

Lung Cancer Screening Using Low-Dose CT

Where are we?

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Disclosures

- None



Lung Cancer

- *It touches all of us!!*
- Canada 2012:
 - 25,600 new diagnoses
 - 20,100 deaths
- USA 2012:
 - 226,160 new diagnoses
 - 160,340 deaths



Lung Cancer

- Leading cause of cancer death for both men and women
- 30% of all cancer deaths
- Annual mortality exceeds that of breast, prostate, colon, kidney, liver, and melanoma combined
- >50% of new cases diagnosed at advanced stage



Lung Cancer



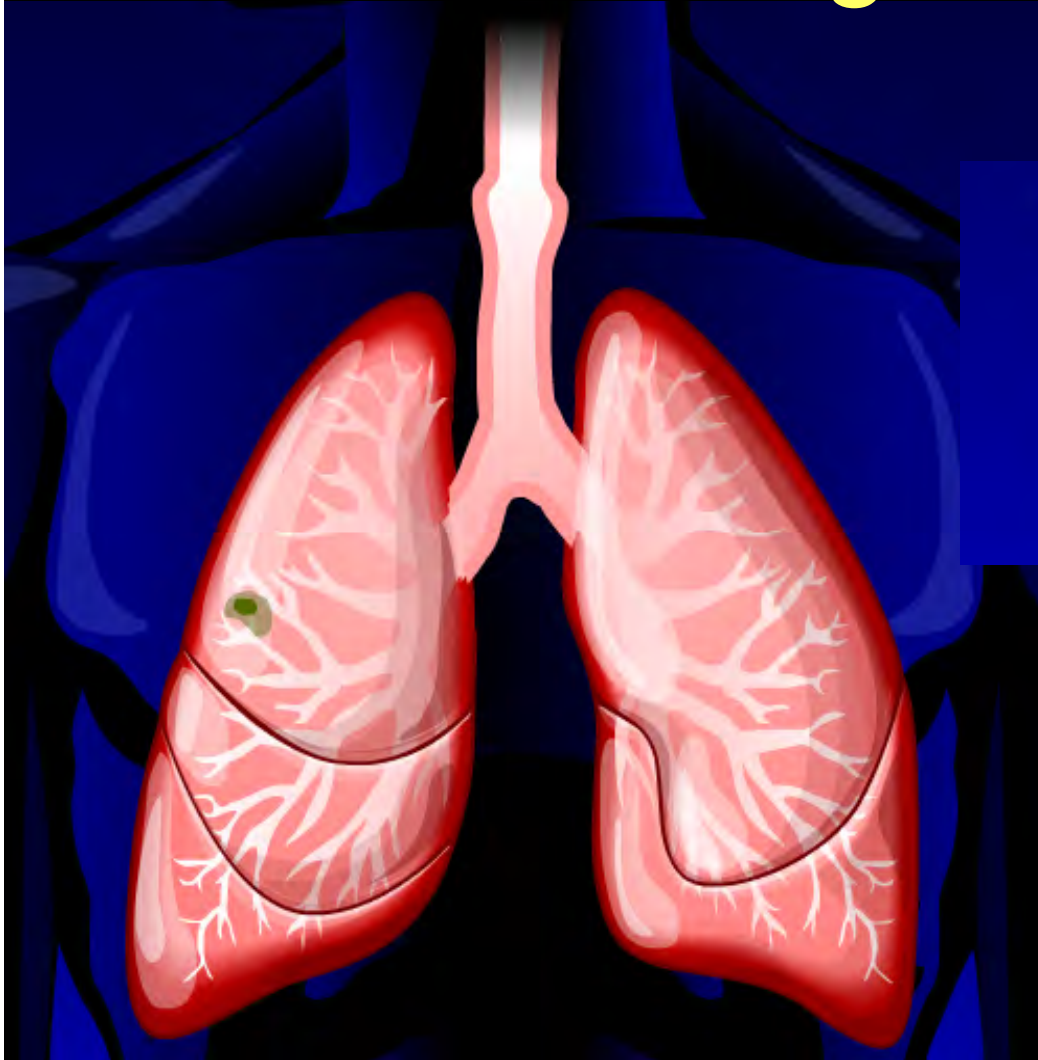
Stage IV



15% 5YS survival



Lung Cancer



Stage I

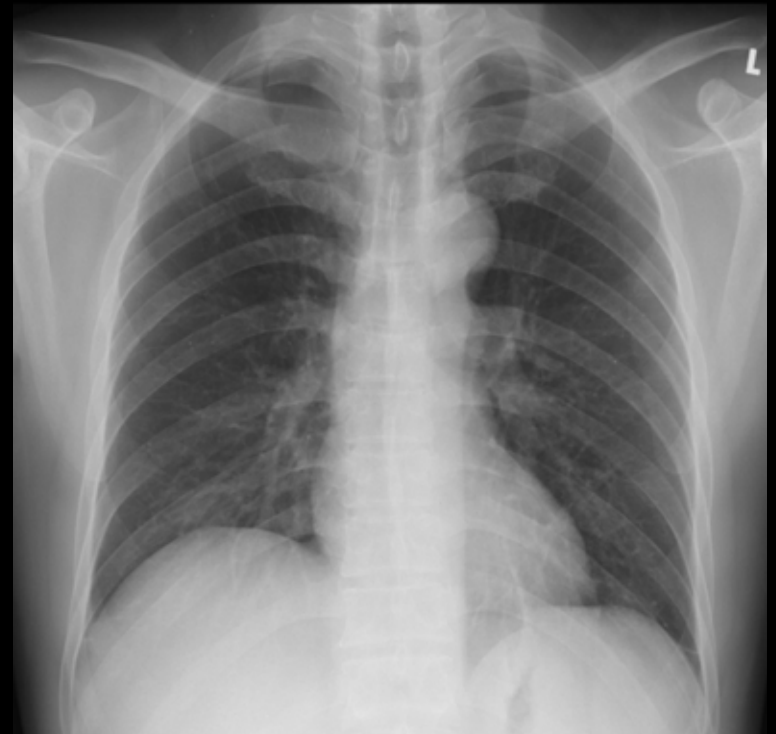


80% 5YS survival



Screening for lung cancer

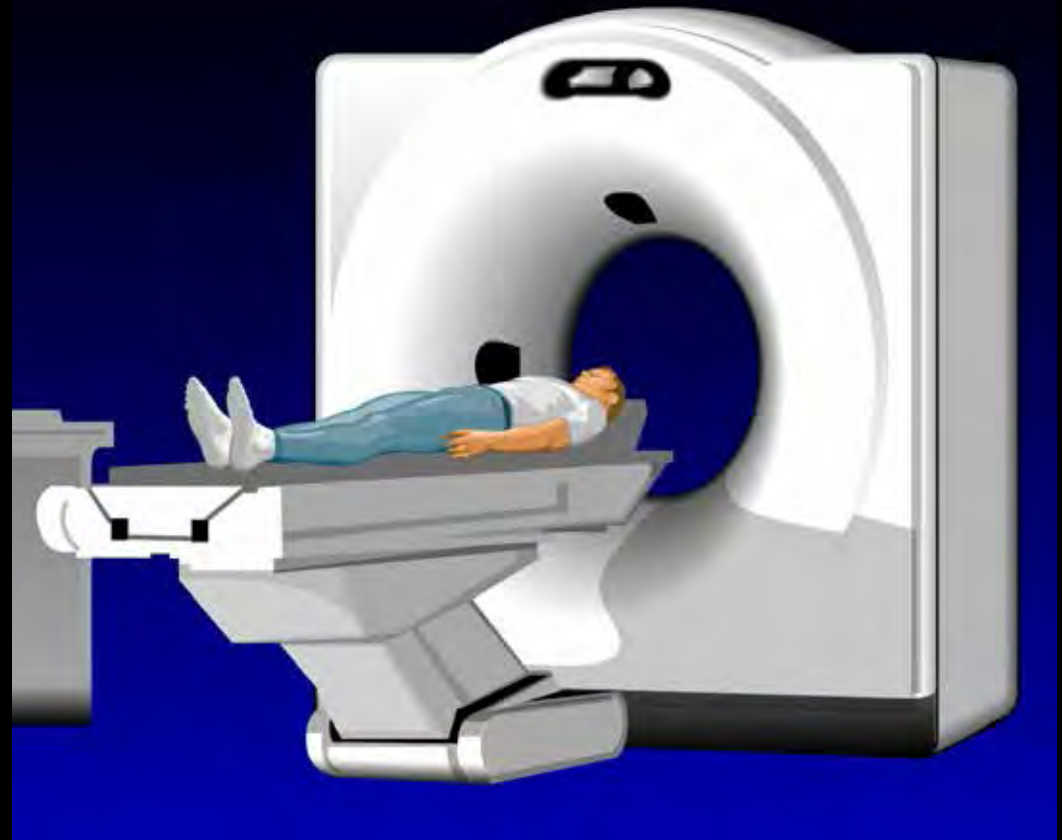
- simple, safe, precise and validated test
- '70's, '80's CXR screening
- No impact on mortality



