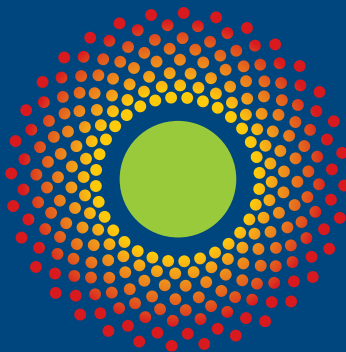


Enroll!

Updates from the Enroll-HD global community

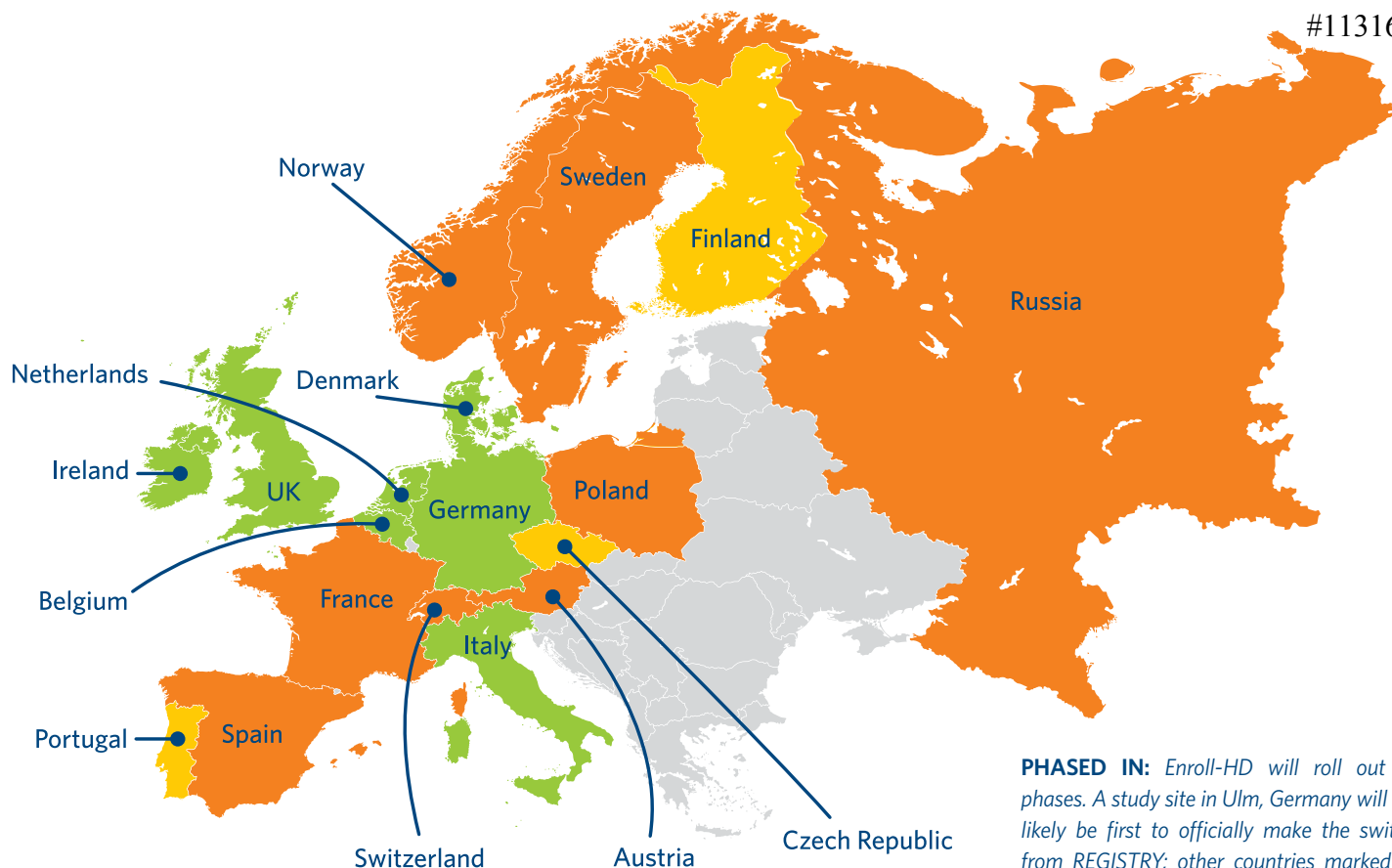


INSIDE THIS ISSUE:

