

# **NCI Cancer Bulletin**

Eliminating the Suffering and Death Due to Cancer

March 6, 2007 Volume 4 | Number 10

#### In this issue:

Study Estimates Overall HPV Prevalence in U.S. Women...1

#### Director's Update...1

Proposed Tobacco Legislation Underscores Need for Research

#### Special Report...3

Study Finds Lung Cancer Screening May Not Reduce Deaths

#### Cancer Research Highlights...3

Children Often Develop Fragile Bones from Cancer and its Treatment

- Strenuous Long-Term Physical Activity Lowers Risk of Breast Cancer
- Radiation and Chemo Before Esophageal Cancer Surgery Improves Survival

#### Spotlight...5

Aromatase Inhibitors Come of Age

#### Featured Clinical Trial...6

Measuring Biological Response to Curcumin

#### Notes...7

NCI Launches Redesigned **Clinical Trials Pages** 

New Communications Guide Available

Women's Health Week Web Site Launched

Special Issue on Cancer Prevention

#### Funding Opportunities...7

NCI's 70th Anniversary: If Memory Serves...7



A Publication of the National Cancer Institute U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES National Institutes of Health NIH Publication No. 05-5498

### **Study Estimates Overall HPV Prevalence in U.S. Women**

Data from the National Health and Nutrition Examination Survey (NHANES) published in the February 28 Journal of the American Medical Association (JAMA) have provided the first national estimate of the prevalence of human papillomavirus (HPV) infection among women in the United States aged 14 to 59. Investigators found that a total of 26.8 percent of women overall tested positive for one or more strains of HPV.

Overall prevalence included both low-risk and high-risk HPV types. Low-risk types of HPV can cause genital warts or other nonmalignant

conditions. High-risk types of HPV can cause cervical cancer, and up to 70 percent of cervical cancers worldwide are caused by two high-risk strains alone—HPV types 16 and 18.

"We think it's important to let women know how common [HPV] is," says (continued on page 2)

### **Breaking News**

Study Finds Lung Cancer Screening May Not Reduce Deaths. See page 3 for a Special Report on new lung cancer research. \*

### **Proposed Tobacco Legislation Underscores** Need for Research

The remarkable decline in smoking rates over the past several decades is a testament to the excellent work

of many in

Director's Update

the cancer and public health communities. But that

on many of the issues raised by tobacco control advocates.

certain populations, including people with less education and those living in poverty.

ing rates were much higher among

NCI is funding ongoing research

does not mean our work on this front is complete.

According to the most recent data, about 21 percent of U.S. adults were current smokers in 2005, but smokTobacco companies, meanwhile. continue to introduce

new products, some of which claim to be "reduced harm," and some of the nation's largest cigarette manufacturers are now even getting into the smokeless tobacco market.

(continued on page 2)

#### (*HPV Prevalence continued from page 1*) Dr. Eileen Dunne from the Centers for Disease Control and Prevention, lead author of the study.

All women aged 14 to 59 selected to participate in the 2003–2004 NHANES, designed to collect health and nutrition measurements from a representative sample of the U.S. population, were eligible to participate in the HPV study. Most eligible women submitted self-collected cervicovaginal swab samples, 1,921 of which could be used for DNA extraction and HPV detection and typing.

Overall, 26.8 percent of women tested positive for one or more strains of HPV. Prevalence of HPV was highest in women ages 20–24. Among all participating women, the prevalence of high-risk types of HPV was 15.2 percent. The prevalence of HPV types 6, 11, 16, and 18—the types targeted by the HPV vaccine Gardasil—was 3.4 percent overall, translating to an estimated 3.1 million exposed women in the studied age groups.

An important limitation of this study, explains Dr. Philip Castle, an investigator in NCI's Division of Cancer Epidemiology and Genetics, is that "this prevalence study is only a snapshot of HPV in the country, but doesn't tell us anything about total lifetime exposure to HPV or the risk of precancer and cancer. Risk is not testing positive at one time point—it's the persistence of carcinogenic types of HPV."

