

# The Power of Many

Data from patient registries help advance research and improve care.

BY RICHARD LALIBERTE

“It just happened out of the blue,” says Jeff Arison of Crystal Lake, IL, explaining the mysterious onset of amyotrophic lateral sclerosis (ALS) when he was 31. He was, he says, “a regular guy.” He loved sports, playing golf, driving cars, and hanging with friends. Then he started having trouble walking and began experiencing muscle weakness in his limbs and extremities. Over the next six to eight months, his symptoms worsened. An orthopedist thought he might have a pinched nerve, but Arison sensed something worse.

He saw a neurologist in February 2011, eight months after his symptoms began. An electromyography (EMG) test to assess the function of his muscles and the nerves that control them was inconclusive. After several visits, his neurologist referred Arison to the Mayo Clinic in Rochester, MN. In October 2011, after four days of testing, including another EMG, a muscle biopsy, an overnight breathing test, two MRIs, and a CAT scan, doctors concluded he had ALS—and his life turned upside down.

Arison is still passionate about his interests, but he is now in a wheelchair and needs a device to help him breathe—all because of a neurologic disorder with yet-to-be-discovered origins.

## LOOKING FOR ANSWERS

Arison’s desire to learn more led him to the Les Turner ALS Foundation in Skokie, IL, where a social worker encouraged him to join the National ALS Registry. The goal of the registry, which was founded a decade ago by Congress, is to collect information from people with ALS nationwide in order to learn more about who gets the disease and why, according to the Agency for Toxic Substances and Disease Registry at the US Centers for Disease Control and Prevention (CDC), which runs the program.

To learn more about potential causes and treatments, ALS researchers need data—preferably large amounts, from people of

varying backgrounds, interests, and locations. Yet ALS is relatively rare, so extensive information-gathering resources are crucial. The National ALS Registry automatically gathers anonymous case data from ALS patients who use Medicaid, Medicare, or services through the Department of Veterans Affairs, in addition to people like Arison, who sign on individually and volunteer their data. Information in the registry can’t be traced back to individuals, and those who participate through government services don’t need to provide consent to have their data included.

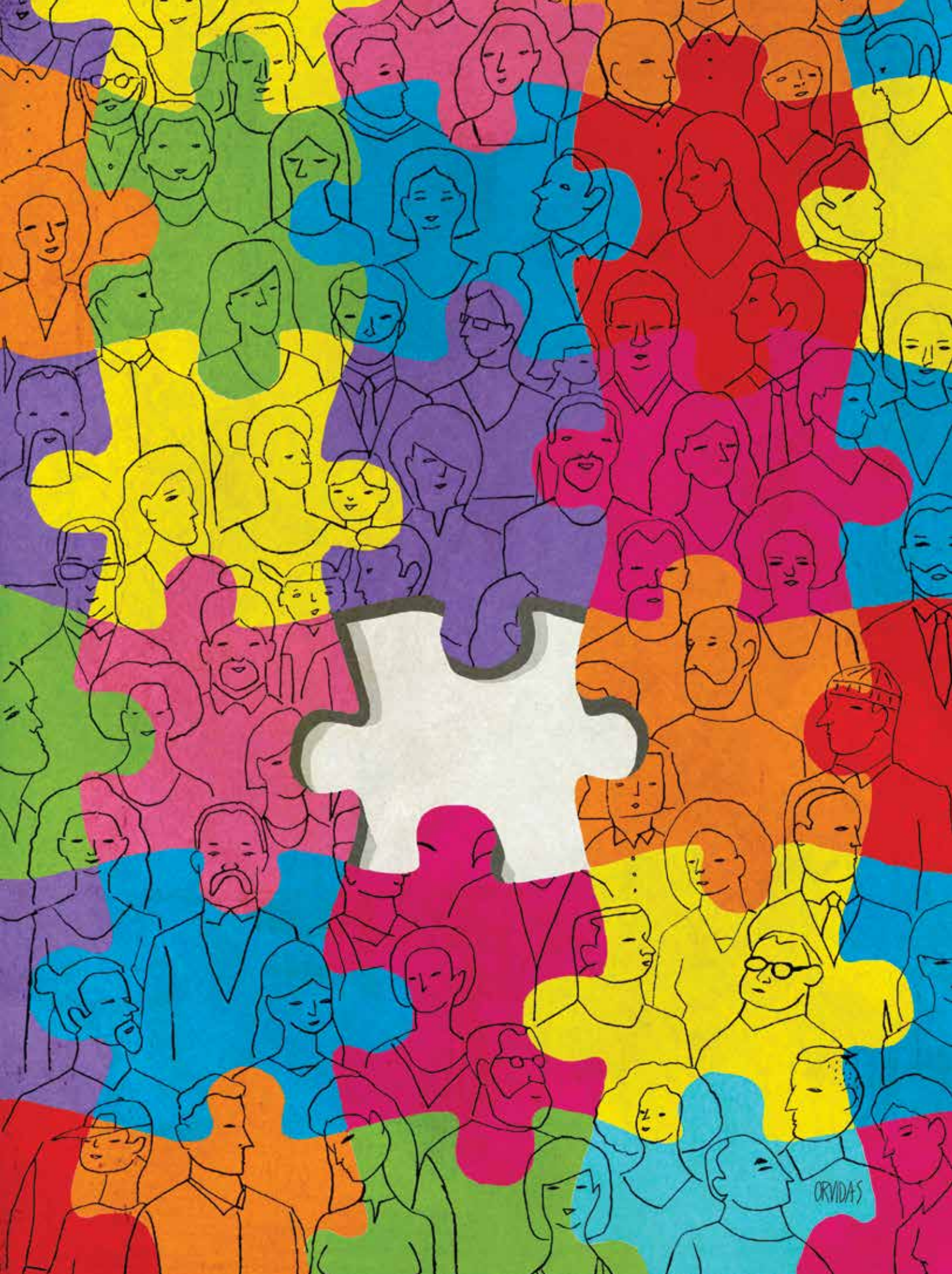
Participants provide details on variables such as family history of neurologic diseases, smoking history, military service—studies repeatedly show that military personnel, regardless of level of service, are twice as likely to die from ALS than people who never served in the military—occupation, hobbies, and exposure to various toxins. In return, the registry can notify patients of clinical trials. “If a clinical trial needs people, anyone in the registry who fits the study parameters automatically gets an email notification and information on how to contact the researchers,” says Andrea Pauls Backman, executive director of the Les Turner ALS Foundation. “That’s a huge asset for both researchers and patients.”

