

When Optimism Is Unrealistic

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As a medical student and later during my residency, I trained for some time in a medical center known for its research and clinical trials. Every week, patients with rare diseases and cancers that had not responded to standard therapy arrived from all over the country, eager to try something new, even if the efficacy of the treatments had not yet been proven.

One of the patients was a woman in her late 30s, a mother of three. Known for her cheery disposition — she reminded the doctors and nurses of a brunette Cathy Rigby — she had melanoma that had spread through her body despite efforts to halt its growth. By the time I met her, she was already the veteran of two clinical trials at the center. Her tumor had responded slightly during one of those studies, but slowing the pace of its growth had come at a significant price. She had endured countless hospitalizations, serious bloating, a punctured lung, overwhelming fatigue and two nearly intractable infections.

Nonetheless, when her cancer began growing again, she eagerly applied for a third study. This time she would participate in one of the earliest studies of a brand-new drug, a Phase I clinical trial, and would have to undergo major surgery before taking the experimental drug.

On the evening before her operation, she joked with the surgical team and shook her head when we asked if she had any more questions. “Haven’t we talked about this enough?” she said smiling and nodding gamely as the head surgeon explained once more that because this was an early-phase trial, it would benefit research but was not likely to be of any therapeutic help to her. Like other such trials, it would test only for toxicity and the maximum safe doses of the experimental drug; generally fewer than 5 percent of patients ever benefit from such early trials.

The woman nodded and waved her hand for the consent form. “I’ve been through this before,” she said to us as she signed the papers. “I know what I am getting into.”

Then, voice lowered, she added: “I’m a mother. I would do anything for a little extra time with my children.”

We all fell silent when she said those words. She seemed to understand the study, and it was hard not to be in awe of her courage and selflessness. But we were also hesitant to probe any further. None of us wanted to deflate her sense of hope. And knowing what we did about the extent of her disease, it was hard not to convince ourselves that optimism, even if based on somewhat false hopes, had to be helpful for someone in her position.

I remembered her words a little over a year later when I heard she had died. Her tumor never responded to the experimental treatment.

For almost four decades, researchers and patient advocates have debated the ethics of informed consent in early-phase clinical trials, studies that test only toxicity and dosing and offer little, if any, therapeutic benefit to those enrolled. A major part of the debate has focused on the motivations of patients who participate. Some research on patient motivations has had disturbing ethical implications, indicating that patients may never fully understand the purpose of trials, despite explanations by the researchers. Others have been more reassuring, noting that patients are driven by a sense of altruism and a desire to help others who may one day suffer from the same disease.

More recently, a few studies have offered what appears to be the happiest of hypotheses. Patients may simply be optimistic and have strong needs to express hope. And because optimism has long been considered an effective coping mechanism for patients with terminal diseases, other researchers have also then assumed that optimism in this context poses few ethical issues.

Now one group of ethicists has just published a study challenging that assumption. It turns out that when it comes to being hopeful, not all optimism is created equal.

The ethicists surveyed 70 patients enrolled in several early-phase cancer trials and asked them about their expectations and understanding of their respective trials. A solid majority understood that the trials' purpose was to advance research, not to treat them. But despite clearly understanding the purpose, and limits, of early-phase trials, the patients were also blinded by what researchers called an "unrealistic optimism," or an optimistic bias, when it came to applying that knowledge to their own particular situations. A majority of patients assumed that the experimental drugs would control *their* cancer and that *they* would experience benefits but not complications.

In essence, they believed they would fare better than the average patient enrolled in the same trial.

"It's the Lake Wobegon effect," said Dr. Daniel P. Sulmasy, senior author and a professor of medicine and ethics at the University of Chicago. "If you have more than 50 percent of patients saying their chances are better than average of avoiding some harm or obtaining some benefit, they are being unrealistically optimistic because you can't say that most people are above average."

Such unrealistic optimism differs from so-called dispositional optimism, or a general optimistic outlook. "This is not about trying to quash hope in dying patients," said Lynn A. Jansen, lead author and an associate director at the Center for Ethics in Health Care at Oregon Health and Science University in Portland. "It's about distinguishing between the different kinds of optimism."

Social psychologists point to smokers who underestimate their chances of getting cancer or gamblers who believe they will beat the odds as classic examples of unrealistic optimism. But unrealistic optimism can be present in anyone, regardless of whether they

have a generally optimistic outlook. “No one is immune to this kind of bias,” Dr. Jansen said. “Optimistic biases are part of human psychology.”

But placed in the context of early-phase clinical cancer trials, unrealistic optimism results in a perfect ethical storm. “You have oncology, a field of medicine that is strongly evidence-based and research-intensive, and you have a population of patients who are experiencing an immediate threat to their lives,” said Dr. Neal J. Meropol, a researcher who has done extensive work on the ethics of early-phase cancer trials and chief of the division of hematology and oncology at University Hospitals Case Medical Center and Case Western Reserve University in Cleveland. “Patients almost invariably take part in early-phase clinical trials because they believe they will personally benefit.”

While the study represents a breakthrough in understanding how different types of optimism affect the informed consent process, doing something about these biases presents a whole different issue. Unrealistic optimism is notoriously difficult to recognize because most individuals are completely unaware that it even exists. “We would probably be able to walk away from these types of biases,” Dr. Jansen said, “if we realized when we were operating under them.”

Dr. Jansen and her colleagues are hoping next to delineate the factors involved in evoking this biased response in patients. By gaining a deeper appreciation of how unrealistic optimism develops, they believe they may be able to help patients and cancer researchers more easily recognize those optimistic biases that impair a patient’s autonomy and compromise the ethics of clinical trials.

“We all need to care about this kind of research,” Dr. Jansen said. “It’s how we advance knowledge and cure disease.”

She added: “We just need to realize that not all optimism is ethically benign.”