Persistence of HPV infection how long the virus remains active in a woman's body—is key to whether exposure to a high-risk type of HPV leads to cervical cancer. "If an infection from specific oncogenic HPV types does not clear within a period of time (about 6 months), it puts that woman at greater risk for cervical precursor lesions," explains Dr. Dunne.

"There's a lot of misunderstanding about HPV's complex natural history," Dr. Dunne continues. "It's not that if you get the infection, you get the disease. It's a common infection, and a lot of them clear [on their own]. (continued on page 8)

#### (Director's Update continued from page 1)

It's with that backdrop that the Senate Health, Education, Labor, and Pensions committee last week held a hearing on legislation recently introduced by Senator Edward Kennedy (D-MA)—and cosponsored by senators from both parties—that would grant the Food and Drug Administration (FDA) the authority to regulate tobacco products.

In its current form, the legislation would grant FDA the authority to:

- Reinstate a rule promulgated by FDA in 1996 that included significant restrictions on tobacco marketing and sales to youth.
- Restrict advertising and promotion of tobacco products to the full extent permitted by the First Amendment.
- Require tobacco manufacturers to provide detailed, brand-specific disclosure of ingredients, nicotine, and smoke constituents in their products.
- Require changes in current and future tobacco products, including the reduction or elimination of harmful ingredients and constituents.
- Strictly regulate products that would be branded "reduced harm."

• Require stronger, more-effective health warnings on tobacco products and advertisements, and ban the use of terms such as "light," "mild," or "low" on labels or in advertising.

Important, complex, and unanswered research questions would be raised by additional regulatory authority requirements. Epidemiology and surveillance research would be required to monitor the impact of any modified-risk products introduced into the marketplace, and research would be needed to determine the biological impact of products with lower levels of nicotine and other toxic constituents both on individual and population levels.

NCI's Tobacco Control Research Branch (TCRB) is funding ongoing research on many of the issues raised by tobacco control advocates, including the effects of advertising and promotion on populations most at risk for smoking. Also, NCI is funding two important efforts that address tobacco products claiming to be reduced harm, one focused on testing such products and the other focused on assessing tobacco use behavior and exposure to toxins among users of such products.

Smoking remains the leading cause of premature, preventable death in the United States, accounting for onethird of all cancer deaths. Whatever the outcome of this legislative process, NCI is committed to its ongoing efforts to tackle the scourge of tobacco by funding cutting-edge tobacco control and prevention research. \*

Dr. John E. Niederhuber Director, National Cancer Institute



# **Special Report**

## **Study Finds Lung Cancer Screening** May Not Reduce Deaths

New research suggests that the use of computed tomography (CT) in lung cancer screening may not reduce deaths from the disease and may expose some individuals to invasive and unnecessary treatments.

CT technology has generated considerable interest as a screening tool because it can detect very small growths in the lungs of current and former smokers. Two large, ongoing randomized studies—the NCI-sponsored National Lung Screening Trial (NLST) and the NELSON trial in the Netherlands—are evaluating whether CT scans can save lives by detecting cancers before they become incurable.

A study in today's *Journal of the American Medical Association* (*JAMA*) addresses this question using data from CT screening studies at the Mayo Clinic, the H. Lee Moffitt Cancer Center, and the Instituto Tumori in Italy. The analysis included more than 3,200 asymptomatic individuals who had smoked for an average of 39 years.

Because the studies lack control groups, Dr. Peter Bach of Memorial Sloan-Kettering Cancer Center and his colleagues used statistical modeling to create artificial control groups. They then compared the results from screening with what might have been expected in the absence of screening. Screening led to a 3-fold increase in the number of lung cancers diagnosed and a 10-fold increase in lung cancer surgeries compared with what was expected without screening. Screening did not save lives and led to additional testing and treatments for growths that may never have caused harm, the researchers found.