Europe joins Enroll-HD
Interview: Taíse Cadore
Where does my data go?
Highlights from Rio

AUTUMN 2013

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PHASED IN: *Enroll-HD will roll out in phases. A study site in Ulm, Germany will likely be first to officially make the switch from REGISTRY; other countries marked in green will soon follow. Nations labeled in orange will be next, followed by those in yellow. Eventually, Enroll-HD in Europe will include about 150 sites in 18 countries.*

EUROPE JOINS ENROLL-HD WHAT DO YOU NEED TO KNOW?

This autumn and winter, Enroll-HD will be rolling out in Europe, replacing the current study REGISTRY. The studies are very similar, although Enroll-HD is larger and will be unified across the globe. But people who have been participating in REGISTRY will notice some differences. Here's what you should know and what you can expect from the change.

Why is REGISTRY changing to Enroll-HD?

The REGISTRY study is only being conducted in Europe. It had a counterpart in North America, called COHORT, but the studies were run differently, so the data doesn't exactly match up and some information is incomplete. Enroll-HD will merge both studies and also include people in other parts of the world, such as Latin America and New Zealand. It will be more systematic, meaning that all the same types of information are collected everywhere. It will be truly global, enrolling as many as 20,000 people on five continents.

Why does having a global study matter?

There are a number of reasons. In Enroll-HD the data and tests will all be standardized and collected the same way everywhere, so that they can be analyzed together. By putting a lot of people together in one study it should be possible to get answers that would be impossible with smaller studies—scientists call this having more statistical power.

In addition, comparing people from diverse ethnic and racial backgrounds and from different cultures can help identify genetic and environmental factors that influence how the symptoms of HD develop and change over time. “Why does person A show symptoms of HD at the age of 60, and person B, with the same number of CAG repeats, experience symptoms much earlier at the age of 45? Enroll-HD is probably our best chance of understanding that,” says Matthew Ellison, an HD family member and project coordinator for the HD Youth Organization (HDYO).

Also, a global study that assesses a lot of participants over a number of years makes it much easier in a couple of ways for researchers to find people who might be interested in and eligible to enter a clinical trial to test an experimental HD drug. Firstly, for a relatively rare disease like HD, it can be slow going for researchers or drug companies to find enough people to

volunteer for their trial. A global study like Enroll-HD means that many more people will hear about upcoming clinical trials. People will be recruited more quickly, allowing trials to be completed more quickly.

Secondly, having lots of clinical information on Enroll-HD participants’ disease signs and symptoms, and their biosamples, means that researchers can fine tune a clinical trial and only invite the ‘right’ volunteers: Those whose

More researchers working with these data and samples make it more likely that someone will make a real breakthrough.

disease stage is most appropriate for the particular drug under test, or have a particular CAG length, or show particular symptoms, or are a certain age—all sorts of different factors. This means that clinical trials will be smarter, and can give answers about a potential drug’s effectiveness more quickly using fewer research volunteers.

Having a worldwide registry of potential study volunteers is unusual for an uncommon genetic disease, and the hope is that it will encourage more scientists, including those in pharmaceutical and biotechnology companies, to focus on HD research to develop effective treatments.

What happens to my information from REGISTRY?

When joining Enroll-HD you will be asked for permission to transfer your data into the new study. However, if you choose not to join Enroll-HD your data will not become part of the new study but will be preserved in the REGISTRY legacy database. Later on, if you change your mind and decide to join Enroll-HD, your data can then be linked up.

Do I have to provide a blood sample to be part of Enroll-HD?

Yes. Giving a blood sample was voluntary under REGISTRY. Now, everyone who joins Enroll-HD will be asked to provide blood. This sample will be used in genetic analysis, to doublecheck the number of CAG repeats. This is called “research genotyping” because it is information used only by scientists researching HD. If you haven’t given blood before the important thing to know is that you will not be told the results of the research genotyping. You will not be told your HD gene status. Even the site staff will not be told, and your research genotyping will not be included in your medical records.

You will also be asked for permission to use your blood sample in other studies. This part is optional. Biological samples can be an important tool to answer crucial questions about HD. For example, genetic information—beyond just the HD gene—might explain why the disease is so different in different people. Other biological information that can be analyzed from the blood will be studied in order to look for biomarkers, signs that can be used to precisely monitor the state of the disease.