## AMASSING INFORMATION

A registry is generally defined as a collection of standardized information about people who share a common condition or experience. “Historically, they’ve been focused mainly—but not exclusively—on research,” says Lyell K. Jones Jr, MD, FAAN, chair of the American Academy of Neurology (AAN) Registry Committee and director of the adult neurology residency program at the Mayo Clinic in Rochester.

Two aspects make them especially useful for studies: They gather information by following people over time, and they aggregate data, which can reveal significant patterns or trends.





ORVIDAS



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“By collecting and pooling data from lots of folks, you get lots of useful information about a given condition,” Dr. Jones says.

Registries are also invaluable for tracking what happens when a new drug or medical device comes on the market. Clinical trials produce valid findings on safety and effectiveness in tightly controlled situations for a finite period of time, but they don't account for problems that may emerge after the study is over. Patients in post-market surveillance registries continue reporting problems or outcomes well after clinical studies have ended or as their disease advances.

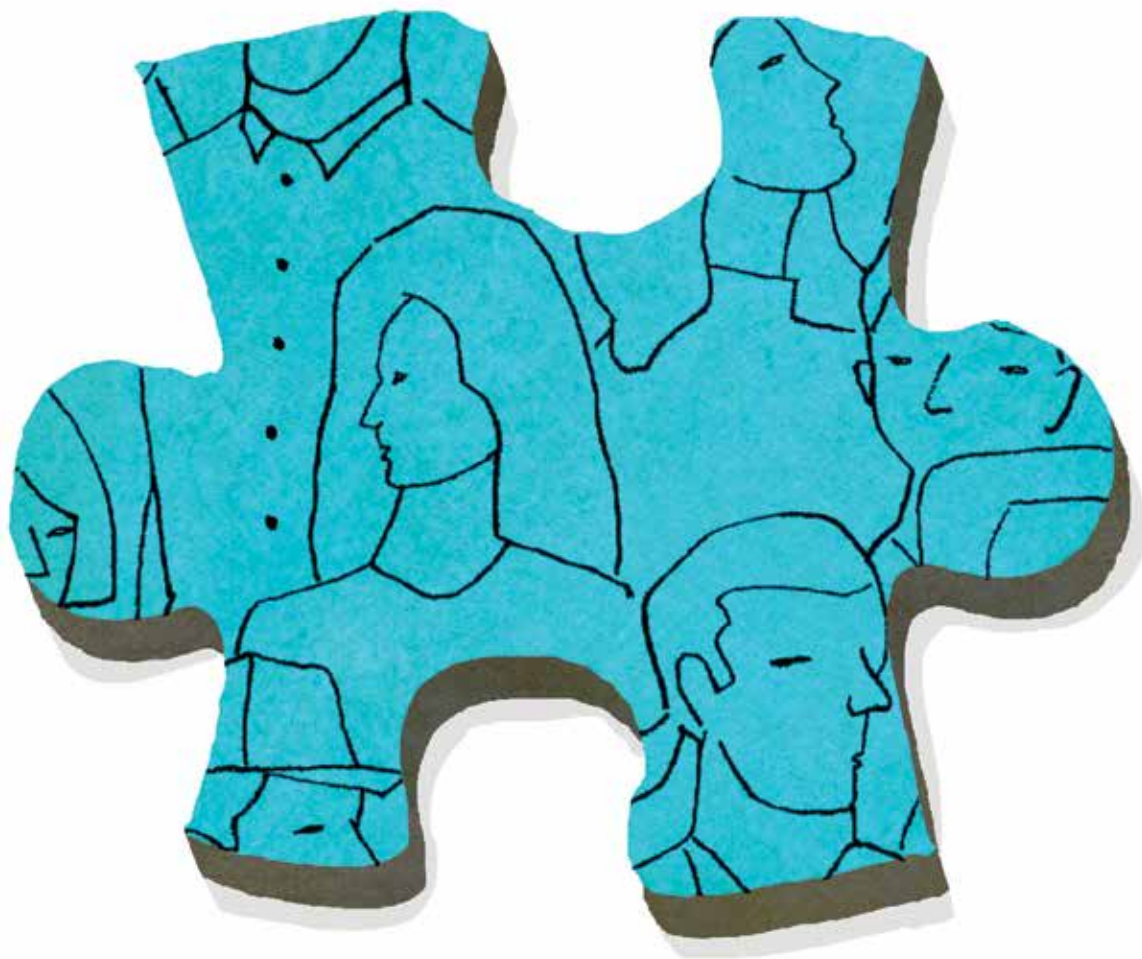
“When treatments enter the real world, that's often when new problems or side effects come to light,” says Sarah M. Benish, MD, FAAN, a neurologist at the Minneapolis Clinic of Neurology and a member of the AAN Registry Committee. “Registries are tools for constantly advancing our knowledge.”