"CT screening is an experimental procedure with numerous potential downsides," says Dr. Bach. These include exposure to radiation, anxiety from false-positive results, and harms caused by detecting and treating an indolent disease.

Participants in the study received an initial CT scan and at least three subsequent exams; they were followed for 5 years.

"The study found no decrease in the number of advanced cases of lung cancers or lung cancer deaths, and that's what is really alarming about the findings," notes Dr. William Black of Dartmouth-Hitchcock Medical Center, who co-authored an editorial in *JAMA*.

The results will be compared with findings last October showing that CT screening resulted in a 10-year survival rate of 88 percent for patients with stage I disease. Reporting their findings in the *New England Journal of Medicine*, the investigators suggested that CT screening in high-risk (continued on page 8)

# Cancer Research Highlights

#### **Children Often Develop** Fragile Bones from Cancer and its Treatment

Research suggests that children treated for cancer are at greater risk years later for bone problems such as osteoporosis and fractures. An article in the April 1 issue of *Cancer* marshals evidence from a variety of studies and sources, leading its authors to conclude that "loss of bone mineral is clearly a common consequence of the treatment of cancer in children and adolescents."

A number of factors appear to contribute, argue Drs. Alessandra Sala and Ronald D. Barr of McMaster University in Hamilton, Ontario. A major factor is multiagent chemotherapy with drugs such as methotrexate and ifosfamide that "have been labeled as especially toxic to bone," yet are commonly used to treat soft tissue and bone tumors. Cranial radiation therapy for children with brain tumors and some of the leukemias and lymphomas can sometimes trigger growth hormone disorders that compromise bone formation. Acute lymphoblastic leukemia is one of the most common childhood cancers, where the disease itself may compromise bone density, and where cumulative doses of glucocorticosteroid treatments most definitely do.

In all of these situations, the heightened physical activity that usually (continued on page 4) (Highlights continued from page 3) occurs in childhood is hindered, impeding patients' ability to accumulate the bone mineral density necessary to avoid osteoporosis in adulthood.

The authors conclude that reduced bone density in "children with cancer is of multifactorial origin, requiring comprehensive strategies for amelioration and prevention." Possible agents that warrant further study are the bisphosphonates and imatinib. Other strategies include more physical exercise, limiting the total cranial radiation dose, and overcoming calcium and vitamin D dietary deficiencies.

#### **Strenuous Long-Term Physical Activity Lowers Risk of Breast Cancer**

California researchers have found that strenuous long-term physical activity decreases a woman's risk of invasive and *in situ* breast cancer, according to study results published in the February 26 *Archives of Internal Medicine*.

Dr. Leslie Bernstein of the University of Southern California and colleagues evaluated 107,034 participants from the NCI-funded California Teachers Study, a prospective study of current and retired female California public school teachers and administrators established in 1995–1996. Researchers collected information on the participants' level of physical activity—moderate or strenuous between high school and their current age (or age 54, if the participant was 55 or older), as well as activity in the past 3 years.

Women who annually participated in more than 5 hours per week of strenuous activity had a lower risk of invasive breast cancer compared with the least active women. Long-term moderate activity and strenuous and moderate activity in the past 3 years were not associated with invasive breast cancer. Researchers also found that women who participated in long-term strenuous or moderate physical activity had a decreased risk of ER-negative invasive breast cancer, but not of ER-positive invasive breast cancer.

Participants had also reported information on relevant breast cancer risk factors, including race/ethnicity, family history of breast cancer, age at menarche, reproductive history, menopausal status, use of hormone therapy and oral contraceptives, height, weight, diet, smoking history, alcohol consumption, mammography screening history, and breast biopsy history. However, these factors did not account for the relationship between exercise and breast cancer.

The authors noted, "In summary, these results provide additional evidence supporting a protective role for long-term strenuous recreational physical activity on risk of invasive and *in situ* breast cancer, whereas the beneficial effects of moderate activity are less clear."

