

National Cancer Institute



NEWSLETTER

American College of Radiology Imaging Network

Winter 2007

Greetings from the NLST Directors

As we begin the New Year, we would like to thank you for your ongoing commitment to the National Lung Screening Trial (NLST). As one of over 53,000 people involved in this trial, you continue to help us obtain crucial information about the effectiveness of lung cancer screening. The screenings have concluded, and we are now in the critical follow-up stage of this trial. The information being gathered in the follow-up stage gives us important insight into how lung screening has affected people's lives.

During this follow-up process, our goal for 2007 is to complete an analysis of the NLST's first year's lung screenings. The information will provide insights into the total number of positive screens. By positive screen we mean a lung screening exam showing a suspected cancer or other significant abnormalities. This analyzed data will tell us how many positive screens from the first year were actually found to be lung cancers. Of the verified lung cancers, we will gain more knowledge of the types, sizes, and cancer stages detected by chest CT and chest X-ray. We look forward to any insights that may be gained regarding possible associations between cancer and participants' geographic locations, age and gender. It will also give us a more accurate idea of how common lung cancer is in a higher-risk population.

Another significant milestone to anticipate will be two academic papers expected late this year. The first will be a large paper describing the trial's unique design. The second and smaller publication will summarize the distinct characteristics of the NLST volunteers (such as age, gender and health history) as well as how all of you came to discover and participate in the trial.

These expected publications are only the beginning steps in the process of making public all NLST results. The follow-up phase of the study will continue through at least through 2009. Only by following up with each of you will we be able to answer the main question of this study: Does screening reduce the number of deaths from lung cancer? Your continued participation in follow-up will help give us the data we need to answer that question. The detailed information our researchers are collecting from each participant is crucial to understand the benefits, if any, of lung screening.

In the future, physicians around the world may be able to give their patients the proper recommendations for lung screening based on rigorous scientific evidence from one of the largest and most comprehensive screening trials ever conducted. Thank you once again for your participation in this landmark trial.

Sincerely,

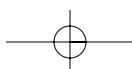
Denise R. Aberle, M.D.
NLST Co-Director
American College of Radiology
Imaging Network

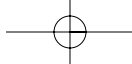
Christine D. Berg, M.D.
NLST Co-Director
National Cancer Institute



Dr. Christine Berg (left) and Dr. Denise Aberle lead the National Lung Screening Trial.

*All Our
Best for a
Healthy
2007!*





The Data and Safety Monitoring Board

From its start, the National Lung Screening Trial (NLST) has had a group of independent experts called the Data and Safety Monitoring Board (DSMB for short) watching the trial. They look at early results from NLST for possible consequences, both positive and negative. If a trend appears, the DSMB notifies the National Cancer Institute and tells the participants. Their main concern is for the safety of all the NLST participants.

This NLST group meets twice a year. In addition to looking at NLST results, they watch for information about other comparable studies. If any of those studies show interesting benefits or harms, the DSMB advises NCI. For example, during the most recent DSMB meeting, board members and the NLST directors discussed the results of a lung cancer screening study recently published in the *New England Journal of Medicine*. The discussion focused on whether the new study results had any possible impact on NLST.

Following the meeting, the NLST directors received a letter written by the chair of the DSMB. This letter states that the DSMB members have been reviewing information from the trial on a regular basis and they believe the trial should continue to try to get answers whether lung cancer screening can decrease deaths from the disease. A copy of this letter is below.

November 6, 2006

Dear Drs. Berg and Aberle:

No randomized controlled trial, utilizing either conventional chest radiographs or chest computed tomography (CT) scans, has thus far demonstrated any mortality benefit as a result of the imaging study in relation to subsequent death from lung cancer in any known patient population. I have the privilege to chair the Data and Safety Monitoring Board for a clinical trial (the National Lung Screening Trial), initiated in 2002 and sponsored by the National Cancer Institute. In this trial, more than 53,000 present or former smokers have been randomly assigned to receive either a chest radiograph or a low dose spiral CT scan for three consecutive years. The goal of the study is to compare the ability of these two approaches to reduce lung cancer specific mortality and to assess the potential harms of these screening programs. The DSMB is composed of clinicians and scientists with expertise in Medical Oncology, Family Medicine, Epidemiology, Pulmonary Medicine, Thoracic Surgery, Thoracic Radiology, Biostatistics, Bioethics, and Internal Medicine. The DSMB has been reviewing the evolving outcome of this clinical trial every six months (most recently on October 30, 2006) and believes unanimously that the trial should continue in its current form. The DSMB has made that conclusion while having also considered the recent report of the I-ELCAP in the *New England Journal of Medicine*.

Sincerely,

Chair

NLST Data and Safety Monitoring Board

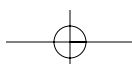
Sponsored by the National Cancer Institute (NCI), the National Lung Screening Trial was carried out at more than 50 sites across the U.S. with coordination provided by both the NCI and the American College of Radiology Imaging Network (ACRIN).

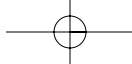
Send questions or comments to:

E-mail address: NLST@nih.gov

Mailing address:

NLST Director of Communications
Early Detection Research Group
Executive Plaza North, Room 3102
6130 Executive Blvd, MSC 7346
Bethesda, MD 20892-7346





NLST Participant Spotlight

Diving into Fitness

NLST participant Adele Kiel smoked for 58 years. She quit five months ago, thanks to a new motivation: competitive swimming. Kiel, 70, who lives on Chicago's South Side, recently qualified for the National Senior Olympics. The Senior Olympics will be held this coming June in Louisville, Kentucky. Kiel will compete in four events.