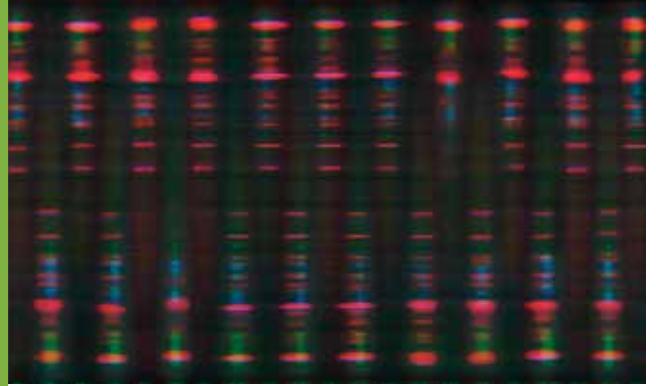
### EXPANDING FUNCTION

As registries grow in number and importance, they're also becoming more diverse in form and function.

Some registries ask patients to fill out information online and provide feedback on a portal where they can see their own information, but not other people's. Some involve phone surveys. Some allow members to share their information with others. Some gather data from patients' medical histories and feed details anonymously into a database, while others gather only information patients agree to provide. Others take a combined approach. Some put patients directly in touch with scientists doing clinical trials, while others act as intermediaries.

Of 51 major registries listed on the National Institutes of Health website, about one-fifth pertain to neurologic conditions, including the Alzheimer's Prevention Registry, the Cerebral





Palsy Research Registry, the Dominantly Inherited Alzheimer Network (DIAN)—Expanded Registry, DS-Connect®: The Down Syndrome Registry, the Myasthenia Gravis Patient Registry, and the National Registry of US Myotonic Dystrophy and US Facioscapulohumeral Muscular Dystrophy. A search tool from the Agency for Healthcare Research and Quality called the Registry of Patient Registries can help people find registries related to specific conditions ([patientregistry.ahrq.gov](http://patientregistry.ahrq.gov)).