#### Radiation and Chemo Before Esophageal Cancer Surgery Improves Survival

A significant survival benefit was evident for the preoperative (neoadjuvant) use of combination chemoradiotherapy and, to a lesser extent, for chemotherapy alone in patients with localized esophageal cancer in a meta-analysis of data from numerous clinical trials that was published online February 15 in *Lancet Oncology*. Traditional management of patients with localized esophageal cancer has been by surgical resection alone; however, "survival is poor...and many patients develop metastatic disease or locoregional recurrence soon after surgery," noted the researchers, led by Dr. Val Gebski of the National Health and Medical Research Council Clinical Trials Centre at the University of Sydney in Australia. Because of the high rate of surgical complications, "focus has turned to neoadjuvant treatment" as a way to improve survival, they added.

The meta-analysis included 10 randomized comparisons of neoadjuvant chemoradiotherapy versus surgery alone (1,209 patients) and 8 studies of neoadjuvant chemotherapy versus surgery in 1,724 patients.

Results for chemoradiotherapy studies showed a 13-percent absolute improvement in survival at 2 years, with similar results for different tumor types: squamous cell carcinoma (SCC) and adenocarcinoma. Analysis of the neoadjuvant chemotherapy studies indicated a 2-year absolute survival benefit of 7 percent. Chemotherapy had no significant effect on all-cause mortality for patients with SCC, although there was a significant benefit for those with adenocarcinoma.

Most of the studies included in the meta-analysis were started before 1994. "[C]urrent trials have used higher doses of radiation (typically 50 Gy) that are likely to result in better downstaging of overt tumours as well as death of micrometastases," the researchers added. \*



# Spotlight

years of an AI alone are more effective at preventing recurrence than 5 years of tamoxifen alone, and that switching women already taking tamoxifen to an AI after 2 or 3 years prevents more recurrences than continuing tamoxifen for a full 5 years. However, it is not clear yet if sequencing tamoxifen and an AI in women who have not yet been treated with hormone therapy confers a benefit over 5 years of an AI alone.

Results from trials where women have switched from tamoxifen to an AI cannot be applied to women who have not yet received any hormone therapy. "It's important to understand that while the treatment is the same, the patients are not the same," says Dr. Beat Thürlimann, president of the International Breast Cancer Study Group. "If you have already taken 2 or 3 years of tamoxifen and survived disease-free, you belong to a favorable prognostic group."

"When you make a decision about treatment after surgery, you don't know if you belong to this favorable category or not," Dr. Thürlimann continues. "With sequencing trials, you're looking at a broader patient population." The Breast International Group trial BIG-1-98 is comparing sequencing of tamoxifen and letrozole to either tamoxifen or letrozole alone after surgery for early-stage breast cancer. The preliminary results from this part of the trial, expected in 2008, will provide valuable information on sequencing hormone therapies in women who have not yet received hormone therapy.

#### **New Questions**

Other questions remain as AIs move to a more prominent position in breast cancer treatment. AIs have side effects of their own, most (continued on page 6)

# Aromatase Inhibitors Come of Age

Aromatase inhibitors (AIs), which interfere with the body's ability to produce the hormone estrogen, are rapidly changing the standard of treatment for breast cancer. Researchers have now taken up the challenge of learning how and when to best use these drugs to reduce recurrence for women with hormone-receptor-positive breast cancer.

Two approaches dominate the development of hormone-based treatments for breast cancer. One approach focuses on preventing estrogen from binding to its receptor and activating cell-signaling pathways that accelerate tumor growth. This strategy led to the development of the drug tamoxifen, which belongs to a class of drug called selective estrogen-receptor modulators (SERMs).

Since its approval by the FDA for the treatment of hormone-receptor-positive breast cancer in 1977, tamoxifen has become a mainstay of therapy. However, many women develop resistance to the drug over time, leading to cancer recurrence. In addition, because tamoxifen binds directly to the estrogen receptor, it can sometimes activate the signaling pathways it was designed to block.