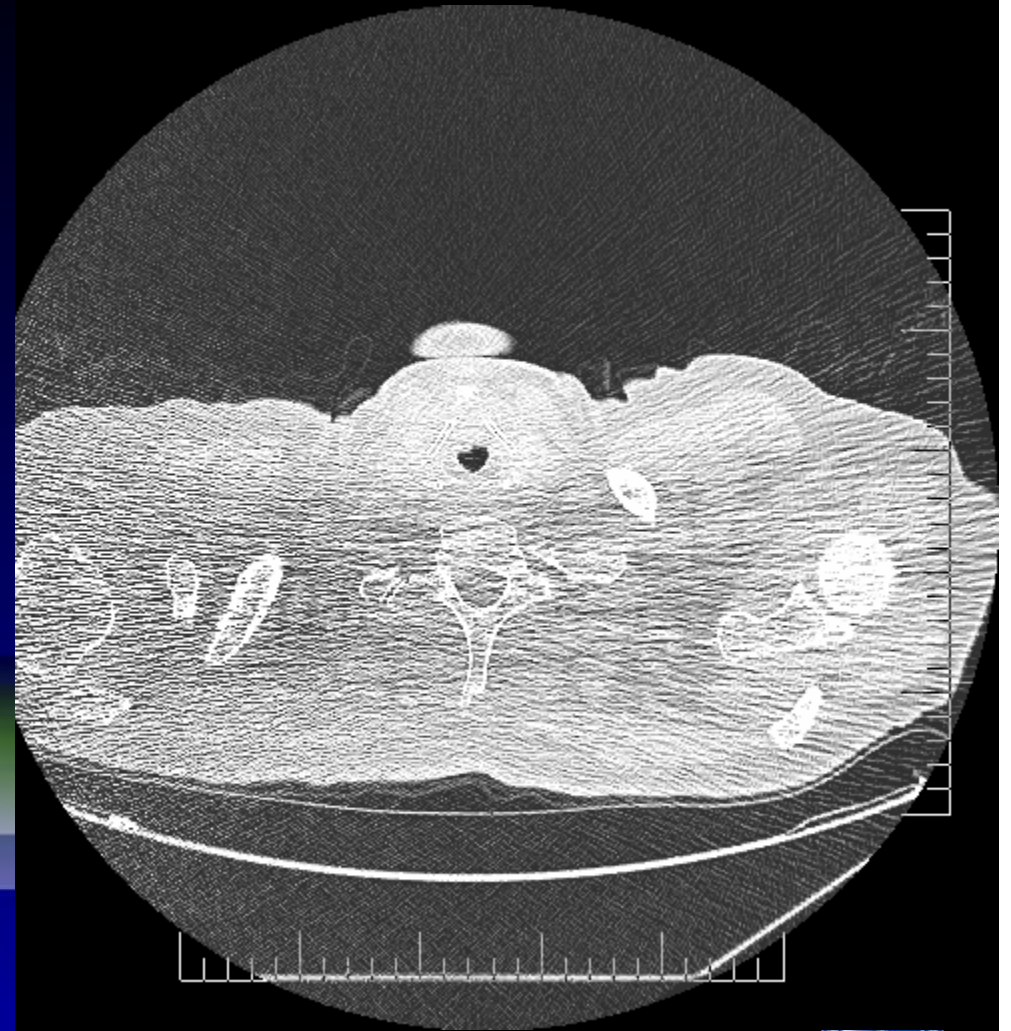
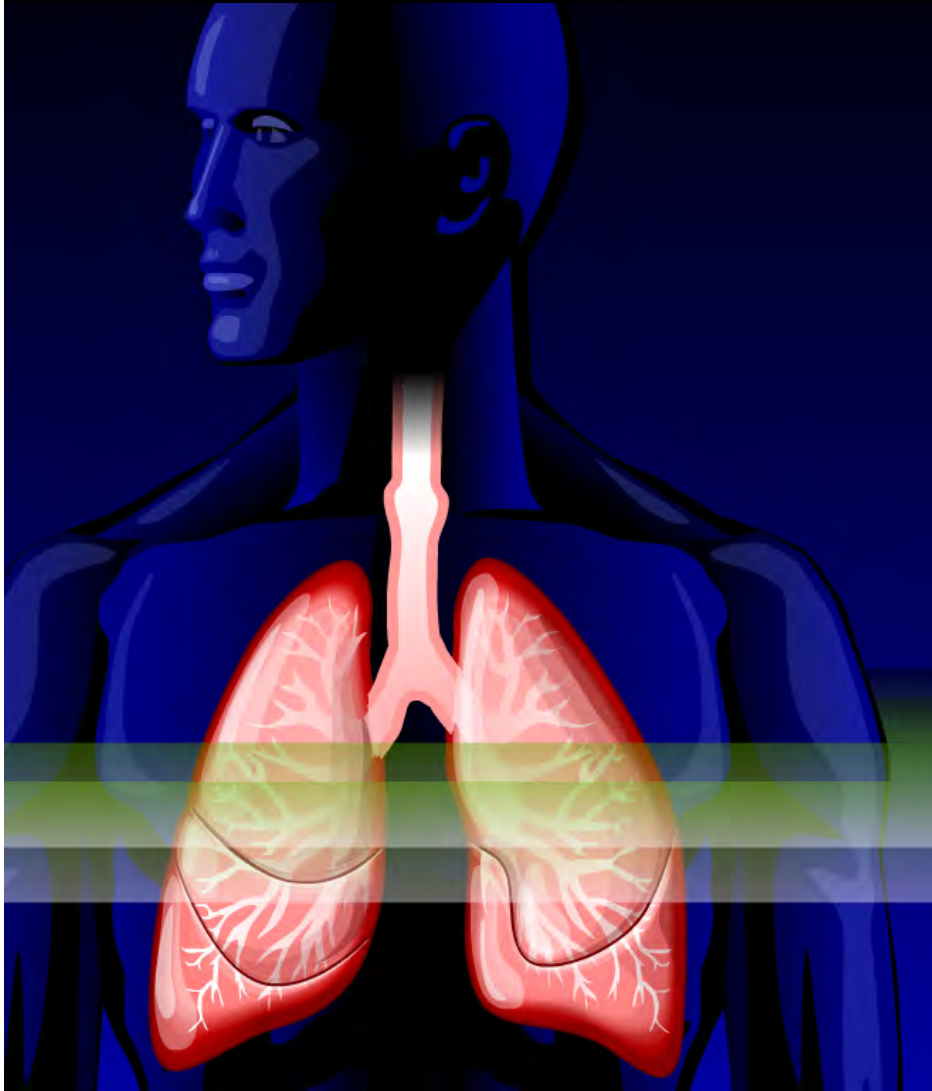
Screening for lung cancer

Low Dose CT

- 120 kV
- 40-60 mA
- 1 mm – 1.25 mm
- widely available



Low-dose CT

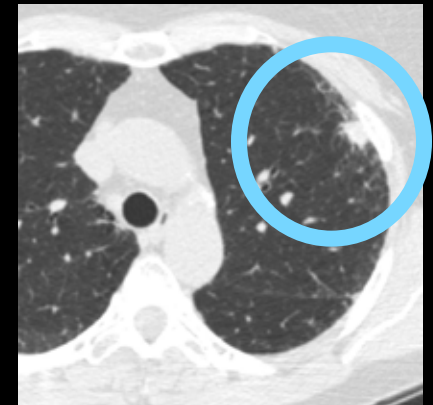
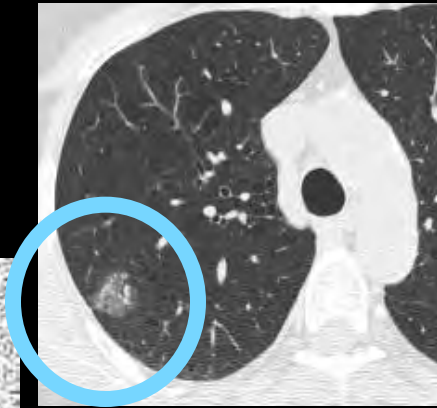
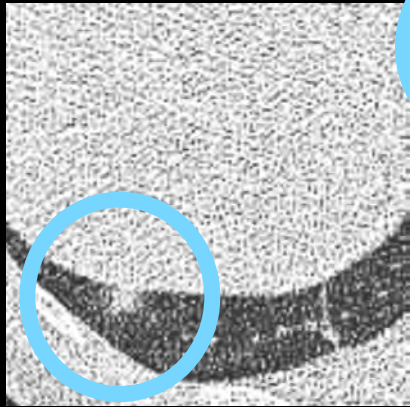


Lung Cancer Screening - Detection

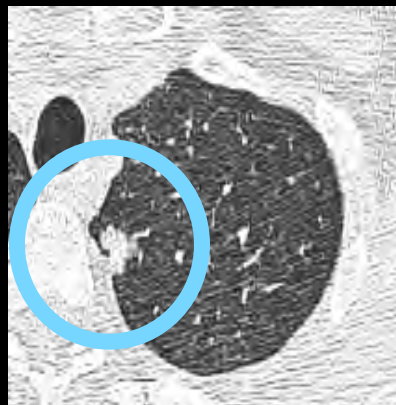
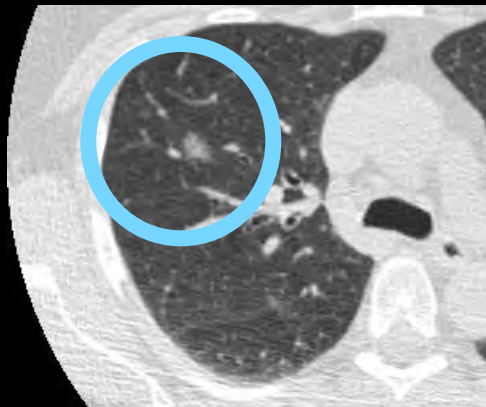
- Nodule detection - not an issue
- Prevalence of lung cancer ~ 1.5% - 2.5%
- Tumour stage ~ 80% stage 1

[Bellomi et al. Cancer Imaging 2009, Pastorino Brit J Cancer 2010]





screen-detected lung cancers
I-ELCAP, PMH, Toronto
peripheral, small, solid, semi-solid, GGO
(~2.3% detection rate)

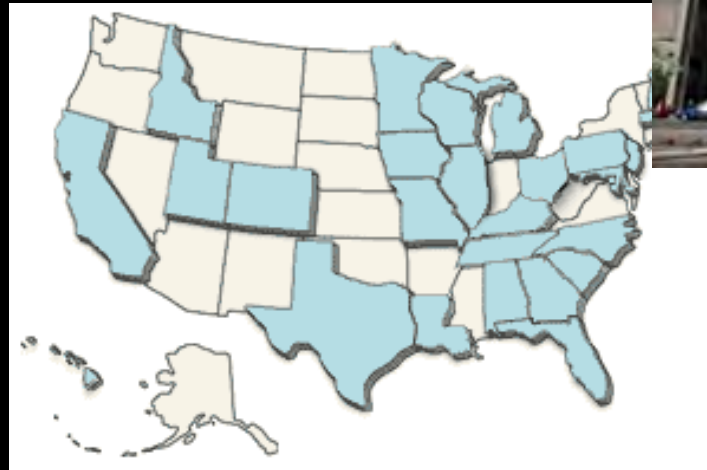


Single-arm trials: Survival

- International Early Lung Cancer Action Program (I-ELCAP)

