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Medical clinical research slows for lack of patients

Enrollment shortages have delayed or canceled trials on experimental therapies. Researchers are trying to reverse that trend, in part by using databases to connect patients with possible new cures.

By Shari Roan

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A year ago, U.S. researchers launched what they deemed a high-priority study to determine if women with an often-fatal type of breast cancer could live longer by taking a specific combination of drugs. If the study found that to be true, the average rate of survival -- four years -- could be significantly extended.

A worthy question to address? It would seem so. But the answer may be a long time coming.

The U.S. arm of the international trial got underway nine months behind those in other countries. And researchers now expect to enroll only 350 U.S. patients of the original 3,500 sought.

Before drugs and therapies to save lives or reduce suffering can reach the market, they must be tested to ensure they're safe and effective. But the reluctance of Americans to participate in clinical trials has been a serious drag on medical research.

Enrollment problems delay more than 70% of clinical trials from one to six months, according to a 2007 survey by CenterWatch, a Boston-based company that publishes information on clinical trials. In cancer care, less than 5% of patients enter clinical trials, even though more than 700 cancer therapies -- many that are highly promising -- clog the research pipeline.

"It's a major issue," says Dr. E. Ray Dorsey, a neurologist at the University of Rochester Medical Center who has studied the issue. "Many trials are started and never finished because they can't complete enrollment. A lot of money is wasted."

A daunting task

To test a promising treatment -- whether a pill, injection or procedure -- researchers usually need large groups of people who have a specific illness and who are, for comparison purposes, of a certain age, ethnicity or gender. Sometimes they even need patients with a particular gene or complication. Then they must track the patients for several months or years to see if the therapy worked and how it compares with the standard treatment.

It's no small task. And with 2,800 drugs and medical therapies now in development -- awaiting solid data on efficacy and outcome -- doctors, researchers and drug companies are finally taking a hard look at how they can persuade more people to participate.

To that end, initiatives to boost clinical trial participation are underway across the country.

Some medical centers are offering simple perks, such as arranging transportation for participants; others are using computer programs that notify doctors if a particular patient might benefit from a trial. Researchers, meanwhile, are avoiding use of the word "subject" and even agreeing to meet with trial participants after the study to answer questions. Everyone, it seems, wants to convince potential participants that they will be cared for and valued.

"It's sort of ironic that there are more compounds available to study than ever before, and most are based on some new scientific principles, yet we are still having trouble recruiting participants," says Diane Colaizzi, executive advisor of the nonprofit Coalition of Cancer Cooperative Groups, founded by research groups to promote study participation.

Although cancer research receives the most publicity, the need for participants plagues almost every area of medical research. This month, the Huntington's Disease Society of America in New York e-mailed its members asking people afflicted with the fatal genetic neurological disease to consider clinical trials.

The letter, from the group's executive director, Barbara Boyle, noted that a recent three-month trial on a potential drug treatment took more than nine months to enroll and another promising trial may take even longer.

"Our scientists and clinicians have done what they can to reach this point," Boyle wrote. "Only you can make the final steps possible."

Researcher failings

Part of the blame for limited participation in clinical trials lies with researchers.

They acknowledge that some trials have been poorly conducted, risking patient health and dimming the public's view of medical research.

Researchers also say they have failed to explain to patients that clinical trials often present two choices of care: the best established treatment or that treatment *plus* an experimental therapy.

"I think there is a misperception by the majority of people that it will take away from their treatment and won't do them any good," says Dr. Raymond DuBois, president of the American Assn. for Cancer Research and provost of M.D. Anderson Cancer Center in Houston. "At a bare minimum, we would offer the standard treatment option."

Patients may fear they would get only placebos -- dummy pills or treatments -- but those are used primarily in trials that assess prevention, rarely in treatment trials.

Nor are clinical trials necessarily a desperate attempt to stay alive only after all other treatment has failed. Says Dr. Robert L. Comis, president of the Coalition of Cancer Cooperative Groups: "Nowadays there are trials for all stages of disease. It's a myth that this is something of last resort."

The one area of medicine in which clinical-trial enrollment is relatively common has positive results to show for it. In pediatric cancer centers, more than 60% of children receive experimental therapies. That decades-long practice, which began out of desperation to treat children who would otherwise die, is now credited with vastly improved rates of survival, such as the astonishingly high cure rate associated with childhood leukemia.