"We knew that tamoxifen was a partial agonist—a weak estrogen," explains Dr. Angela Brodie, professor of pharmacology and experimental therapeutics at the University of Maryland, who has worked on the development of AIs for more than 35 years. "So we thought it might not be optimally effective on tumors...and that it could cause side effects. In fact, it does increase the risk of stroke and endometrial cancer."

#### A Different Mechanism

Als take a different approach to hormone therapy—they prevent the bodies of postmenopausal women from producing estrogen rather than blocking its activity. Als accomplish this by interfering with the enzyme aromatase, which catalyzes the final step in the synthesis of estrogen from its steroid precursors.

Two different types of AIs are in use in the clinic today. Steroidal AIs, such as exemestane (Aromasin), bind permanently to aromatase. Nonsteroidal AIs, such as anastrozole (Arimidex) and letrozole (Femara), bind reversibly to aromatase and compete with the precursors of estrogen for the enzyme.

Both steroidal and nonsteroidal AIs have been shown in large-scale clinical trials to be superior to tamoxifen in extending survival in women with metastatic disease, and in preventing recurrence when used as primary adjuvant therapy. In addition, treatment with an AI after a full course of tamoxifen continues to improve recurrence-free survival, compared with cessation of hormone therapy.

The challenge remains to determine the best schedule for up-front AI treatment. Studies have shown that 5

#### *(Spotlight continued from page 6)*

importantly loss of bone density, which can be especially hazardous for women already at risk for osteoporosis. Therefore, tamoxifen may still provide a more favorable risk/benefit ratio for some subgroups of women, which need to be identified.

In addition, the role of AIs in premenopausal patients remains to be defined. While AIs alone may not have an effect in premenopausal women, because the ovaries can override the inhibition by producing a large amount of aromatase, clinical trials are now testing AIs in premenopausal women in combination with drugs such as goserelin, which suppress ovarian function.

Because AIs have also reduced the occurrence of contralateral breast cancer in several studies, researchers are now testing the compounds as chemopreventive agents. Two large scale trials have begun testing exemestane and anastrozole in women at high risk for developing breast cancer. Although tamoxifen was approved in 1998 for the prevention of breast cancer in high-risk women, fewer women than expected have chosen to take it.

"One reason [healthy] women don't want to take tamoxifen is fear of side effects," explains Dr. Jennifer Eng-Wong, a clinical oncologist in NCI's Center for Cancer Research. If AIs prove to have both efficacy in preventing breast cancer occurrence and acceptable side effects, they and the new generation of SERMs such as raloxifene will provide women at high risk with additional options to help prevent the disease. \*

By Sharon Reynolds



# **Featured Clinical Trial**

#### **Measuring Biological Response to Curcumin**

Name of the Trial

Phase II Chemoprevention Study of Curcumin in Current Smokers with Aberrant Crypt Foci (UCIRVINE-UCI04-2-01). See the protocol summary at http://cancer.gov/clinicaltrials/UCIRVINE-UCI04-2-01.

#### **Principal Investigators**

Dr. Richard Banya, University of Illinois at Chicago; Dr. D. Kim Turgeon, University of Michigan; and Dr. Frank Meyskens, University of California, Irvine

#### Why This Trial Is Important

Colorectal cancer remains the second leading cause of cancer death in the United States despite effective screening methods and proven therapies. In an effort to reduce colorectal cancer incidence and death, researchers are exploring ways to prevent the disease using drugs or other chemicals (chemoprevention).

Dr. Frank Meyskens

Microscopic lesions in the lining of the colon called aberrant crypt foci (ACF) are thought to be precursors of colon polyps and, ultimately, malignant tumors. ACF lesions typically display biomarkers that may indicate precancerous development. In this trial, researchers are exploring the ability of a substance called curcumin to affect these biomarkers and possibly stop the progression to cancer. Curcumin is a component of turmeric, a spice commonly used in curry powder.



of smokers have ACF lesions.

