications, thus facilitating country and site selection for approved sponsors, and reducing the administrative burden for sites by having this feasibility information curated centrally. To create a new site entry in GSID-HD, go to this address: <http://qbagent.chdifoundation.org/Android/Public/submitGSIDSiteAdd.php>

You will be presented with the form you see below, which you should complete. The record for a site that has already been added to the database can be accessed via a unique hyperlink that was assigned at initial submission.

For support or information concerning GSID-HD, or to be resent your site's unique hyperlink, please contact: gsid@enroll-hd.org

Any queries regarding application for the HD Clinical Trial Site Certification scheme should be addressed to: hdsite@euro-hd.net

Update: Clinical trials

Jenny Townhill and Tim McLean, Central Coordination



LEGATO-HD: This phase 2 safety and efficacy trial of laquinimod, sponsored by Teva Pharmaceuticals, completed enrollment in May 2017. The study is underway in the Czech Republic, Germany, the Netherlands, Italy, Portugal, Spain, the UK, Russia and North America, and the 351 participants will continue regular study visits for up to 12 months of treatment. Teva recently announced the results of CONCERTO, its laquinimod study in relapsing-remitting multiple sclerosis (RRMS). Although the primary endpoint for this study was not met, and there are no plans to continue investigating laquinimod for RRMS, there were positive results on several secondary and exploratory endpoints. This suggests that further exploration of laquinimod as a treatment for neurodegenerative disease is worthwhile.



Open Pride: This open-label extension to Pride-HD, Teva's phase 2 study of pridopidine, closed for recruitment in 2016, having enrolled around 250 participants at sites in the US, Canada, Russia, Australia and eight European countries. Participants will receive treatment for up to 104 weeks, pending regional approvals. The protocol includes a sub-study whose aim is to develop algorithms for objectively quantifying chorea by analysing data obtained from a wearable device linked to a smart phone. The sub-study is underway in the US and Canada, and there are plans to start recruitment in Europe in the coming months. It is open to all participants in the main study.



Photo: ARTIFOX, Gabriele Stauner



HD-DBS: This investigator-initiated trial of pallidal deep brain stimulation for HD, which is sponsored by the University of Düsseldorf, is underway in Germany, Switzerland and Austria. To date, 16 out of a total of 50 participants have been randomised. The investigation of DBS as a potential treatment for severe chorea is important because there is currently no adequate treatment for this. The study is recruiting and clinicians in participating regions are encouraged to refer potentially eligible participants to the surgical sites. Eligible patients are those with uncontrolled choreic symptoms for which current pharmacotherapy is proving unsuccessful, and who are able to give their consent. For further information, or help identifying potential participants via the Enroll-HD database, please contact Pauline Kleger: pauline.kleger@euro-hd.net

For queries or feedback regarding these studies, please contact Jenny Townhill: jenny@euro-hd.net



Enroll-HD launches clinical training platform

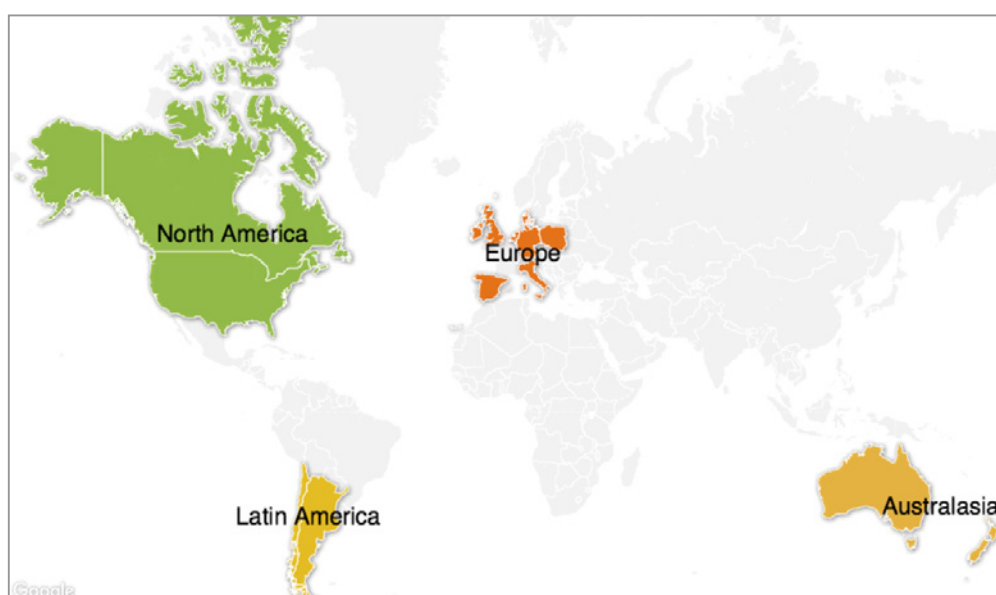
Olivia Handley, EHDN Global Platform Manager

The Enroll-HD platform is now offering platform services, a unique operational resource for clinical research that is intended to speed up and facilitate HD research.

