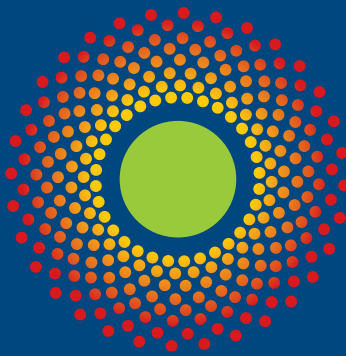


Enroll!

Updates from the Enroll-HD
global community



INSIDE THIS ISSUE:

Family Ties: the Bjorklunds

Improving Care

Q&A: Site Coordinator Dawn Rogers

JUNE 2014

HDSA ENDORSES ENROLL-HD

The US national patient-advocacy organization announces its support for the study

In February, the Huntington's Disease Society of America officially endorsed the Enroll-HD study—the first time that the national nonprofit patient-advocacy organization has signed on to any research project. “There aren't a lot of times in science that you can call something a potential game-changer, but this is one of those times,” says Louise Vetter, Chief Executive Officer of the HDSA.

Because the organization's mission is to support the entire HD community, HDSA hasn't put its weight behind studies of individual drugs or treatments before, says Vetter. But because it is inclusive and has such broad goals, Enroll-HD is different. “This is more than your average study,” she says. “It's a platform from which future HD science will be made possible.” The HDSA membership will have the chance to learn more about the study this month at the annual convention in Louisville, Kentucky.

HDSA plans to help raise awareness about the study with an educational campaign through its 54 local chapters and affiliated organizations nationwide. The idea is to make sure that everyone who might be interested in participating hears about it, and to demystify how the study works and what it involves. “We want there to be broad community awareness so that people can decide whether or not to get involved,” says Vetter.

The HDSA board spent a long time talking over the decision, says board member Jang-Ho Cha, MD, PhD, who has been involved in HD research at universities and pharmaceutical companies for decades. Ultimately, they agreed that Enroll-HD's aim of accelerating all HD research was worth endorsing. “This study is so important for laying the groundwork for the clinical trials

that we anticipate will be coming down the road,” he says.

There are roughly 7,000 “orphan diseases” like HD that affect a relatively small number of people. Pharmaceutical companies

that want to test new drugs for these diseases often struggle to find enough study participants. Without enough people, “a lot of companies will walk away from that disease, even if there's a good scientific rationale and unmet medical need,” says Cha. Enroll-HD is helping to establish many clinical centers with trained experts who know how to assess people with HD, and a registry of potential volunteers who may be willing to participate in drug trials. These tools will catch the attention of pharmaceutical companies and help bump HD to the top of their priority list.

“There aren't a lot of times in science that you can call something a potential game-changer, but this is one of those times.”

— Louise Vetter

Both Cha and Vetter emphasize that getting involved in research is a personal decision. Not everyone may want to participate. But everyone who wants to do so should have the opportunity. “Everyone asks what they can do,” says George Yohrling, PhD, Director of Medical and Scientific Affairs at the HDSA. “The greatest thing they can do is get involved in the research process. You don't have to sit on the sidelines waiting—you can be an active participant in the fight against HD.”

The potential of Enroll-HD to speed up how drugs are tested is valuable, says Vetter—it allows the research community to find out quickly whether something works, and use that information to move to the next step. “Enroll-HD provides a concrete way to

get involved without having to get tested [for the HD gene] or make decisions about therapies,” says Vetter. “It's a simple way to do something, and that's important.”



Huntington's Disease
Society of America

FAMILY TIES

For the Bjorklund family, being involved in research is all about hope

Erika Bjorklund will be having what anybody would call a busy summer. She's just finished her second year of medical training to become an osteopath, which means that after weeks of intense studying she'll have a marathon test in June that covers everything she's learned in the past two years. As soon as that's over, she'll fly from her home state of Washington to the Huntington's Disease Society of America convention in Kentucky in June. But when she heard that an HD research study needed control volunteers to provide a sample of spinal fluid—and the procedure had to be done at a hospital in Iowa—she didn't flinch. On her way back from Kentucky to Washington, she's stopping off in Iowa to get a spinal tap.

It's not just her: The whole Bjorklund family goes the extra mile for HD research. Erika's older sister Melissa, who has the expanded HD gene, is now volunteering for her second study, a drug trial to test a treatment for HD. The studies are in Seattle, a drive of about an hour and half from her home in western Washington state, so their mother Cindy takes time off work every week or two to drive Melissa there and back. Despite the inconvenience, they're both enthusiastic about the study. "I feel optimistic that it's going to help me," Melissa says. "It's also

helping other people, testing other things for them—for the future. I do it for both reasons."