NLST participant Adele Kiel

Kiel began swimming three years ago around the time she volunteered in the NLST. She was having trouble with her legs and thought some exercise would help. "I had not been swimming for 50 years when I joined this swim team, but most of us are real amateurs. It's fun! Your body responds and you feel energetic," says Kiel. She reports losing weight and feeling like a whole new person. "I think more seniors need to be aware that they can become healthy and do new things".

Swimming is not Kiel's only activity – not by a long shot. She has worked as a painter, editor, and sculptor, although recently she has devoted much of her energy to swimming rather than creating her life-sized animal sculptures that are featured in several Chicago galleries. To prepare for the Senior Olympics in June, Kiel lifts weights to improve her leg strength. She adds, "I'd love to learn to kayak, go tubing, and learn to scuba dive."

This former smoker says, "I've never been an athlete. I encourage a lot of people—they see me and they really try harder. I've been a role model to some of them." Kiel saw an ad in the newspaper for the NLST, and called for more information because she wanted to see what her lungs looked like. Each annual lung screening was very interesting. Kiel had just completed a follow-up survey at the time of this interview and was pleased to note there wasn't much to report.



Adele Kiel's sculpture "Dragon" is composed of welded steel and copper.

NLST by the Numbers

NLST Participants: 53,464

Participant Exams: 148,011

Gender:

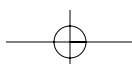
Male: 31,545 Female: 21,919

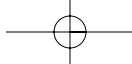
Participants' Age at Time of Study Enrollment

< 60: 22,872
 60 - 64: 16,362
 65 - 69: 9,525
 ≥ 70: 4,705

NLST Screening Sites:

59 sites in 28 states in the U.S.



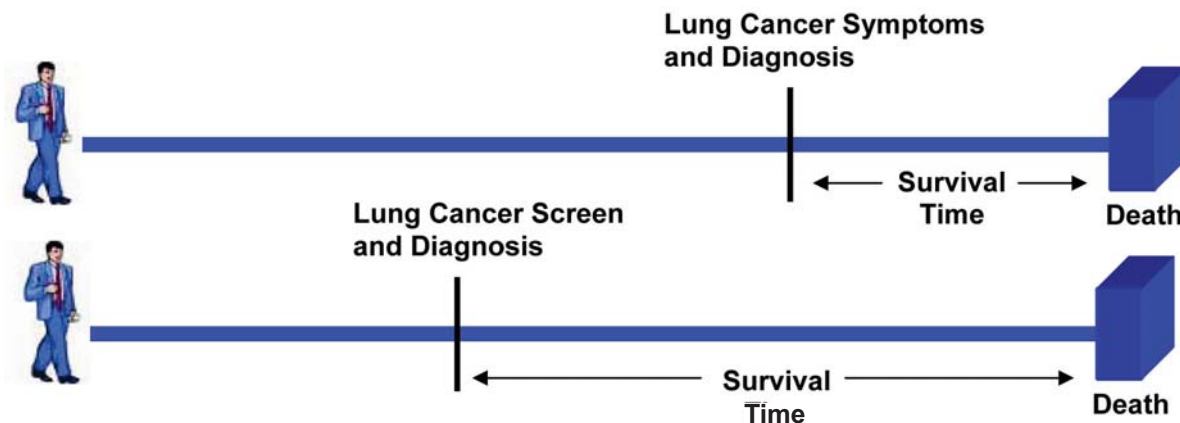


Why the NLST Measures Mortality Instead of Survival

A cancer survival rate is the ratio of the number of patients alive after diagnosis of the disease relative to that of all patients with a diagnosis of the disease. In casual conversation about cancer treatments, it is appropriate to use the phrase “survival rate.” Survival, however, is not an acceptable measure of the effectiveness of a screening test. Three biases (effects that lead to distortion of study results) are described below.

Lead-time Bias

Lead-time bias can happen when cancers detected by screening are diagnosed earlier, making the patients appear to have lived longer from the time of their diagnosis. As illustrated below, end-of-life is ultimately not delayed by early detection as compared with time of death in an unscreened population. The NLST is designed to avoid lead-time bias.



In the first picture, lung cancer is diagnosed when the individual develops symptoms. In the second picture, the individual is screened, resulting in the earlier diagnosis of lung cancer. With screening, the lead time in diagnosis will increase "survival time" even if death is not delayed.

Length Bias

Not all cancers behave the same; some are very aggressive while others are more slowly growing. Length bias refers to the tendency of the screening test to detect more cancers that are indolent (slow growing and often painless). In fact, some cancers are so indolent that they will never grow large enough in a person's lifetime to cause medical problems. Because of the longer period when these indolent cancers can be detected prior to any symptoms, the screening test detects more slowly growing cancers. The survival rate in patients with screen-detected cancers is longer because the screened cancers are more indolent, but the improved survival is not attributable to early treatment.

Over-diagnosis Bias

There is another bias that can happen when a screening test detects slow-growing cancers that would not have affected a patient's natural lifespan. Over-diagnosis bias causes lung cancer survival measurements to be falsely inflated. In fact, the surgery and other therapies that patients with these non-deadly cancers will undergo may result in greater harm than the effects from their non-deadly cancers.

The NLST Measures Mortality

The NLST will avoid these biases by using an appropriate outcome measure for screening tests: the disease-specific mortality rate. A disease-specific mortality rate is the ratio of number of deaths due to the disease compared to the total number of persons in the trial. By measuring the study population from the time of screening (or no screening) rather than from the time of cancer diagnosis, the resulting data will not be subject to lead-time, length-time, or overdiagnosis bias.

Using this technique, NLST investigators will be able to determine whether chest x-rays or spiral CTs reduce deaths caused by lung cancer. A reduction in mortality rather than the apparent increase in lung cancer survival would demonstrate real benefits to those at high risk for lung cancer.

