NIH StrokeNet

How the NINDS is improving and accelerating clinical trials for stroke.

BY TOM VALEO

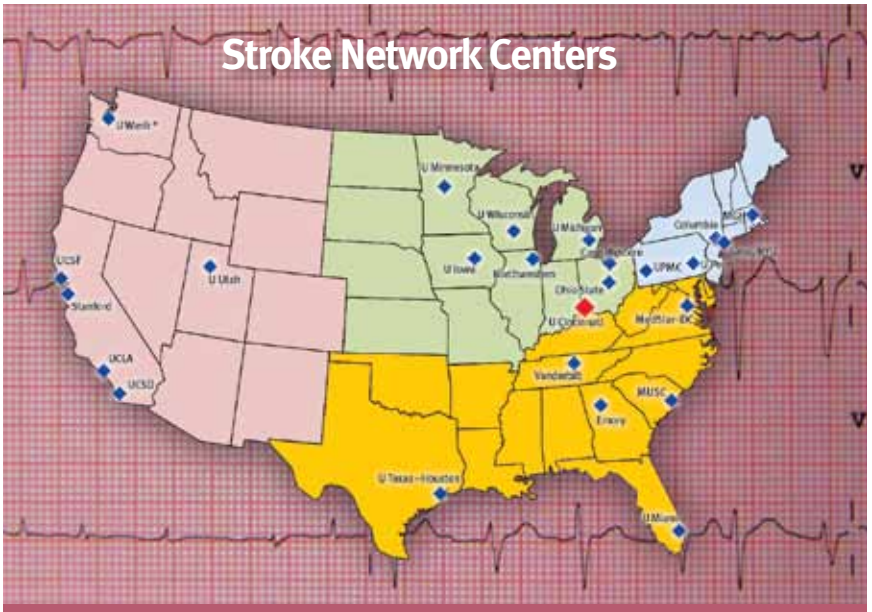
A world's fair amounts to a small city that springs up suddenly with an elaborate infrastructure—buildings, water and sewage pipes, electrical lines, roads—and an army of employees. When the fair closes, the city becomes a ghost town. Nothing is salvaged for the next fair, which must be built from scratch again.

Clinical trials work much the same way. Each one involves the creation of a "city" for designing the experiment, recruiting subjects and researchers, analyzing data, managing the budget, and monitoring countless other details. Then, after several years, when the trial is completed, the infrastructure is abandoned.

Wouldn't it make more sense to build the infrastructure once and use it over and over again?

When it comes to stroke research, that's precisely what the National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health (NIH), has achieved by creating NIH StrokeNet. This network of 25 institutions, plus satellite hospitals, will coordinate clinical trials for stroke prevention, treatment, and recovery. The centers—strategically placed in almost every region of the United States—are linked to hospitals in their region so that trials can involve a larger number of people and results can be shared quickly to have the greatest impact on patient health.

NINDS believes that NIH StrokeNet can accelerate the search for better ways to prevent, treat, and recover from strokes while at the same time reducing redundant costs. "NIH StrokeNet will allow the most promising therapies to quickly advance to the clinic—to improve prevention, acute treatment, or rehabilitation of the stroke patient," says Walter J. Koroshetz, M.D., NINDS deputy director and Fellow of the American Academy of Neurology (FAAN). "We need to have



NIH StrokeNet National Clinical Coordinating Center
University of Cincinnati

NIH StrokeNet Regional Coordinating Stroke Centers
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Emory University School of Medicine
Massachusetts General Hospital/Partners HealthCare
Medical University of South Carolina
MedStar Health Research Institute, MedStar NRH, Georgetown University
MedStar Health Research Institute, MedStar Washington Hospital Center
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a balance of approaches to decrease the burden of illness due to stroke."

STREAMLINING ADMINISTRATION

NIH StrokeNet will create an infrastructure capable of managing everything from the design of a research project to the details involved in writing contracts, paying bills, and analyzing data. "We expect to see lots of savings—in money and time—because we won't have to build up the trial infrastructure again and again," says Petra Kaufmann, M.D., director of the NINDS Office of Clinical Research, which directs the planning of clinical trials, and member of the AAN.

For example, every clinical trial needs an institutional review board (IRB) to make sure the participants are treated fairly and ethically. Normally, each site conducts its own local IRB review of the trial procedure (called a protocol). But with NIH StrokeNet, all sites will rely on a single, central IRB at the University of Cincinnati that will monitor all clinical trials for the entire network.

"That avoids the need for the same protocol to be reviewed at multiple universities by many committees," Dr. Kaufmann explains. "NIH StrokeNet will save time because you won't have many separate entities doing the same thing. There will be one board in charge."

NIH StrokeNet will also create standard trial agreements and contracts so administrators "won't have to reinvent the wheel each time," Dr. Kaufmann notes.

Once clinical trials are up and running, the data they produce will funnel into the Data Management Center for StrokeNet at the Medical University of South Carolina, where Yuko Palesch, Ph.D., is the principal investigator. This will streamline the process and also make the data more available for future trials. What's more, NIH StrokeNet will make all data available to other researchers around the world.

The Importance of Participating in Clinical Trials

Clinical trials depend on recruits—people who volunteer to participate in the testing of new drugs, devices, and procedures. But people cannot volunteer if they don't know which clinical trials are available. To remedy this problem, NIH StrokeNet is developing a website that will make trial information readily available.

"Eventually, patients, investigators, and industry will be able to see what trials are going on," says Joseph Broderick, M.D., at the University of Cincinnati. "This will help those interested to get connected to trials."