If you’ve already given blood as part of REGISTRY, you don’t have to do it again, although you may be asked to volunteer a new sample, which could be used in gene modifier and biomarker studies. You don’t have to provide a urine sample.

1178
PEOPLE
CURRENTLY
SIGNED UP
FOR ENROLL-HD
AS OF SEPT 30, 2013

What else will be different at the visit?

Not much. The people at the study site or clinic that you visit will be the same for Enroll-HD as for REGISTRY. You'll still be asked to take tests that measure mental function and look for emotional problems. If you've already given all your family history and personal history, you won't have to go through that again—just provide updates.

It depends on your site, but some of the cognitive tests will probably be new or slightly different. Enroll-HD combines the most accurate and useful tests from both REGISTRY and COHORT, and will also add some state-of-the-art tests that improve upon the old ones. Some tests will actually be shorter. For example, REGISTRY included a three-minute word fluency test in which you were asked to name words beginning with the letters F, A, and S. It will be replaced with a similar version that is only one minute long. One new test is being added called the mini-Mental Status Examination. It includes 30 questions and simple problems that assess memory, attention and concentration, like repeating a phrase, spelling backwards, or drawing a shape.

Will the visit be longer or shorter?

In most cases the visit will be slightly longer: Between 45 minutes and one hour. In REGISTRY your doctor did not have to do all the tests at every annual visit. In Enroll-HD, a core set of tests must be completed at every site for every participant at every annual visit; this is what makes the data more useful to researchers. Sites also have the option to add on additional tests that provide more information. These can bring the entire visit up to two and a half hours.

How is my information kept private?

The same system to de-identify participants that was used for REGISTRY will be used for Enroll-HD: Some basic personal information that you provide is used to create an "HDID", a 9-digit code. At the clinic, your medical information that your doctors look at is under your name. But any data collected as part of Enroll-HD that will leave the site and go into the database is only associated with that 9-digit ID number, and not your name. Even the people running the study at CHDI and its research partners, Outcome/Quintiles and the European Huntington's Disease Network, can't access names. See "Where does my data go?" on page 5 in this issue for more information.

Blood samples are protected by another layer of privacy;

before they are sent to the repository in Italy where they are stored they get a new ID number that is separate from the HDID.


Who gets access to this data?

Researchers all over the world can apply to Enroll-HD for access to data—more researchers working with these data and samples make it more likely that someone will make a real breakthrough. As long as the researchers are qualified to carry out the proposed work, as judged by the Enroll-HD Scientific Publication Review Committee, permission will be granted. The data and samples that these researchers would get access to are all recoded and all potentially identifying information (like the site where you were seen) is removed. Even the HDID is removed and replaced with another number to keep your identity private. Researchers also have to sign special agreements assuring that they will follow ethical standards of research and keep all information confidential.

How long will Enroll-HD last?

It doesn't have an official end date. The idea is for it to go on for many years, but you can quit at any point if it becomes too burdensome. "It's important for people to know that they essentially sign up for the long haul, but they can opt out at any time if it's too much for them," says Ruth Fullam, a member of the European Huntington's Disease Network, which coordinates the study in Europe. "They don't have to carry on, and it won't affect the quality of their care." But the longer participants stay with it, the more valuable the data becomes, because it shows how the disease affects people over time. Having that information for many thousands of people in Enroll-HD will be the best way to quickly judge the effectiveness of any experimental drugs that participants volunteer to test in clinical trials.

When is the changeover to Enroll-HD happening?

A site in Ulm, Germany, is expected to be the first in Europe, probably in mid to late October. Other sites in Germany, the UK and the Netherlands will probably be next, but not all the sites in one country will transition at the same time. Next will likely be Belgium, Denmark and Italy. Within 18 months, all 150 European sites in 18 countries will be part of Enroll-HD. 



Taíse Cadore, president of the Brazilian HD association, spoke at the World Congress.

