understanding of the potential effect of chemotherapy, she said.

In an editorial accompanying the article, H. Sam Wieand, PhD, explains that the absolute survival benefit cannot be determined from the relative risk reduction unless one also knows the probability of survival without treatment. Wieand, a Professor of Biostatistics at the University of Pittsburgh, presented two scenarios. In the first scenario, the probability of survival without chemotherapy is 98%, and the absolute survival benefit and relative risk reduction with chemotherapy are 1% and 50%, respectively. In the second, the chance of survival without chemotherapy is 50%. Although the relative risk reduction in this scenario is also 50%, the absolute survival benefit is 25%. Wieand suggested that far more patients would agree to undergo chemotherapy for an absolute survival benefit of 25% than for one of only 1%. However, presenting the patients only with the relative risk reduction would not distinguish between these two scenarios.

Another expert agreed with this conclusion. “I think absolute risk is better understood and the way most oncologists probably present risk,” said Jimmie Holland, MD, Professor and Vice Chair of Psychiatry and Behavioral Sciences at Memorial Sloan-Kettering Cancer Center in New York. “This [study] gives it some scientific underpinning.”

Open communication between doctor and patient is critical. Doctors must take the time to explain adjuvant therapy to patients, and they can use tools (such as graphs or charts) to help patients understand the risks and benefits of adjuvant chemotherapy, Chao said.

Holland said patients can do their part by learning as much about adjuvant chemotherapy as possible from sources like the American Cancer Society (ACS) and the National Comprehensive Cancer Network. Bringing a second person to the consultation or taping the discussion so it can be reviewed later also can be helpful, she added. And above all, patients “shouldn’t be intimidated to ask questions because that’s their right,” Holland said.

Chao said her study highlights a need for more research into what factors influence decisions about adjuvant treatment, which may be very different from factors that influence decision making in the metastatic setting. “Everyone has different motivations for choosing a therapy or not,” she said. “But to me, the basic understanding [patients must have] is that adjuvant therapy doesn’t help everyone. It may increase your chance of a cure, but it can’t guarantee it.”

**Benefit of Clinical Trials to Participants Questioned**

Writing in *The Lancet* (2004;363:263–270), researchers from the Dana-Farber Cancer Institute say there’s not much evidence patients participating in cancer clinical trials have better outcomes than those who do not participate.

Jeffrey Peppercorn, MD, MPH, and colleagues reviewed 24 published studies describing 26 comparisons of outcomes for patients who participated in clinical trials with those who did not to determine whether there was a discernible “trial effect”—a measurably better outcome for those who participated. Fourteen of these 26 comparisons showed some evidence of better outcomes among trial participants. However, only eight comparisons limited the control group to individuals who met eligibility criteria for the trials in question. Of these eight comparisons, only three showed a benefit to those enrolled in the study. Studies showing a trial effect were more likely to involve pediatric cancers and hematologic malignancies and were more often from the period before 1986. No studies showed worse outcomes for people who participated compared with other patients.

“We found a few instances in which cancer trial participants may have had better outcomes than nonparticipants, but the limitations of the...
data we reviewed made it difficult to establish a definitive link between trial participation and improved outcome,” said coauthor Steven Joffe, MD, MPH, in a statement.

Most of the comparisons were retrospective cohort analyses, and few controlled adequately for potentially confounding factors like comorbidities, socioeconomic status, or treatment differences like hospital volume or care in a specialized cancer center, the authors wrote.

However, that doesn’t mean cancer patients should be discouraged from participating in trials. “Clinical trials are critical to the advancement of cancer care, but it is important that people who enroll in a study understand that their participation is intended primarily to benefit future patients,” said Peppercorn, a clinical fellow at the Dana-Farber Cancer Institute.

“It is important that we not overpromise the potential results and outcomes of participation [in clinical trials],” agreed Harmon J. Eyre, MD, Chief Medical Officer of the ACS and CA Editor-in-Chief.

But Eyre questioned whether doctors really are giving patients false hope, and he worried that the study might discourage some patients from taking part in critical research. “This study may lead patients, their families, and even health care providers to the faulty conclusion that participating in clinical trials has no benefit,” he said.

Although no two trials are the same, Eyre noted that many do offer participants certain advantages. Patients may get access to treatments that aren’t otherwise available and that may be safer or more effective than standard treatment, for instance. Patients in trials may be more carefully monitored for changes in their condition and for side effects of treatment. Participants may also be offered a greater number of treatment options, even if they haven’t exhausted standard options.

