

# Division of Cancer Prevention Update

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**National Cancer Advisory Board  
November 2012**

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# Scientific Directions – November 2012

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- 1. Clinical Studies and Large Trials**
- 2. Agent Development and Decision-Making**
- 3. Overdiagnosis and Precancerous Lesions**
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# 1. Clinical Studies and Large Trials

## *The* NEW ENGLAND JOURNAL *of* MEDICINE

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### Colorectal-Cancer Incidence and Mortality with Screening Flexible Sigmoidoscopy

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## Clinical Studies and Large Trials

# Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial: Colorectal Cancer Results

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**Flexible sigmoidoscopy at baseline and year 3 or year 5 vs. usual care (155K participants)**

- **21% relative reduction in incidence for screened group (proximal and distal): 3 per 1,000 persons over 10 years**
- **26% relative reduction in colorectal cancer mortality for screened group (distal only): 1 per 1,000 persons over 10 years**

# Clinical Studies and Large Trials

## Screening Trial Resource Availability

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**PAR Approved for utilizing the PLCO biospecimen resource to bridge gaps in cancer etiology and early detection research**

- **Promotes use of resource by streamlining permission and adding funding for projects**

**Public use data sets and website for PLCO and National Lung Screening Trial (NLST) data available**

**<http://biometry.nci.nih.gov/CDAS>**

- **Cancer Data Access System to manage data release**
- **Website gives summary materials & access info**

## Patient and Physician Guide: National Lung Screening Trial (NLST)

### What is the purpose of this guide?

To explain the benefits and harms of low-dose computed tomography (CT) screening for lung cancer in people at high risk for the disease. The NLST showed a reduction in deaths from CT screening compared to chest X-ray screening. The Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial recently showed that chest X-ray screening (compared to no screening) did NOT reduce the chance of dying from lung cancer.

### Who participated in the NLST?

Current or former cigarette smokers within the past 15 years, 55 to 74 years of age, with at least 30 pack-years of smoking [Pack-years = packs per day x number of years smoking]. Participants must have had no symptoms or signs of lung cancer or other serious medical conditions, and be medically fit for surgery.

## Study Findings: Low-dose CT versus Chest X-ray screening

53,454 current and former smokers were randomly assigned to be screened once a year for 3 years with low-dose CT or chest X-ray. Here's what happened after an average of 6.5 years:

	Low-dose CT 26,722 people		Chest X-ray 26,732 people
<b>Benefit: How did CT scans help compared to chest X-ray, an ineffective screening test?</b>			
4 in 1,000 fewer died from lung cancer	13 in 1,000	versus	17 in 1,000
5 in 1,000 fewer died from all causes	70 in 1,000	versus	75 in 1,000
<b>Harm: What problems did CT scans cause compared to chest X-ray?</b>			
223 in 1,000 more had at least one false alarm	365 in 1,000	versus	142 in 1,000
18 in 1,000 more had a false alarm leading to an invasive procedure, such as bronchoscopy, biopsy, or surgery	25 in 1,000	versus	7 in 1,000
2 in 1,000 more had a major complication from Invasive procedures	3 in 1,000	versus	1 in 1,000

## "Take home" messages

Lung cancer screening with CT scans is the only screening test shown to lower the chance of dying from lung cancer. The effect of screening may vary depending on how similar you are to the people who participated in the study. The benefit of screening may be bigger if your lung cancer risk is higher. The harm may be bigger if you have more medical problems (like heart or severe lung disease), which could increase problems from biopsies and surgery.

For perspective, the reduction in deaths from lung cancer with CT screening is larger than the reduction in deaths from the target cancers of other common screening tests, such as mammograms for breast cancer.

There is a tradeoff: CT screening decreases your chance of death but increases your chance of having a false alarm.

If you choose to have CT screening, it is important to have it done at a medical center with special expertise in lung cancer screening and treatment.

## Most important thing you can do

**DON'T SMOKE.** Regardless of your screening decision, avoiding cigarettes is the most powerful way to lower your chance of dying overall or suffering or dying from a variety of diseases, such as lung cancer, emphysema, heart or vascular disease. For example, at age sixty-five, 89 in 1,000 male current smokers will die of lung cancer in the next 10 years versus 4 in 1,000 never smokers. For women, the corresponding figures are 55 in 1,000 versus 5 in 1,000.

For help quitting, call 1-800-QUIT-NOW.