TAÍSE CADORE

This year brings new attention to HD across Latin America as Rio de Janeiro hosts the World Congress on Huntington's Disease and Enroll-HD gets underway across the region, says Taíse Cadore, president of the Associação Brasil Huntington (Brazilian Huntington's Association), a nonprofit support and education organization based in São Paulo. She has been involved in the association since 2003 when a family member

was diagnosed with the disease. She knows from personal experience how difficult it can be in Brazil and in other Latin American nations to access information and find knowledgeable medical help—but, she predicts, that is now beginning to get easier.

For the Brazilian HD community, what's the significance of having the World Congress in Rio?

It's a very big moment for HD in Latin America, not only because of Enroll-HD but because of the Congress. This is the first time it happened in Latin America—a milestone. The Congress is our opportunity to say to the government and to others: Let me tell you about Enroll-HD, let me tell you about this disease. It is an opportunity to get government, families and the technical community focused on HD.

What's the current state of knowledge about HD in Brazil, and what needs to improve?

Here, we have two realities. In cities such as São Paulo, Rio, Brasília, Belo Horizonte, Porto Alegre—the big capitals—there are one or two physicians who specialize in HD, but it's difficult and sometimes expensive to get an appointment. It's not very accessible. In the countryside HD is not very well known. There may be no access to a lot of care that HD patients require, like nutrition, physiotherapy, and so forth. We as an association are working on this, but we don't have the resources or support and sponsors to send physicians there who have the knowledge to train the local physicians. Enroll-HD will provide an opportunity to say [to those doctors]: These are the centers in Brazil that are an excellent reference, and you can find a lot of information there.

What kinds of projects is your HD association working on?

Our mission is to communicate and link people. For example, medical students look to us to understand the disease, and we put them in contact with families as a way for them to get more knowledge. For people who just found out that the disease is in the family, we have a list of doctors who are ready to treat. And if someone from an HD family calls with the name of their doc-

tor, we'll call that person and introduce ourselves—then, if another family from the same city calls, we'll refer them to that doctor, who is already treating one family.

Another recent example: A new company that offers home care services found us on the Internet. We educated them about the services that HD patients need and now we can present this as a possible resource for families.

We are also working on a project to present to the government of Brazil to include HD training in the health system. A lot of physicians don't even know about the disease. So for example, if you need to retire early because of your HD, a physician or retirement systems expert may not understand the nature of the disease. Some of them would say: Come back in six months and you'll be better. These are the kind of issues that we face daily.

What do you think Enroll-HD has to offer in Brazil?

Latin America has so few resources. Enroll-HD will not only be an opportunity to find a cure but also a way to get more resources to families. It's not that we're expecting that the physicians will cure participants, but it will be much easier to get more health professionals involved in HD.


This is the most important result for the families in Latin America. We are coming from a history in which nobody knows how to deal with it, and there's no point of reference. Now there is an opportunity to start to talk about HD.

All these points are linked. Without Enroll-HD there's no point in talking so much about the participation of families. With the study there's a real opportunity for countries that don't have resources, and for dedicated professionals who can deal with HD.

You gave a talk at the World Congress titled "The role of HD families in driving scientific progress". What did you say?


Why families should be part of scientific studies like Enroll-HD, and what we, as families, get back from participating. In the community at large there is so little technical information. By participating in this kind of study you will better understand the science. You can build your hope with knowledge. This is essential for families nowadays.

Families have to be more aware of what's happening too. Some families, when they find out they have the disease, question what will happen should they have children. For the most part they don't understand the genetics. We need to spread this kind of knowledge.

The big message is that we need this kind of opportunity to change the history, from a disease nobody knows about to one where there is knowledge. This is my broad view. I hope I'm right! 

WHERE DOES MY DATA GO?

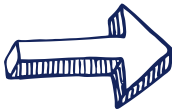
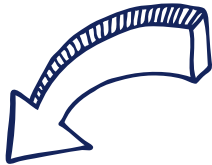
Enroll-HD will make data available to scientists all over the world while protecting the privacy of study participants. This works through a process of double de-identification. All data collected as part of the study is maintained separately from your own medical records. Your name is never entered into the Enroll-HD

database. Instead, your data is associated with a 9-digit code, the HDID. Then, before any of this information is made available to research scientists, other identifying data such as your birthdate and location are removed, and it is assigned a new ID number separate from the HDID. This way, data can be shared widely, but people's identities are still concealed. 



It Starts With You

Your health information is recorded by clinic staff and put into a computerized "electronic data capture" system separate from your medical records.