For Erika, who is gene-negative, there are no immediate payoffs involved in flying to Iowa to get a lumbar puncture—only hassles and risks. But she's determined to do whatever she can to help HD research. "If I'm going to be a clinician, and expect my patients to be in trials, I need to be willing to do it myself," she says. It won't be the first time the family has gone out of their way to be involved in studies; a few years back the family vacation to California included a detour to the Gladstone Institute outside San Francisco, where Melissa donated blood for genetic research. And a family trip to Texas had to be rescheduled last winter so that she could be sure not to miss her first appointment for a new drug study.

The Power of Optimism

Erika and Melissa's father, who had HD, died when the sisters were young. They both decided to get tested and found out on the same day almost 10 years ago that Melissa had the HD

2351
PEOPLE
CURRENTLY
SIGNED UP
FOR ENROLL-HD
IN 10 NATIONS
AS OF JUNE 1, 2014



Melissa (left), Erika (center) and Cindy Bjorklund at Erika's white coat ceremony, the kickoff to her medical training.

“Believing you can make a difference by being involved in these trials can be helpful.” —Cindy Bjorklund



Erika (left) and Melissa Bjorklund (right). Both sisters are enthusiastic about HD research.

gene and Erika did not. At the time, Erika was just about to begin culinary school. After she finished she decided instead to pursue a career in medicine and research in order to help people with HD. “I want to be a clinical neurologist doing research studies,” she says. “Unless people are doing research, learning about outcomes, we can’t really figure out what is the best way to treat people. There are so many questions with HD that still need to be answered.”

Melissa began volunteering for trials of new drugs in 2012, when she signed up for the Reach2HD study of the new compound PBT2. As in many drug trials, some people were given the active drug and others given a placebo, an inactive compound, but they weren’t told which they were getting. Melissa and her whole family were sure she was taking the drug because they all could see that she was improving. During the six months that the trial went on her speech was becoming clearer and she was functioning better.

After the study was over it turned out Melissa had been taking the placebo – a good example of how powerful the placebo

effect can be, and the reason why any new drugs have to be tested against inert pills, to make sure that the active ingredients in the drug is actually improving symptoms. She thinks the reason she was doing better was probably because she thought she was taking the drug, and she expected it to work. Her mother thinks it was partly the sense of being involved in a constructive effort to improve treatment of HD. “To me, this is a real lesson in the power of the mind, and the human spirit to believe in something,” says Cindy. “It brought home the message that having hope and believing you can make a difference by being involved in these trials can be helpful. It was fascinating.”

Melissa is now in another drug study, for an extended-release version of tetrabenazine (Xenazine) that might have fewer side effects. It seems to be helping her balance and movements, she says.

As the primary caregiver, it falls to Cindy to do all the paperwork, request family medical leave from her job, and regularly drive to the study site. “There are definitely hardships,” she says. “But I don’t regret any of it.” Cindy and Melissa make the best of the trip by making a day of it: Going shopping in the city after the study visit, or going out for lunch. “They try to make it fun,” says Erika. The site staff at Evergreen Health also makes it a pleasure, Cindy and Melissa both say. “It can be a commitment, but it’s worth it in the end, for most people,” says Melissa. “I’d recommend it. It’s really hopeful for the future. It helps everybody.”

All three Bjorklunds feel optimistic that studies are finally now getting off the ground to test treatments for HD. One reason that all three are open about their family’s HD history is due to this sense of optimism about the future. “It’s made me very proud of both of my daughters for being involved in the HD community, for being involved in research trials on Melissa’s part, and learning about how to help people with neurological diseases on Erika’s part,” says Cindy. “In that way, we have a really positive family story.”

*The Bjorklund family graciously volunteered to share their research experiences and have their names made public because they feel that raising awareness about HD research is important and helps reduce stigma. Enroll-HD participants wanting to share their stories with **Enroll!** can always choose to remain anonymous if they wish.*

IMPROVING CARE WITH ENROLL-HD

Analyzing success could make health care better for everyone

Improving how a disease is treated doesn't always require a scientific breakthrough. It can be as straightforward as identifying which medical centers already have the healthiest patients, finding out exactly what they do to ensure their patients' health, and getting other clinics to use those methods. Such "quality improvement" projects have already made a big difference in the lives of people with cystic fibrosis and cardiac disease. The Enroll-HD Care Improvement Committee (CIC), an international group of researchers involved with the study, is now beginning to apply these principles to HD. The goal: "To create a world where the care of

The goal is "to create a world where care of current patients is simply better."

—Martha Nance

current patients is simply better," says Martha Nance, MD, one of the co-chairs of the CIC.

