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EHDN News

EUROPEAN **HUNTINGTON'S DISEASE** NETWORK

Picture courtesy of Fabio G. Festa, Wonderlust Pictures, for the Italian Huntington's Disease Network

CALLING ALL REGULAR MEMBERS:
VOTING OPENS FOR THE 2018 EHDN ELECTIONS ON 1 AUGUST.
PLEASE MAKE YOUR VOICE HEARD!
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Celebrating Registry

On 6 June, the Italian Huntington's Disease Network organised a flash mob in Milan's Piazza del Duomo, at which a 67 metre-long replica of the huntingtin gene was unravelled. The event was planned to mark the 25th anniversary of the identification of the huntingtin gene, but this year also sees another major landmark: the closing of the pioneering observational study Registry.

REGISTRY

This edition of the newsletter is dedicated to Registry, its achievements, and the global study and platform which has taken over from it, Enroll-HD.

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Bernhard Landwehrmeyer

First, a little history...

Laura Spinney

The man who had the vision that became Registry was none other than Bernhard Landwehrmeyer, the first EHDN Chair and the study's principal investigator.

Soon after he arrived at the University of Ulm in Germany, in 1999, Landwehrmeyer was charged with setting up a three-year trial of a potential disease-modifying treatment for HD called riluzole. The trial required the participation of more than 500 patients, which meant that sites from more than one European country would have to get involved. It was a logistical challenge, but with colleagues in six countries he pulled it off.

Even while the riluzole study—called the European Huntington's Disease Initiative—was running, its architects acknowledged that it would be a shame to let the trial infrastructure go to waste once it was over, so they began to think how they could maintain and expand it. CHDI got involved, the EHDN was born, and in 2004—with the invaluable funding and support of CHDI—so was the longitudinal observational study Registry.

The main goal of Registry was to fill a yawning gap in knowledge about HD. "We only had cross-sectional data at the time," recalls Raymund Roos, the PI of one of the first sites to join the study, and later one of the highest recruiting, the Leiden University Medical Centre in the Netherlands. "The longitudinal dimension provides so much more information."

Raymund Roos

But making the dream a reality wasn't without its challenges. "The first challenge was to convince both sites and participants that such a project could be sustained over the long term," says Landwehrmeyer, no mean feat when funding cycles tend to last three or at most five years. "The second was to convince them that this enterprise would benefit the entire community, that every capable and interested party would have access to the data and biomaterials we would gather."

Given Europe's cultural and linguistic diversity, ensuring that everyone was on the same page scientifically and clinically required agreement on such things as rating scales and quality control, which in turn required a huge effort in terms of translation of materials. "We were helped by being able to meet regularly in person," says

The first Language Area Coordinators meeting, Reisensburg, Germany, April 2004. From left to right: Olivia Handley, Matilde Laura, Jenny Townhill, Bernhard Landwehrmeyer, Amandine Rialland, Asunción Martínez, Marie-Noëlle Witjes-Ané.

Landwehrmeyer. "To some extent, it was an exercise in confidence-building."

From the beginning there was a strong emphasis on the practical: the study would take advantage of the way healthcare is organised in Europe to integrate the research as far as possible into existing care practices, and the findings would inform clinical care decisions. That approach paid off. "When you look systematically at your patients," says Roos, "then inevitably your care improves." Patients also benefited from feeling more actively involved in HD research.

Eventually, the study brought together 161 sites across 17 countries. It expanded to cover a wider range of participants and began to explore factors that might influence the onset and natural history of this monogenic disease. "From the get-go we were intrigued by the prospect that we might be able to identify genetic modifiers of HD, but to do that we needed reliable data on its onset," says Landwehrmeyer. Registry's cohort of experienced clinicians provided that data, and in 2015 the consortium published a paper in *Cell* identifying genetic factors that modify the onset of HD—one of the study's achievements that its PI is proudest of.

The *Cell* paper changed researchers' understanding of HD, reinforcing earlier indications that at the heart of the disease is an instability in DNA, such that the number of CAG repeats in the huntingtin gene might increase over a patient's lifetime. That in turn raised the possibility that therapies that interfere with the molecular machinery responsible for that instability might modify the course of the disease.