1. Your HDID

To protect your identity, your name is not included in this database. All the health information taken down for Enroll-HD is linked only to a 9-digit "HDID."

2. Locked Down

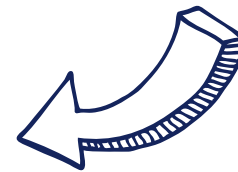
The information is stored in a secure server in the UK, the same systems that banks and hospitals use to protect sensitive information. The UK was chosen because it has the highest standards for data protection.

3. Keeping Secrets Safe

Before researchers can see it the data are further stripped of identifying details, such as your birthday or where it was collected.

4. A New Identity

Each record gets a new ID number and is moved onto a new server, for extra protection.



Putting Data to Work

Now, researchers studying HD can apply to get access to the de-identified data.

HIGHLIGHTS FROM RIO

In September, nearly 500 people gathered in Rio de Janeiro, Brazil for the 2013 World Congress on Huntington's Disease. It was the first large global conference focused on the research and care of HD held in Latin America, drawing people from 41 nations. International HD experts presented the latest scientific and medical advances, and regional specialists described research projects and efforts to improve HD care across the continent. In addition to the scientific and medical updates, the conference included patient and family perspectives on living with HD in Latin America and around the world.


The first plenary session brought home how significant it is for Latin America to host a world HD conference. Rodrigo Osório, president of the Agrupación Chilena de Huntington in Chile, said that as many as 120,000 Latin Americans are affected by HD in some way, but top-notch care can be hard to find. In some countries, genetic testing is not widely available, and misdiagnosis is more common than it should be.

Enroll-HD, the first global HD study to include participants across Latin America, was the subject of a special plenary session. The study will eventually involve as many as 3,000 people in sites in Argentina, Brazil, Chile, Peru, Venezuela and possibly other nations.

Each day, two sets of talks were held at the same time; one session was aimed primarily at scientists and medical professionals, and the other was for families, patients, and other people affected by HD. Speakers included academic scientists, neurologists and other medical professionals, as well as people from HD support

organizations and those personally affected by the disease. Italian HD expert Elena Cattaneo, PhD, who was recently appointed a permanent member of Italy's senate, talked about her research exploring what the huntingtin protein is and how it works. Several talks described the new drugs that could start being tested in people as early as 2014. Others focused on improving access to genetic counseling, an Australian project to protect people against genetic discrimination, and ways to improve life with HD. CHDI neurobiologist Ignacio Munoz-Sañjuan, PhD, introduced FactorH, an independent effort to help Latin Americans with HD gain access to housing, basic social services and medical care.


Nearly 100 family members attended the conference, and several talks discussed ways of coping with the physical and emotional demands of the disease. British television journalist and war correspondent Charles Sabine, who found out he was gene positive in 2005, described his own experience. He pointed out that effective treatments for HD will probably emerge gradually over time—meaning that long-term collaborative partnerships between researchers and patients are going to be crucial.

The congress was a landmark in Latin America, says neurologist Monica Haddad, MD of the Universidade São Paulo, one of the conference organizers. It inspired the shared sense that the best way to improve the lives of people with HD is for professionals and people affected by the disease to work together in this collaborative spirit. 

For more detailed notes on the conference, see the daily conference reports written by Ed Wild, MD and Jeff Carroll, PhD at <http://en.hdbuzz.net/138>

WHAT IS AN OBSERVATIONAL STUDY?

Instead of testing an experimental drug to see if it works, an observational study such as Enroll-HD simply measures the changes over time in people with a particular medical condition. It is a "longitudinal" study, meaning that it tracks people at regular intervals over years. These people are compared with the "controls", another group of people who do not have HD but are similar in other ways. Studying a disease over time in a real-world setting like this can provide a wealth of information that can impact quality of care and contribute to scientific knowledge about the disease.

For a disease like HD that usually changes very slowly these kinds of studies are particularly important since they reveal how things usually play out over the course of that disease. Knowing how HD usually unfolds makes it possible to tell whether an experimental drug is actually working, because it slows down or stops those changes. Enroll-HD is a prospective observational study, meaning that it is planned in advance, rather than relying on people to look back and remember how things have changed. 

Enroll! is a publication of CHDI Foundation, Inc., a not-for-profit biomedical research organization that is exclusively dedicated to rapidly 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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