Platform services are provided by the Enroll-HD platform team, whose 45-plus members have expertise in the setting up of clinical studies and the support of clinical trials. This includes experience with regional regulatory requirements, translation of study materials, database design and implementation, study management, process development, site selection and participant eligibility. Each platform service has been assigned at least one subject matter expert (SME) who has specialist knowledge in that area.

The Enroll-HD platform is a product of the partnership between CHDI and EHDN. This partnership, known as One Study Team, seeks to operate as a unified network of HD-related clinical research operations, and to provide a broader skill set than either partner organisation can offer alone. At the core of the platform is the Enroll-HD study, a global observational study with over 14,000 participants.

To make best use of the platform services, a group planning a study or trial should first determine its requirements. For example, will the study make use of the Enroll-HD electronic data capture system? Will participant eligibility listings be extracted from the Enroll-HD database? Do licence permissions need to be sought? Each requirement will then be matched to a platform service and SME. The vision is that the SME will provide information and guidance to the group on how best to set up and implement a specific aspect of the study. Needless to say, this will work best when the Enroll-HD platform team and the study group communicate regularly and clearly.



The global spread of Enroll-HD

**Elena Bellosta**

Update: Fellowship Exchange Programme

Nine applicants were selected in the first round of the Fellowship Exchange Programme (FEP) to be organised jointly by the EHDN and the International Parkinson and Movement Disorder Society—European section (MDS-ES). The EHDN would like to express its gratitude to the MDS-ES, whose collaboration made it possible for three extra fellowships to be offered in 2017, and also to the host clinics that agreed to receive the fellows for the duration of their placements. Since one successful application* from the previous round of the FEP was carried over for personal reasons, current fellows number 10. They are:

- Elena Bellosta from Zaragoza, Spain
- Ahmed Dashan from Cairo, Egypt
- Nataliya Grigorova from Sofia, Bulgaria*
- Yang Jing from Sichuan, China
- Xiaoyan Li from Hangzhou, China
- Pasquale Nigro from Perugia, Italy
- Mayke Oosterloo from Maastricht, the Netherlands
- Marina Peball from Innsbruck, Austria
- Nikhil Ratna from Bangalore, India
- Natalia Szejko from Warsaw, Poland



Pasquale Nigro and EHDN grant manager Fionnuala Margreiter at the European Academy of Neurology meeting in Amsterdam on 25 June

Future editions of this newsletter will track the fellows' progress as they complete and report back on their placements.



SEED FUNDS

Looking for a publication?

Publications generated by EHDN-supported projects are now listed on the new EHDN [website](#). They include publications based on seed fund projects and studies conducted with data or samples from Registry participants. If you have published research supported by EHDN and do not find your publication listed there, please contact Christine Capper: Christine.Capper-Loup@siloh.ch

Seed funds are intended to support pilot studies that will eventually kickstart larger projects. The next deadline for applications is 1 November 2017. More information about the programme and how to apply can be found [here](#).

**Christine Capper-Loup**



The e-health interface



Topaz social worker Lia de Jager using the video-calling system

E-health for HD

Jesseke de Man, Policy Advisor, Topaz Overduin

At Topaz Overduin, a specialised HD centre at Katwijk in the Netherlands, we have developed an innovative e-health and e-learning platform that we hope will enable patients to remain at home for longer.

HD patients frequently express the desire to live in their own homes for as long as possible, and though many HD centres try to facilitate this, it often isn't possible because of the physical distance it creates between the patient and the clinicians who have the expertise to treat them. Our e-health platform, which we launched in 2015, is designed to overcome this obstacle, principally through video calling.

The patient at home is equipped with a touch screen that they operate by means of simple icons. Via this interface, they maintain regular video contact with Topaz social workers, carers and therapists, sharing agendas, receiving instructions, sending video messages, and participating in relaxation exercises and games. They can also use the system to stay in touch with family members and carers, without leaving the environment in which they feel secure.