## BENEFITS OF REGISTRIES

### IDENTIFYING PATIENT PRIORITIES

As a child, Joy Aldrich didn't know why she felt so clumsy. "I did everything I could to avoid school on days we had fitness tests in gym," she says. "I couldn't run without falling down and I couldn't jump, so other kids made fun of me." At age 14, she got an explanation through her mother, who'd had similar problems as a child but had been thought to have a mild case of polio.

When Aldrich's mother, at that point in her 40s, had a cast removed after breaking her ankle, her podiatrist noticed that the muscles in the affected leg had atrophied much more than normal. After countless doctors' appointments, a neurologist made the diagnosis: Charcot-Marie-Tooth disease (CMT), a group of inherited disorders in which genetic mutations damage nerves or the protective sheath around them. The damage can interfere with nerve signals to the muscles and trigger symptoms such as weakness in the limbs, loss of muscle, and difficulty walking. Aldrich's mother's genetic mutation caused a form of the disease called CMT1A, which is autosomal dominant, meaning that each of her children had a 50 percent chance of inheriting the mutated gene. EMG tests helped establish that both Aldrich and her brother had the defect.

"It was actually a relief to get a diagnosis and have a reason why I couldn't do certain things," Aldrich says. When at age 40, her symptoms, like difficulty walking, started becoming worse, she reached out to the Hereditary Neuropathy Foundation (HNF, [hnf-cure.org](http://hnf-cure.org)), which advocates primarily for people with CMT variants, and joined the Global Registry for Inherited Neuropathies (GRIN), a joint venture between HNF and Hannah's Hope Fund.

"Our goal is to understand the disease, help with preclinical research, and provide a tool for clinical trial design and recruitment," says HNF founder Allison Moore, who also has CMT. GRIN participants provide data about family history, specific genetic variations, and willingness to join a clinical trial. They also share details about how mobile they are, what interventions they use, and how much pain they experience.

## Reservations about Registries

Despite the benefits, some people are cautious about enrolling in registries. "The first things that come up are privacy and data security," says Lyell K. Jones Jr, MD, FAAN, chair of the American Academy of Neurology Registry Committee. "Extraordinary security measures are in place to make sure your data are protected."

Still, patients aren't always convinced. "You can tell them there's no way somebody can get in and find their personal data, but many people may not find that reassuring enough," says Lewis B. Holmes, MD, of Massachusetts General Hospital for Children.

Another obstacle is the time it takes to fill out forms or complete surveys. "We ask ourselves every year whether we should change the way we get information," says Dr. Holmes. His registry gathers data through phone calls, in part to ensure that participants answer every question, which enhances the quality of information in the database.

People may also be frustrated by what registries don't provide. For example, the GeneMatch DNA-gathering program associated with the Alzheimer's Prevention Registry doesn't tell you if your genetic code contains the apolipoprotein E4 gene, which is known to boost the risk of Alzheimer's, unless you become part of a clinical trial that requires you to learn this information. And registries may not provide a portal where you can access your own data.

On the research side, registry databases are sometimes criticized for having inconsistent, unverified, or biased data.

Such concerns don't matter to Jeff Arison, who has amyotrophic lateral sclerosis (ALS) and joined the ALS National Registry. "I can't think of any downsides," he says. "If I can help find a cure, that's awesome."

### LEVERAGING ONLINE COMMUNITIES

HNF also offers access to what has become a valuable adjunct: an online discussion and support community provided in partnership with a platform called Inspire. The online community has played a pivotal role in bringing patient realities to light and driving research into underexplored topics. Recently, for example, online discussions about CMT-associated pain led the foundation to analyze GRIN data and conduct a survey of CMT patients, which revealed that the majority experienced pain and/or took medications to control it.

"We hadn't realized the depth and breadth of what people were experiencing," says Tina Tockarschewsky, director of medical and

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public affairs at HNF. “The data gave us more leverage to advocate for greater attention.” A pharmaceutical company that previously lacked data on pain in CMT is now exploring new therapies.

