

Virtual Mentor

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MEDICAL NARRATIVE

Volunteers and the Great Unknown: Interview with Clinical-Trial Participants

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Don't think, try.

—William Harvey, physician (1578-1657)

In one of the earliest recorded clinical trials, British physician Edward Jenner decided to test his theory that infection with the cowpox virus provided protection from the more deadly scourge of smallpox. Jenner's approach, however, is also a bioethicist's worst nightmare. In the waning days of the 18th century, there was no such thing as informed consent, institutional review boards, or human-subjects protection. So, without much fanfare, Jenner simply transferred pus from a cowpox pustule to an incision he created on the arm of his 8-year-old test subject, James Phipps, and subsequently exposed the boy to smallpox. Luckily for Phipps, Jenner's idea did not prove fatal: cowpox exposure did offer smallpox protection. When the Royal Society of London declined to publish his findings, Jenner simply turned to more pediatric subjects to prove his point. As legend has it, this included his own infant son [1].

In the end, Jenner's ideas—if not his methods—were not as far-fetched as first imagined. While his discoveries were responsible for the first smallpox vaccine and earned him a place in medical history as the father of immunology, much has changed in the way physicians interact with patient research subjects since Jenner's time. After the trials at Nuremberg and the Declaration of Helsinki, the rights and protection of the patient-subject are at the forefront of any modern research trial [2].

What motivates people to participate in research protocols today? Entire departments and layers upon layers of federally mandated paperwork exist to protect both the scientific integrity of research as well as the health and well-being of human test subjects. One fundamental detail, however, has not changed in the days since Jenner exposed neighborhood children to smallpox: clinical research must necessarily contain an element of the unknown. Yet people still participate.

I decided to interview some clinical-study participants to see what they had to say about their decision to participate in a study and whether or not they would do so again. The studies represented were a trial that compared a new cancer drug to existing therapy and two preclinical research studies in which normal (non-sick) volunteers underwent neurological imaging or donated bone marrow for laboratory studies. Given the diversity of study aims, the answers of study participants may surprise you. And in a way, their thoughts about participating in clinical-research

projects embody the same spirit of inquiry that first set Jenner on his way over 200 years ago.

In their own words. “Why would anyone want to do that?” This is one of the first questions that comes to mind when one considers the uncharted waters of a clinical protocol. Yet as those close to patient-subjects make clear, sometimes it is the promise of something new and different that makes a study appealing. “My mom participated in the study because we were out of options at that point,” a family member said, referring to a study that was designed to test the efficacy of a new medication to treat a particular kind of cancer.

The drug she had been taking...stopped working, and the side effects of interferon were nearly killing her. We heard about Gleevec and weren't sure she would qualify for the clinical trial...but we thought, if she qualified, then why not? We had nothing to lose. She wasn't paid, but the promise of a new drug gave us hope when we were already expecting the worst.

This particular patient-participant's disease was so advanced at the time of therapy initiation that she eventually succumbed to it. The drug she received, however, is now standard therapy for this type of leukemia (chronic *myelogenous* leukemia) and has had a profound influence on pharmaceutical drug design. “Ultimately my mom knew she was fighting a losing battle,” her daughter noted. But, “I think she would have done it again, especially to be on the trial for a drug that revolutionized the therapy of CML as we know it.”

The same thread of hope is also a part of the motivation for a normal volunteer who participated in a different study that involved donating bone marrow for laboratory research. “If I truly believe in the utility and promise of clinical studies,” he said, “then I feel obligated to participate in whatever way I can to further the research goals of others, even if it means enduring slight discomfort.” This thought is echoed by a participant in the same trial who, even though she initially thought the bone-marrow-donation process was too painful to consider doing again, decided the right trial might change her mind. “Well, actually maybe I would do it again if it was something to help children or a disease like cancer or MS,” she said. “Clinical research is a wonderful thing, and it should be funded more,” she said.