## 2. Agent Development and Decision-Making

# Agent Development

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**The PREVENT Cancer Program implemented and the first two semi-annual application cycles completed (42 applications)**

**12 applications approved and task orders awarded**

- **New drugs (6)**
- **Surrogate biomarkers (3)**
- **Vaccines (3)**

# Agent Development and Decision-Making

## Early Phase Prevention Trials

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**Phase 0-I-II Cancer Prevention Trials contract recompleted and awarded**

- Primary mechanism for early phase trials
- Identify & test biomarkers of efficacy
- Develop trial models for identifying agents

**Contract trials completed this year**

- Atorvastatin, sulindac, inulin in colorectal cancer
- Polyphenon E/green tea in prostate, bladder cancer
- Zileuton + celecoxib in lung cancer
- Resveratrol, atorvastatin in breast cancer

# Agent Development and Decision-Making

## **Making Better Decisions About Agents**

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**Overarching Goal: Determine positive and negative predictive values of preclinical models for clinical development**

- **Constructed a model for predicting the outcome of long-term animal tumor assays from the results of short-term morphological assays**
- **Applied to 6 morphological assays**

### **3. Overdiagnosis & Precancerous Lesions**

## **Overdiagnosis Workshop & Initiative**

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**Workshop led to recommendations for scientific next steps in basic and translational research**

**EDRN pilot project to discover and develop biomarkers or molecular signatures that can distinguish indolent cancers from progressive cancers**

- Includes prostate, breast, and lung cancers**

# Overdiagnosis and Precancerous Lesions

## Companion Imaging & Biomarkers PAR

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**Co-sponsored with Division of Cancer Treatment and Diagnosis**

**PAR for pre-clinical and clinical studies that correlate cancer imaging methods with biomarkers to:**

- **Detect cancers at the earliest stages**
- **Reduce false-positive tests**
- **Reduce overdiagnosis of cancer**

# Overdiagnosis and Precancerous Lesions

## Overdiagnosis Research Consortium

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**Joint project with Division of Cancer Biology**

**Propose a consortium to build on existing resources and collaborate with other groups**

- **Characterize cellular and molecular patterns of indolent vs. potentially lethal lesions**
- **Determine the cellular and molecular phenotypes of early lesion cells and associated microenvironment**

## 4. Cancer Immunoprevention

# Vaccine Studies from PREVENT

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- A multi-antigen vaccine for prevention of MNU induced ER+ rat mammary cancers
- Characterization & testing of potential antigens for immunization against murine colon cancer
- Plac-1 vaccine for breast cancer prevention

# Cancer Immunoprevention

## PAR for Detection of Pathogen-Induced Cancer

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- **> 20% of cancers are associated with microbial pathogens**
- **Premise: infectious pathogens and host cells play a joint role in modulating cancer-related pathways**
- **Goal: to develop new molecular signatures for risk of progression and early detection of pathogen-induced cancer**

## 5. International Collaborations

### **China Cancer Screening Trial Feasibility Study**

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**Confirm NLST results in urban Chinese population**

- **Differences in the histology of lung cancer, genetics, and health care systems in China vs. U.S.**
- **Feasibility study in 4 cities for a long-term randomized 3-arm screening trial**
  - 1. Helical chest CT exam annually**
  - 2. Helical chest CT biennially**
  - 3. Annual screening for liver disease/cancer**

# International Collaborations

## Translating PDQ into Chinese

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- **Joint project with NCI Office of Communications and Education and three medical centers in China**
- **Pilot: a subset of the PDQ health professional summaries to be translated and made available to medical professionals and students**

## 6. Cancer Prevention Fellowship Program

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- **Applications more than doubled since 2007**
- **Class of 2013 will have 11 fellows (a 10% success rate)**
- **NIH Evaluation Set-Aside funds awarded to conduct a comprehensive evaluation of career paths and outcomes of former Fellows**

## 7. New Approaches to Clinical Prevention Studies

# Non-Cancer Trials to Find Prevention Signals

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### Diabetes Prevention Program Outcome Study (DPPPOS) Collaboration with National Institute of Diabetes and Digestive and Kidney Diseases

- Examine if metformin or lifestyle intervention can modify cancer incidence, especially in obesity-related cancers (breast, colon & rectum, endometrium, pancreas, esophagus, gall bladder, and kidney)

### Aspirin in Reducing Events in Elderly (ASPREE) Study with National Institute on Aging & Australian govt.

- Funding collection of biospecimens from this randomized trial testing aspirin in 19,000 healthy people age 70 and older

# New Approaches to Clinical Prevention Studies

## **Reciprocal Control Design for Trials**

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- **Large numbers of participants must be followed for years in definitive prevention and early detection trials**
- **The reciprocal control design to increase efficiency**
  - **Participants in each arm receive an intervention for a particular disease but also serve as controls for a different intervention and disease in the other arm**
- **Panel Session at the Society for Clinical Trials Annual Meeting, May 2013: “The Reciprocal Control Design for Trials in the Early Detection and Prevention of Disease”**

# **New Approaches to Clinical Prevention Studies**

## **NCI Community Oncology Research Program (NCORP)**

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**Two existing community-based cancer research programs**

- **Community Clinical Oncology Program Network (CCOPs and Minority-Based CCOPs)**
- **National Community Cancer Center Program (NCCCP)**

**Planning a new community-based program to align these programs to expand the scope of research**

- **Clinical trials**
- **Cancer care delivery & health services research**
- **Cancer disparities research**