Registry had another goal: to accelerate recruitment into clinical trials. "I think we have been pretty successful in this," says Landwehrmeyer, "because recruitment times in regions that have access to the database are substantially shorter than in those that haven't."

For Roos, one of Registry's most important contributions has been to reveal the great variation in the clinical manifestation of the disease—the fact that it is not one but a family of diseases. It has also stimulated more awareness of HD in general, and more commitment to finding effective treatments among stakeholders.

The work carries on with Registry's successor study, Enroll-HD, which adds greater temporal depth to the knowledge of HD's natural history that Registry has provided over the last 14 years. Enroll-HD is still in its infancy, but in providing a roadmap for HD research going forward, it has already achieved one very important psychological goal: "It is concrete proof of continuity," says Landwehrmeyer.

Registry: an overview

Jenny Townhill,
Central Coordination

At completion, the EHDN Registry study was the largest study of Huntington's disease to date, and a highly successful demonstration of the power of collaboration between clinicians, researchers and the patient community.

Registry was a prospective, longitudinal, multinational, multicentre observational cohort study conducted across 161 specialist HD clinical sites in 17 European countries. Through annual visits, it collected standardised clinical data and biospecimens on HD gene carriers, individuals affected by HD, HD family members and control participants. The first participant was recruited on 17 August 2004, recruitment closed in 2017, and the last participant was enrolled on 15 August of that year.

14,851 participants contributed clinical phenotypical data, including assessments of motor, cognitive, behavioural, quality of life and functional abilities. More than 90% of participants completed the core clinical assessments and only 1% withdrew from the study. Of those participants who contributed clinical data, 11,261 also donated biosamples (blood and urine) for use in exploratory biomarker studies and large-scale genetic modifier studies.

Three-quarters of Registry participants had clinically diagnosed or manifest HD. These were distributed more or less evenly across disease stages, but with the lowest proportion in stage 5 (advanced disease). 15% of all participants were premanifest, meaning they were known HD gene-expansion carriers who had not yet presented with clinical symptoms; 3% were at-risk, meaning they came from an HD family but did not know their genetic status; and 7% were controls.

The vast amount of data and biosamples collected in Registry represents an immensely valuable resource for the study of HD that has already been exploited in numerous research projects. These have generated publications, facilitated basic research and clinical development in HD, contributed to our understanding of the disease and its progression, and informed the clinical care of HD patients.

Since 2012, Registry sites and participants have been transitioning to the Enroll-HD global study. All Registry data have been curated and prepared for import into the Enroll-HD database, with the datasets being combined when participants enroll in the new study. The Enroll-HD protocol has a modified and refined set of assessments with respect to Registry, but the two are sufficiently similar to allow for the creation of a single clinical database and biorepository that combines their longitudinal depth. Not all Registry participants will transition to Enroll-HD, because many are at too advanced a disease stage for inclusion or are deceased. Hence the Registry database and biosample repository continue to be available for research as a stand-alone resource.

The substudies

Jenny Townhill, Central Coordination

The Registry protocol was designed to accommodate optional assessments and to pilot additional scales or scale adaptations tailored towards specific participant groups or areas of research interest. This meant that it generated a number of spin-off studies, or substudies. The following is a whistlestop tour of three of these, after which Aileen Ho will present the Quality of Life substudy which she led.

Physiotherapy

The purpose of this was to evaluate the suitability of various physical outcome measures for use in trials designed to improve physical functioning in HD. Registry sites in the UK and the Netherlands, and one non-Registry US site, recruited 76 participants. Three of the 11 assessments examined—the Berg Balance Scale, the Physical Performance Test and the Timed Up and Go Test—showed excellent reliability and low minimal detectable difference across disease stages, suggesting that of the physical tests commonly used with HD patients, these would be the most appropriate for use as outcome measures.

Lifestyle factors

This was designed to replicate the findings of a retrospective 2010 Australasian study which suggested that avoiding a passive lifestyle could delay the onset of HD symptoms. It was also hoped that it would inform the development of a cross-sectional prospective study of the role of lifestyle factors in HD, with a view to providing HD patients with lifestyle strategies that could delay onset. The substudy, which recruited 147 participants in eight countries, failed to replicate the findings of the Australasian study.

