Lung Cancer Screening: Why It's More Than Just a Scan

Mark Block, M.D.
Chief, Division of Thoracic Surgery
Memorial Healthcare System

Sept. 21, 2019

Lung Cancer Screening…..

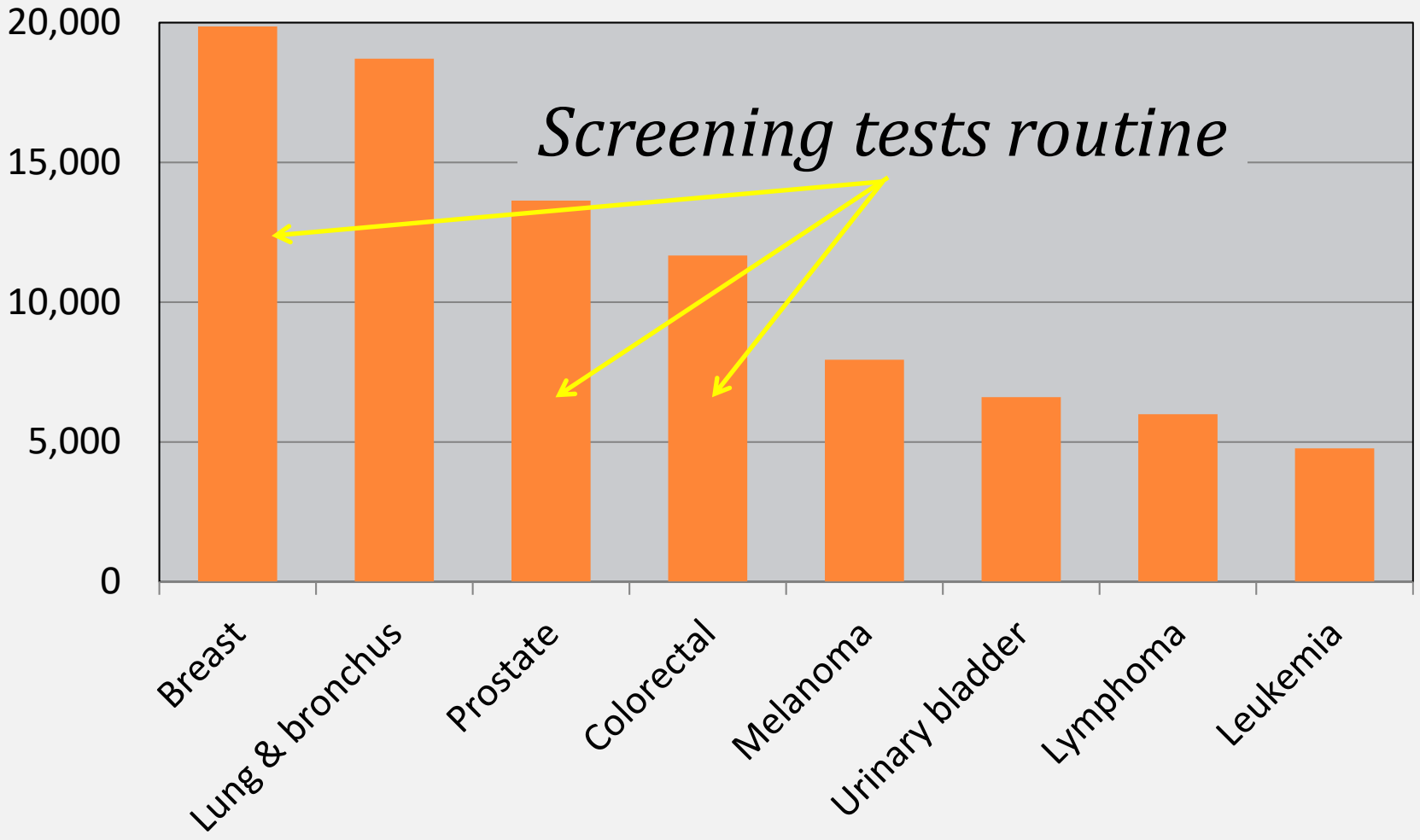
"…the opportunity to realize the greatest single reduction of cancer mortality in the history of the war on cancer."

James Mulshine, MD
Associate Provost and Vice President for Research
Rush University Medical Center

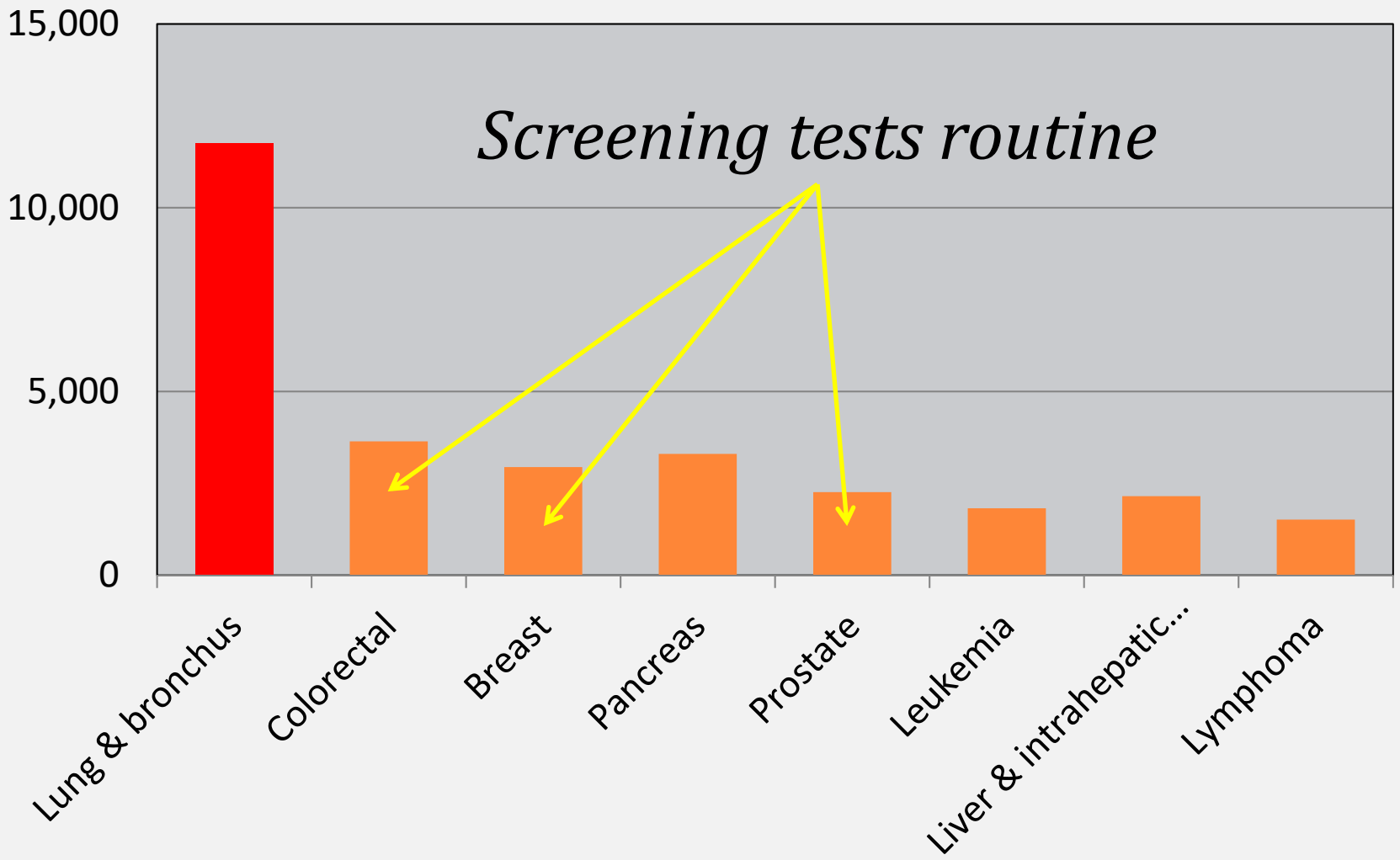
Cancer Statistics, 2018

American Cancer Society
Cancer Facts & Figures, 2018

Estimated Cancer Cases, Florida, 2018



Estimated Cancer Deaths, Florida, 2018



History of Lung Cancer Screening

- Chest x-ray ⟶ Negative
- Sputum cytology ⟶ Negative
- Chest CT ⟶ ?

2352

Prevention and Early Diagnosis of Lung Cancer

Supplement to ***Cancer***

The Mayo Lung Project

A Perspective

Robert S. Fontana, M.D.

Department of Medicine, Mayo Clinic, Rochester, Minnesota.

BACKGROUND. The Mayo Lung Project (MLP) was a randomized, controlled, clinical trial designed to determine whether intensive radiologic and cytologic screening for lung carcinoma could reduce lung carcinoma mortality significantly.
METHODS. Half the MLP population was encouraged (and reminded) to undergo free chest X-rays and free sputum cytology tests every 4 months for 6 years,

Cancer, 2000

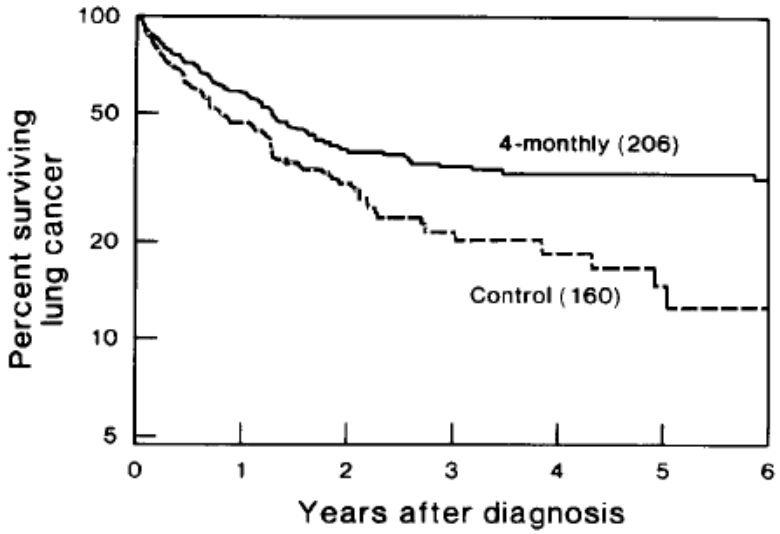
1971 – 1983
N = 9211 men, heavy smokers

Randomized:

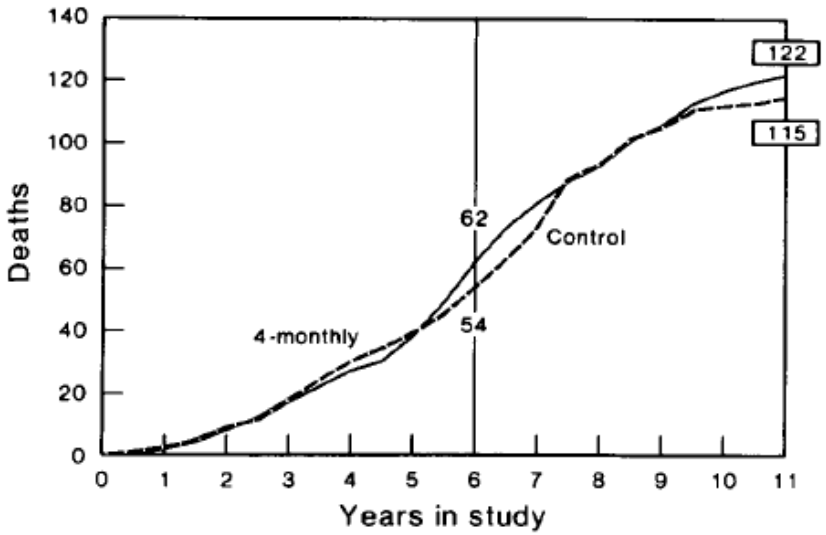
- CxR + sputum q 4 months
- CxR + sputum annually

Mayo Lung Project: Results

Lung Ca Survival

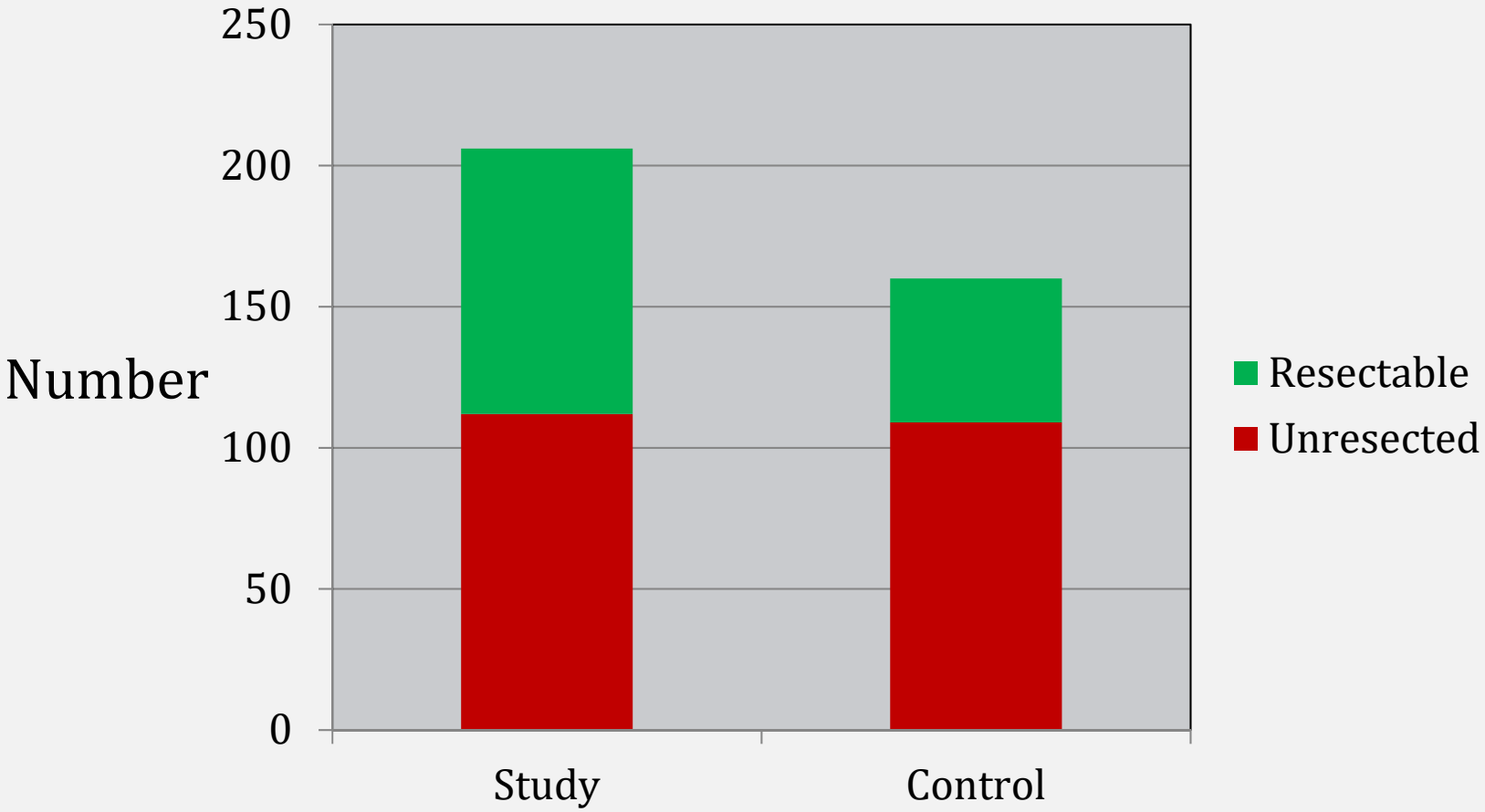


Cumulative Lung Ca Deaths



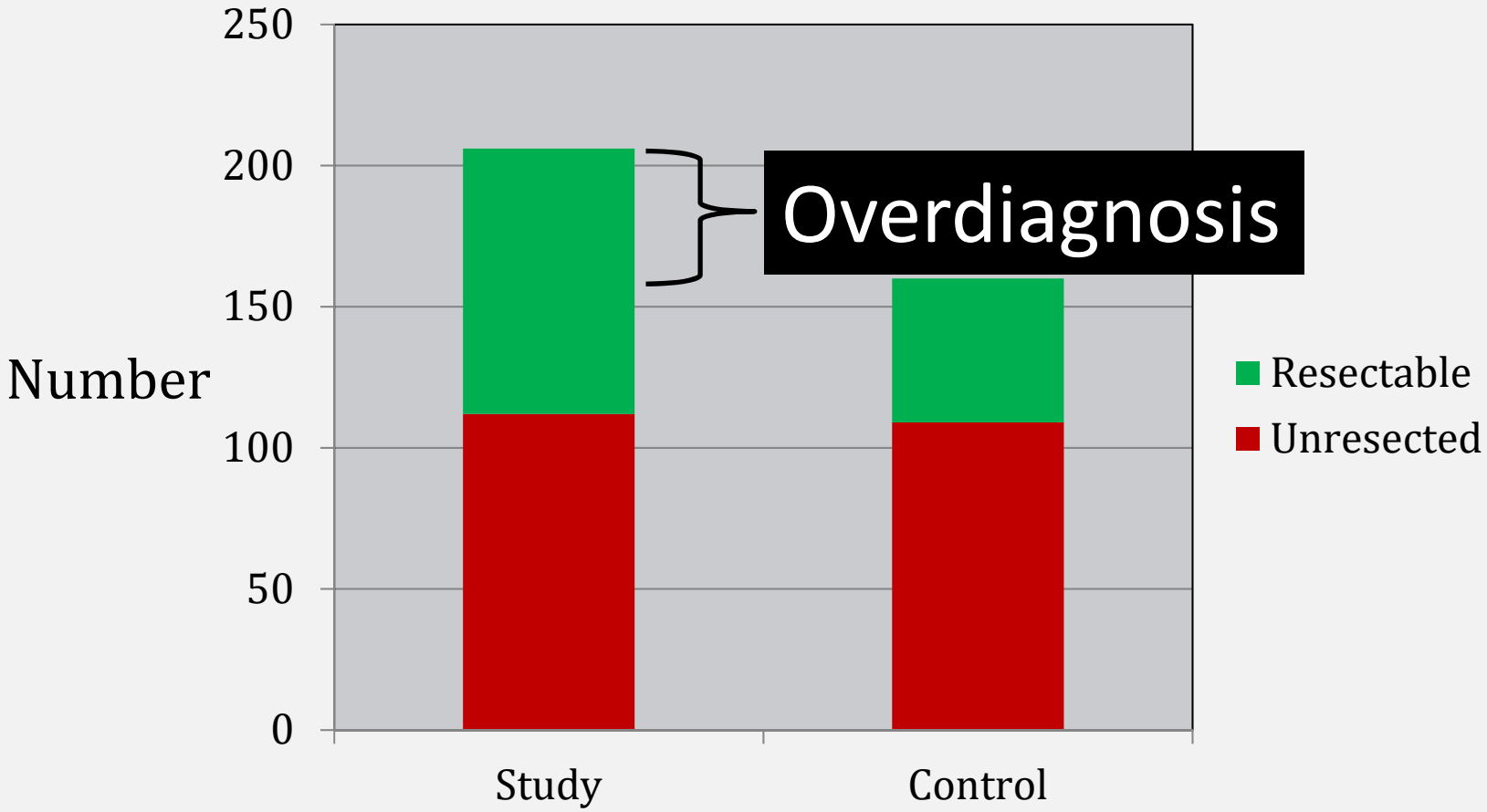
Mayo Lung Project: Results

Discovered Lung Cancers:



Mayo Lung Project: Results

Discovered Lung Cancers:



ONLINE FIRST

Screening by Chest Radiograph and Lung Cancer Mortality

The Prostate, Lung, Colorectal, and Ovarian (PLCO) Randomized Trial

Martin M. Oken, MD
Willam G. Hocking, MD
Paul A. Kvale, MD
Gerald L. Andriole, MD
Saundra S. Buys, MD

Context The effect on mortality of screening for lung cancer with modern chest radiographs is unknown.

Objective To evaluate the effect on mortality of screening for lung cancer using radiographs in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial.