I-ELCAP

- 27,456 (4782 PMH)
- non-randomized
- 10YS
- up to 92%*



*Henschke et al,
New Eng J Med 2006*

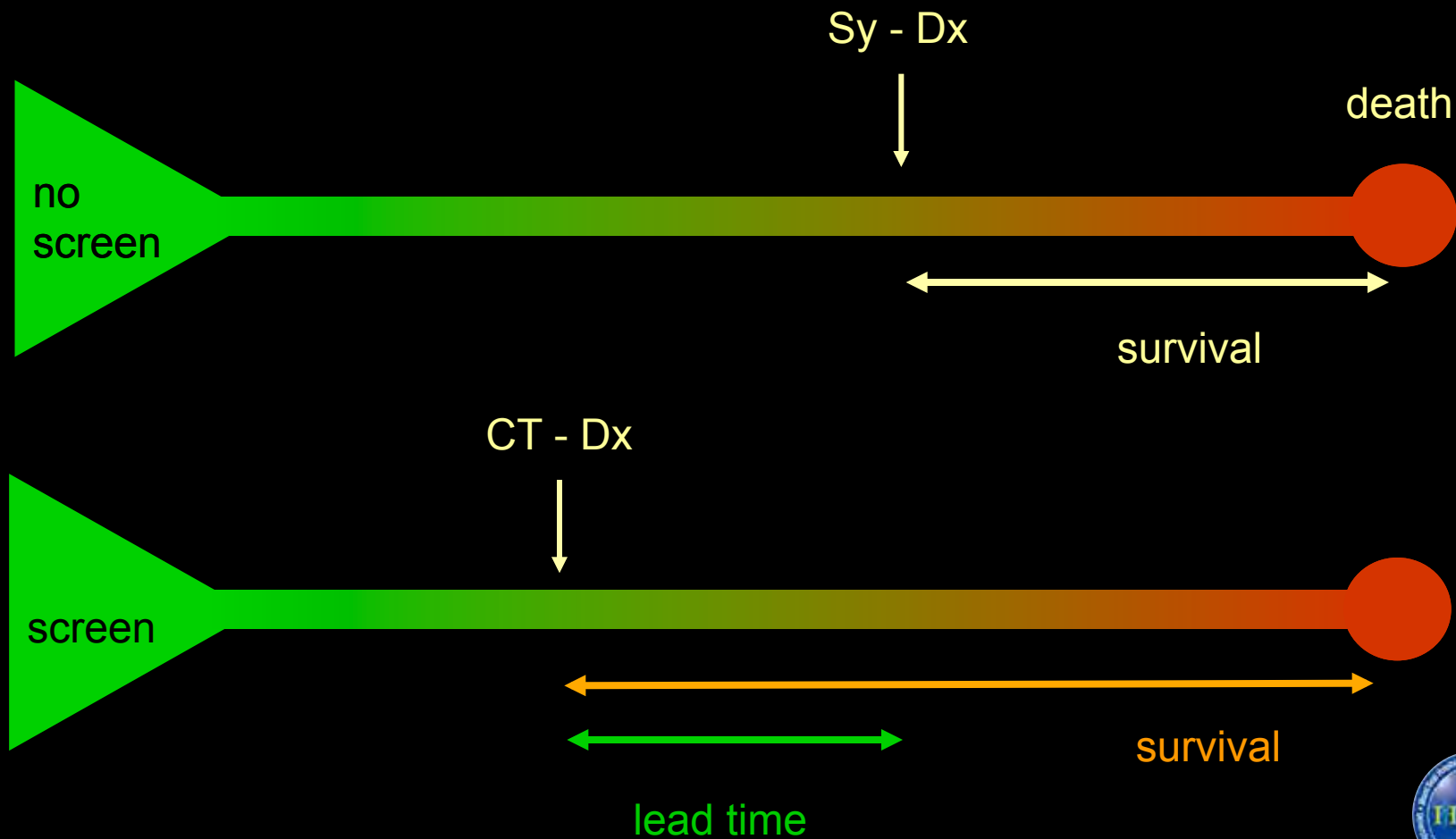


Survival vs. Mortality

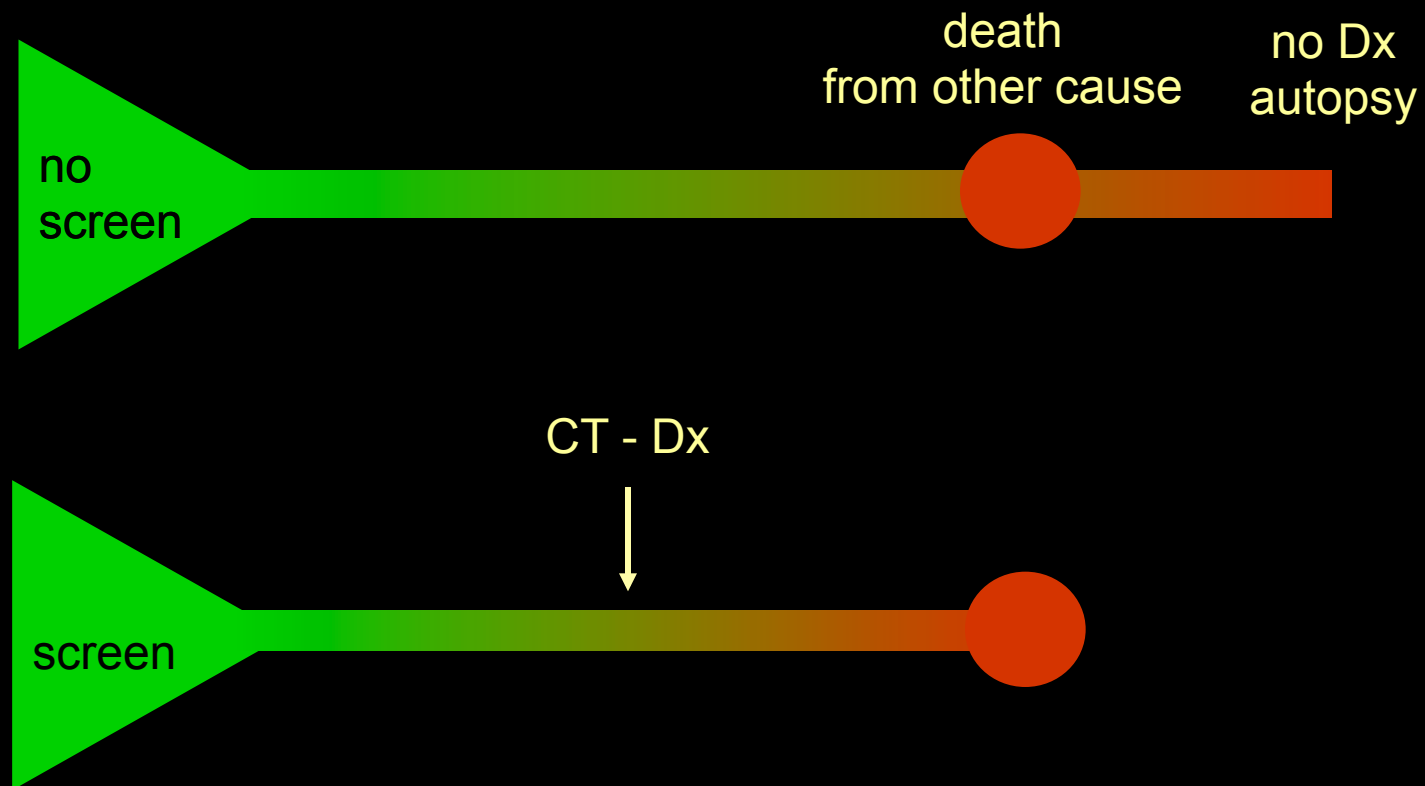
- longer survival \neq reduced mortality
- survival biased by
 - lead time bias
 - overdiagnosis
 - length time bias
 -



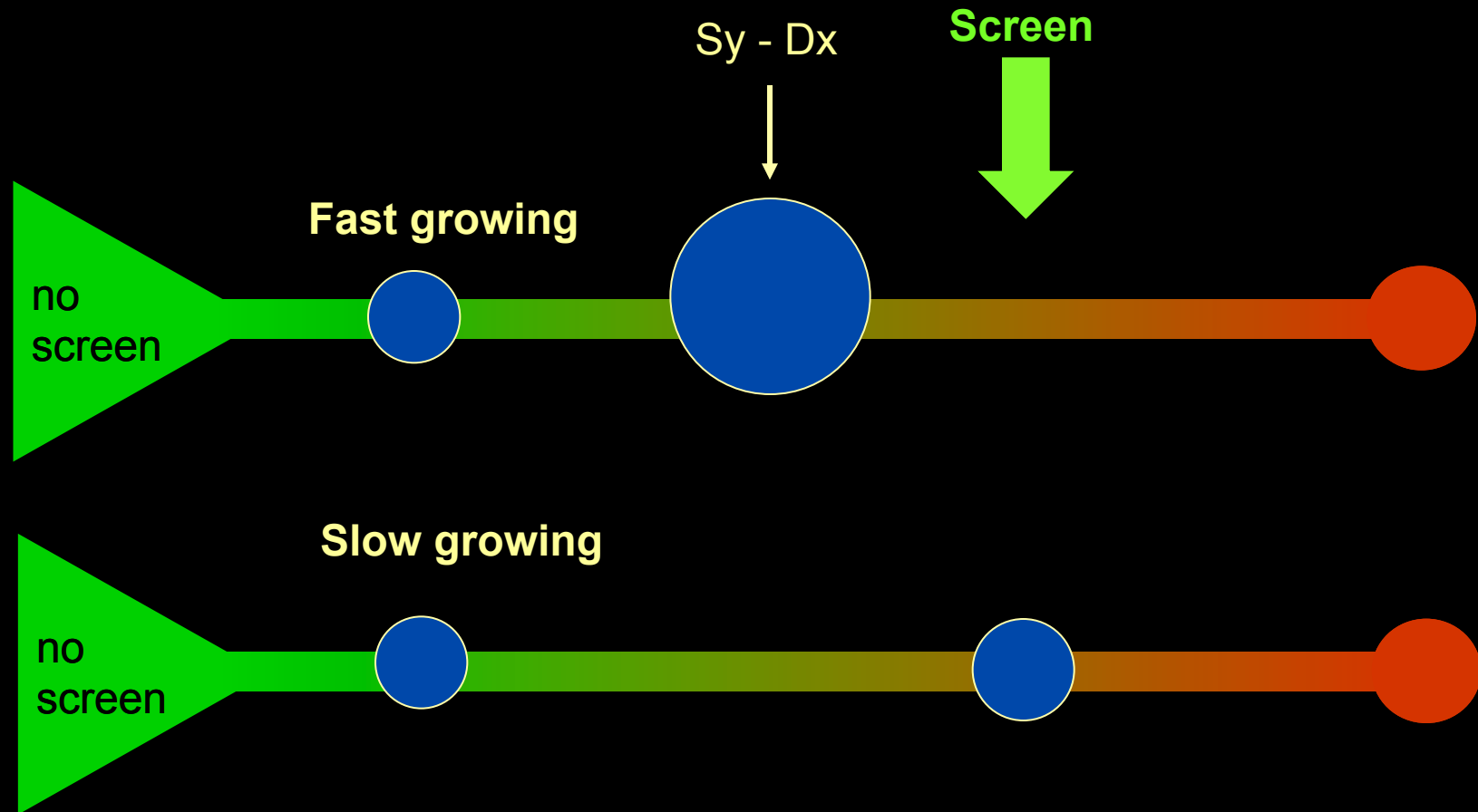
lead time bias



overdiagnosis bias



length time bias



Length time bias = screening test tends to capture slower growing tumours which are more likely to have a favourable prognosis