Juvenile onset HD

Juvenile onset HD (JHD) presents with a markedly different set of symptoms and course to the adult form of the disease. Standard rating scales are used to assess the adult-onset HD phenotype, and modified versions of these were evaluated for their ability to better capture the symptoms and progression of JHD. 78 participants took part, in 12 countries, and the study generated larger datasets than JHD researchers have had access to in the past. These gave rise to a number of publications, on subjects including the pharmacological management of JHD and the experience of parents of children with the disease.

The Quality of Life substudy: mission accomplished

Aileen Ho, University of Reading

"You cannot measure what you do not understand, and you cannot understand what you cannot measure." These words or similar are often attributed to the physicist Lord Kelvin, but they could also be applied to Huntington's disease.

The impact of HD on the lives of those who are affected by it is immense but difficult to quantify. Clinician's ratings and clinical assessments are essential, but so too is the patient's perspective. Questionnaires that measure quality of life have been devised for healthy populations and for other diseases, but they don't necessarily capture all the ways in which HD affects health and wellbeing. Acknowledging the need for a similar instrument tailored to HD, EHDN supported an investigator-initiated Registry substudy whose goal was to refine and robustly validate a questionnaire that

sensitively reflects the full impact of HD on a patient's life, and translates it into a quantifiable score.

Starting with words that HD patients used in interviews with our team, we developed a list of questions that reflects the issues that concern them. Those questions that statistical analyses revealed to be the most informative were then selected to produce a carefully calibrated instrument. In the context of the EHDN substudy, this instrument was then refined and validated in a large-scale study involving 541 patients from 29 Registry sites and six care homes in the UK—patients who covered the full spectrum from premanifest to late-stage disease.

The substudy has now been completed, and the result is a one-page questionnaire called the Huntington's Disease health-related Quality of Life questionnaire, or HDQoL. Like a bespoke suit, the HDQoL captures the reality of living with HD, specifically. It reflects four distinct domains or areas of impact expressed in patients' own words: Physical-Functional, Cognitive, and two components of Behaviour (Mood-Self and Worries, where Mood-Self combines measures of mood and self-image). These map onto the classic triad of HD symptoms, and underscore the importance of the behavioural dimension of the disease. Indeed, the separation of the behavioural component into two sub-components is novel, and a product of this approach.

Overall, there is robust psychometric support for the refined HDQoL across disease stages, showing that it is fit for purpose. We believe that this patient-derived instrument is the fastest and most faithful (to patients' lived experience) of its kind, and that its use in clinical trials will allow the effects of any intervention on the triad of HD symptoms to be investigated in a more patient-centred way.

The HDQoL is freely available for use in clinical practice and research, along with the companion report, and we hope that the information it provides will improve understanding of the impact of care practices and clinical interventions on patients' lives.

For further information please follow this link: www.hdqol.info. Queries should be addressed to: webmaster@hdqol.info

Supporting clinical trials

Jenny Townhill and
Tim McLean,
Central Coordination

A key aim of Registry was to facilitate and expedite clinical trials and studies, and in this it succeeded.

Among the trials that have been supported over the last decade by Registry and the associated infrastructure of the EHDN Central Coordination and regionally based language area coordinators, or LanCos, are the following:

- Medivation HORIZON
- CHDI Pearl-HD
- Pfizer Amaryllis
- Siena Biotech Selisistat
- Teva Pride-HD
- Teva LEGATO-HD

The level of support provided was tailored to the requirements of each sponsor and study, beginning at the protocol development stage. The HD community could be confident of the robustness of the scientific design, and ethical integrity, of studies whose protocols had been developed with the help of the EHDN protocol advisory service, reviewed by the EHDN Scientific and Bioethics Advisory Committee and endorsed by the EHDN Executive Committee.

The detailed clinical characterisation of patients recruited at Registry sites facilitated the assessment of study feasibility. Through Registry, EHDN established durable working relationships with HD clinical sites, and this also sped up the process of identifying sites with the skills, resources and track records in running clinical trials, that meant they were able to deliver high-quality data in a timely fashion.