Design, Setting, and Participants Randomized controlled trial that involved 154 901

JAMA, 2011

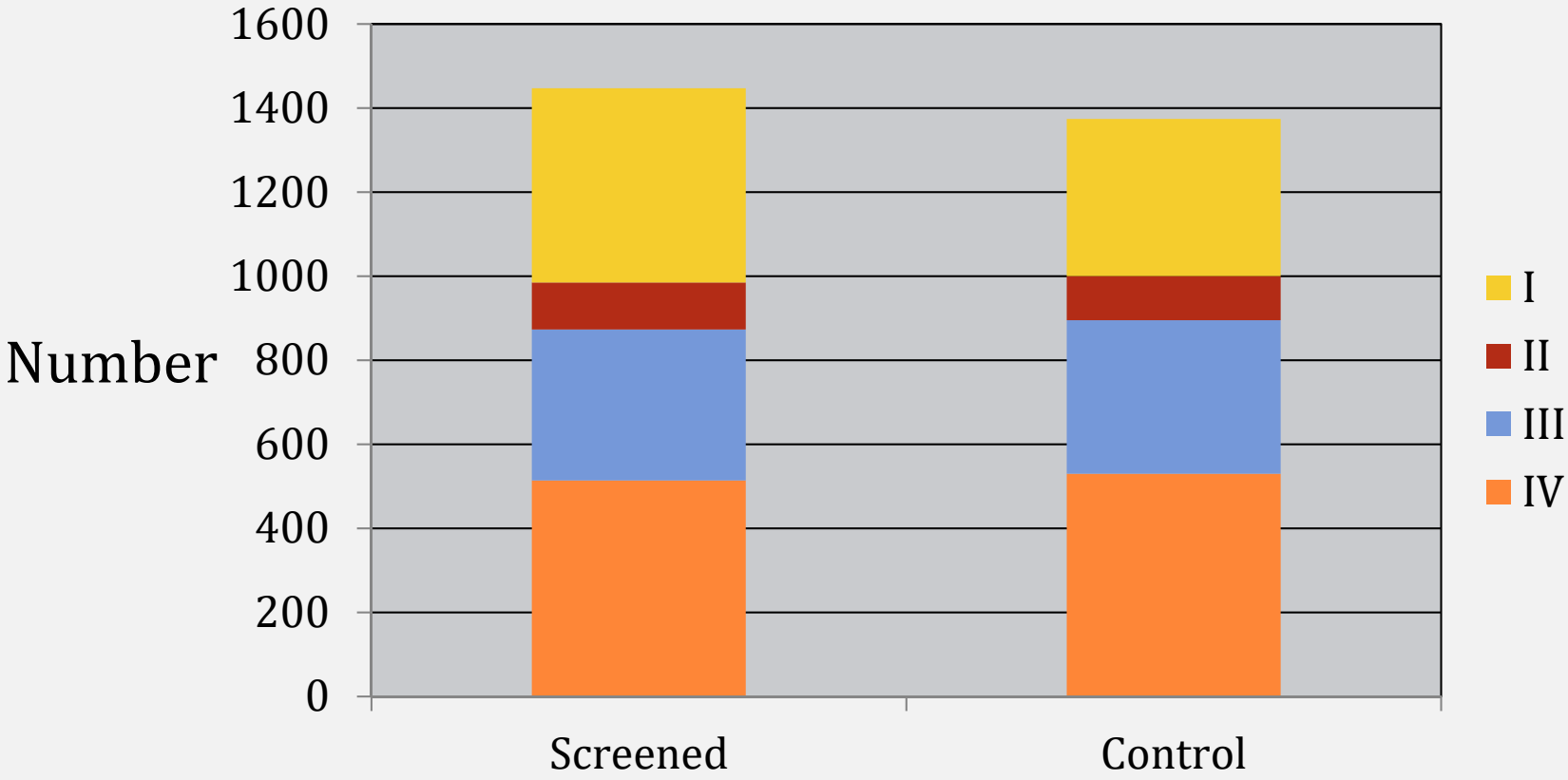
1993 – 2001
N = 154,901
Age: 55 – 74 years

Randomized:

- Annual CxR (77,445)
- Usual care (77,456)

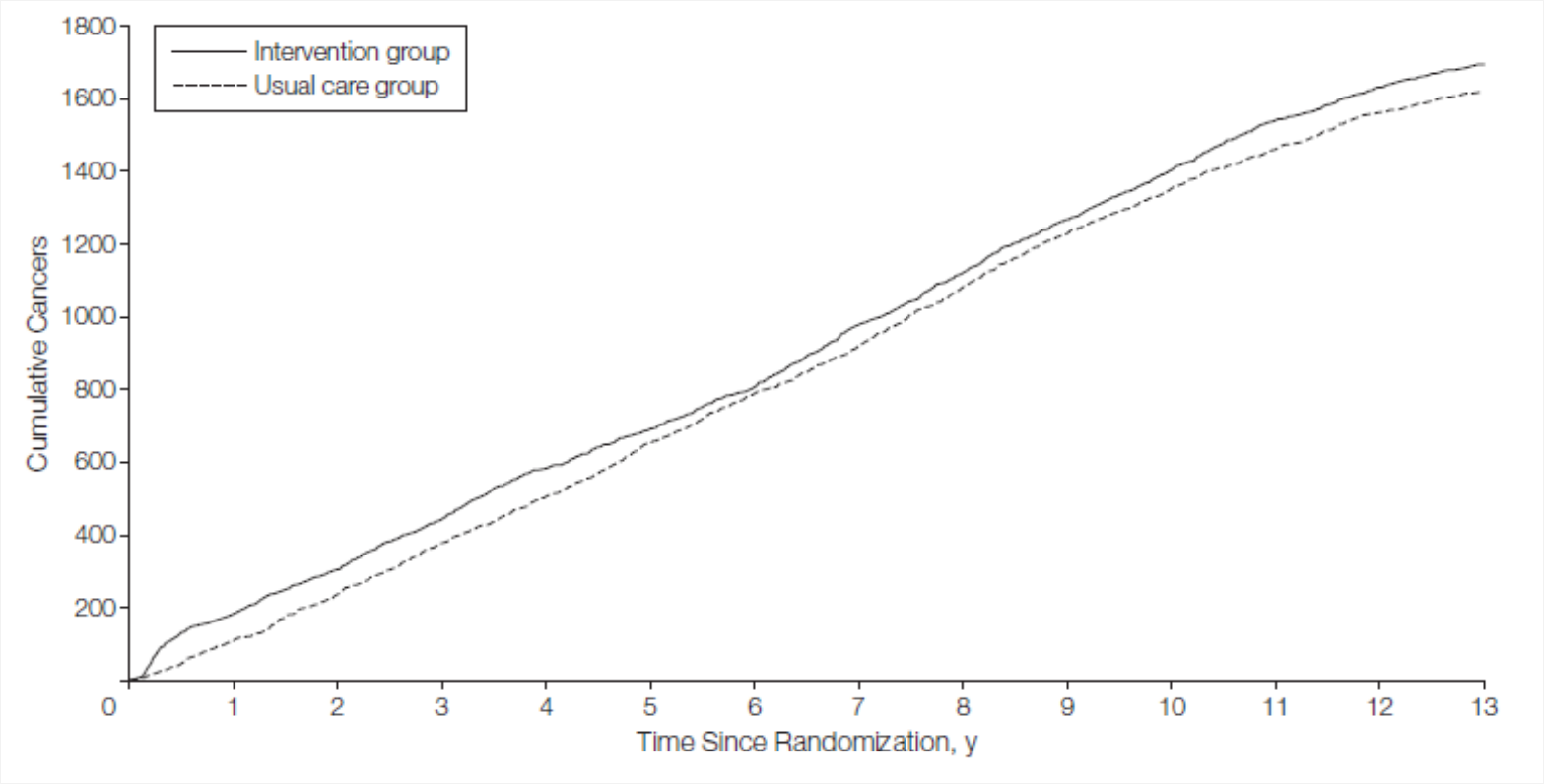
PLCO: Results

Stage of discovered NSCLCs:



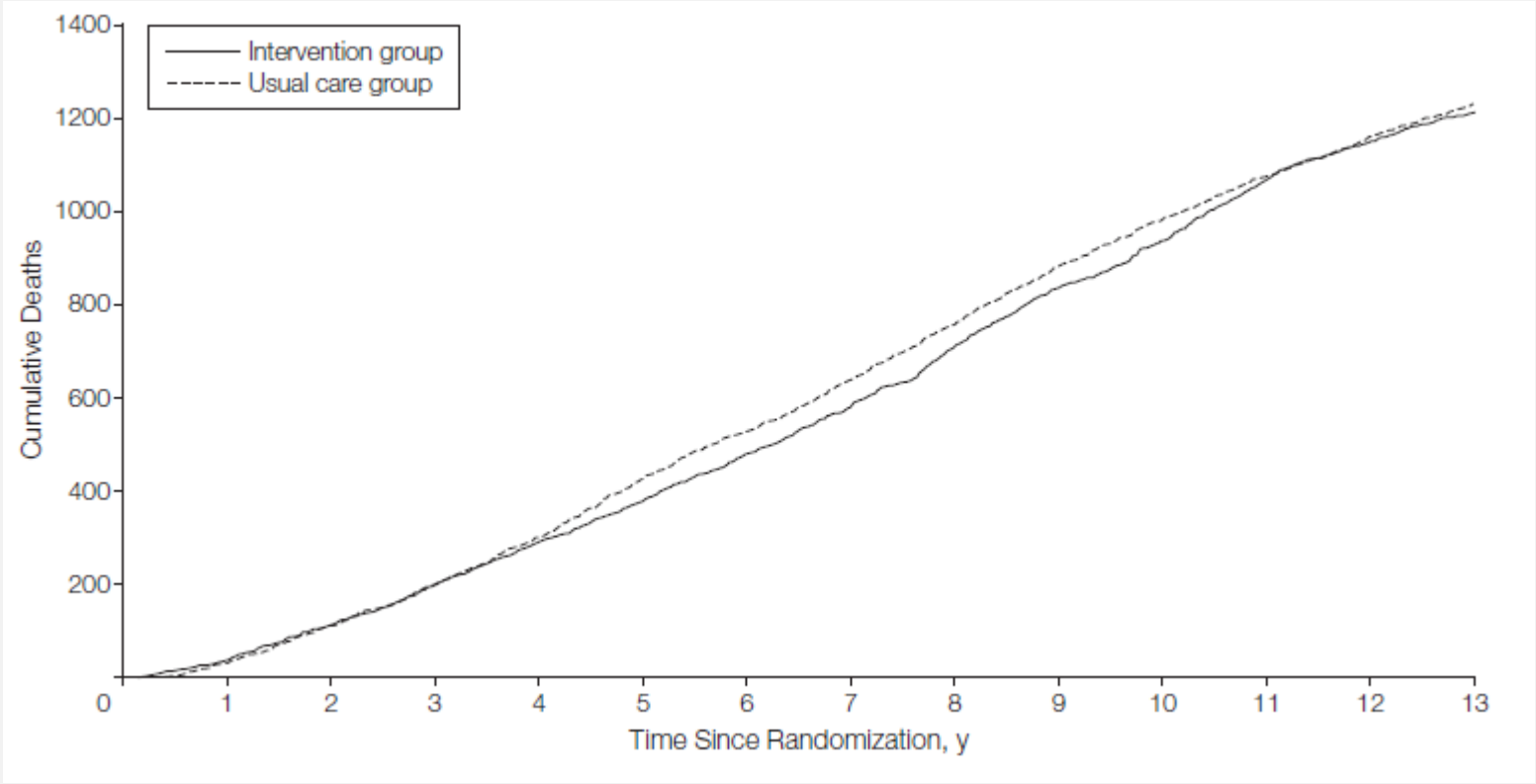
PLCO: Results

Cumulative Lung Cancers Detected



PLCO: Results

Cumulative Lung Cancer Deaths



Early Lung Cancer Action Project: overall design and findings from baseline screening

Claudia I Henschke, Dorothy I McCauley, David F Yankelevitz, David P Naidich, Georgeann McGuinness, Olli S Miettinen, Daniel M Libby, Mark W Pasmantier, June Koizumi, Nasser K Altorki, James P Smith

Summary

Background The Early Lung Cancer Action Project (ELCAP) is designed to evaluate baseline and annual repeat screening by low-radiation-dose computed tomography (low-dose CT) in people at high risk of lung cancer. We report the baseline experience.