The basic idea is straightforward. Every HD center has their own preferred ways of treating the symptoms of the disease—for example, tending to prescribe one psychiatric drug over another, or recommending every patient (or none) to a particular type of physical therapy. Some of these methods are undoubtedly more effective at treating symptoms or keeping people healthier than others, but without hard data on who does better, it's impossible to tell. The only way to know for sure is to compare the results from many people at many different centers. Because Enroll-HD is collecting data from clinics around the world, it's an opportunity to make these broad comparisons across different regions and identify

SUCCESS IN CYSTIC FIBROSIS

About 14 years ago, the Cystic Fibrosis Foundation (CFF) began analyzing data from its national registry of people with the disease in order to improve routine care. CF and HD are both genetic diseases, and both affect about 30,000 people in the US. CF causes thick mucus to impair lung function and digestion, and it is serious: Fifty years ago, few children born with it survived to reach grade school.

When the CFF began comparing statistics across the 120 different specialized care centers in the US it discovered a big range of outcomes, with people at a few centers living much longer than others. "That was news, because every center was doing the best they could and thought they were providing the best possible care," says Eugene Nelson, DSC, MPH, a specialist in quality improvement in health care at the Dartmouth Institute in New Hampshire, USA. They discovered that the main causes of premature death were poor lung function and low body weight. Next, CFF looked closely at what the top centers were doing right. Some

examples included making sure that each patient came in for regular visits four times a year, aggressively treating lung infections, and making sure that every patient got an annual flu vaccine to protect the lungs, stayed at a healthy weight, and took all their medications.

From these observations the foundation drew up guidelines for the whole CF medical community. With Nelson as a consultant they organized collaborative networks so that everyone involved in treating CF could learn about the most effective methods for maintaining lung function and healthy weight. As part of that program, teams from 20 centers would come together three times a year to analyze the way they provide care, compare it against the best, and systematically improve how they do it. Each center would also track the changes in outcomes over time. The CFF also made data on each center public, so that all the clinics could measure their progress against the average and the best.

Today, people with CF are much healthier; the average predicted lifespan of

people with the disease reached 41.1 years in 2012, up from 31.3 years in 2002, and is still climbing. New medications are part of that success, but big benefits came from using the patient registry to track health outcomes, getting patients and families involved, and setting up learning networks so that best practices are adopted widely and rapidly.

A similar kind of process has helped improve the care of rheumatologic diseases in Sweden, and treatment of irritable bowel disease in children in the US, and it can work in HD too, says Nelson, who is advising the Enroll-HD Care Improvement Committee: "Wherever you have a chronic condition, these methods tend to apply." The crucial steps include bringing together the whole "community of practice"—experts in every aspect of the disease, plus patients and families, and the data and statistics experts that can analyze the information. "Cystic fibrosis is an extraordinary example, but there are others waiting to happen," says Nelson. "The chances are quite good that if the approach is applied with fidelity, it can lead to real improvements."

“best practices”—the treatment choices that on average lead to the healthiest, best-functioning patients.

It may be surprising that this hasn't been done before, but because HD is an “orphan” disease, meaning that it affects relatively few people, few studies have been able to compare current practices to see which are most effective. Experienced HD doctors rely on their knowledge and best judgment in treating their patients, but not all doctors who treat HD have this experience, and even the best instincts can be misleading. “We really don't know what aspects of what we do are actually important,” says Nance, who is director of the HDSA center of excellence at Hennepin County Medical Center. “We have no idea whether one antidepressant works better than another in terms of treating depression—or maybe no antidepressant works better.” The data collected within Enroll-HD can answer some of these questions.


Identifying best practices can make a big difference in the lives of people with chronic disease. A quality improvement project in cystic fibrosis (CF) has increased the lifespan of people by 10 years since 2002 (see sidebar, “Success in Cystic Fibrosis.”) “Just by putting forward these standards of care, and organizing the care teams according to best practices, they were able to actually increase life expectancy,” says Joe Giuliano, CHDI director of clinical operations. “That's ultimately what we're all about, to improve the lives of people with HD and their families.”

A similar effort launched in 2009, the Parkinson's Outcome Project, has found “dramatic variation” in how well people do with the disease at different clinics that specialize in Parkinson's disease, says Peter Schmidt, PhD, the vice president of research and professional programs for the National Parkinson Foundation, who is in charge of the project. “In medicine, there's an assumption that any one physician could be exchanged for another—that the most important thing is which pills patients are given, and what they're told to do,” says Schmidt. “We rarely consider the performance of a physician,” or take into account the way that a center's staff works together to ensure that patients get all the services they need. But in fact the data collected for the Parkinson's project show that the doctor and the care site account for about 25 percent of the differences in health and quality of life in PD patients. This project has already identified a way of organizing health care that makes a big difference in depression, one common problem in PD.

Getting the best treatment can have a big impact on mood, energy, and ordinary life activities.