"Though it has been used for centuries in traditional medicine, we're very early in the clinical development of curcumin as a chemopreventive agent," Dr. Meyskens said. "This trial is a proof-of-principle study to see if curcumin really can affect the relevant biomarkers in humans. If it

does, we can then design a larger cancer prevention trial based on demonstrated biological response rather than on results from epidemiological studies."

#### Who Can Join This Trial

Researchers will enroll 48 current smokers with at least 8 aberrant crypt foci. See the list of eligibility criteria at http://cancer.gov/clinicaltrials/ UCIRVINE-UCI04-2-01.

**Study Sites and Contact Information** Study sites in Illinois and Michigan are recruiting patients for this trial. See the list of study contacts at http://cancer. gov/clinicaltrials/UCIRVINE-UCI04-2-01 or call NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237) for more information. The toll-free call is confidential. \*

An archive of "Featured Clinical Trial" columns is available at http://cancer.gov/ clinicaltrials/ft-all-featured-trials.

### Notes

#### NCI Launches Redesigned Clinical Trials Pages

NCI recently posted a redesigned Clinical Trials portal area at http:// www.cancer.gov/clinicaltrials. Based on feedback gathered during user testing, the main Clinical Trials menu page and other key pages have been simplified. It is now easier to locate summaries of clinical trial results organized by type of cancer or topic. Improvements to NCI's basic and advanced clinical trials search forms give users better orientation and search help. The portal area also features educational materials about clinical trials, information about major NCI-supported clinical trials, and information for researchers about conducting clinical trials.

#### New Communications Guide for Breast Cancer Screening Available

Designing Print Materials: A Communications Guide for Breast Cancer Screening is a practical guide developed to improve the quality of information provided by breast cancer screening programs to consumers. A result of collaborative efforts by the NCI-sponsored International Cancer Screening Network, it offers a summary of informational materials and decision tools used internationally by breast cancer screening programs to communicate with women about mammography.

Free copies of the guide can be ordered at https://cissecure.nci.nih. gov/ncipubs/search.asp. A downloadable version is also available online at http://www.appliedresearch.cancer. gov/ibsn/publications/guide.html.

#### Women's Health Week Web Site Launched

The Department of Health and Human Services recently launched a Web site for the 8th Annual National Women's Health Week, which will kick off on Mother's Day, May 13, and will be celebrated until May 19.

During the week, families, communities, businesses, government, health organizations, and other groups will work together to celebrate progress in women's health; bring attention to and create understanding of women's health issues; encourage women to get regular check-ups; provide free or reduced cost screenings for women nationwide; and educate women about steps they can take to improve their physical and mental health and prevent disease. \*

70 YEARS OF EXCELLENCE ■ CANCER RESEARCH

#### If Memory Serves...

In their 1938 deliberations over NCI's expenditures, the National Advisory Cancer Council considered purchasing 15 to 20 grams of radium for research on treating cancer with radiation. However, they decided against such a large amount of radium, expecting that a supervoltage x-ray machine would soon be available for the same purpose. \*

For more information about the birth of NCI, go to http://www.cancer.gov/aboutnci/ncia.

#### Special Issue on Cancer Prevention

Don't miss next week's special issue of the *NCI Cancer Bulletin*, which will focus on cancer prevention. The issue will feature articles about NCI's prevention research activities, as well as a list of resources for additional information. \*

#### **CCR Grand Rounds**

March 13: Dr. Mina J. Bissell, Distinguished Scientist, Lawrence Berkeley National Laboratory. "Context and Tissue Structure Determine the Pattern of Gene Expression and Phenotype in Normal and Malignant Breast."

March 20: Dr. Kevin Gardner, Head, T Cell Transcription Regulation Group, Laboratory of Receptor Biology and Gene Expression, NCI Center for Cancer Research. "Genomic Approaches to Understanding Mechanisms of Gene Regulation: Perspectives from the Bench to the Bedside."