Methods ELCAP has enrolled 1000 symptom-free volunteers, aged 60 years or older, with at least 10 pack-years of cigarette smoking and no previous cancer, who were medically fit to undergo thoracic surgery. After a structured interview and informed consent, chest radiographs and low-dose CT were done for each participant. The diagnostic

Interpretation Low-dose CT can greatly improve the likelihood of detection of small non-calcified nodules, and thus of lung cancer at an earlier and potentially more curable stage. Although false-positive CT results are common, they can be managed with little use of invasive diagnostic procedures.

Lancet 1999; **354:** 99–105
See Commentary page

Introduction

In the USA in 1998, there were an estimated 160 000 deaths from lung cancer and an estimated 172 000 new

N = 1000
Age 60 and over
10 pack-year smoking history
CxR + low dose Chest CT

Lancet, 1999

ELCAP: Results

Discovered Lung Cancers:

Stage	CT	CxR
I	23	4
II	1	1
III	3	2

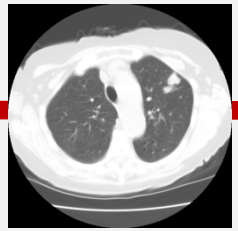
Problems with Screening Trials:

- *Overdiagnosis*

  Diagnosis of cancers that would have never become clinically significant

- *Lead-time bias*

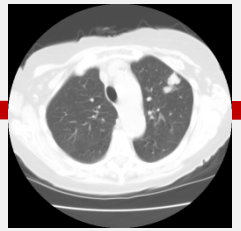
Lead-time bias:

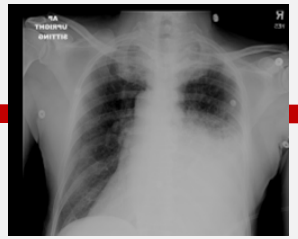


7 6 5 4 3 2 1 0

Time (years)

Lead-time bias:



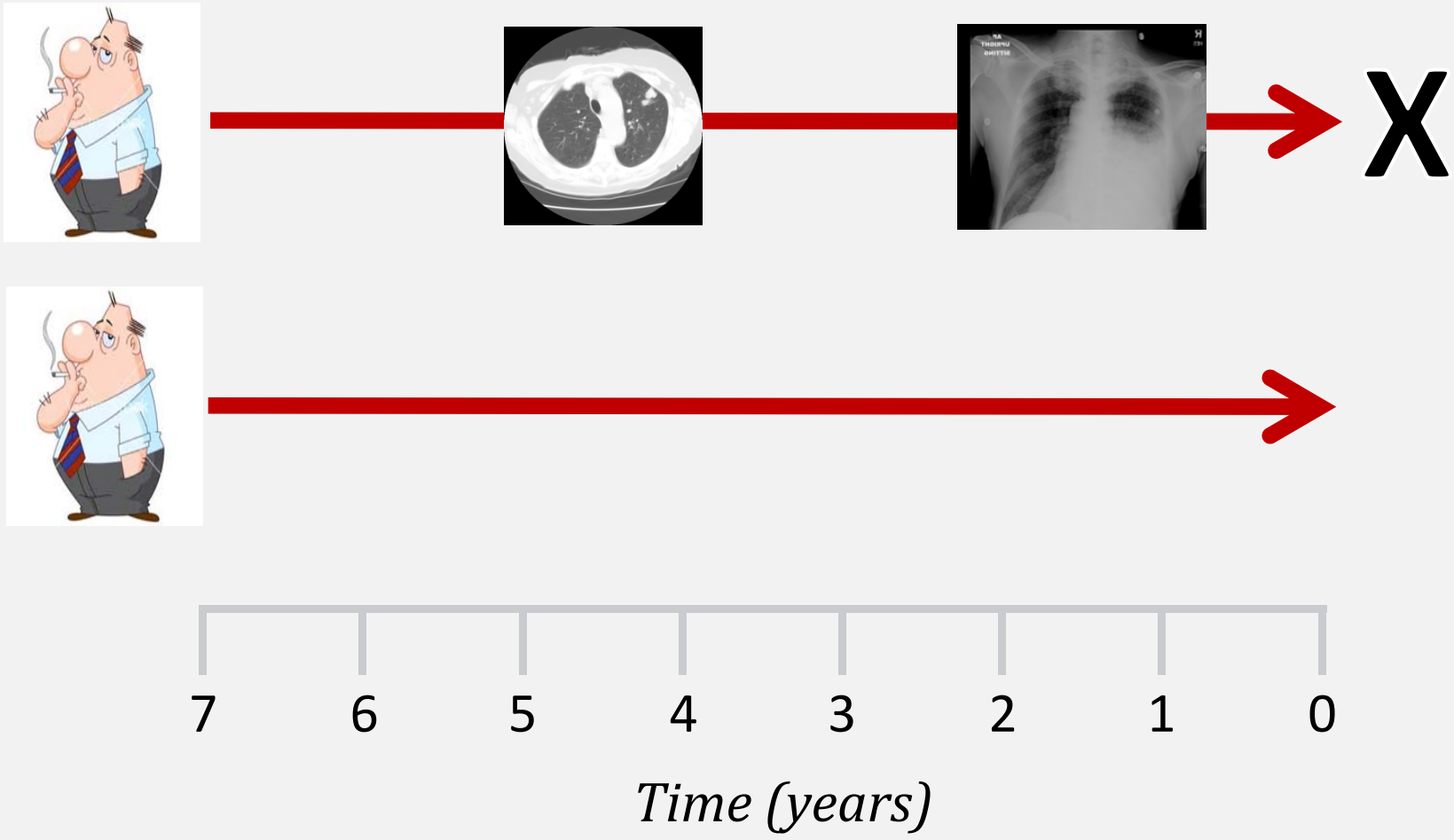


X

7 6 5 4 3 2 1 0

Time (years)

Lead-time bias:



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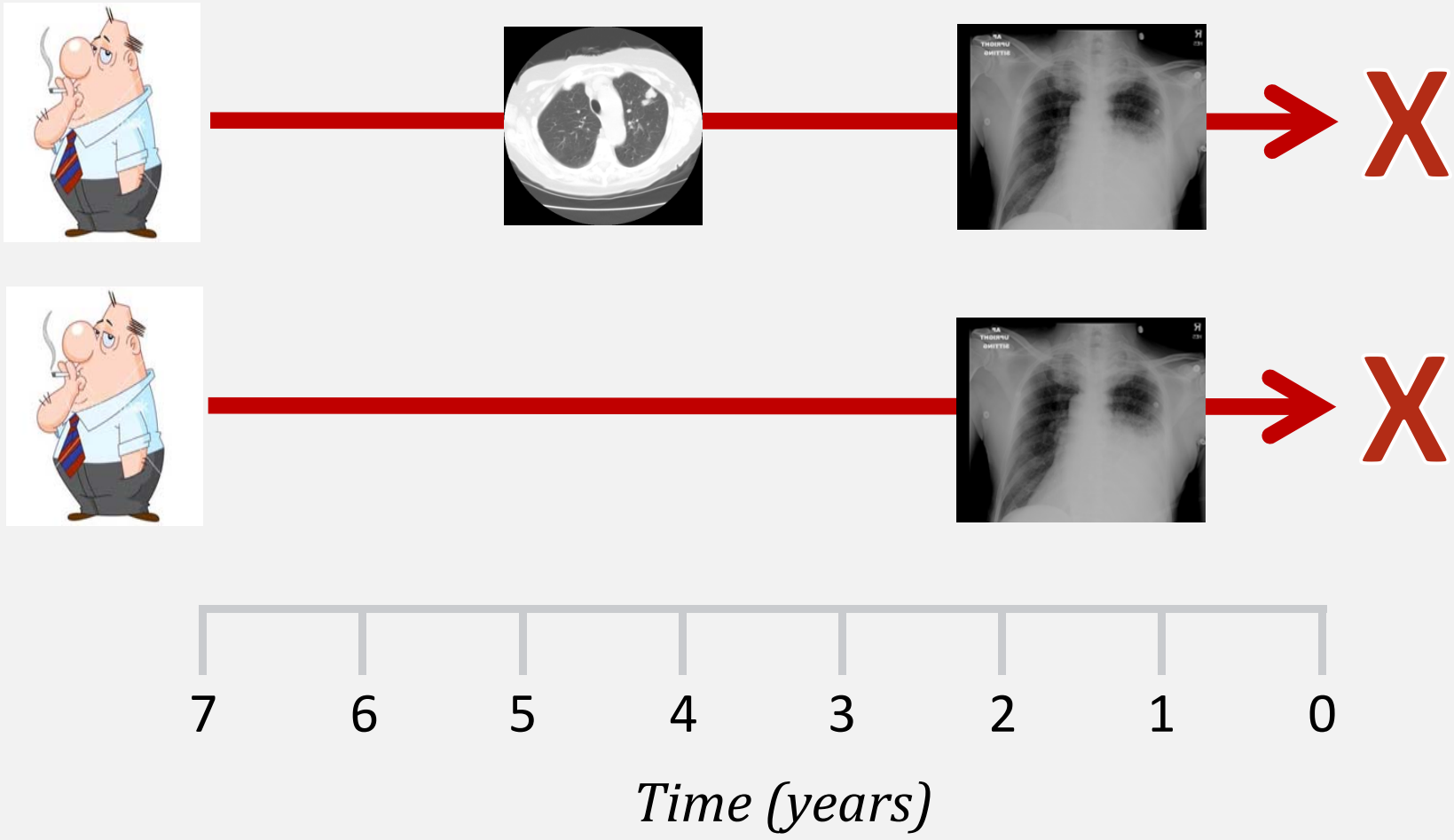
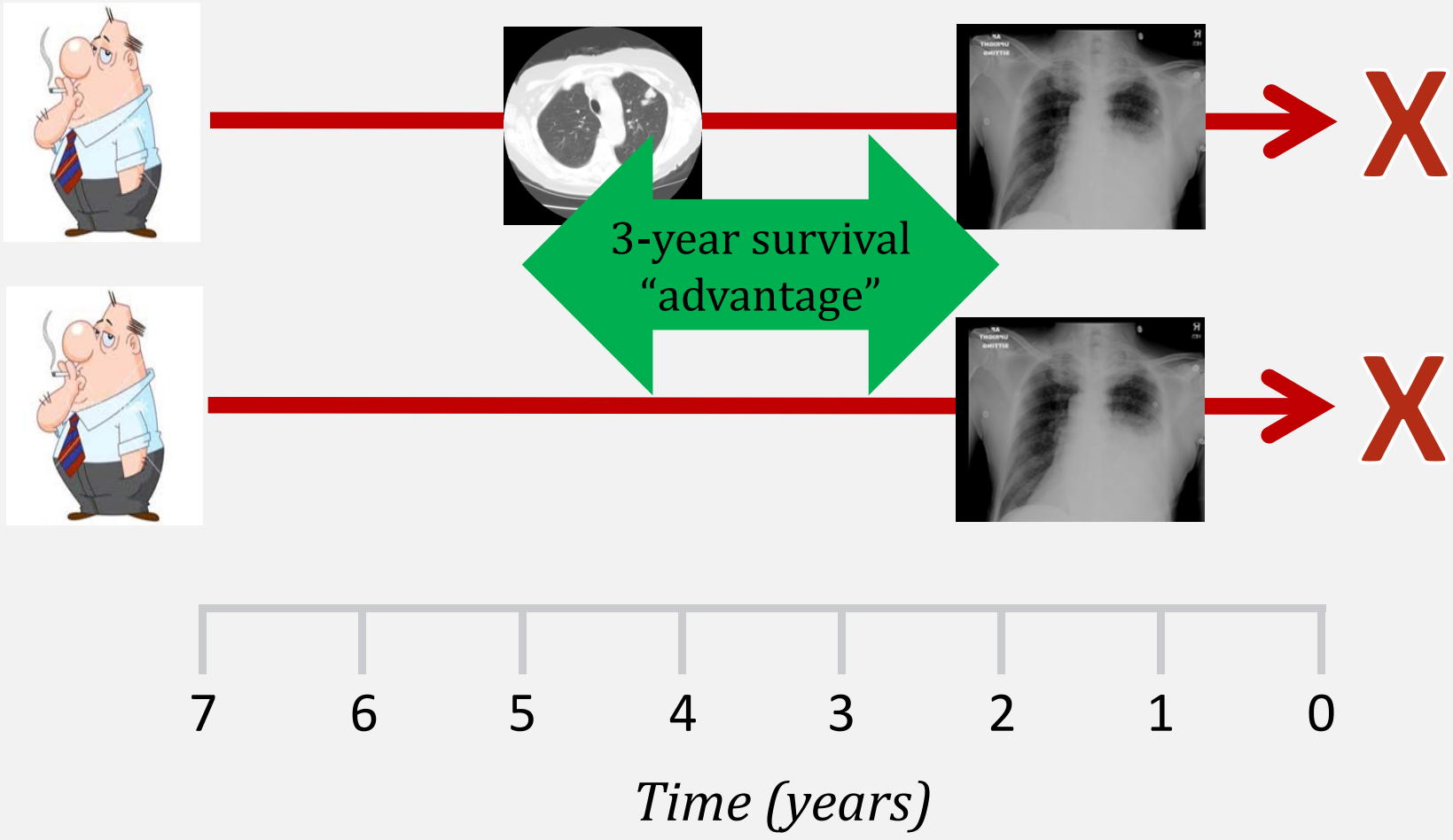


Lead-time bias:



U.S. Preventive Services Task Force

Division of the Agency for Healthcare Research and Quality (AHRQ)

"The USPSTF concludes that the evidence is insufficient to recommend for or against screening asymptomatic persons…."

Lung Cancer Screening Recommendations (2004)

www.uspreventiveservicestaskforce.org

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*

NEJM, June, 2011

33 Sites
$300,000,000

National Lung Screening Trial

- Age 55-75 years
- >30 pack-year smoking history
- Enrolled between 2002-2004
- Annual scans (T0, T1 and T2)
- >4 mm considered positive test