“Treatment offered in most trials is equivalent to or incrementally more effective than the current standard of care, and there are numerous examples of real advances that led to dramatic improvements in survival and quality of life among participating patients,” Eyre said. “We should not lead participants to believe that trial participation is likely to improve their survival, but it is true that participating patients have small chance of substantial benefit from a new therapy.”

Eyre pointed out that Peppercorn and colleagues noticed a trial effect for childhood and hematologic cancers, areas of rapid progress during the time these data were collected. During such a period, trial participants may benefit from access to new treatments; when little progress is being made, a trial effect is less likely. The problem facing both patients and oncologists, he said, is that it’s often difficult to predict which trials provide access to the next big breakthrough.

There is also evidence that trial participation has a positive impact on quality of life for some patients, even in Phase 1 oncology trials, which are designed to study safety rather than efficacy (JAMA 2003;290:1,075–1,082). Participating in a trial that offers even a relatively small chance of direct benefit is an important coping strategy for some patients, Eyre said. For others, the opportunity to help future patients is a source of pride and comfort.

Finally, trial participation offers some patients the opportunity to receive their care from leaders in academic oncology who might not currently be accepting many new patients outside of certain trials, Eyre noted.

Of course, there are downsides to trials, also. Patients in randomized trials do not have a choice concerning which treatment they receive, insurers may not cover the cost of participation, and patients may be inconvenienced by more frequent testing or time and travel commitments associated with participation.

Nevertheless, Eyre said clinical trials are crucial. “Because clinical trials often benefit tomorrow’s patients and sometimes help today’s
patients, the ACS will continue to promote participation in these trials.”

LESS LETHAL SMOKING STILL A PIPE DREAM

The notion of tobacco harm reduction—that there may be a “safer” way to smoke—is one that holds great appeal for smokers unwilling or unable to kick the habit and for the tobacco companies that profit from it. But two recent studies add weight to the argument that quitting is still the only certain way to reduce the health risks of tobacco.

The first, published in BMJ (2004;328:72–80), compared lung cancer risk among smokers of high-tar, regular-tar, and reduced-tar cigarettes. Researchers from the Massachusetts Institute of Technology and the ACS found that low-tar and very low-tar cigarettes were no less harmful than those with regular or medium-tar levels.

“The data underscore that terms like ‘light’ and ‘ultra light’ are misleading because they imply less health risk but do not correspond to less hazardous cigarettes,” said coauthor Michael J. Thun, MD, MS, Vice President of Epidemiology and Surveillance Research at ACS.

Nearly 1 million men and women (non-smokers, former cigarette smokers, and current cigarette smokers) participating in the ACS Cancer Prevention Study II were analyzed. The tar rating of the brand of cigarette smoked in 1982 was compared with mortality from cancer of the lung, trachea, or bronchus over the next six years. Cigarettes were categorized as “very low tar” (0 to 7 mg tar per cigarette), “low tar” (8 to 14 mg tar per cigarette), “medium tar” (15 to 21 mg tar per cigarette), or “high tar” (22 mg or more per cigarette). The statistical analyses controlled for factors including age, race, education, marital status, diet, occupation (including asbestos exposure), and cardiovascular or respiratory comorbidities.

As expected, people who never smoked had virtually no risk of lung cancer. Those who smoked high-tar brands (which typically are unfiltered) had the highest risk; compared with current smokers of medium-tar cigarettes, their hazard ratios were 1.44 for men and 1.64 for women.

But lung cancer risk among people who smoked low-tar or very low-tar cigarettes was indistinguishable from that of smokers of medium-tar brands. Hazard ratios were 1.17 and 1.02 among men smoking very low-tar and low–tar brands, respectively, and 0.98 and 0.95, respectively, among women. None of these values were significantly different from the hazard ratio for smokers of medium-tar brands (set at 1.0 for this statistical analysis).

The way people smoke is the likeliest explanation for the findings, Thun said. The tar and nicotine content listed on cigarette labels is based on measurements from a smoking machine, but studies have shown “there’s a very poor correlation between machine-measured yield and what people are actually taking in,” he explained.

People who smoke reduced-tar cigarettes don’t necessarily lower the amount of chemicals they inhale because they tend to inhale deeper, hold the smoke longer, and puff more often than smokers of regular-tar brands. They also tend to smoke more and may, inadvertently or not, cover ventilation holes in the cigarette filter that are designed to dilute the smoke with air.

Compensation in smoking behavior is also the most likely explanation for the findings of a second study examining the effect of smoking fewer cigarettes on the level of carcinogens in the body. Researchers from the University of Minnesota Cancer Center Transdisciplinary Tobacco Use Research Center reported in the Journal of the National Cancer Institute (2004;96:107–115) that smoking fewer cigarettes did not result in a proportional reduction in metabo-