

By Barry E. Katz



CLINICAL TRIALS

Do you have what it takes?

Conducting pharmaceutical research can supplement your income, but if landing big bucks is your motivation, think again. Being a research investigator takes time and commitment, but it can pay both real and intangible rewards.

FIVE YEARS AGO, DR. CHARLES PARABOSCHI AND OTHER MEMBERS OF HIS Yardley, Pennsylvania, cardiology group decided to become investigators in a nationwide study of an experimental drug for unstable angina and non-Q wave myocardial infarction. They found the experience intellectually exhilarating.

Today, the group, Mercer-Bucks Cardiology, runs about 10 clinical trials of drugs at various stages of research. Paraboschi serves as the principal investigator in trials of medications for heart failure, hypertension, and high cholesterol. The drug the group helped test for Merck & Co. pharmaceuticals back in '95—Aggrastat—has since been approved and is prescribed by cardiologists worldwide.

“When you’re out in private practice, it gets real easy to get what we sometimes refer to as the ‘local doc mindset,’” says Paraboschi,

38. “You just sort of see your patients, do the day-to-day work, you can fall behind with your continuing education, you may not be reading the journals as actively as you would like, and so your knowledge base can slip. When you do clinical trials, it’s one way of keeping up with cutting-edge therapies...

“It also has, we believe, a modest but probably real effect at differentiating us from our competitors. If we’re trying to be academic and doing clinical trials and we’re at the cutting edge of medical therapies, then our referrals and other physicians in the community, I think, perceive that in a very positive light.”

Secondary income

About 46,000 physicians will supplement their incomes this year by conducting clinical trials, mostly for pharmaceutical companies, according to CenterWatch Inc., an organization that provides drug-research information to physicians, consumers, and the pharmaceutical industry. Pinched by managed care, doctors in small practices as well as large groups often find it’s an excellent way to diversify revenues while steering their careers in more satisfying directions.

With more than 1,000 new drugs, biologics, and vaccines in development, the pharmaceutical industry is intensifying its research activities. Spurred by recent advances in genomics, the demand for trial subjects and trained investiga-

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● Dr. Charles Paraboschi, a cardiologist in Yardley, Pennsylvania, says, **“When you do clinical trials, it’s one way of keeping up with cutting-edge therapies... It also has, we believe, a modest but probably real effect at differentiating us from our competitors.”**

tors is expected to balloon in coming years, and drug companies are increasingly looking to private-practice physicians for help. An estimated 56,000 doctors will be conducting drug trials three years from now, according to Center-Watch projections.

So what kind of money should a physician expect to make?

A physician starting out in drug research might bring in between \$2,500 and \$15,000 per patient, with 36 to 45 patients a year—three separate studies—typical for doctors new to trial work. Some group practices find clinical trials account for as much as a quarter of their income but only a tiny fraction of their patient loads.

The amount of pay depends on a lot of things—the length of the trial, the complexity of the disease being treated, the difficulty in finding patients to enroll, the extent to which patients must be monitored, the frequency of follow-up visits, and other factors.

“There are clinical trials that can only be run in the hospital ... in the ICU, and that kind of clinical attention certainly demands much more time and diligence,” says Deborah Bowe, 46, a Cleveland internist who helped her colleague, an endocrinologist, run research studies of drugs for diabetes, acne, and hormone problems. “On the other end of the spectrum, there might be a trial of a new acne medication or a medication for freckles. Certainly, that kind of attention and diligence in monitoring takes a lot less time and effort.”

An acne or cholesterol study

that involves just one office visit and a couple of blood tests, for example, might pay \$500 a patient. Some long-term sleep studies supervised by specialists, on the other hand, gross \$20,000 to \$30,000 per patient.

Generally, a primary-care physician could expect to receive \$2,700 a patient for a Phase III study with 15 patients, says Tracy Blumenfeld, the president and CEO of Physicians Clinical Research Solutions, a Wayne, Pennsylvania, company that matches doctors with research sponsors. Payments are usually made in increments over the course of a study, usually with 10 percent up front to cover start-up costs.

The physicians’ biggest expense is personnel.

Paraboschi’s group pays two people—a clinical research associate and an RN—whose sole responsibilities are to help run clinical trials. They do much of the patient screening and follow-up.

“A physician needs to be a physician first and see patients,” Paraboschi says. “If you are going to have patients in your office for follow-up for different clinical trials, you as a physician want to spend as little of your personal time as is necessary on the non-physician aspects of (clinical trials)—in other words, paperwork. Signing documents. Calling patients to arrange follow-up.