Exports from the Registry database accelerated recruitment by identifying potentially eligible participants meeting high-level study inclusion criteria, and giving sites a head start when it came to pre-screening. The

operational support provided by the EHDN Central Coordination and LanCo teams, who regularly interact with sites and local researchers and patient organisations, helped resolve operational issues quickly, and improved communications.

Standardised training and certification on one of the key outcome measures used in clinical trials, the Unified Huntington's Disease Rating Scale (UHDRS) motor scale, is provided via an online training platform. Previously this was hosted on the EHDN website, but it is now available via the Enroll-HD website. Training on the standard assessment of behavioural symptoms of HD (PBA-s) is provided via interactive webinars for small groups of trainees. Improving inter-rater reliability and ensuring that site staff are adequately trained improves the chances of detecting treatment effects in trials.

Looking to the future, the EHDN and Enroll-HD platform teams are continuing and expanding the work of Registry by providing trial support to pharmaceutical and academic partners globally. In this, they are able to leverage the wealth of experience in study start-up, and solid working partnerships with HD sites, that Registry built up over its 14 years of existence.

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REGISTRY

Adding to the literature

Michael Orth, Central Coordination

The unparalleled large collection of clinical data and biomaterials that Registry made possible enables research projects to be conducted on a scale that could not previously be imagined.

An example is the work carried out by the Genetic Modifiers of Huntington's Disease (GeM-HD) consortium, which will expedite the search for genetic disease modifiers and which would not have been possible without access to thousands of datasets, since the power of such studies depends heavily on numbers.

Equally important is work to identify clinical phenotypes, and several studies have made use of Registry data to better understand the motor, cognitive and behavioural phenotypes of HD. More clearly defined clinical phenotypes facilitate the understanding of phenotype–genotype relationships, which can in turn be harnessed for the development of novel treatments. But they are also useful in the evaluation of current treatment strategies, including symptomatic therapies, and in cross-continental comparisons of HD phenotypes. Such comparisons have revealed, for example, that clinical phenotypes are similar throughout North America and Europe, which is encouraging in view of the increasingly global nature of clinical trials.

In all, more than 50 scientific publications have been published using Registry data—of which some examples are listed below—and others are in preparation. More can be expected as researchers continue to exploit the Registry legacy database.

On genetic modifiers of HD

- Lee JM *et al.* CAG repeat expansion in Huntington disease determines age at onset in a fully dominant fashion. *Neurology.* 2012 Mar 6;78(10):690-5.
- Genetic Modifiers of Huntington's Disease (GeM-HD) Consortium. Identification of genetic factors that modify clinical onset of Huntington's disease. *Cell.* 2015 Jul 30; 162(3):516-26.
- Keum JW *et al.* The HTT CAG-expansion mutation determines age at death but not disease duration in Huntington disease. *Am J Hum Genet.* 2016 Feb 4;98(2):287-98.

On HD clinical phenotypes

- Rickards H *et al.* Factor analysis of behavioural symptoms in Huntington's disease. *J Neurol Neurosurg Psychiatry.* 2011 Apr;82(4):411-2.
- Hart EP *et al.* Better global and cognitive functioning in choreatic versus hypokinetic-rigid Huntington's disease. *Mov Disord.* 2013 Jul;28(8):1142-5.
- Hubers AA *et al.* Suicidal ideation in a European Huntington's disease population. *J Affect Disord.* 2013 Oct;151(1):248-58.

Legacy database

Christine Capper-Loup,
Central Coordination

Though Registry is now closed, the data that were collected during its lifetime will remain accessible as a legacy database. This is in preparation and should become available in September 2018, to coincide with the EHDN plenary meeting in Vienna.

The legacy database provides a unique source of information on more than 14,000 Registry participants, including manifest, premanifest and at-risk individuals, and gene-negative and community controls. The Registry data of those Enroll-HD participants who took part in the older study may also be transferred to the new one with their agreement.

A large amount of curation has been devoted to increasing data quality in the legacy database. All successful applicants for data mining projects were asked whether they had encountered any issues with the datasets provided to them, and if they had performed any curation of their own, before undertaking their projects. Their responses were used to identify potential problems with the datasets, most of which concerned missing data. Other issues were corrected where possible.

A team has been created to prepare the legacy database. The members had a first face-to-face meeting in October 2017 and have also held several conference calls. A first quality control (QC) analysis of the data has been performed, and after a further QC analysis, the database will be finalised.