randomized trials: mortality end point

Study	Country	Design	Year started	Subjects
LSS	USA	CT vs CXR	2000	3318
DANTE	Italy	CT vs obs	2001	2472
NLST	USA	CT vs CXR	2002	53000
NELSON	NL-B	CT vs obs	2003	15822
DLCST	DK	CT vs obs	2004	4104
ITALUNG	Italy	CT vs obs	2004	3206
MILD	Italy	CT vs obs	2005	4479
LUSI	Germany	CT vs obs	2007	4000
				> 90,000



“Lung Cancer Screening Using LDCT Reduces Deaths”

Nov 4th, 2010



thestar.com

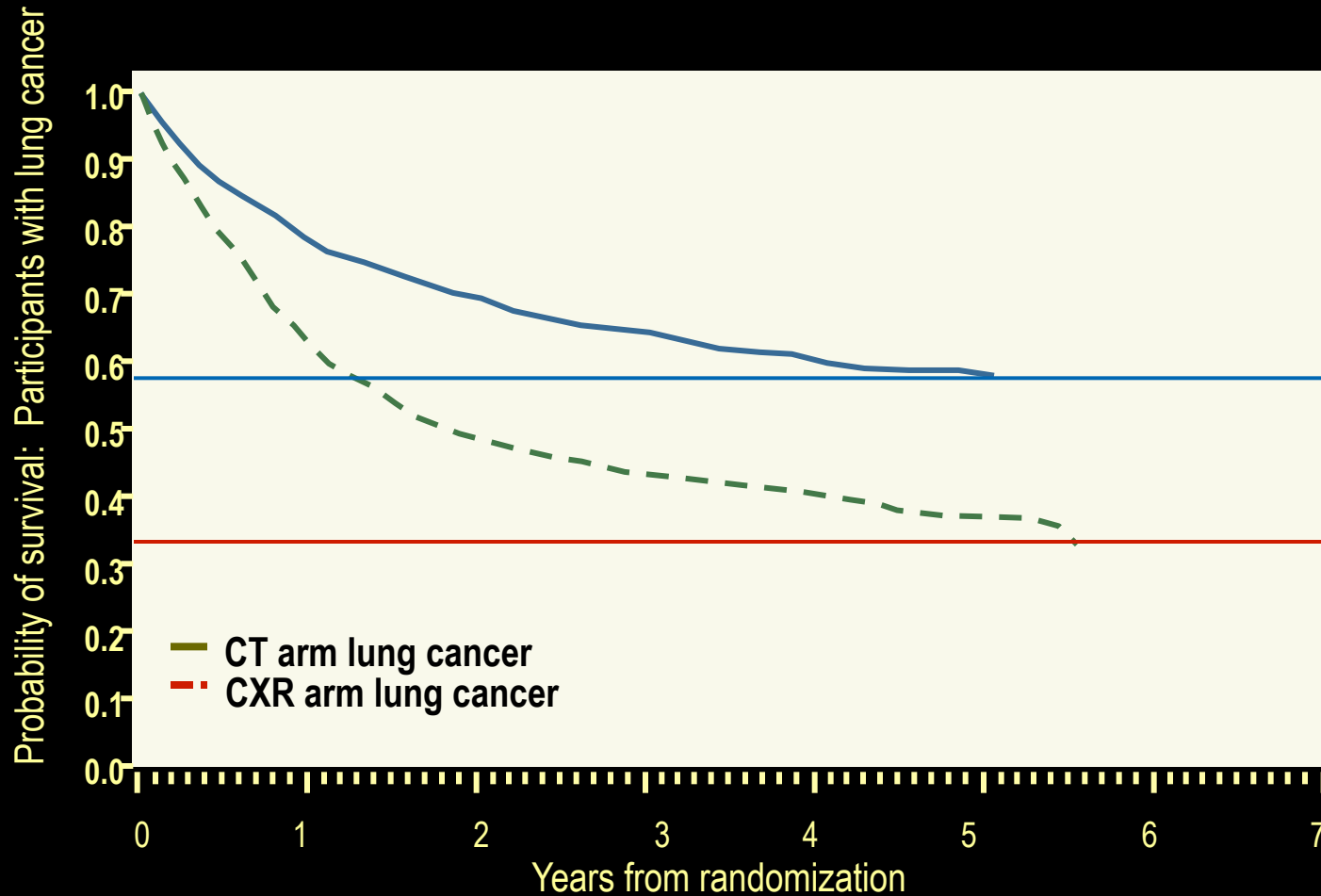


CNN Health



NLST initial trial results, showed 20% mortality reduction among trial participants screened with low-dose CT compared to CXR screened subjects

NLST – lung cancer survival



courtesy of NLST



National Lung Screening Trial

- The facts: 20% mortality benefit
 - The hope: change recommendations for lung cancer screening
- impact on health care policy



Where are we?



Screening - Issues to be discussed

- nodules and false positives
- radiation exposure – how long screen?
- cost-effectiveness
- who should be screened
- who's in charge
- present and future



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Lung Cancer Screening – nodules

- 5.1% - 51.4% of patients have nodules
- 80-99% are benign
- how deal with all of the nodules?

Bepler et al, Cancer Control, 2003



Screening CT results

- no nodules
- small nodules
- large nodules



Screening CT results

- no nodules

- small nodules

- large nodules



“negative”
annual repeat



Screening CT results

- no nodules



“negative”

annual repeat

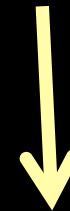
- small nodules



“negative”

annual repeat

- large nodules



“positive”

1-3 months follow up,
biopsy, etc.



positive screening CT

	definition	%
<i>ELCAP Henschke Lancet 1999</i>	1-6mm	23.3
<i>Italian SS Pastorino Lancet 2003</i>	6mm	29
<i>LSS (NCI) Gohagan Chest 2004</i>	4mm	20.5
<i>Mayo Swenson Radiology 2005</i>	any	51
<i>Toronto (n=1000) Roberts Can Ass Rad J 2007</i>	5mm	25.7
<i>Toronto (n=3352) Menezes, Roberts Lung Cancer 2009</i>	5mm	18
<i>NLST 2011</i>	4mm	27.3

(false) positive screening CT

- smaller threshold size for a qualifying nodule = larger number of “positive screening CT” scans

Toronto (n=3352) <i>Menezes, Roberts Lung Cancer 2009</i>	5 mm	18
NLST 2011	4 mm	27.3
proposal from the I-ELCAP	7 / 8 mm	



Lung Cancer Screening

- how to deal with all of the nodules?
 - Define threshold of nodule size
 - Surveillance
 - protocol
 - size + growth



nodule follow up (5mm)

- solid lesions ≤ 5 mm
– “negative”, no follow up
- annual repeat



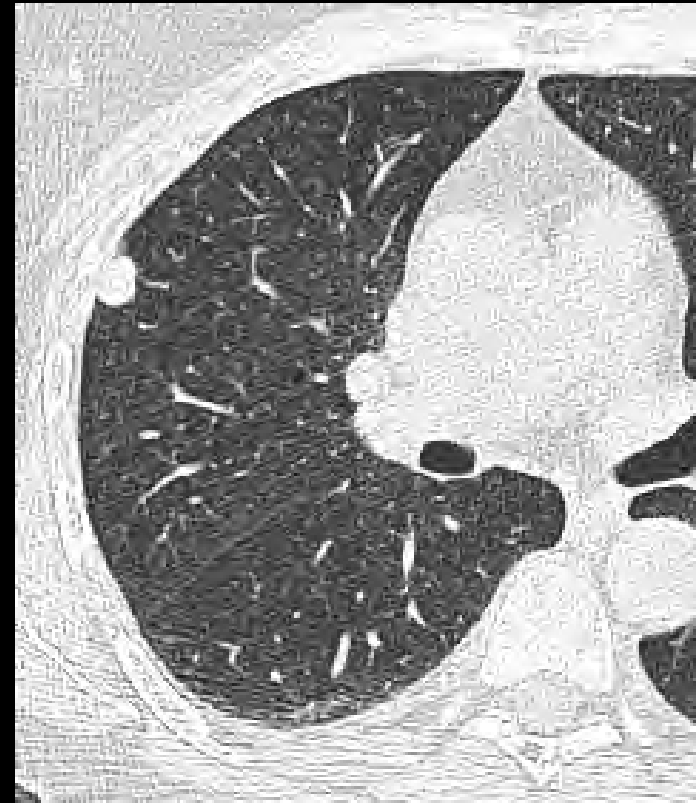
nodule follow up (5mm)

- solid lesions ≤ 5 mm
 - no follow-up
- solid lesions 5 – 10 mm
 - surveillance of growth (rpt LDCT at 3 mth)
 - doubling time 30 – 360 days = malignant