Twenty-eight home-based patients currently use the secure video-calling system. Prior to its implementation, case managers conducted face-to-face meetings with

patients every six-to-eight weeks. Now they make contact once a week, on average. Both psychological support and certain forms of therapy, such as speech therapy, can be delivered via the platform. Evaluations indicate that the system enables patients to stay at home for longer and improves the quality of patient-expert communication. Not only does it allow for better continuity of care, it can also help defuse volatile situations, and the vast majority of patients who have used it have recommended it to others.

Alongside the e-health platform, we have also developed a [public online platform](#) with the help of patients, carers and professionals. This is a database that HD patients and carers can use to obtain information and teaching videos, provide feedback, and ask and answer questions. It also enables them to contact specialists and to find out about scheduled meetings. We feel confident that these new platforms will improve care for HD patients, and so improve their quality of life.

A visit to Topaz Overduin was organised on 18 September 2016, for delegates attending the EHDN plenary meeting in The Hague. For further information about the centre's e-health and e-learning platforms, please contact Jesseke de Man: J.deMan@topaz.nl



Aim high: Lysle Turner recounts his adventures in a good cause

On 19 May 2016, Lysle Turner became the youngest South African to reach the summit of Mount Everest. When he got there, the 26-year-old planted a flag bearing the names of 200 people who had lost their lives to HD. As he recounts here, the 2016 attempt was his second, the first having been abandoned under dramatic circumstances.

On the morning of 25 April 2015 an earthquake struck the Himalayas. The day being a whiteout, I was in my tent writing my journal and reading when it happened. In a flash I was up and hopping around my two-man tent, trying to keep my balance while shoving my feet into my high-altitude boots. As I unzipped the tent and looked up at Everest, I heard the ominous sound of a serac or ice pinnacle detaching itself from a neighbouring mountain, followed by the rumble of an approaching avalanche.

That rumble marked the beginning of the end of my first attempt to climb the world's highest peak. As I ran for the safety of a bigger supply tent, I caught a glimpse of the approaching wave of destruction and thought that some of us, perhaps all of us on the mountain, might die. Grabbing another climber who was watching in shock, I dived into the tent. My mind went blank until we surfaced, and my first recollection as a survivor is

of the sight of blood on snow. I looked down and saw that my jacket was also covered in blood. I expected to feel pain, but the blood wasn't mine. I started shouting names, and from that moment on my energy, as well as that of other survivors, was directed towards rescuing fellow climbers.





Eight days after the earthquake I left Nepal, but I knew that I would be back, and a year later I reached the summit. The feeling that I experienced as I stood on top of the world is hard to describe, but perhaps those reading this can understand me if I say that it felt like a cure had been found for HD. There is no cure, yet, but in my family—four generations of which have been devastated by the disease—the youngest generation is finally free of it, having no gene expansion carriers. Knowing that contributed to my exhilaration that day.

“I achieved my goal in 2016, but 2015—the year of the earthquake—was the greater learning experience for me.”

Climbing Everest, for me, was all about raising awareness of HD. It was something I could put myself through on behalf of those who are fighting the fight,

who climb an Everest each day, and of those who have lost the fight. And though I achieved my goal in 2016, 2015 was the greater learning experience for me, because it was then—in the aftermath of the earthquake—that I learned to embrace adversity, and to look upon it as an opportunity to grow.

My reward has been a whole new family: the HD community, which was with me every step of the way. Whenever I meet someone affected by HD who is reluctant to reach out to their community, I tell them about this family, because those of us who belong to it are on the same page. We understand each other, and knowing that is what inspires me. Before leaving Base Camp on both attempts to climb the mountain, I added names of members of this family to the flag I carried. Writing out a name, I tried to imagine the person it belonged to, and the daily challenges they faced. It may have taken two attempts, but the flag reached the summit. It got there in the end.



All photos kindly provided by Lysle Turner



Photo: ARTIFOX, Gabriele Stautner

Dates for your diary

Save the dates for

- [30th European College of Neuropsychopharmacology Congress](#), Paris, France, 2-5 September 2017
- [European Huntington Association Conference](#), Sofia, Bulgaria, 22-24 September 2017
- [17th European Congress of Neurosurgery](#), Venice, Italy, 1-5 October 2017
- [4th Conference on Animal Models for Neurodegenerative Disorders](#), Liblice, Czech Republic, 22-24 October 2017
- EHDN2018 Plenary Meeting, Vienna, Austria, 14-16 September 2018 (details to follow)