CCR Grand Rounds are held 8:30 to 9:30 a.m. at the NIH campus in Bethesda, MD, in the Clinical Center's Lipsett Amphitheater. \*

#### **Funding Opportunities**

For a complete listing of current NCI funding opportunities, please go to the HTML version of today's *NCI Cancer Bulletin* at http://www.cancer.gov/ncicancerbulletin/NCI\_Cancer\_ Bulletin\_030607/page9. \* (*HPV Prevalence continued from page 2*) The important thing is that women have routine cervical cancer screening with Pap tests, and appropriate groups of women receive the preventative vaccine that's now available."

The baseline data provided by this study may help researchers determine the public-health impact of HPV vaccination, explain the authors. However, "This is one piece of the big puzzle," says Dr. Dunne. "Looking at diseases such as genital warts, cervical cancer precursors, and cervical cancer will also be necessary to monitor vaccine impact."

"What we need...is a surveillance program that's linked to HPV vaccination uptake over a long period of time, so we can see the impact, and also any potential adverse effects, of an HPV vaccine," agrees Dr. Castle. "By monitoring benefits and risks of HPV vaccination, we can optimize the use of HPV vaccines to achieve the greatest good for women." \*

By Sharon Reynolds

#### **Headline Readers Beware**

While the February 28 *JAMA* study about HPV prevalence in the United States has generated a great deal of publicity, some of the media coverage is confusing and potentially misleading. Take, for example, the following headlines which appeared in three major newspapers and a cable TV network Web site last week:

"Study: 1 in 4 U.S. Women Infected with Cervical Cancer Virus"

"Millions of Women Carry HPV Strains that Vaccine Can Block"

"Millions In U.S. Infected With HPV; Study Finds Virus Strikes a Third of Women by Age 24"

"Study: Virus Hits 1 in 4 Women" "While it's true that, based on projections from the survey, millions of women were infected with HPV at the time the survey was conducted, it is not accurate to say that these women are at high risk for developing cervical cancer," said Dr. Philip Castle. "Only some HPV types cause cervical cancer and only if they persist for many years. The vast majority of HPV infections, even by those types which cause cervical cancer, go away within a year or two without treatment.

"It's important for people to understand that two strains of HPV—16 and 18—have been found to cause 70 percent of cervical cancers if they persist and are left untreated," continued Dr. Castle. "But even if HPV16 and 18 infections persist, they do not always cause cancer. This is why it's important for the public to clearly understand the role of all types of HPV in causing cervical cancer and other diseases, especially when considering who to vaccinate and at what age." \* (Screening continued from page 3) individuals could prevent 80 percent of lung cancer deaths.

The huge contrast between the two studies reinforces the idea that randomized clinical trials are needed to understand what is going on, says Dr. Black. The most likely reason for the discrepancy was that the first study used survival as the primary measure of outcome while the second used mortality, he says.

"The new study is well done and critically important," says Dr. Christine Berg of NCI's Division of Cancer Prevention, who is co-leader of NLST. "The findings underscore the importance of a prospective trial to address this question with mortality as an endpoint."

The editorial suggests that while rigorous cancer-screening trials are expensive and time-consuming, they are cost-effective compared with the broad adoption of expensive screening interventions that cause more harm than good.

Dr. Bach is awaiting the NLST results, but he went into the study hoping and expecting that CT was going to work. "We were all very disappointed because, like everyone else, we want to have a solution to this terrible disease," he says. \*

By Edward R. Winstead

#### Featured Meetings and Events

A calendar of scientific meetings and events sponsored by the National Institutes of Health is available at http://calendar.nih. gov/app/MCalWelcome.aspx \*

For more information on cancer, call 1-800-4-CANCER or visit http://www.cancer.gov. *NCI Cancer Bulletin* staff can be reached at ncicancerbulletin@mail.nih.gov.