To simplify the analysis for applicants requesting access to both Registry and Enroll-HD, a short version of the database will be prepared, called the Registry dataset (RDS). This will be very similar to the Enroll-HD periodic dataset and will use the same recoded IDs. To reduce the risk of participant identification, outlier values will be aggregated, and instead of seeing dates users will see the number of days from baseline.

It will still be possible for researchers to obtain access to data that are not in the RDS, and to de-aggregated data, by requesting a specific dataset and following a procedure similar to the one currently in place for such a request. The procedure for obtaining access to the RDS will however be simplified compared to that for a specific dataset, involving a generic review of the project by the chairs of EHDN's Scientific and Bioethics Advisory Committee, and a decision by the chairs of the EHDN Executive Committee.

Data mining

Among the more than 100 applications for data mining projects that EHDN has received since Registry got underway, are projects looking at factors influencing age at onset and disease progression. There have also been applications for Big Data projects, such as the IBM (Modelling HD clinical assessments and comprehensive HD progression) and PsychoGenics (Computational outlier analysis of GWA phenotypic dataset – a machine learning exercise) projects.

A summary of data mining projects is available on our website: http://www.ehdn.org/hd-clinicians-researchers/previous-ongoing-research/ (under projects supported by EHDN, Clinical Research Projects). Publications that have been generated by EHDN-supported projects can also be viewed via that link.

We encourage applications for access to the RDS or specific datasets, which can be made via the following portal: https://www.euro-hd.net/html/projects/proposals/file/_/new (login required).

Any queries relating to the procedure should be addressed to: Christine.Capper-Loup@siloah.ch

Enroll-HD takes up the baton

Laura Spinney


Cristina Sampaio

Enroll-HD, the global successor study to Registry in Europe and Cohort in the US, held its first congress in Quebec City, Canada, over 20-22 May. The meeting was attended by all those scientists and clinicians who make the study function day-to-day, and according to CHDI's Chief Medical Officer Cristina Sampaio, it was an unqualified success. More than that, she said, it was "uplifting".

"Enroll-HD is an observational study embedded in a clinical research platform," she said. "I don't think the majority of those working on it had really grasped that, until the congress." But she stressed the importance, going forward, of the platform concept: "The reason it makes sense to keep going is because we can build new studies on top of the platform, and keep testing new hypotheses against the sample."

Enroll-HD is a vast machine, Sampaio said, and many of those involved only see a small part of it—like the blind men patting the elephant in the well-known parable. At the congress, they saw how the different parts come together to create a really powerful platform for clinical research. They saw how the data and biosamples collected in Enroll-HD are being put to use, and they realised that they were participating in a much more ambitious project than they had imagined. "It had an eye-opening effect," she said. "There was a sense of excitement, they saw the great value of their efforts, and that increased their commitment to the project."

The congress showcased platform studies that are already making use of the Enroll-HD infrastructure, such as the cerebrospinal fluid collection initiative HDClarity, alongside a number of innovations that are gradually being rolled into the study. These are designed to optimise the data being collected, the population being studied, and the study infrastructure.

One important goal of the Enroll-HD team going forward, for example, is to shift the study population away from the later stages of the disease towards earlier ones, including premanifest individuals. This shift is already underway, and the aim is to achieve a 50-50 balance of manifest-premanifest by 2025. Attracting the premanifest group to research is challenging, however—as a survey presented at the congress made clear. Those who carry the HD mutation but don't yet have symptoms are often employed, leading busy lives, and disinclined to engage with research or healthcare systems. The Enroll-HD team is therefore exploring ways of drawing them in virtually, via an app and web-based registry.

Another challenge the study faces is how to manage the sheer quantity of data coming in, along with the implications for the collection of that data of the European Union's General Data Protection Regulation (GDPR), which came into effect on 25 May. It is also modernising its biorepository, and putting in place plans to conduct systematic analyses of the samples in that repository. The goal of this last innovation is to ensure that those research groups requiring access to Enroll-HD samples are not forced to repeat the same analyses, but instead get direct access to the results of those analyses. "As machines go," Sampaio said, "Enroll-HD is a highly dynamic one, and it will always need to adapt to the changing needs of clinical research, and the changing regulatory environment."