"I think the real issue here is that in adult medicine, the clinical trial process is not an integral component of the entire treatment paradigm," Comis says. "What we're trying to do is make it more mainstream."

Information access

Brad Silver was diagnosed with brain cancer in 2003 and was scheduled for surgery almost immediately thereafter. After 90 minutes, the surgeon found Silver's pregnant wife in the waiting room. "We can't do surgery," he told her. "You'll have to tell him because I have to go."

The tenor of a follow-up appointment with an oncologist was equally dismal. That doctor told Silver he had two months to live. So Silver called everyone he knew who had contacts in medicine. Within a week, he had an appointment at UCLA to explore an experimental treatment.

Most people are unaware they are candidates for clinical trials, neurologist Dorsey says. A survey presented last year at the annual meeting of the American Society of Clinical Oncology found that 60% of newly diagnosed cancer patients hadn't been told about clinical trials as a treatment option.

After undergoing the standard therapy of surgery, radiation and chemotherapy, Silver underwent the experimental therapy -- a vaccine made of protein from his tumor. Silver, now 39 and living in Ohio, has had no recurrence of cancer.

He relied on moxie and connections to find a life-saving, experimental treatment. But researchers are now trying to bring clinical trials to the masses -- via computer databases -- instead of forcing people to search for them. The largest database, ClinicalTrials.gov, sponsored by the National Institutes of Health, lists federally and privately supported clinical trials for a wide range of diseases and conditions.

The site was founded in 2000, but a 2007 federal law expanded its trials to include a wider range of conditions. Further, the law requires researchers listing their studies to report their results -- including negative ones.

Another database, TrialCheck at CancerTrialsHelp .org, was launched in 2003 and lists all industry- or government-sponsored cancer trials currently recruiting. The service uses information from ClinicalTrials.gov to ensure the studies have met government safeguards. But then it goes further. Besides trying to avoid dense medical terminology, TrialCheck has begun to offer a service that allows users to call a clinical trial specialist with the American Cancer Society for questions about a particular study or clinical trials in general. Visits to the website have quadrupled in the last year.

Another type of matching service, this one for breast cancer patients, launched nationwide in November. BreastCancerTrials.org allows patients to enter information about their cancer history into a secure online database. The record is then used to match the patient with breast cancer trials across the country.

Looking ahead

The databases are only a first step. As electronic medical records become the norm, researchers hope to tie the records into an automated clinical trial matching system that will alert doctors and patients alike. One company, Impac Medical Systems of Sunnyvale, Calif., offers this service to oncology practices that use its health records software. After a patient's health record has been entered into a computer, the software searches TrialCheck to see if that person may be eligible for clinical trials.

Comis describes the ultimate goal for patients: "They will have access to their own health records and they can say to their doctor, 'It says here I'm eligible for three studies. Why didn't you talk to me about that?' "

Researchers and patient advocates in various states are also fighting for federal legislation that would require insurance companies to pay for the patient care involved in clinical trials, following 23 states -- including California -- that already have such laws. The federal bill was developed specifically to address enrollment in cancer trials, which make up a majority of clinical research. Called the Access to Cancer Clinical Trials Act, it was introduced by Sen. Sherrod Brown (D-Ohio) last year and is before a House committee.

Though the research sponsor, such as a drug company, usually provides the drug or therapy free of charge, some insurance policies don't pay for care, such as blood tests, scans or examinations, linked to the treatment, says Dr. James Thomas, director of clinical trials at the Ohio State University Comprehensive Cancer Center.

Other researchers are simply extending basic courtesies to boost enrollment.

Some trial steering committees include a patient advocate to make sure patient concerns and views are represented, Dorsey says.

And more people will enroll, studies have found, if researchers assure them they'll take the time to brief the participants when the study is over.

"Companies are required by law to inform investors of the results of trials, but there is no law that anyone needs to inform the participants about the results," Dorsey says.

A study published in December by Dorsey reported on the results of a nationwide conference call between investigators and patients or their caregivers who had participated in a study on Huntington's disease. Over 90 minutes, the experts answered questions, explaining that the drug had failed to improve symptoms.

"They were disappointed," Dorsey says of the participants. "But I think they felt appreciated for their efforts."

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