3 months



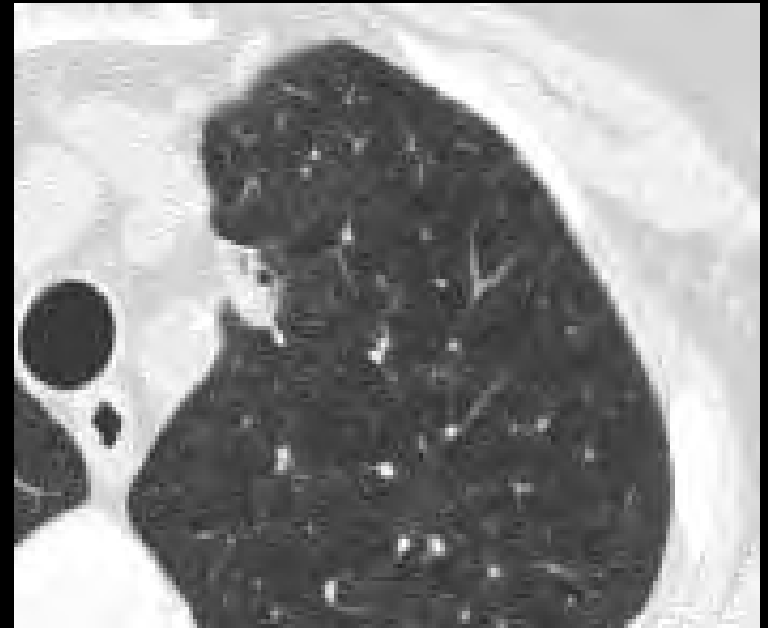
doubling time 72 days

combined small cell-large cell neuroendocrine carcinoma





3 months



mucinous adenocarcinoma



SPN – additional imaging



Sep 13, 2006



Oct 12, 2006

resolution

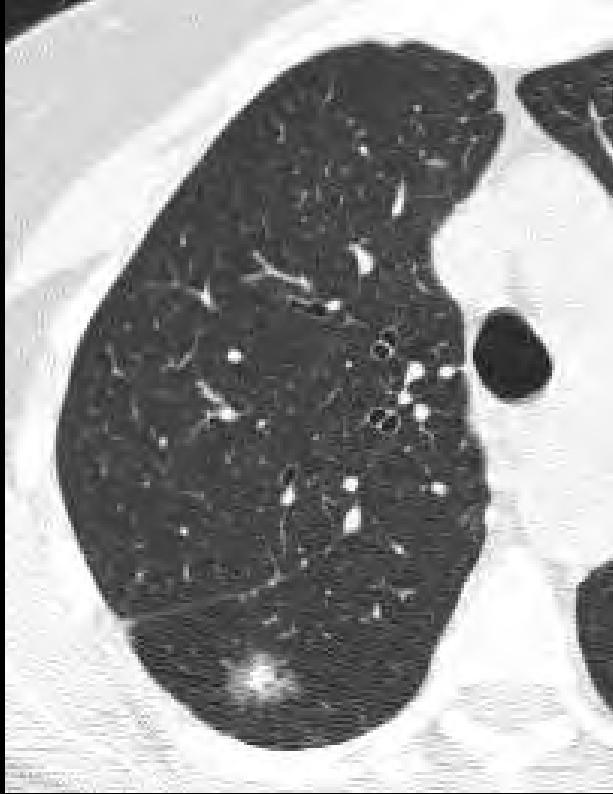


no further action

nodule follow up

- solid lesions ≤ 5 mm
 - no follow up
- solid lesions 5 – 10 mm
 - surveillance of growth
- **part-solid lesions**
 - risk of malignancy relates to size and growth of **solid** component





3 months



same size, higher density

adenocarcinoma

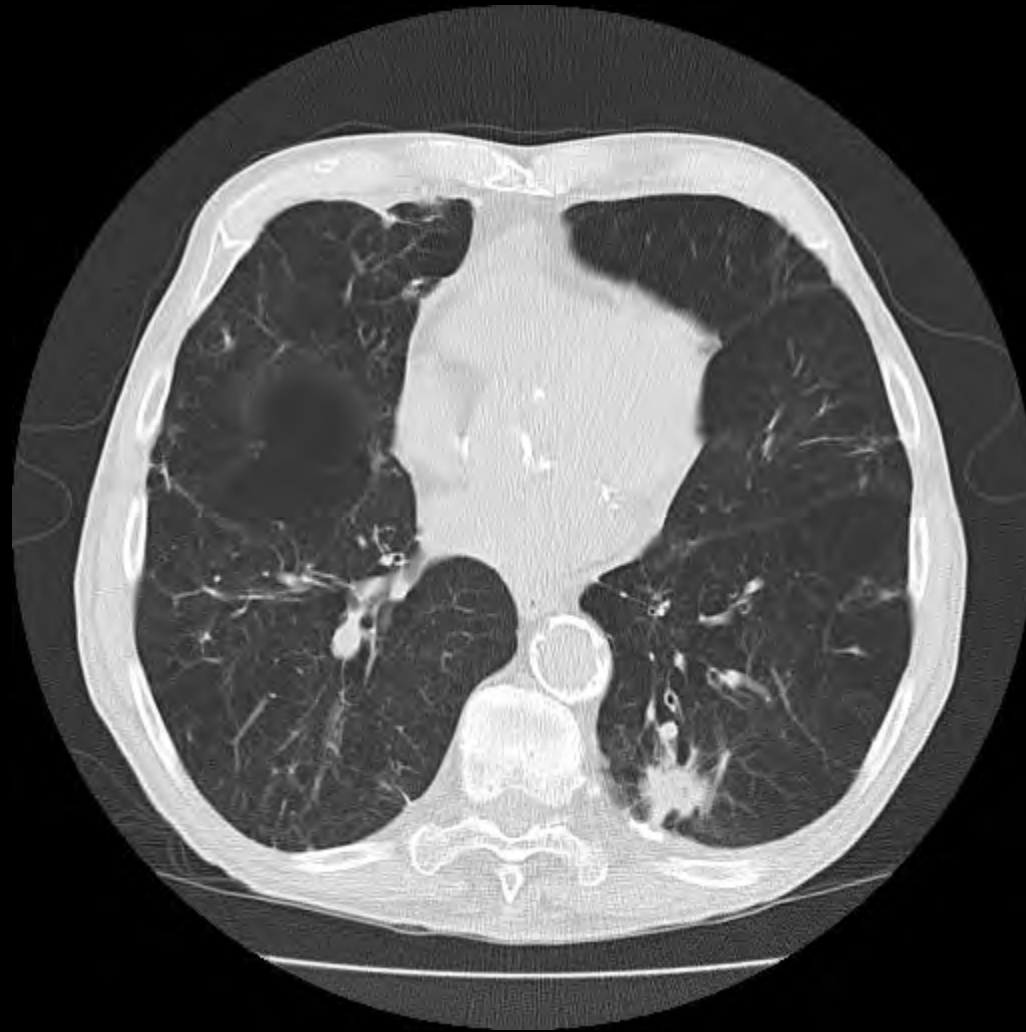


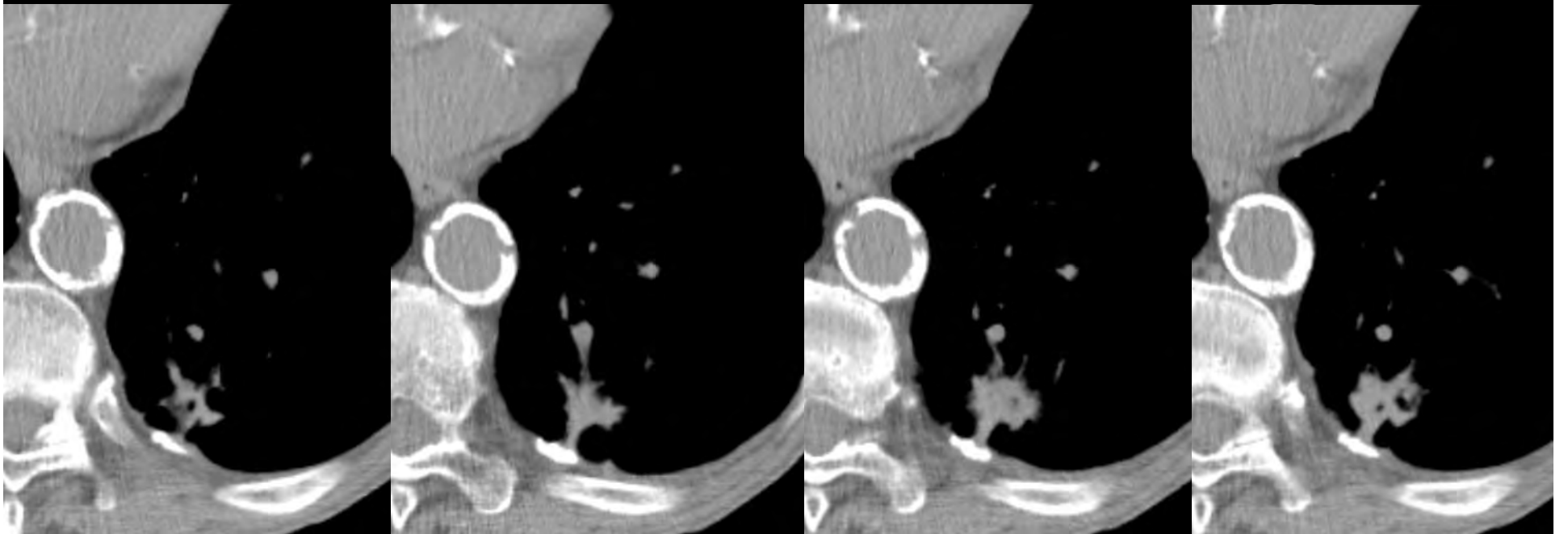
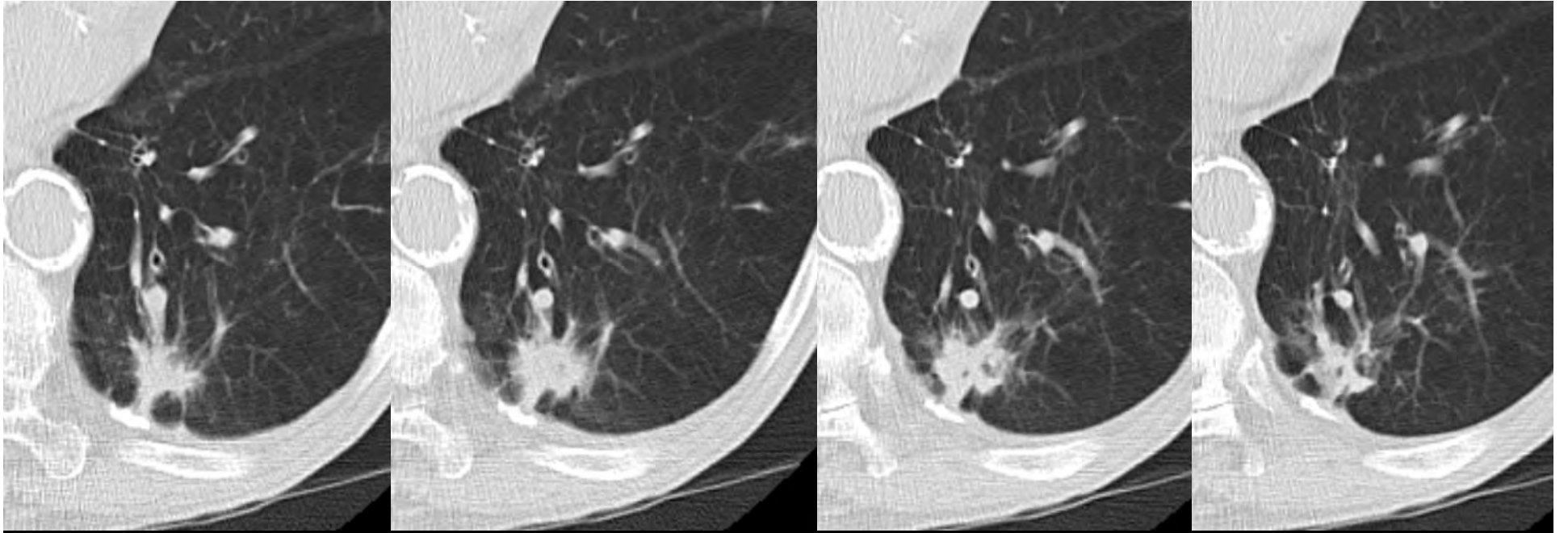
nodule follow up