“Patients who come into the office purely for follow-up of a trial can frequently have their data collected by a nurse practitioner or even an RN for certain blood-pressure trials. You need to admin-

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Phases of Drug Research

Before clinical trials involving human subjects can begin, a pharmaceutical company must thoroughly test its drug in the lab, often with animals and human cells. If the test results are suitable to the Food and Drug Administration, the company can initiate drug tests in humans.

Clinical trials typically are carried out in three phases. Each phase requires a larger test-patient population. After the FDA approves a drug for marketing, pharmaceutical companies sometimes sponsor a fourth level of study to compare it to other drugs or determine its long-term effectiveness. Here, according to CenterWatch Inc., are the major phases of drug research:

Phase I

PURPOSE: Assess drug safety. Determine how drug is metabolized. Identify side effects as dosages increase.

NUMBER OF PATIENTS: 20 to 100.

Length of trial: Several months.

OUTCOME: 70 percent of drugs pass Phase I.

Phase II

PURPOSE: Determine drug efficacy, often by randomized trials involving a test group and a control group. Further assess safety.

NUMBER OF PATIENTS: Up to several hundred.

LENGTH OF TRIAL: Two months to two years.

OUTCOME: Approximately 33 percent of drugs pass Phase II.

Phase III

PURPOSE: More thorough look at drug efficacy, safety, and benefits. Further document adverse reactions.

NUMBER OF PATIENTS: Several hundred to several thousand.

LENGTH OF TRIAL: Several years.

OUTCOME: Seventy to 90 percent of drugs pass Phase III and are given FDA approval for marketing.

ister that and oversee that—and the FDA is very specific about your responsibility for the appropriate conduct of that trial as the principal investigator. But you need to pay for personnel to do that.”

There are options to taking on additional staff. “There are companies that provide study coordinators on a project basis,” Blumenfeld says. “For those projects, typically the coordinator company will come in and, for 40 or 50 percent of the budget, they’ll share the budget and the risk of the study with the physician. There are a lot of those companies out there, and they’re terrific for doctors who don’t want to deal with hiring those people and managing those people.”

This way, according to Blumenfeld, overhead is kept at a minimum because a physician is just sharing revenue. Hiring an experienced coordinator is especially critical for a physician just beginning clinical trial work.

“Most drug companies are on very strict timelines,” Blumenfeld says. “Their biggest fear is that new physicians don’t understand the regulations, they don’t understand the process, they’re going to slow down the whole process of recruiting patients—they’re not prepared. So they’re very reluctant to work with new investigators on clinical trials...”

“The most important thing a new investigator needs to do is be willing to hire either

on a part-time basis or on a contract basis an experienced study coordinator. In lieu of having a physician or principal investigator with experience, you need to have someone who knows the regulations, knows how studies run, knows what’s entailed, understands what the sponsors are looking for, and typically the study coordinator is the one who knows that.” Still, it’s important to keep an eye on the bottom line.

“If you’re going to start hiring study coordinators and data-management people, it can get fairly expensive,” Blumenfeld says. “So you’ve got to have a fairly sizeable research program to cover those expenses.” With 15 patients in a typical clinical trial, a coordinator should be part time. “You need to be running at least three to four clinical trials of that size (at once) to have a full-time coordinator there,” she says.

There can be other expenses, as well. Physicians might have to arrange for additional locked storage space or, perhaps, buy a centrifuge. They might need extra phone and fax lines. Some doctors invest in special software to manage their trials, though a physician’s current data-management system might work fine.

“IRBs (institutional review boards that monitor drug studies) will charge fees to review protocols, but that’s frequently picked up by the sponsor,” says Paraboschi.

The time factor

Depending on how an office’s cost accounting is done, a physician’s time could also be considered a big expense. “If a physician has patients coming out of his eyeballs, and he can’t get home until 11 o’clock every night because he or she is just seeing patients all day long, then clinical trials might not be right for that person,” Paraboschi says. Doctors need to figure out how to coordinate their research with their busy practices. Being part of a group makes it a lot easier.

“In a group practice, one of the key things that we try to do is to be as diversified as possible, going to multiple hospitals, taking care of multiple patients from multiple referrals,” Paraboschi says. “Doing clinical trials makes sense for us, because if one physician’s time is taken up administering this and seeing (trial subjects) and follow-up, then another cardiologist’s time is available to seeing patients.”

Physician-investigators find many of their trial subjects among their own patients. The rest come from referrals and advertising campaigns. John Winder, a Toledo allergist who runs the Toledo Center for Clinical Research alongside his private practice, recruits many trial subjects at health fairs and by advertising on television, radio, in newspapers, and over the Internet.