A number of experimental huntington-lowering therapies are moving towards clinical trials, including one that is the product of a collaboration between CHDI and New Jersey-based PTC Therapeutics, that could potentially be swallowed as a pill. All of these efforts should be regarded with cautious optimism, Sampaio said. For now, she and her colleagues are working hard to fine-tune Enroll-HD, so that it can support those trials and accelerate them towards outcomes that, the entire community hopes, will be positive.

EHDN elections 2018

Jamie Levey, Central Coordination

It is time for elections at EHDN and we have the great opportunity to get out and vote for the Executive Committee (EC) and the Scientific and Bioethics Advisory Committee (SBAC)!

The EC is responsible for governing the EHDN, directing and overseeing its activities and establishing its strategy. The SBAC advises the network and the EC about scientific and ethical aspects of research. It also reviews research projects that require access to Registry data and bio-samples, and that seek funding under the seed fund scheme.

All regular EHDN members can vote—that's over 2,400 people! Historically voter turnout has been quite low in EHDN elections, but it is important that as many regular members as possible participate so that the network is properly represented. So please join in and make a difference!

This year there are five seats open on the EC, with two current members standing for re-election: EC co-chair Anne Rosser, and plenary meeting programme chair Lesley Jones. The EC has made a concerted effort to seek nominees from EHDN regions that are not regularly represented on the committees, notably the south and east of Europe, and to raise the profile and participation of younger HD clinicians and researchers, in order to keep new ideas and experiences flowing in. Seven seats are open on the SBAC.

Regular members may vote for each open position. This means that each regular member has five votes for the EC and seven votes for the SBAC, however they may only vote once per candidate. Committee members are elected for a term of four years.

Voting opens on Wednesday 1 August and closes on Friday 14 September, when the 2018 EHDN plenary meeting gets underway. Regular members will receive an email when the voting period opens, and may then vote via the following link (login required).

Come out this election period and VOTE!

Three grant deadlines

EHDN's Grants and Collaborations Manager, Fionnuala Margreiter, reminds members that three grant deadlines are fast approaching:

- Courses and workshop grants from the European Molecular Biology Organization, next deadline 1 August 2018
- Individual research fellowships offered under the European Commission's Marie Skłodowska-Curie Actions programme, next deadline 12 September 2018
- Funding opportunities from the Jacques and Gloria Gossweiler Foundation, for research projects on the non-pharmacological treatment of the symptoms of movement disorders, next deadline 1 October 2018

Follow our Grants and Collaborations Manager on Twitter **@EHDN_GRANTM** for the latest news on EU funding and events and policy developments in the domain of rare diseases.

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Update from Roche

In June, the EHDN posted on its website a letter from Roche, in which the company introduces itself and lays out its plans for future clinical trials of the experimental molecule RG6042, formerly known as IONIS-HTT$_{Rx}$.

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News from CHDI

The scientific presentations from the 13th Annual HD Therapeutics Conference, held in Palm Springs, California, from 26 February to 1 March 2018, are now available online, as is a postcard from the last two conferences in the series, narrated by Charles Sabine.

Cristina with her parents

The patient's view:

Interview with Cristina Ferreira

Cristina Ferreira saw Registry from one remove, as her mother's carer. This year she will join Enroll-HD in her own right. Here she tells us about her family's experience of a major observational study of HD, and the lessons she took away from it.

Tell us something about yourself.

I was born in Mozambique in 1971 and moved to Portugal as a child. I was trained as a lawyer but I currently work as a legal advisor in the city hall of a beautiful little town south of Lisbon, called Palmela. I am a proud mother to Sofia, 16, who plays the saxophone and is studying music at the Lisbon Metropolitan School of Music. Out of hours, I volunteer for research and for various HD associations, including the European Huntington Association (EHA). I also paint and write poetry.

How did you learn that your family was affected by HD?

My mother was diagnosed with HD in 2012, which is when I became aware of my own risk. I suspected that she had HD before that, because a cousin had been diagnosed with it, but she was only tested after my father died. She was showing behavioural and psychiatric symptoms by then, and he had been her main carer. After he died, she was hospitalised for a month and that's when she took the test.