- solid lesions ≤ 5 mm
 - no follow-up
- solid lesions 5 – 10 mm
 - surveillance of growth
- solid lesions > 10 (15?) mm
 - immediate bx?



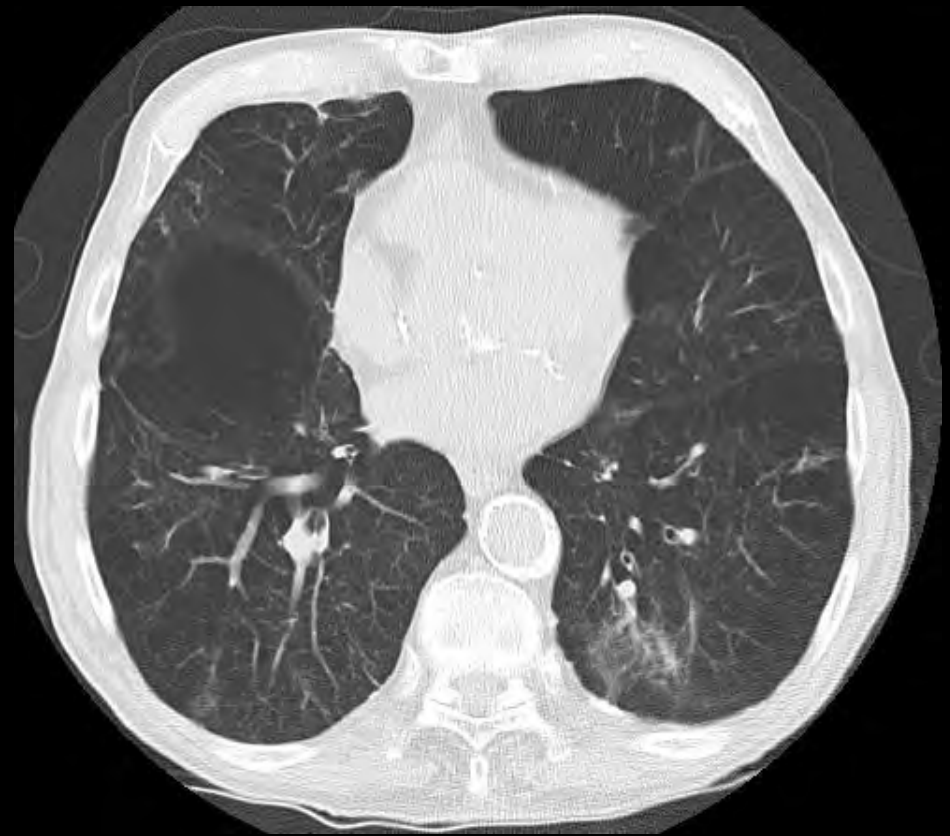
example: screen-detected nodule







baseline



3 months follow up



examples: screen-detected nodules

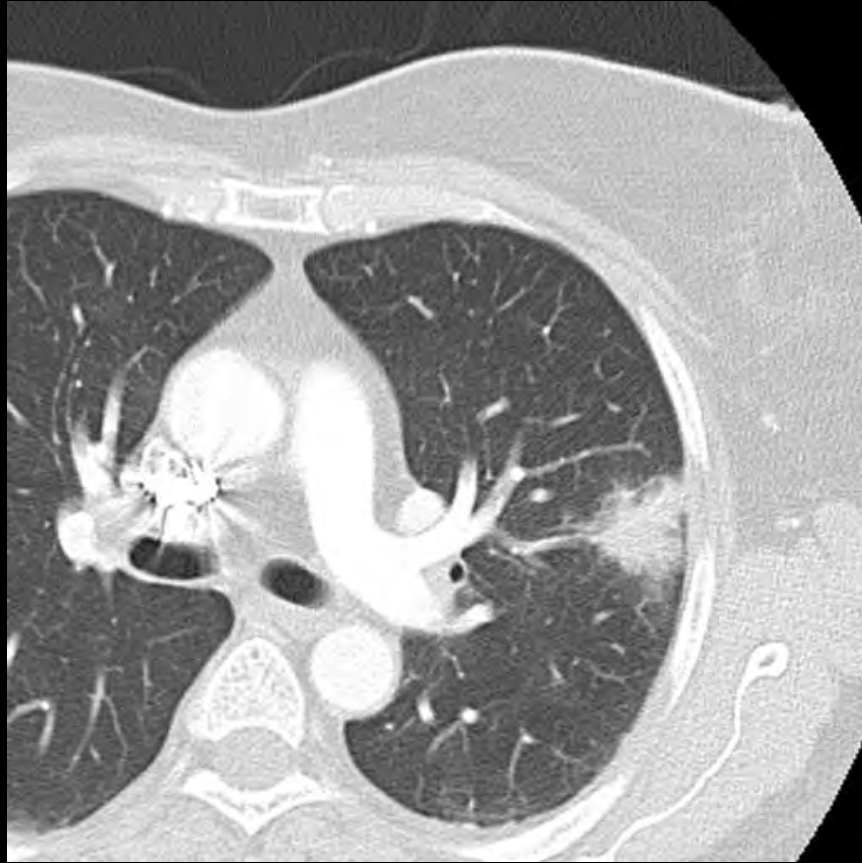


baseline

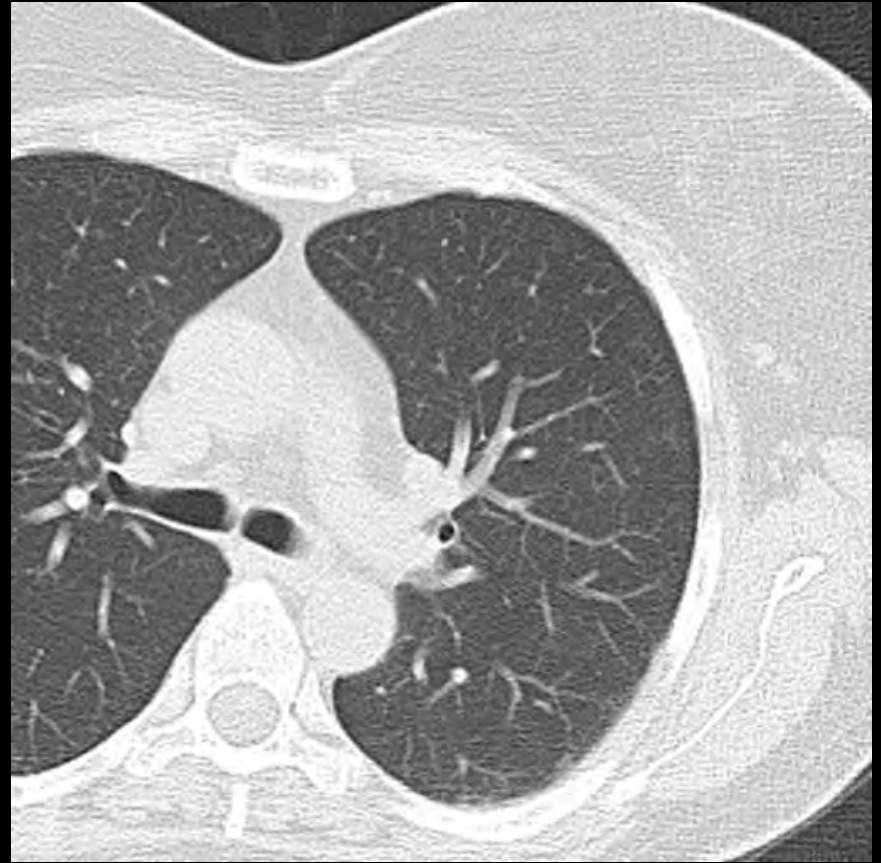


3 months follow up





June 23rd



July 29th



false positives

- 4782 participants
- simple algorithm based on size and growth
 - 130 biopsies (2.7%) recommended
 - 20 biopsies (0.4%) for benign lesions



Screening - Issues to be discussed

- nodules and false positives
- radiation exposure – how long screen?
- cost-effectiveness
- who should be screened
- who's in charge
- present and future