Patients can't volunteer for acute stroke trials, of course—no one can plan for that—but trials that focus on prevention and recovery might provide numerous opportunities for patients who are interested in volunteering.

"We want patients to know how critical it is that they and their families are willing to participate in research," Dr. Broderick says. "It's not always easy, particularly when you're having a stroke and someone starts talking to you about entering a clinical trial. That's the last thing you want to think about at such a time. However, that's how we develop treatments that work."

In the late 1980s, when there were no treatments at all for people experiencing a stroke caused by a blocked artery, researchers created a clinical trial for a new substance known as tissue plasminogen activator (tPA). The drug proved extremely effective at dissolving clots when administered within three hours of the first symptoms. Patients who participate in the trial and received tPA often walked out of the hospital completely recovered.

"Those people probably had radically different lives because they participated in that clinical trial," Dr. Broderick says. "I saw a patient I treated in 1987 or 1988. He had a big stroke and was treated with tPA. He's still walking and talking normally 25 years later. That's an example of how participating in research can change your life."

HELPING PATIENTS GET INVOLVED

NIH StrokeNet will also make it easier for patients to get involved in clinical trials. "Trials are the best way to evaluate new therapies. However, in order to conduct them in a timely manner, we need more people to volunteer," says Dr. Kaufmann. "There's a lot of education that needs to be done. Physicians need to think about trial opportunities for their patients as well as educate patients, their families, and the public about the importance of volunteering for trials. We find that people who participate in clinical trials value the experience and feel, regardless of the outcome, that they get something out of it." (See box, "The Importance of Participating in Clinical Trials.")

Recruiting people who are having a stroke poses a major challenge. In response to this challenge, Dr. Kaufmann plans to make information available to paramedics and emergency department staff reminding them of clinical trials for stroke patients.

Dr. Kaufmann also plans to use advertising to encourage stroke patients to participate in clinical trials designed to help them recover from a stroke and prevent another. "Advertising clinical trials can be very costly, and we have to be good stewards of taxpayer dollars. We carefully balance the cost of advertising against what we get out of it," Dr. Kaufmann says.

AT THE READY William F. Katz, Ph.D., of University of Texas Callier Center for Communication Disorders in Dallas, wants to conduct a clinical trial of his electromagnetic articulograph to help stroke patients regain the ability to pronounce words clearly.

"With NIH StrokeNet, we can test which approach works best, effectively measuring the impact of advertising."

ASSISTING CURRENT AND PLANNED TRIALS

NIH StrokeNet will assist some trials already in progress as part of the NINDS Neurological Treatment Trials Network. For example, the Platelet-Oriented Inhibition in New TIA trial is investigating whether aspirin combined with the antiplatelet clopidogrel (sold as Plavix) is effective for preventing another stroke in patients who have just had a transient ischemic attack or a minor ischemic stroke. Another, the Stroke Hyperglycemia Insulin Network Effort, is examining the effect of careful glucose control in people with diabetes who have just had a stroke.

In addition, NIH StrokeNet will incorporate two recently funded trials. One, known as MISTIE III, is designed to determine the effectiveness of using a catheter to deliver the clot-buster known as tissue plasminogen activator (tPA) directly to the site of a blockage in the brain. The other, known as CREST2, compares a combination of intensive medical management and carotid endarterectomy (in which plaque is surgically removed from the carotid artery) to intensive medical management alone; in addition, CREST2 compares intensive medical management and carotid artery stenting to intensive medical management alone.

NINDS anticipates that new projects funded by NIH StrokeNet should start to receive approval within the next year, according to Scott Janis, Ph.D., program director of the Office of Clinical Research at NINDS. "It will take a couple of years to be fully functional, but some projects should be approved fairly soon," Dr. Janis says. "We have made tremendous progress in a very short time."

The grants will go to applicants who want to study some aspect of stroke prevention, treatment, or research. Plenty of topics await investigation. For example, much effort has gone into developing catheters that can remove a clot from a blocked brain artery, but their effectiveness remains ambiguous, according to Ralph L. Sacco, M.D., FAAN, executive director of the Evelyn McKnight Brain Institute and Miller Professor of Neurology, Epidemiology, and Human Genetics at the University of Miami. He would like to see a clinical trial that would settle the matter. "Some recent studies [of clot-removing catheters] have failed, so I'd like to see if newer devices are more effective," says Dr. Sacco, who will help direct the Miami Regional Coordinating Center, one of the 25 regional stroke centers created by NIH StrokeNet.

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> —PETRA KAUFMANN, M.D.

William F. Katz, Ph.D., a professor of linguistics at the University of Texas Callier Center for Communication Disorders in Dallas would like to conduct a clinical trial of his electromagnetic articulograph. The device—which monitors muscle movements of the tongue, lips, and jaw—is designed to help stroke patients regain the ability to pronounce words clearly.

"We glue little sensors to the tongue. When the patient talks, the sensors track the position of the tongue—its velocity, acceleration, trajectory, and so on," Dr. Katz explains. "Patients can look at the screen and see a transparent mesh model of their mouth, with an avatar of their own tongue moving in 3D as they speak."

REACHING PATIENTS AROUND THE WORLD

The Clinical Coordinating Center for NIH StrokeNet will be at the University of Cincinnati, which will serve as the hub for two dozen other sites, according to Joseph Broderick, M.D., FAAN, chair of Neurology and Rehabilitation at the University of Cincinnati medical school and research director at the University's Neuroscience Institute.

"We're a coordinating center, but the work will be done across country, some trials will involve sites and networks in other countries as well," says Dr. Broderick, who will serve as the principal investigator of the Clinical Coordinating Center. "In that respect, the Center will be touching patients across the U.S. and around the world." NN

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