In HD the first step will be to see what is actually being done now, so the committee is now working on an online survey that the group hopes to send to all active Enroll-HD sites in June. It will establish the basic facts for each center—what services they offer, who is on the HD care team, how often patients are seen, and how the clinic is organized. “It will give us some understanding of the context of care,” says Jan Frich, MD, PhD, of the University of Oslo and currently a visiting professor at the Yale School of Public Health. Meanwhile, a working group is starting a small-scale analysis of data from REGISTRY (the long-term study that preceded Enroll-HD in Europe) to begin identifying which medical practices might be most relevant to improving quality of life—the first step in zeroing in on what really makes a difference. “We'd like to learn more about how the model of care may actually have an impact on the patients and family,” says Frich.

In cystic fibrosis, lung function and body weight are easy to measure and clear signs of how well a patient is doing, but HD does not have any such obvious benchmarks yet. “In some patient groups it's easier to identify the relevant measures, but it's a huge challenge in HD. But I think it's worth trying,” says Frich. “HD is a complex disease with many symptoms, and my guess is that we'd need several indicators rather than just one.” Candidates include measures of motor function, behavioral symptoms, or possibly body mass index (weight), but the main focus will be the overall wellbeing of the patient and family. To begin with, one possible yardstick to compare different practices and centers will be patient quality of life, which can be roughly measured with a symptom checklist. Obviously, quality of life is affected by more than just medical care, but getting the best treatment can have a big impact on mood, energy, and ordinary life activities.

The promise of quality improvement projects is being able to make a big difference in health care now, even before any great new drugs are invented. In PD, says Schmidt, the numbers suggest that excellent neurological care is equivalent to a drug that reduces the impact of the disease by 15 percent—potentially a big difference in many people's lives. Meanwhile, the challenge in quality improvement projects is figuring out which aspects of treatment make a big difference. A lot of measurements are required to tease apart which parts of care are the most important. It's also important to have a wide range of practices to compare. Because Enroll-HD is a large international study, it has both of these ingredients. “The strength of Enroll-HD is having the numbers to ask these kinds of questions,” says Nance. “The power is in the numbers.” 



BEHIND THE SCENES WITH... DAWN ROGERS

As a coordinator for the Enroll-HD site in Manchester,

UK, Dawn Rogers works with people who have signed up to participate for this and other HD studies. For the time being, she is also doing another job: Helping make sure that all the study sites in the UK transition smoothly from REGISTRY to Enroll-HD. As a study monitor, Dawn Rogers travels the length of the United Kingdom “from Aberdeen to Cornwall,” visiting sites that are preparing to transition to double-check that data is accurately collected and well-maintained. It’s a lot of travel, but she likes it. Because she stops in on each site individually, sooner or later she meets nearly everyone who is involved in the UK branch of the study.



Dawn Rogers, site coordinator at the University of Manchester, UK

on any history of behavioral or motor problems. The site visits also involve training—for example, on the cognitive assessments or the problem behaviors assessment. I’ve got to know a lot more people in this role. It’s lovely to feel a bigger part of the HD network.

The other half of the week you’re in Manchester.

What is your work like there?

I’m involved in the recruitment of patients—but actually, we have a lot of patients who want to take part, so I don’t do a lot of actively going out and finding people. I’m involved in organizing the clinics, and do the majority of the research assessments with people. I’m also involved in a number of clinical trials coming up.

When you visit sites around the UK as a study monitor, what do you do?

We check the data against medical notes and family records, and meet with coordinators there. We want to make sure the records of clinical characteristics are as accurate as possible. We check through the medical notes to make sure the site staff have picked up

What’s your favorite part of the job?

I love meeting the patients! I love talking to them about research as well, and explaining about Enroll-HD. We’ve generally had a very positive vibe from patients about the study. They’re excited that it’s gone global and is going to be a much larger cohort.

The assessments for Enroll-HD can be tedious for study participants. How do you make it fun?

I try to put people at ease as much as possible. We have a real continuity of staff at Manchester, so families meet with the same people each year. They appreciate that we’ve remembered details about them. In terms of making the assessments fun, I’m not sure we’ve achieved that! We try to let people know we want to support them. We try to encourage people not to put too much pressure on themselves. You have to relax people, because it can be stressful for them. I’ve been tested on these tasks too, and I know they’re not easy. Being a rater, I was expected to be good at them, but as I tell people, I made errors too. People get a giggle out of that.

What do you tell people about getting involved in research?

We let people know that it’s really useful information. A lot of people are keen to be involved in other research as well, and we let them know that this is what we use to see if they’re suitable for those studies. It’s all connected, it’s an important network. A lot of people are keen to be involved in whatever way they can.

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