“We all keep our eyes peeled,” says Para-

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boschi, whose group has 25 to 50 people enrolled in clinical trials at any given time. "When we find somebody who might fit a particular protocol, we approach that patient and we tell them about the protocol, what commitment it might take on their part, what benefits might accrue or might not accrue to them. We find that most of our patients—as long as the protocol isn't scary in any way, which we wouldn't do—tend to be very cooperative. They like to participate. Most people have some element of altruism; they want to participate..."

"Some patients want to participate because it's a way for them to get medications that aren't FDA-approved yet. One of our heart-failure protocols that we're about to start is going to be with people who are pretty sick. And we have access to a medication in its early stages of development that might make them feel a little better. For some motivated patients, that's all they need."

Each patient has to be screened to make sure he or she meets the study criteria. But often, a new investigator will find fewer patients than expected willing to enroll. Some just may not agree to be part of a study. Or their family members will object. Others may be going on vacation.

"When a sponsor or a research institute comes to you, they're going to ask you: How many patients can you enroll in this trial?" says Paraboschi. "Invariably, whatever you think you can enroll, you should cut it in half because patients who you thought might be interested aren't, patients who you thought for sure were going to be candidates may have some very small exclusion criterion that you hadn't thought about. You're only going to be able to enroll half of what you thought to start with, and to be really successful at clinical trials, you need volumes of patients."

Before physicians agree to participate in a trial, it's important to study the trial's guidelines, do chart reviews to make sure they can enroll the right number of patients, and look

at their schedules to see if the study requirements conflict with their own vacations or other commitments, Blumenfeld says.

"They need to think through all the logistics," she says. "There's nothing that upsets a sponsor more than going through all this effort, having an investigator meeting, doing the initiation, paying for the IRBs, paying study start-up fees, and then having a doctor not enroll. It's far better for a physician to say, 'You know what? I really don't think our site can accommodate this study at this point in time,' than to take something on that they can't do."

The ethics of clinical trials

Some pharmaceutical companies offer bonuses ranging from \$200 to \$2,000 to doctors as incentives to speed up enrollment. Sometimes, a physician will split his bonus with another doctor who has screened and referred patients for the study.

"There are always bonuses," says Isaiah Jenks, the founder and part owner of The South Florida Clinical Research Group in Miami Beach, a company that brokers and manages clinical trials for six physician groups in Dade County, Florida. "They are usually done very quietly."

Blumenfeld says she hasn't seen many bonuses being offered lately because of ethical questions about the practice. The concern is that some physicians could be so focused on getting enrollment bonuses that they could place patients in studies who shouldn't be there.

Another ethical question involves the extent to which physicians can exploit their patients' trust in them by persuading them to enroll in trials. A doctor isn't supposed to recommend to a patient that he or she participate, just present the information that is clearly spelled out in the informed-consent form, Blumenfeld says.

Physicians' profits, like gross income, vary. "We did an analysis once, and we found for the typical internal-medicine general

practice, they're looking at a 20 to 24 percent profit margin on a clinical trial," Blumenfeld says. "That would be after physician expenses, coordinator expenses, and procedures."

Winder says he nets 40 to 50 percent on the 20 to 25 drug studies he conducts each year. Some private-practice specialists affiliated with The South Florida Clinical Research Group see as much as 70 to 80 percent profit, says Jenks.

But physicians and researchers warn about unrealistic expectations. Some doctors, especially if they are conducting only one clinical trial, make just enough to cover their expenses and their time as if they were seeing patients in their practice, says Paraboschi.

"This is not something that you would get rich at," says Bowe, the Cleveland internist.

More than anything, they say, it's hard work. And any physician not ready to make the necessary commitment should stay away from clinical trials. "The motivation to (participate) in clinical trials as a private practitioner should not be because it's a major financial windfall," Paraboschi says. "It is a way to diversify your income stream, and that's one of the positives. But much more important, we believe, is that performing clinical trials makes us better physicians by being on top of our game in various areas. When you do a heart-failure trial, you better be a heart-failure expert..."

"If you aren't willing to become an expert or put in the time to really know what you're dealing with, then doing a clinical trial is not for you. We do clinical trials predominantly because of the effect of making us better doctors, differentiating ourselves from our competitors. And the finances—we're happy if the finances pay our overhead, diversify our income stream a little bit, give us a little more income. But with 11 doctors in the group, no one's getting rich on these." ■

Barry Katz wrote about physician-politicians in the January/February issue of UO.