U.S. Cancer Screening Trial Reports More Diagnoses, but No Fewer Deaths from Annual Prostate Cancer Screening

Huntsman Cancer Institute one of 10 sites participating in study

March 18, 2009, Salt Lake City-Six annual screenings for prostate cancer led to more diagnoses of the disease, but no fewer prostate cancer deaths, according to a major new report from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial. Huntsman Cancer Institute (HCI) at the University of Utah is one of the 10 sites that enrolled participants onto this trial. The PLCO was designed to provide answers about the effectiveness of prostate cancer screening.

“What this report tells us is that despite our best design as to the most effective way to prevent deaths from prostate cancer, the only way we can know what works for certain is doing large-scale studies over several years, such as the PLCO study,” says Randall Burt, M.D., HCI’s senior director of prevention and outreach. “The results of this large, long-term trial tell us that there is little benefit to most men from current methods of prostate screening. In fact, many men may suffer more from the side effects of prostate cancer treatment, such as impotence and incontinence, than would ever suffer from the consequences of the disease itself. Our patients need a better way of determining which tumors will progress and thus need treatment.”

The U.S. Preventive Services Task Force, whose recommendations are considered the gold standard for clinical preventive services, recently concluded that there is insufficient evidence to assess the balance of benefits and harms of prostate cancer screening in men younger than age 75 and recommended against prostate cancer screening in men age 75 and older.

There were 76,693 men in the PLCO trial that was conducted at 10 centers around the United States. Of the men in the trial, 38,343 were randomly assigned to screening with annual prostate-specific antigen (PSA) tests for six rounds and digital rectal exams (DRE) for four rounds. A DRE is an exam whereby a doctor inserts a lubricated, gloved finger into the rectum and feels for anything that is not normal. The other 38,350 men were randomly assigned to usual care, but received no recommendations for or against annual prostate cancer screening.

Of those men who were screened annually, 85 percent had PSA tests and 86 percent had DREs. Men in the usual-care arm sometimes had these tests as well, due to the growing public acceptance of such screening. Screening by PSA in this usual-care group increased from 40 percent at the beginning of the study to 52 percent of men by the last screening year, and screening with DRE ranged from 41 percent initially to 46 percent by the last screening year. Men in the screening arm were referred to their usual health care provider for follow-up testing for prostate cancer if their PSA level was greater than 4.0 nanograms per milliLiter (ng/mL) or if a DRE found an abnormality.

This report includes data for all participants at seven years after they joined the trial and for 67 percent of participants at 10 years after they joined the trial. Other important findings include:
At seven years, 22 percent more prostate cancers were diagnosed in the screening arm (2,820 men vs. 2,322 in the usual-care group). This excess is continuing to be observed in data collected up to 10 years (currently a 17 percent excess, 3,452 men vs. 2,974 men).

The vast majority of men in both groups who developed prostate cancer were diagnosed with relatively early stage II (out of IV stages, of which IV is late stage) disease, and the number of later-stage cases was similar in the two groups. However, using the Gleason scoring system, which assesses tumor aggressiveness, men in the usual-care group had more prostate cancers that fell into the Gleason 8 to 10 range, which marks them as more aggressive. The smaller number of men with prostate cancer with a Gleason score of 8 to 10 in the intervention group may eventually lead to a mortality difference between men in the two groups but data analyzed so far have not shown such a difference.

Men in both groups who were diagnosed with prostate cancer at the same stage received similar treatments for their disease. This reflects the PLCO study design policy of not mandating specific therapies.

At seven years, 50 deaths were attributable to prostate cancer in the screening group and 44 deaths were attributable in the usual-care group. Through year 10, there were 92 prostate cancer deaths in the screening group and 82 in the usual-care group. The difference between the numbers of deaths in the two groups was not statistically significant. Thus there was no detectable mortality benefit for screening vs. usual-care.

“NCI wants to understand why some prostate cancers are lethal even when found early by annual screening, and what approaches can be used to identify these more aggressive cancers when they can be effectively treated,” said Christine Berg, M.D., NCI leader of the PLCO trial and senior author of the study.

Another report in this same online publication of the NEJM is from the large European Randomized Study of Screening for Prostate Cancer (ERSPC), which shows a 20 percent reduction in the rate of death from prostate cancer but with a high risk of over diagnosis. In the ERSPC, unlike the PLCO trial,
men were referred for follow-up testing if their PSA level was 3.0 ng/mL or higher and were also screened, on average, every four years as opposed to annually in the PLCO.

“The results of this study provide useful information to men in the general population,” reports Saundra Buys, M.D., the leader of the study conducted at HCI. “In our study, screening found more men with early stage prostate cancer, but that knowledge didn’t translate to fewer deaths. These findings confirm what we have known for some time, which is that the decision to screen or not to screen needs to be thoughtfully made, taking into account individual patient risk factors, particularly family history of prostate cancer, as well as the wishes and values of the patient. Now that results of the study are in, researchers can concentrate on learning to identify which prostate cancers are aggressive and which can bear ‘watchful waiting.’ Diagnosing prostate cancer early isn’t enough to prevent prostate cancer death if the disease is aggressive, but diagnosing it at all may not be necessary for slow-growing cancers.”

The PLCO data are being made public now because the study’s Data and Safety Monitoring Board (DSMB), an independent review committee that meets every six months, saw a continuing lack of evidence that screening reduces death due to prostate cancer as well as the suggestion that screening may cause men to be treated unnecessarily. The DSMB also supports continued follow up of all participants so that every participant is tracked for at least 13 years from entry onto the trial.

The PLCO is a large-scale clinical trial, sponsored and run by NCI’s Division of Cancer Prevention, begun in 1992 to determine whether certain cancer screening tests can help reduce deaths from prostate, lung, colorectal and ovarian cancer. The underlying rationale for the trial is that screening for cancer may enable doctors to discover and treat the disease earlier.

Nearly 155,000 women and men between the ages of 55 and 74 have joined the PLCO trial. At entry, participants were assigned at random to one of two study groups: One group received routine health care from their health providers. The other received a series of exams to screen for prostate, lung, colorectal, and ovarian cancers. Screening of participants ended in late 2006. Follow-up of participants is anticipated to continue for several more years.
A Q&A on the prostate screening results from the PLCO is available at
http://www.cancer.gov/newscenter/pressreleases/PLCOprostateResultsQandA.