Modality	N
Chest CT*	26,722
Chest x-ray	26,732

NEJM, June, 2011

NLST: Key Findings

- 20% reduction in deaths from lung cancer

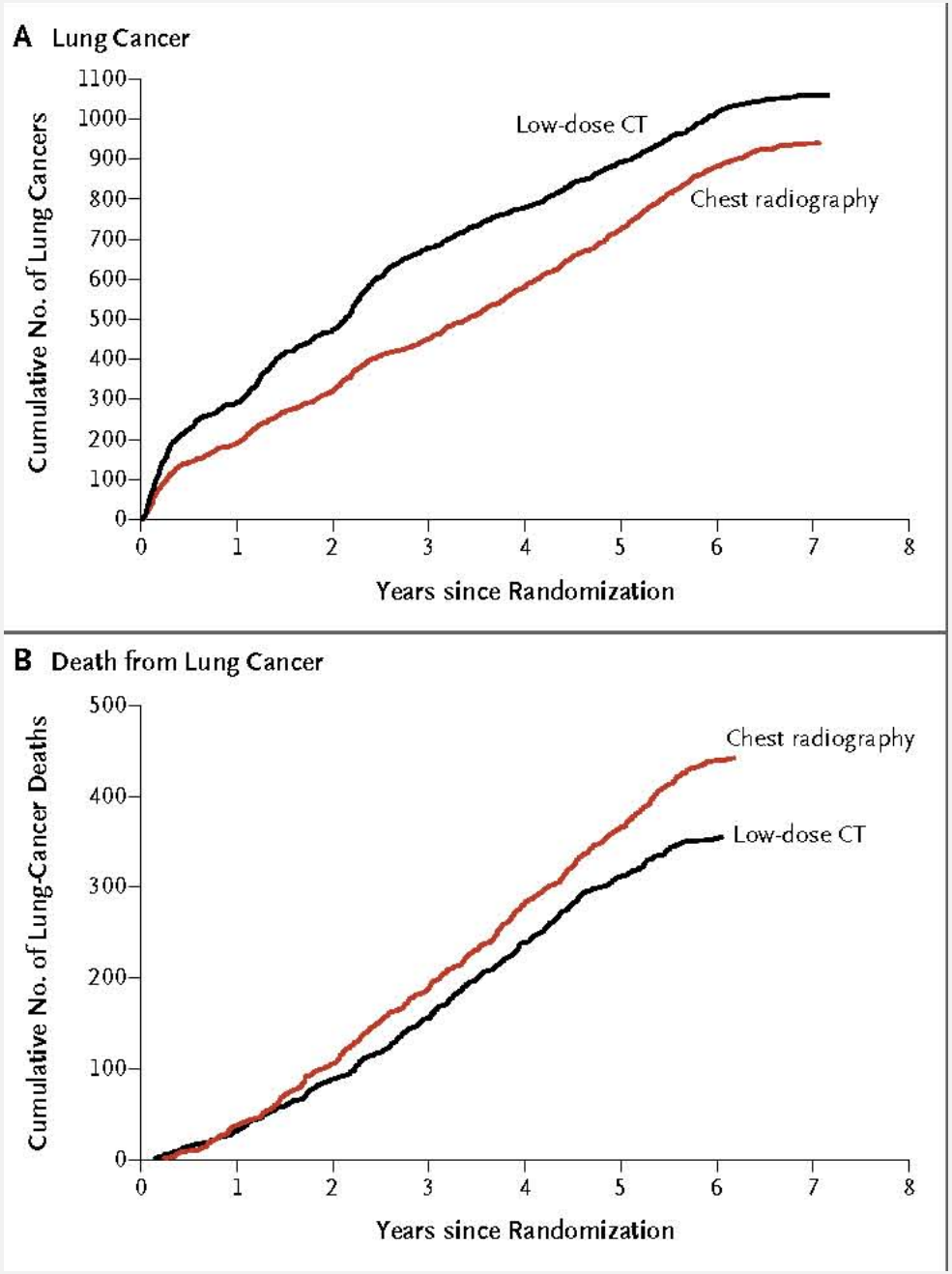
NLST: Key Findings

- 20% reduction in deaths from lung cancer

- 6.6% reduction in overall mortality

Cumulative Lung Cancers

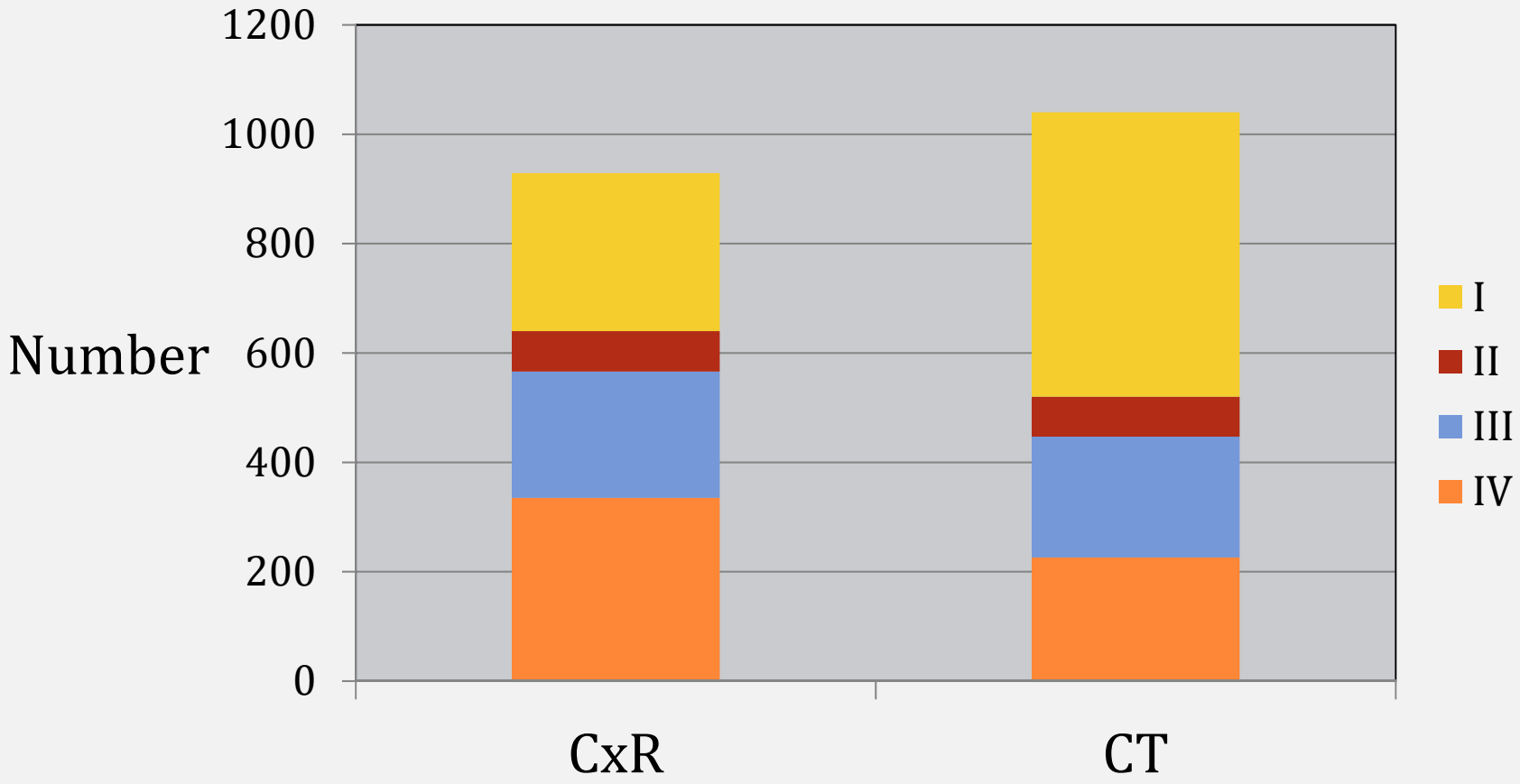
Cumulative Deaths from Lung Cancer



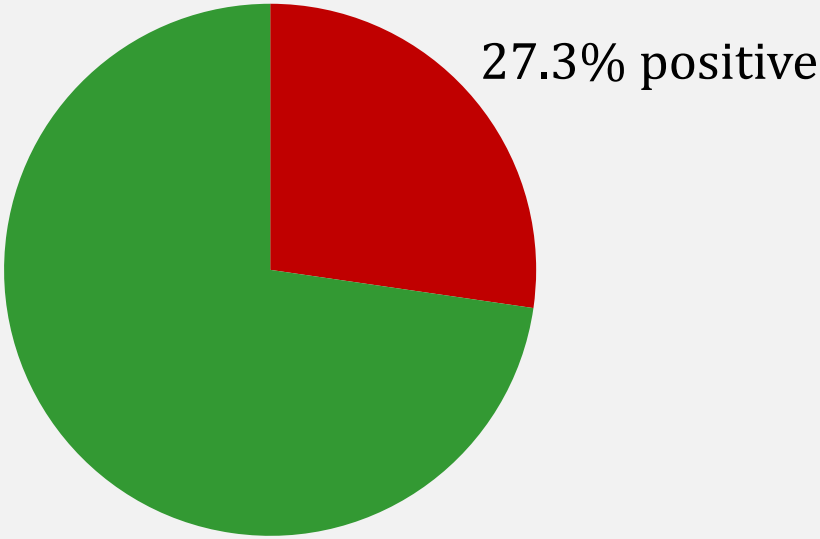
NEJM, June 2011

NLST: Stage Shift

Stage at Diagnosis:

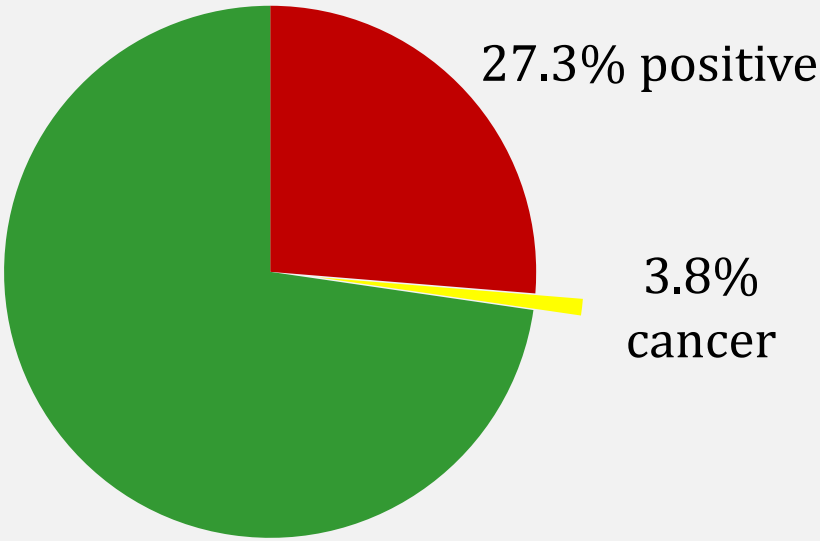


NLST: CT Findings



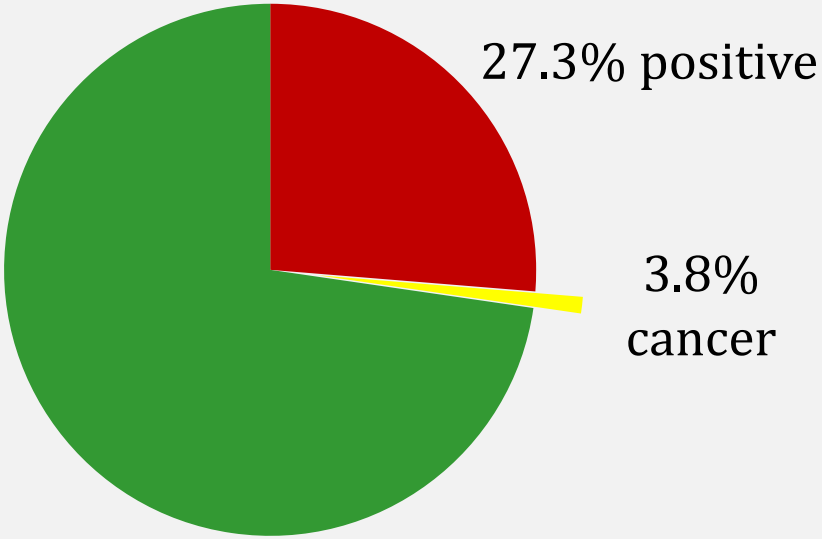
Prevalence scan

NLST: CT Findings

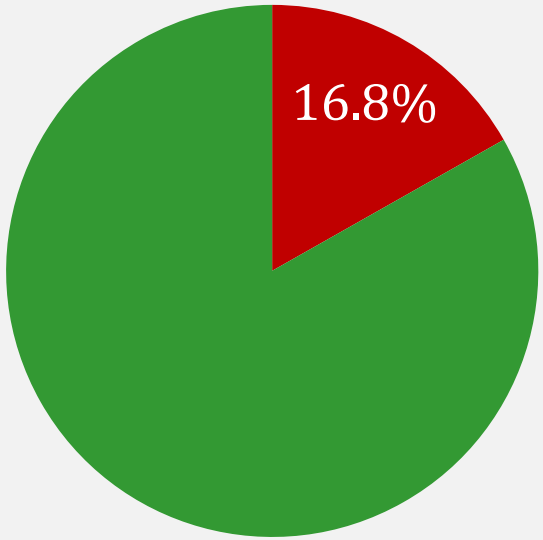


Prevalence scan

NLST: CT Findings

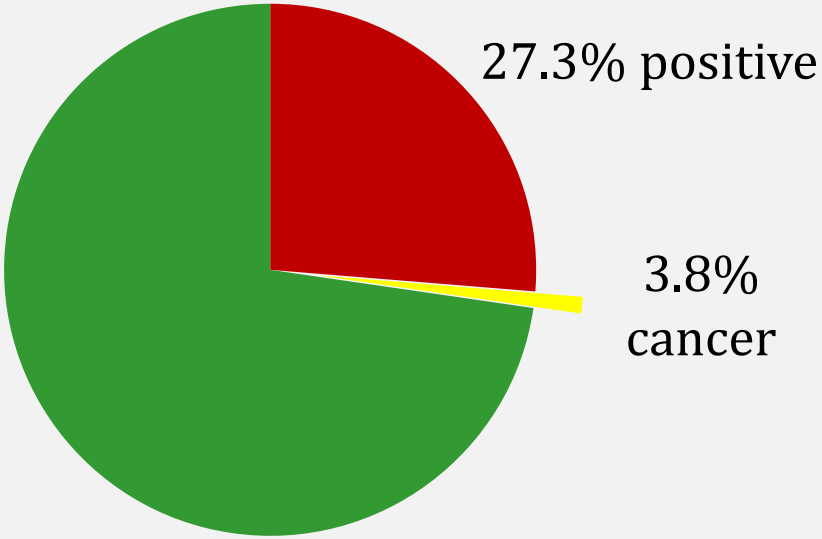


Prevalence scan

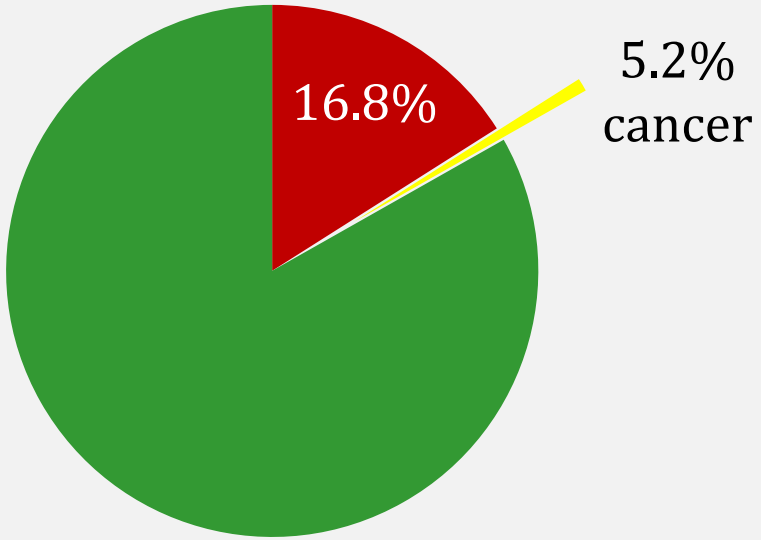


Incidence scan

NLST: CT Findings

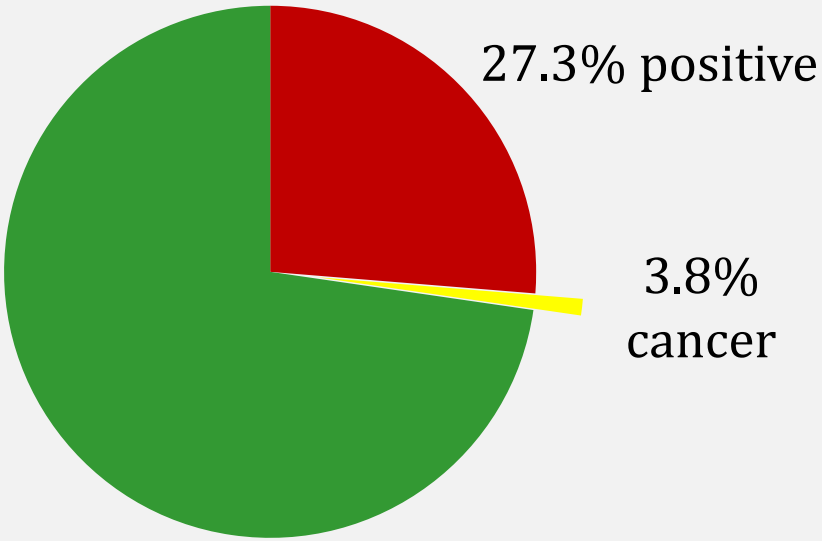


Prevalence scan

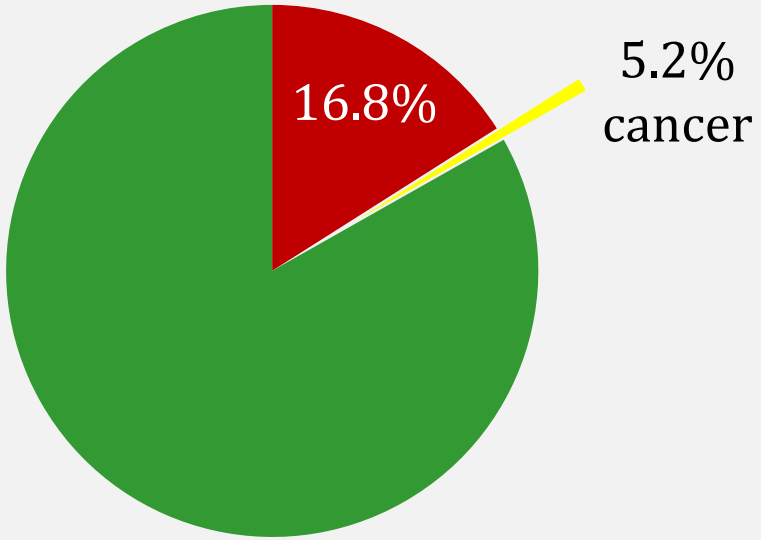


Incidence scan

NLST: CT Findings

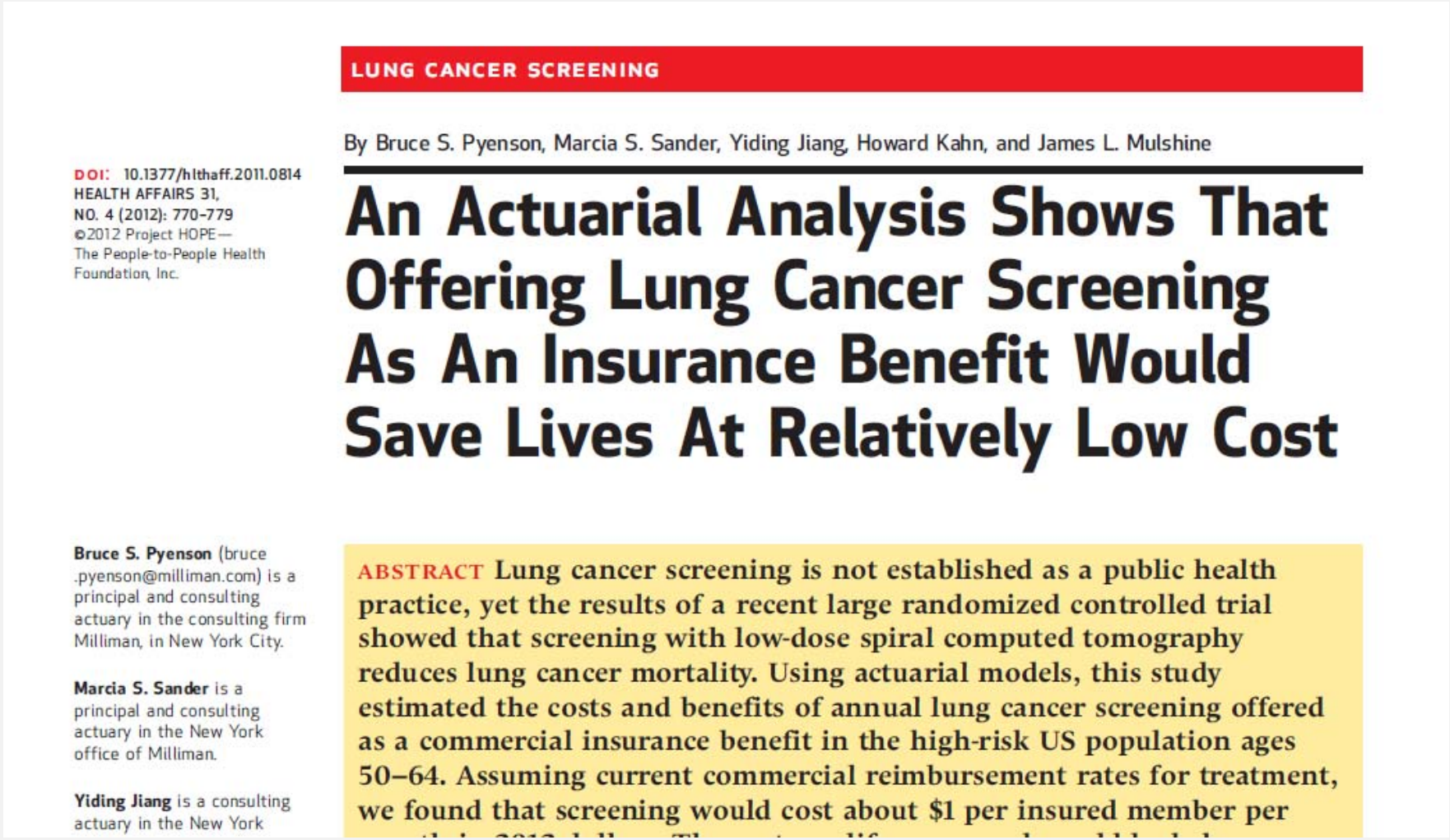


Prevalence scan



Incidence scan

- Lung cancer incidence = 645/100,000 person-years
- 96% of positive findings were not cancer



LUNG CANCER SCREENING

By Bruce S. Pyenson, Marcia S. Sander, Yiding Jiang, Howard Kahn, and James L. Mulshine

DOI: 10.1377/hlthaff.2011.0814
HEALTH AFFAIRS 31,
NO. 4 (2012): 770–779

An Actuarial Analysis Shows That Offering Lung Cancer Screening As An Insurance Benefit Would Save Lives At Relatively Low Cost

Bruce S. Pyenson (bruce.pyenson@milliman.com) is a principal and consulting actuary in the consulting firm Milliman, in New York City.

Marcia S. Sander is a principal and consulting actuary in the New York office of Milliman.

Yiding Jiang is a consulting actuary in the New York

ABSTRACT Lung cancer screening is not established as a public health practice, yet the results of a recent large randomized controlled trial showed that screening with low-dose spiral computed tomography reduces lung cancer mortality. Using actuarial models, this study estimated the costs and benefits of annual lung cancer screening offered as a commercial insurance benefit in the high-risk US population ages 50–64. Assuming current commercial reimbursement rates for treatment, we found that screening would cost about $1 per insured member per

Age 50-64 years, >30 pack-year smoking history

Health Affairs, April 2012

Cost of Treatment

Treatment Year	Stage A	Stage B	Stage C
Year 1	$82,087	$132,464	$142,750
Year 2	$20,159	$42,945	$85,956
Year 5+	$11,364	$24,209	$48,456

Health Affairs, April, 2012

Per Member per Month Cost for Screening Coverage

Type of Cancer	Cost
Cervical	$1.10
Colorectal	$0.95
Breast	$2.50
Lung	$0.76

Health Affairs, April, 2012

Cost per Life-year Saved

Type of Cancer	Screening Technique	Cost per life-year saved (2012 dollars)
Cervical	Pap smear	50,162
Colorectal	Colonoscopy	18,705
Breast	Mammography	31,309
Lung	Low-dose chest CT	11,708 – 26,016

Health Affairs, April, 2012

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cost-Effectiveness of CT Screening in the National Lung Screening Trial

William C. Black, M.D., Ilana F. Gareen, Ph.D., Samir S. Soneji, Ph.D., JoRean D. Sicks, M.S., Emmett B. Keeler, Ph.D., Denise R. Aberle, M.D., Arash Naeim, M.D., Timothy R. Church, Ph.D., Gerard A. Silvestri, M.D., Jeremy Gorelick, Ph.D., and Constantine Gatsonis, Ph.D., for the National Lung Screening Trial Research Team*

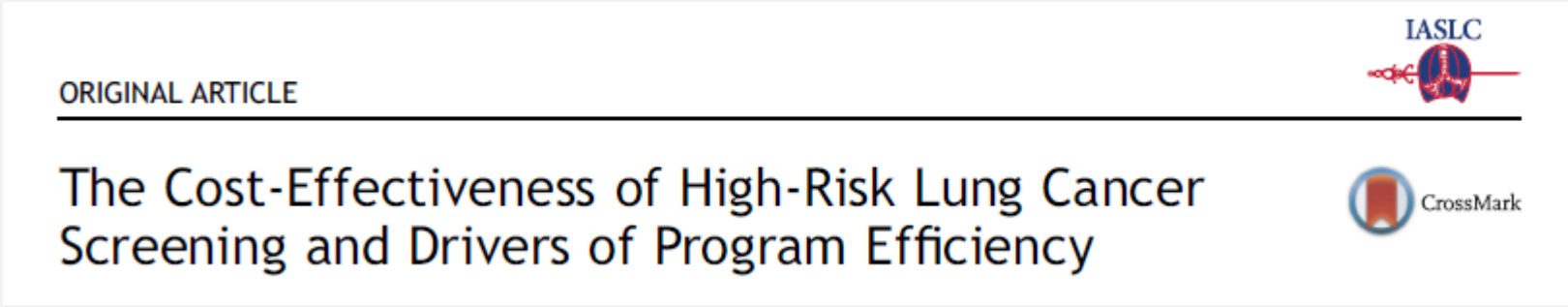
NLST: Cost Analysis

Characteristic		Cost per QALY* (US $)
Sex	Male	147,000
	Female	46,000
Age at Entry (years)	55-59	152,000
	60-64	48,000
	65-69	54,000
	70-74	117,000
Smoking Status	Former	615,000
	Current	43,000