Online forums also foster discussions about topics such as medication side effects, cost of care, and anti-inflammation diets. “There’s been a lot of conversation about opioids and pain management,” says Aldrich, who moderates HNF’s Inspire community discussions. “In many cases, medication is becoming difficult to get, or traditional pain management programs aren’t very helpful. That leads to discussions of cannabis and other alternative therapies.” Some people experiencing devastating setbacks, like amputation due to an infection following a CMT-related surgery, have even brought up suicide.

“The registry and the Inspire community are separate entities, but when I see patterns in online conversations, I can remind the community to report a given topic in the registry so it can be used more formally for research,” Aldrich says.

Other registries promote these difficult but important discussions in other ways. For example, registries designed to improve quality of care may encourage doctors to ask patients specific questions that are associated with better outcomes. The Axon Registry®, which gathers data on patient care in neurology practices, for instance, credits clinicians with meeting a quality measure if they talk with patients about advance health care directives at least once a year. (For more information about the Axon Registry, visit [bit.ly/NN-AxonRegistry](http://bit.ly/NN-AxonRegistry)).

## ASSESSING RISK

Ultimately, insights from registries help those who contribute data. For example, the North American AED Pregnancy Registry was established in the 1990s to help researchers learn more about the risks of antiepileptic drugs (AEDs) for pregnant women and their children. Data from the registry have helped provide important guidance for both clinicians and women in balancing the benefits of taking specific AEDs to manage serious symptoms related to epilepsy, mood disorders, migraine headaches, and chronic pain with the risks of drug-related birth defects.

Data collected from 10,200 women have contributed to numerous studies published on the AED Pregnancy Registry’s website, [aedpregnancyregistry.org](http://aedpregnancyregistry.org). For example, a 2012 study published in *Neurology* that evaluated the safety of antiepileptic medications found that some drugs had many more associated risks than others.

“Valproate is the most dangerous,” says registry director Lewis B. Holmes, MD, retired chief of the Medical Genetics Unit at Massachusetts General Hospital for Children. As noted in the 2012 study, registry data confirmed an association of valproate

with an increased risk of birth defects if taken while pregnant, including spina bifida, distinct facial features such as cleft lip or palate, and heart abnormalities.

Just as important, data from the AED Pregnancy Registry suggested that drugs such as lamotrigine (Lamictal) or levetiracetam (Keppra) are safer than valproic acid or topiramate (Topamax), Dr. Holmes says. This is invaluable knowledge for women weighing the risks and benefits of different AEDs.

## CONNECTING TO CLINICAL TRIALS

Access to clinical trials is as vital to researchers as it is to patients. “The staggering fact is that 80 percent of studies are delayed because researchers can’t find eligible participants in the desired time frame,” says Jessica Langbaum, PhD, principal scientist at the Banner Alzheimer’s Institute and associate director of the Alzheimer’s Prevention Initiative, which runs the Alzheimer’s Prevention Registry. “That’s an unacceptable problem.”

The Alzheimer’s Prevention Registry ([endalznow.org](http://endalznow.org)) matches people willing to participate in clinical trials with researchers seeking subjects. Participants who sign up receive monthly newsletters and emails notifying them about open studies. Registry participants then reach out to researchers. “We collect minimal information,” Dr. Langbaum says—mainly basic data like year of birth, zip code, and race or ethnicity. “That’s a different model from registries that may collect detailed information and send targeted invitations,” she says. “We chose a model that requires the lowest commitment or effort to make it very easy for participants.”

## PROVIDING DATA FOR RESEARCHERS

Some registries, including the National ALS Registry and the Alzheimer’s Prevention Registry, gather a different form of data: biological samples, which go to disease-specific biorepositories where researchers can obtain tissue or DNA for direct analysis.

“Participants are giving the ultimate gift,” Pauls Backman says—especially those who pre-register to donate postmortem samples to the ALS biorepository after they die.

For living participants, the process is simple: A person or package arrives at your home with a kit to collect a swab of saliva or a sample of blood, hair, or nail clippings. “The hope is to connect the dots between genetic causation, presentation in bodily tissues, and clinical progression of the disease,” Pauls Backman says. “That might lead to biomarkers, which would be a huge advance in diagnosis—and the sooner you get treatment, the better the quality of life.”

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**WEB EXTRA:** To learn how the myasthenia gravis community is expanding its Patient Registry, go to [bit.ly/NN-MGFA-Registry](http://bit.ly/NN-MGFA-Registry).