Lung Cancer Screening

Radiation Risk - Low Dose Chest CT - NLST

- 96 CT scanners at NLST sites, 2003-2007
- mean $CTDI_{vol}$ = 3.4 mGy (S.D.=1.7 mGy)
- mean Effective Dose = 2.0 mSv (S.D.=1.0 mSv)
- Range = 0.5 – 7.0 mSv

- F. Larke et al at RSNA 2008 (SSG18-09)



Lung Cancer Screening

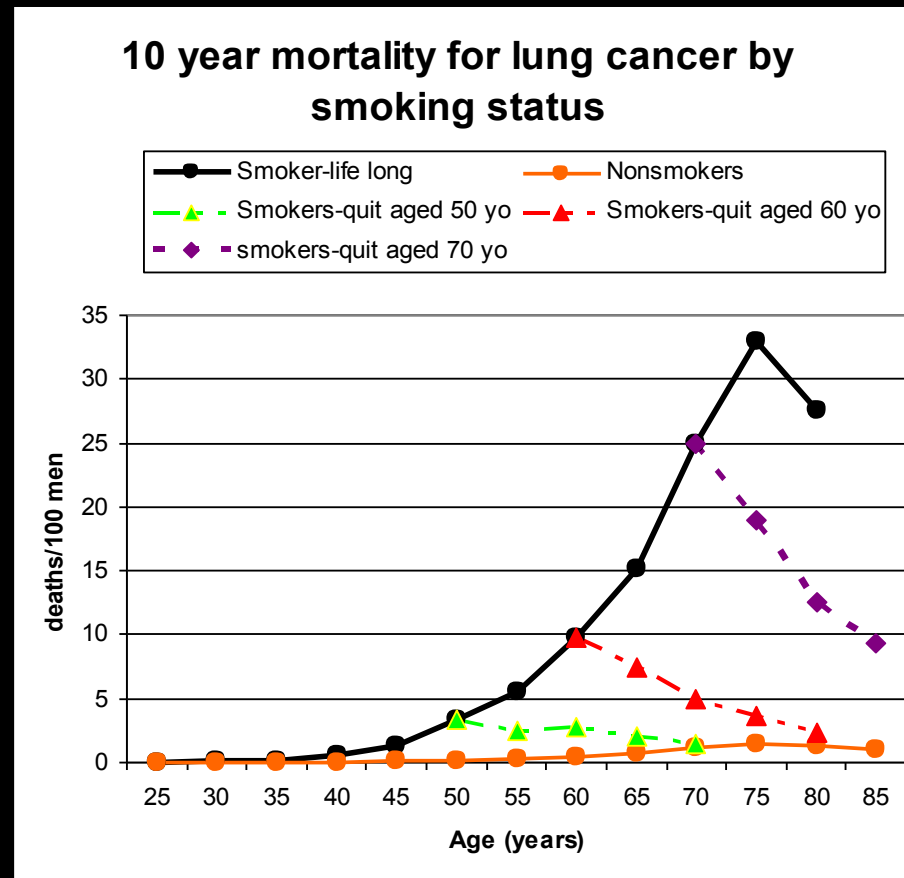
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 - Range = 0.5 – 7.0 mSv
-
- standard chest CT: 8 - 9 mSv
 - screening chest radiograph: 0.08 – 0.12 mSv
 - transatlantic flight: 0.25 mSv
 - mammography: 0.7 mSv



Screening – how long?

- detectable risk factor or disease marker
 - smoking and ex-smoking population

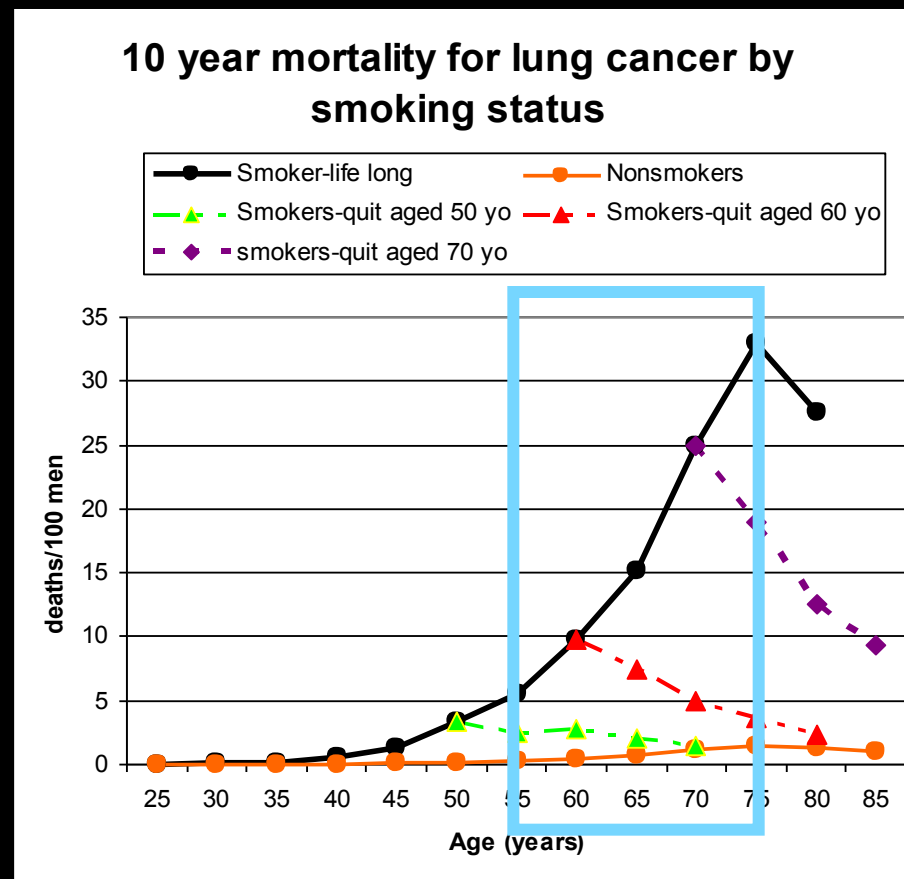


courtesy
N Young, NZ



Screening – how long?

- risk to die from lung cancer ↑ 55 years – 75/80 years



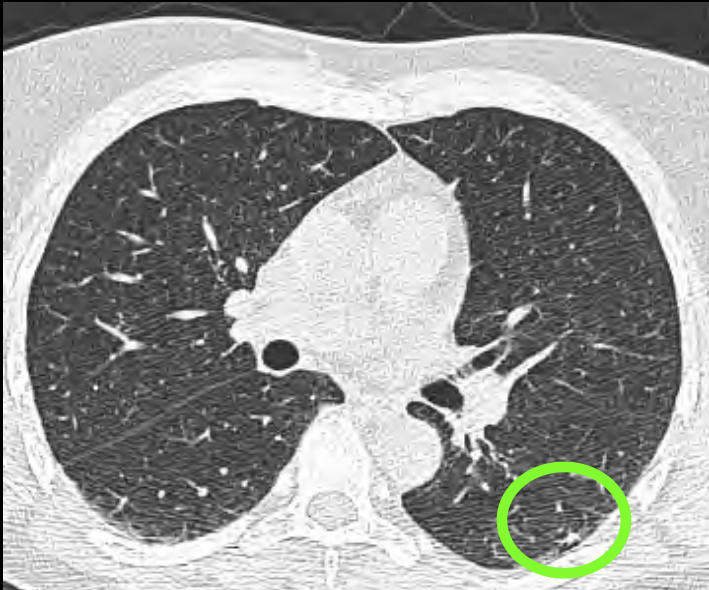
courtesy
N Young, NZ



Lung Cancer Screening

Timeline for screening: 50 – 55 yrs to 75 - 80 yrs

How often? annual / every 2-3yrs?



baseline



annual
(no show)



2 years





2006



2007



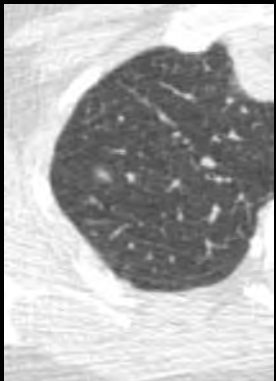
2010



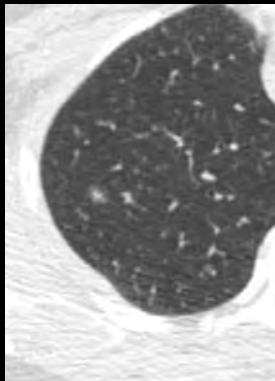
Lung Cancer Screening

Proposal

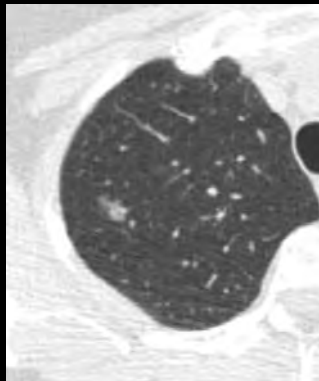
- baseline + 1 annual
- if no change - biennial



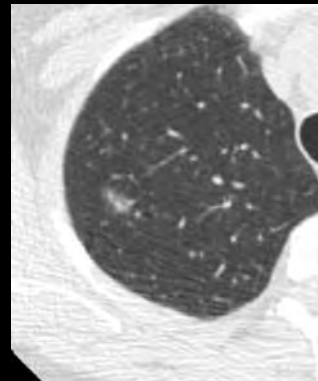
2006



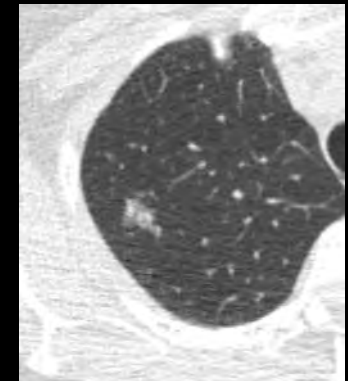
2007



2008



2009



2011



Screening - Issues to be discussed

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Lung Cancer Screening – Feb 2013

- not paid for by OHIP
- not standard of care
anywhere in the western world
- research only
 - international (USA, Europe, Japan)
 - national (Pan-Canadian, 7 sites) enrollment
closed in Dec 2010



Lung Cancer Screening – Feb 2013

- not research
- not clinical

no options for

study participants

people at risk

collaborating/referring physicians

disguised screening

“emphysema, COPD, hemoptysis”

full dose contrast-enhanced CT

non-standardized follow up of nodules



Lung Cancer Screening – Feb 2013

- not research
- not clinical

no options for

study participants

people at risk

collaborating/referring physicians

disguised screening

“emphysema

full dose

non-stand



hemoptysis”

enhanced CT

follow up of nodules



Lung Cancer Screening – Whom?