*QALY: Quality adjusted life year

NEJM, 2014

Cost-Effectiveness



Cressman, et al. *J Thor Oncology*, May, 2019

- Stratified NLST patients into high/low risk based on $PLCO_{m2209}$ score (> 2% risk/6 years).
    - Age, education, smoking history
    - Coexisting COPD, Family history of lung cancer
    - BMI

- Simulated outcomes for
    - High risk, screened
    - High risk, unscreened
    - Low risk, unscreened

In 2004 the USPSTF said:

"…the evidence is insufficient to recommend for or against screening asymptomatic persons…."

www.uspreventiveservicestaskforce.org

Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement DRAFT

DRAFT

DRAFT

DRAFT

DRAFT

Summary of Recommendation and Evidence

DRAFT

The U.S. Preventive Services Task Force (USPSTF) recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in persons at high risk for lung cancer based on age and smoking history.

DRAFT

This is a Grade B recommendation.

July 30, 2013

Annals of Internal Medicine | CLINICAL GUIDELINE

Screening for Lung Cancer: U.S. Preventive Services Task Force Recommendation Statement

Virginia A. Moyer, MD, MPH, on behalf of the U.S. Preventive Services Task Force*

Description: Update of the 2004 U.S. Preventive Services Task Force (USPSTF) recommendation on screening for lung cancer.

Methods: The USPSTF reviewed the evidence on the efficacy of low-dose computed tomography, chest radiography, and sputum cytologic evaluation for lung cancer screening in asymptomatic persons who are at average or high risk for lung cancer (current or former smokers) and the benefits and harms of these screening tests and of surgical resection of early-stage non–small cell lung cancer. The USPSTF also commissioned modeling studies to provide information about the optimum age at which to begin and end screening, the optimum screening interval, and the relative benefits and harms of different screening strategies.

Population: This recommendation applies to asymptomatic adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.

Recommendation: The USPSTF recommends annual screening for lung cancer with low-dose computed tomography in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. (B recommendation)

Ann Intern Med. www.annals.org

For author affiliation, see end of text.

* For a list of the members of the USPSTF, see the Appendix (available at www.annals.org).

This article was published online first at www.annals.org on 31 December 2013.

Dec. 31, 2013

AAFP has reservations…..

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Evidence Lacking to Support or Oppose Low-dose CT Screening for Lung Cancer, Says AAFP

Inability to Make Harms/Benefits Comparison Precludes Definitive Recommendation

January 13, 2014 04:50 pm Cindy Borgmeyer – Citing a paucity of high-quality evidence on which to base a comparison of relative harms and benefits, the AAFP today released an "I" recommendation regarding the routine use of low-dose CT scans in screening high-risk, older smokers for lung cancer.

The Academy's action puts it at odds with a recommendation issued last month (www.uspreventiveservicestaskforce.org) by the U.S. Preventive Services Task Force (USPSTF).

Jan. 13, 2014

AAFP has reservations…..

"…reviewed the USPSTF's recommendation … and had significant concern with basing such a far reaching and costly recommendation on a single study."

….about excessive intervention

The risks attendant in such a long-range screening protocol cannot be ignored….

…"there's going to be a considerable amount of testing that's going to be required, including some biopsies and some bronchoscopies and some other procedures that have risk to them…."

….about excessive intervention

"A shared-decision-making discussion between the clinician and patient should occur regarding the benefits and potential harms of screening for lung cancer."

The bottom line….

…most important when talking with these high-risk patients: Don't forget to address the elephant in the room.

"If they're currently smoking, a better thing to do by far is to stop smoking. This is not a substitute for stopping smoking."

Barriers to Screening

Estimated that <5% of eligible patients are screened

Barriers:

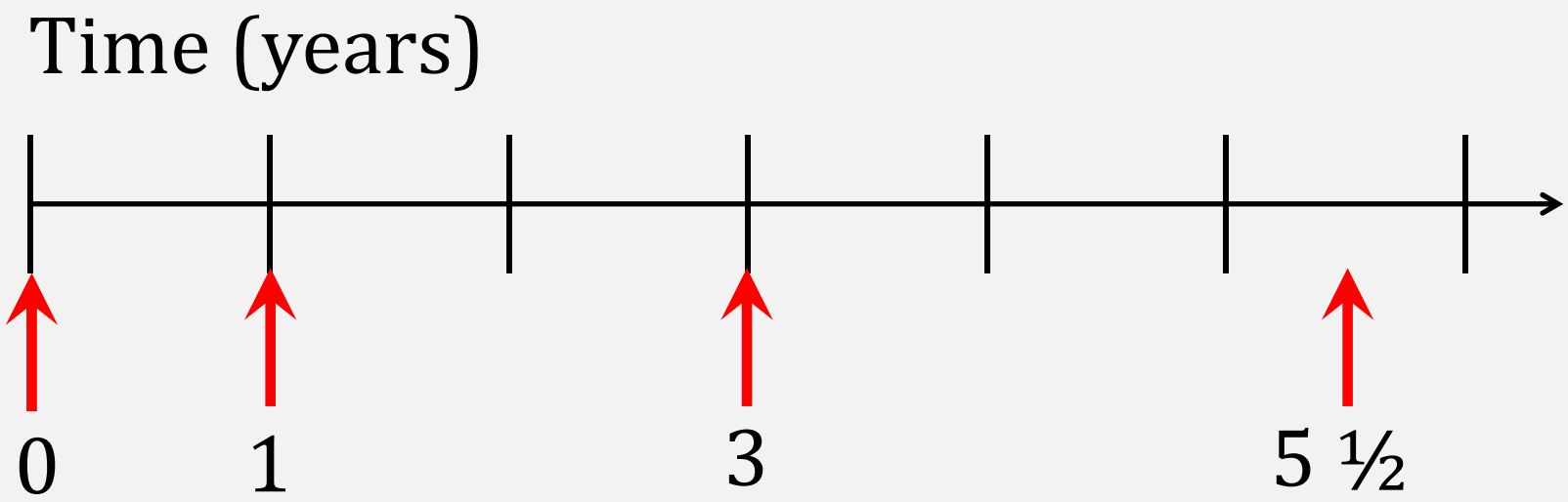
- Uncertainty about outcomes
- Concern about overdiagnosis
- Education
- Lack of available screening centers
- Logistics (e.g. SDM visit requirement)

NELSON Lung Screening Trial

- Randomized European trial
- 10 year results presented at IASLC 2018 meeting
- N = 15, 792

Modality	N
Chest CT	7,900
No screen	7,892

NELSON Lung Screening Trial



- LDCT
- Indeterminate: 2 month f/u for volume doubling time

NELSON Lung Screening Trial

Results:

- Follow-up at 10 years for 93.7% of participants
- 86% compliance rate
- False positive rate = 59.4%

Overall lung cancer detection rate = 3.2%

Baseline	1 year	3 years	5 ½ years
0.9%	.08%	1.1%	0.8%

NELSON Lung Screening Trial

Results – Lung Cancer Deaths:

214 study arm vs. 157 control arm

LC mortality rate-ratio:

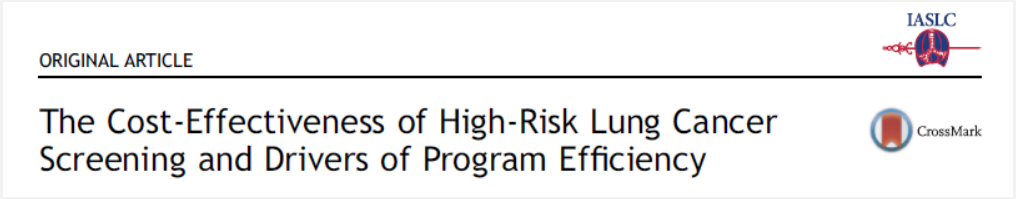
- Men = 0.74 (p = 0.0003)
- Women = 0.61 (p = 0.0054)

NELSON Lung Screening Trial

Results – Other findings:

Stage shift no different after 1 year,
but less favorable after 2 ½ years.

Cost-Effectiveness


ORIGINAL ARTICLE

IASLC

The Cost-Effectiveness of High-Risk Lung Cancer Screening and Drivers of Program Efficiency

CrossMark

Results:

- Reduced number to be screened by 81%
- High risk screening cost $20,724 (Canadian) / QALY
- Higher cost of non-curative care (drug costs, immunotherapy) improve cost-effectiveness

Where do we go from here?

Academic	Community
• Further define high risk pool • Standardize management protocols to reduce variability and cost • Biomarkers	• Build robust programs • Engage primary physicians • Outreach, especially to vulnerable and underserved populations • Enhance smoking cessation • Track results

Why It’s More Than Just a Scan:

- Engagement
- Process
- Management
- Results

Lung-RADS™ Version 1.0 Assessment Categories Release date: April 28, 2014

Category Descriptor	Category Descriptor	Primary Category	Management
Incomplete	-	0	Additional lung cancer screening CT images and/or comparison to prior chest CT examinations is needed
Negative	No nodules and definitely benign nodules	1	Continue annual screening with LDCT in 12 months
Benign Appearance or Behavior	Nodules with a very low likelihood of becoming a clinically active cancer due to size or lack of growth	2	
Probably benign	Probably benign finding(s) - short term follow up suggested; includes nodules with a low likelihood of becoming a clinically active cancer	3	6 month LDCT
Suspicious	Findings for which additional diagnostic testing and/or tissue sampling is recommended	4A	3 month LDCT; PET/CT may be used when there is a ≥ 8 mm solid component
		4B	chest CT with or without contrast, PET/CT and/or tissue sampling depending on the *probability of malignancy and comorbidities. PET/CT may be used when there is a ≥ 8 mm solid component.
Significant - other		S	
Prior Lung Cancer		C	

"…the opportunity to realize the greatest single reduction of cancer mortality in the history of the war on cancer."

James Mulshine, MD
Associate Provost and Vice President for Research
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