Financial reward. The promise of hope is indeed a powerful motivation. Yet the question of financial remuneration is also powerful and one of the most complex issues involved in clinical studies. To avoid coercion, money offered to participants cannot be deemed excessive. Yet, particularly for the non-sick volunteers needed to serve as healthy controls for many types of studies, shouldn't there be some payback for donation of time and the experience of undergoing unpleasant and often painful procedures? Who is to say how much is enough (or too much)? And does money of any kind make people more likely to participate? The answer appears to be more convoluted than one might imagine. As one participant stated,

I donated bone marrow for a friend's PhD research project. The money was nice (I was paid \$150), but I mostly donated because I liked the idea of being included in my friend's project. As a future physician, I wanted to know what it was like to donate bone marrow, so I would understand what patients experience during bone-marrow biopsies.

This thought was echoed by another participant in the same study who remarked,

While I was compensated for my time and discomfort, this was not the primary motivation for participation. Knowing that part of me might be used to help better understand disease and perhaps lead to an improved diagnostic method or therapy was rewarding enough.

A third participant who also donated bone marrow concurred. "Well, for the money, yes," she said, when asked why she participated. "But also for the science factor. Depending on what it was for, I wouldn't need to be paid to consider it."

Sometimes, this same sense of curiosity leads people to participate in multiple studies. Another participant in the bone-marrow study remarked, "While a laboratory technician...I participated in several studies that involved transcranial magnetic stimulation (TMS) and MRIs. I was not compensated for the studies, but I participated because I was fascinated by the science and really interested in seeing the scans of my own brain."

Would you do it again? Repeat participation in future studies is—of course—the best way to gauge a clinical subject's overall experience on a research protocol. For the volunteers interviewed here who were not sick, the overwhelming answer seems to be affirmation of the promise of clinical research. As one participant put it,

I would definitely do it [donate bone marrow] again. Since then, I have donated blood for basic science research....The first time I did it, the guy unfortunately missed three veins and couldn't get any blood. I would still go back. I love the idea that I can contribute to science.

Another volunteer on the bone-marrow protocol added, "I hope to continue in whatever way I can to help researchers pursue their studies."

Yet participation in a clinical study of any kind is not an entirely benign experience. It is sometimes difficult to tell whether the new drugs and devices being tested are working. "She did start to feel better," a family member noted about a cancer patient participating in a trial evaluating a new medication. "But the course of the illness...and her death were about the amount of time the doctor had predicted, regardless of the [drug]." Furthermore, the time commitment required for evaluation of new therapies can be exhausting for people who are already sick. As the daughter of one participant put it: "I think my mom was getting frustrated with the constant appointments." Even for normal volunteers who participate in studies that do not

involve long-term follow-up, there is still the upfront commitment of time, not to mention sometimes unpleasant procedures. “No, I wouldn’t do it again. It was too painful,” remarked a study participant in reference to a bone-marrow donation.

Much has changed since the early days of medical research, but what will never go away is the challenge of finding a way to pursue progress when that progress requires human experimentation. Participation in a clinical study of any kind is a significant commitment. Yet it seems that such studies will continue to move ahead thanks to the sense of purpose felt by patients and normal volunteers alike. This general optimism is perhaps best summarized by an individual who lost her mother to cancer: “...I knew the medicine probably wasn’t going to make a miracle happen, but at least the [experimental] drug gave us all something new to have hope and faith in. And even if [it] didn’t help my mom, we were at least playing a part in something that maybe would work for someone else’s mother. I am sure my mom would agree.”

References

1. BBC. Historic figures: Edward Jenner (1749-1823). http://www.bbc.co.uk/history/historic_figures/jenner_edward.shtml. Accessed February 24, 2009.
2. The World Medical Association. World Medical Association Declaration of Helsinki. 2008. <http://www.wma.net/e/policy/b3.htm>. Accessed February 24, 2009.

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