Ready, Set, Go... Stop:
Lessons Learned From Cancer Prevention Trials

Clinical studies in cancer prevention will yield better results if researchers put in the planning time to avoid some of their inherent pitfalls, according to speakers at a symposium held at the 22nd annual meeting of the American Society of Preventive Oncology in Bethesda, Md. The symposium, aptly titled "Ready, Set, Go... Stop," covered issues relating to informed consent, problems raised by patients’ different coping styles, minority recruitment, and what happens when a clinical trial must be stopped.

True informed consent helps ensure patient compliance and trust, but "informed consent in oncology has been less than ideal," said Robert T. Croyle, Ph.D., associate professor of psychology at the University of Utah, Salt Lake City. However, today, he said, sensitive issues in genetic testing and increased federal scrutiny are setting higher standards for informed consent in cancer prevention trials.

Croyle said informed consent in oncology has evolved from giving subjects very little information to smothering them with details, often written in scientific jargon. He said the traditional approach has been to focus on the content of the informed consent form, whereas a newer and better approach focuses on informed consent as a process rather than a piece of paper. He made several specific suggestions for researchers planning and administering cancer prevention trials (see sidebar).

The benefits of taking the time to make informed consent a truly meaningful process, Croyle said, are numerous: patients have a greater sense of control, feel an alliance with their trial contact person, may be inspired by the thought of contributing to science, and are more likely to be compliant during later stages of a trial.

Patient compliance in cancer prevention trials will be higher if researchers factor in the knowledge that participants fall into two general camps when it comes to coping — monitors and blunters, said Suzanne M. Miller, Ph.D., director of psychosocial and behavioral medicine at the Fox Chase Cancer Center, Philadelphia.

Monitors and Blunters

Monitors, as she defines them, are patients who tend to be hyperattentive to a threat, such as a cancer diagnosis; perceive themselves as more vulnerable and at greater risk; and show lower expectations of control and need lots of reassurance. Monitors are the ones who "make the oncologist’s beeper go off in the middle of the night," said Miller. Monitors are not more globally anxious, but become anxious in certain situations, such as during participation in a clinical trial, she said.

In contrast, blunters are patients who tend to tune out a threat to avoid stress, have lower levels of perceived vulnerability, and tend to downplay risk. But ironically, both groups of patients can become noncompliant in a cancer prevention trial, said Miller. The monitor can become so anxious that he or she says, "I’m so stressed I can’t bear to go in and find out if I have cancer," while the blunter says, "I don’t have any symptoms; why should I go in?" In either case, noted Miller, the patient becomes noncompliant with the clinical trial regimen.

Miller said for both groups of trial participants, telephone reminder calls coupled with counseling helps. The monitors are encouraged, supported and reassured by such telephone calls, while the blunters are assured of the importance of their coming in.

Cautionary Tales

While there are now more minorities in trials sponsored by the National Cancer Institute, difficulties still remain in minority recruitment to prevention trials, said Otis W. Brawley, M.D., director of NCI’s Office of Special Populations Research. He said there is still widespread mistrust of science among minorities, especially African Americans, and that many have a fatalistic view of life and death that discourages them from being fully informed participants in clinical trials.
An inherent mistrust of science can encompass well-meaning legislators as well as scientists, said Brawley. He related the reaction of an African American to news of the 1993 legislation requiring inclusion of minorities in federally funded National Institutes of Health trials: “We always thought they wanted to experiment on us, and now there’s a law that says they have to.” That fatalistic view also can be manifested when a minority patient says, “Do me whatever you want; I’m going to die anyway,” said Brawley.

That overzealousness can also backfire when researchers analyze minority data subsets without regard to their numbers within the general population, or to the fact that racial designations can no longer be so neatly defined, said Brawley.

For example, he cited subset data from a North Central Cancer Treatment Group trial of 5-FU/levamisole as adjuvant therapy for colon cancer patients that contradicts subset data from a similar Southwest Oncology Group trial. The NCCTG trial found that the adjuvant regimen was most effective for women and younger patients, while the SWOG trial found that the regimen was most effective for men and the elderly. “We should only look at subset data when we’re looking for something very specific,” said Brawley. Otherwise, he added, the results can be confusing.

Stopping a Trial

Researchers must always be prepared to stop a cancer prevention trial if the data warrant it, said Gilbert S. Omenn, M.D., Ph.D., executive vice president for medical affairs at the University of Michigan. As former principal investigator of the NCI-funded Beta Carotene and Retinol Efficacy Trial — known as CARET — Omenn was faced with the heavy responsibility of calling a halt to CARET in January 1996. Brawley cautioned researchers against being overly zealous in recruitment of and inclusion of minorities in cancer prevention trials, which he said can lead to a “medicalization of race” that somehow suggests blacks are inherently different. Such overzealousness can also backfire when researchers analyze minority data subsets without regard to their numbers within the general population, or to the fact that racial designations can no longer be so neatly defined, said Brawley.

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One Investigator’s Tips for Building Patient Trust

For researchers planning and administering cancer prevention trials, Robert T. Croyle, Ph.D., associate professor of psychology at the University of Utah, has some highly specific advice for building patient trust and ensuring compliance:

• Make sure that what subjects are being told is consistent across the trial’s stages — recruitment, consent and education, randomization and intervention — and across trial staff members. To build trust, said Croyle, what is said before and after the consent form is presented should match up.

• Try to tailor the consent form to the patient and include his or her prior beliefs (such as cultural traditions) in presenting information. That way, the consent form is likely to be better understood.

• Use organizing devices, such as discreet chunks of type, subheadings, and bullets in the consent form, rather than one long unbroken written text. Croyle recommended looking at Web sites for ideas on organizing information.

• Use printed materials as a backup, but employ oral and aural means of communication to explain the trial to the participant. For example, the patient could be given an audiotape of a face-to-face interaction with the researcher who explains the trial.

• Make use of interactive technology, as was done with a CD-ROM to inform participants in a breast cancer gene trial.

• Involve family members in the informed consent process — if desired by the participant — to help remember information and offer support.

• Assess the readability level of the informed consent form before it is used and be willing to toss it out and start again if it is on too high a level.

• Explain the “why” as well as the “what” of the trial, especially when it comes to randomization. “Getting people to really understand randomization is worth the time and effort,” said Croyle.