SCIENCE

THE INS AND OUTS OF CLINICAL TRIALS

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There are currently around 50,000 clinical trials underway in the US, according to the Center for Information and Study on Clinical Research Participation; but 80% of these are delayed at least a month because of unfulfilled enrollment. In a medical climate where new drugs can take up to 15 years to reach the market, every minute counts. So why do clinical trials still face recruitment problems?

"Everyone is afraid of getting a placebo," said Gwen Darien, former director of survivor and patient advocacy at the American Association for Cancer Research and former editor-in-chief of *CR* magazine. "Conversations about clinical trials don't tend to be very nuanced, and one thing people don't understand is that you're not a guinea pig. You're receiving an experimental drug, but it's a drug that has shown evidence of being an effective treatment. That's why it's being tested."

In fact, it's very rare that a patient in a clinical trial will receive a placebo, says Dr. James Doroshow, director of the division of cancer treatment and diagnosis at the National Cancer Institute. "The control arm is almost always what is thought to be the standard of care," he explained. "The randomized trials that the NCI supports usually involve testing drugs A, B and C against drugs D, C and F, or surgery plus drug against surgery alone. Just receiving a new treatment is extremely rare."

But this misconception isn't the only factor that contributes to the lack of enrollment in clinical trials. Dr. Bob Young, chairman of the board of scientific advisors for the NCI and former president of the Fox Chase Cancer Center, says there are multiple factors: "Patients don't know where to find them," he said. "Or their doctor either doesn't know about them or doesn't want to participate. Clinical trials are complex – they often require additional work on the part of the physician, and there are only 24 hours in a day."

That was Darien's experience while undergoing treatment for stage II non-Hodgkin's lymphoma. During the time she was treated, a clinical trial was underway for Rituxin, which has subsequently become the standard of care for the disease. But Darien was never asked to participate. "It isn't something you come in thinking about, and my doctor didn't offer the possibility," she said. "It's possible that there was nothing available for me at that point, but even in subsequent years I wasn't asked to participate

in any quality of life trials or survivorship trials.

"Everyone says when you go into the doctors' office, have a list of questions," she continued. "And one question you should ask is am I eligible for any clinical trials."

There's also a psychological factor. "There are many people who want their doctor to tell them what the best treatment is and then get it," Young said. "It frightens them to think that they're participating in a study. They want their doctor to definitively tell them that treatment B is the right treatment for them."

Doroshow concurs. "There's a lot of patient choice that goes into this, and there are individuals who simply do not want a computer to decide," he said. "There are patients who just don't like that. I have experienced that perspective from individuals of every education level – it's very personal. Getting one treatment or another based on randomization is not everyone's cup of tea."

So why should patients enroll in clinical trials? Young has a few answers. "Clinical trials are good for patients," he said. "They're generally performed in institutions in the context of people who have a particular expertise or special interest in that disease. One of the things that is seen in clinical trials is that if you're testing whether new treatment A is better than standard treatment B, very frequently the patients on the standard treatment alone do better than the average patient because the people involved with their care have so much experience with the disease."

And that's not the only reason. "The faster we get done with trials, the faster we know whether treatment A is better than treatment B," said Young. "We learn that certain things work and other things don't, and with the cost of medical care always on the rise, that's very important."

The high cost of medical care: it's a topic familiar to most Americans as premiums inflate and paychecks shrink. Unsurprisingly, it also plays a role in clinical trials. "For a practice to participate in clinical trials, there is a major intellectual as well as financial commitment that has to be made," said Doroshow. "It takes time, and that time is very tough to make available. You need additional personnel."

He mentioned a practice that had been "incredibly successful" with clinical trials in the past: "They lost money," he said. "They put their own profits into making these studies available because they thought their patients would benefit. If budget times were different and our appropriation was different, we would like to cover the costs incurred by our sites. They shouldn't have to take a loss to do this."

Patients could encounter cost-related obstacles as well, Young notes. "In some areas of the country, there are difficulties with reimbursement for normal patient care costs, and it's a significant problem," he said. "Medicare and insurers say, we're not in the business of paying for experimental therapy."

The answer? Both docs say infrastructure improvements are key. "Standardizing clinical trials across cooperative groups would be an enormous benefit," said Young. And Doroshow says that solution is already in the works: "We're working very hard to standardize the way information is collected so that if you participate in a range of trials, we will be able to provide you with software," he said. "That's something I've been working on for close to five years. The more standardized it is, the more efficient it is."

In the meantime, however, 80 to 85% of cancer patients are still treated by community oncologists, who don't participate in clinical trials to the extent that providers in academic centers do. So patients looking to enroll in trials have to be their own advocates, seeking out the studies that are right for them. Resources include:

* CancerConsultants
* CenterWatch
* Current Controlled Trials
* EmergingMed
* New Medicines in Development Database
* Physician Data Query
* TrialCheck

Young encourages patients to look into whether a clinical trial could be right for them. "The reality is that somewhere around 3 to 4% of patients with cancer participate in clinical trials, while somewhere between 20 to 40% of all cancer patients could be eligible," he said. "Which means that the pace of getting answers to our questions is remarkably slower than it should be."

"It’s great when somebody wants to help society and help themselves," Darien said. "This is an area where those two motivations coexist."

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