NOT everybody

limit advertisements and promotion



Lacy Atkins / The Chronicle

*“Demand a CAT Scan”
advertising campaign*

who should be screened

people at risk



Risk Factor #1: *Smoking*

BRITISH MEDICAL JOURNAL

LONDON SATURDAY SEPTEMBER 30 1950

SMOKING AND CARCINOMA OF THE LUNG

PRELIMINARY REPORT

BY

RICHARD DOLL, M.D., M.R.C.P.

Member of the Statistical Research Unit of the Medical Research Council

AND

A. BRADFORD HILL, Ph.D., D.Sc.

Professor of Medical Statistics, London School of Hygiene and Tropical Medicine; Honorary Director of the Statistical Research Unit of the Medical Research Council

“public health classic”



Risk Factor #1: *Smoking*

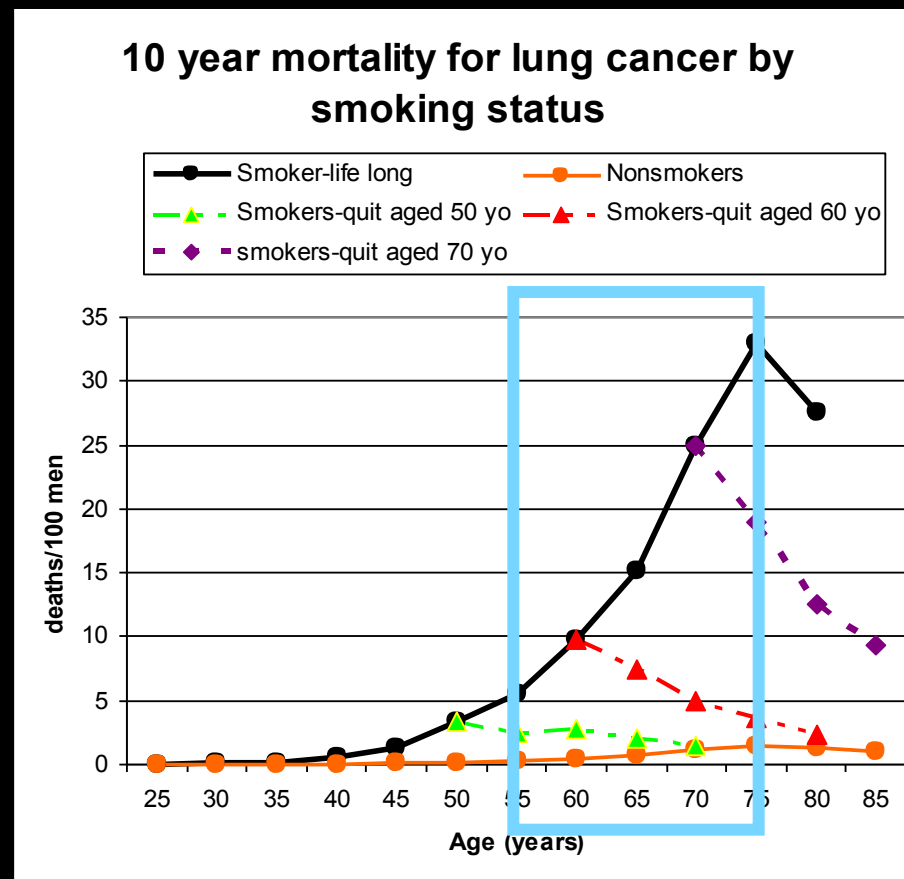
- 10 pack-year?
- 30 pack-year?

- second hand smoking?



Risk Factor *Age*

- risk to die from lung cancer 55 years – 75 years



courtesy
N Young, NZ



people at risk

- Ontario: population ~ 2 million
- 55-75 years old
- 18% *current* smokers 360,000
- 44% *ever* smokers 880,000

screening compliance 25% - to be screened:

- *current* smokers 90,000
- *ever* smokers 220,000



people at risk - cancers

- 18% *current* smokers 360,000
- 44% *ever* smokers 880,000

cancer prevalence: 1.5%

- *current* smokers 5,400 lung cancers
 4,050 Stage 1 (75%)
- *ever* smokers 13,200 lung cancers
 9,900 Stage 1



Lung Cancer Screening – Whom?

risk factors: age (>50 – 55 years)

smoking (10-30 pack-years)



Inadequate as sole criteria for risk



Lung Cancer Risk Assessment Model

Pan-Canadian Lung Cancer Study

individual profile

predictive regression model

socio-demographic factors, smoking exposure, medical and radiographic data

- age
- smoking history
- history of COPD (self-reported)
- chest X-ray in last 3 years
- family history
- education
- body mass index

M Tammemagi & PLCO Study Group



Lung Cancer Risk Assessment Model

Pan-Canadian Lung Cancer Study

individual profile

- detection rate >2.6%
 - + spirometry
 - + biomarker
 - + sputum analysis



M Tammemagi & PLCO Study Group

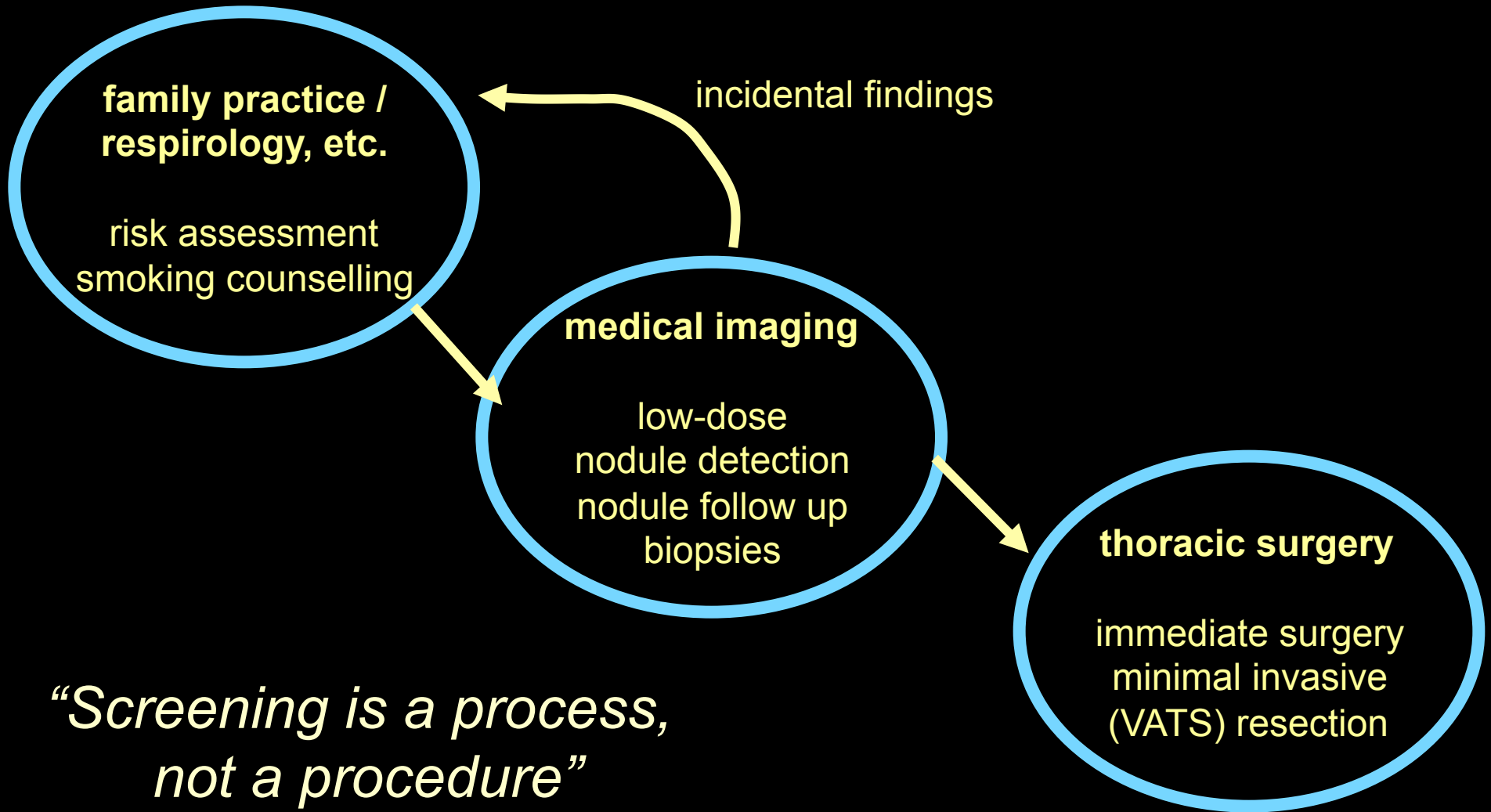


Screening - Issues to be discussed

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Lung Cancer Screening – network



*“Screening is a process,
not a procedure”*



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Lung Cancer Screening – April 2013

- cannot be prevented- it is happening now!
- need for quality control
- need for updated guidelines



Lung Cancer Screening recent guidelines

- International Association for the Study of Lung Cancers (IASLC)
 - July 4, 2011
- National Comprehensive Cancer Network (NCCN)
 - November 4, 2011
- American Lung Association (ALA)
 - April 23, 2012
- American Cancer Society (ACS)
 - January 11, 2013
-



Lung Cancer Screening recent guidelines

- most guidelines follow NLST
- recommends low-dose CT screening for
 1. current or former smokers
 2. age 55 to 74
 3. smoking history of at least 30 pack-years
- general population should not be screened
- chest x-rays are not recommended
- screening not an alternative to smoking cessation
- screening useful when access to treatment centers



Summary

Lung Cancer Screening

- 1. Defined the screening population
- 2. Outlined the technical requirements of CT Screening
- 3. Algorithm for follow up of positive screening cases
- 4. Explained why it is not the SOC in Canada
- 5. Canadian outlook - hopeful