Did your mother join Registry straight away?

Cristina's mother, Pureza (L). And on the right, being entertained by her granddaughter Sofia.

Yes, right after her diagnosis. She was enrolled by the neurologist who had diagnosed her at the Santa Maria Hospital in Lisbon—the same neurologist who still follows her, as it happens. The neurologist persuaded us of the importance of collecting data from as many patients and families as possible, to add to knowledge about HD. For us, at the time, the point was also to track the

evolution of my mother's illness and to give her access to future clinical trials and experimental treatments. We simply went up four floors to the centre that was running the study. The baseline visit took about half a day and there were annual visits after that, during which the staff collected samples and clinical data.

Untitled. By Cristina Ferreira's alter ego, Vicente Cravo

What was your role?

Since I hadn't had the genetic test at that time, I couldn't be assigned to either the control or at-risk groups, so I took part as a caregiver. My mother was already pretty symptomatic. Her speech was hard to understand, she was in a wheelchair, she had dystonia and a lot of chorea and dysphagia, so I stayed close to her and translated her to the Registry personnel.

What was the day-to-day experience of participating in Registry like?

The staff covered multiple specialities and were very well trained for collecting the data. In general our experience was excellent. We were impressed by the organisation, getting reimbursed for transport costs was easy, and the assessments were bearable for my mother, especially since I was there to reassure her. The only problem was a slight lack of flexibility in terms of scheduling. For example, my mother is not good in the mornings. If she had a morning appointment, she could be sleepy, bad-tempered and uncooperative. I explained this several times to the Registry staff, they took note of it, but still the next appointment would be in the morning. These little details make a big difference, especially to patients in the advanced stage of HD, and ultimately they affect the quality of the data collected. The experience highlighted to me the importance of listening to the patient's and carer's voices.

What do you think Registry has achieved, from a patient's or carer's point of view?

It threw light on exactly who HD patients are, where they are and what their lives are like. We are all aware in this community that we are in a race against time. The data collected in Registry will help in the validation of outcome measures, which will in turn accelerate the setting up of clinical trials and the transfer of new therapies to the clinic. That's hugely valuable, even if those therapies come too late for my mother. The data will be useful in social, legal and political domains too—informing analyses used to allocate health resources to rare diseases, for example.

You are about to join Enroll-HD, but your involvement in the community goes deeper than that, doesn't it?

HD-COPE meeting, London, February 2018

Yes. After keeping my distance for a while, I got involved in the Portuguese HD association. Because of that I went to the EHA conference in Sofia, Bulgaria last year.

Representing the Portuguese Alliance of Rare Disease Associations (APDH) on Rare Disease Day 2018

> *"It was a revelation: I discovered the human kaleidoscope that is the HD community."*

My background in advocacy turned out to be useful, too. Through the EHA I got involved in HD-COPE, an international coalition whose goal is to give HD families more of a voice in clinical research. In February we had a first meeting with Roche, who are designing the protocol for a large clinical trial of the huntingtin-lowering therapy that showed so much promise in a phase 1 trial last year. We're helping them make that protocol as patient-friendly as possible. The first thing the Roche team said to us was "thank you". I consider that a historical moment: it told us that we had already made a difference.

When you think about the future now, how do you feel?

Full of hope! As I said recently to Bernhard [Landwehrmeyer], it feels as if we've been scanning the horizon for spaceships for a long time now, and soon they will be landing in our gardens.

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Dates for your diary

Save the dates for:

- 11th FENS Forum of Neuroscience, Berlin, Germany, 7-11 July 2018
- EHDN2018 Plenary Meeting, Vienna, Austria, 14-16 September 2018 (registration closes 31 July)
- International Congress of Parkinson's Disease and Movement Disorders, Hong Kong, 5-9 October 2018
- Annual Health Care Summit, Geneva, Switzerland, 8-9 October 2018
- EANS2018 – the 18th European Congress of Neurosurgery, Brussels, Belgium, 21-25 October 2018
- World Orphan Drug Congress 2018, Barcelona, Spain, 6-8 November 2018
- Huntington Study Group's HSG 2018: Unlocking HD, Houston, USA, 8-10 November 2018