The Management of Screen Detected Lung Nodules - Navigating the Guidelines

CAR 2016

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Inspiring Minds

Disclosure

- Speakers bureau, Roche

- 1. Apply nodule management guidelines for lung cancer screening (canmeds medical expert, communicator, collaborator)
- 2. Identify the limitations of existing guidelines (canmeds scholar, professional).
- 3. Compare the various guidelines (e.g., Lu-RADS, LUNG-RADS, NLST, Risk calculators) (canmeds scholar).
- Presentation Summary
- Screening CT for lung cancer is beginning to move out of the research domain and into clinical practice. With the publication of the Canadian Task Force on Preventative Health Care recommendations in March 2016 (final recommendation not known at the time of writing), public interest in CT screening is anticipated to increase and all adult institutions can expect to see requests for CT screening exams. Various guidelines are available to assist with the safe reporting of screening CTs. We will review the available guidelines including LUNG-RADS, LU-RADS, NLST, and risk profiling. Limitations of the guidelines and specific situations where the guidelines are difficult to apply will be addressed. Differences in various guidelines, including differences in the definition of a positive scan, will be outlined to help radiologists understand the underlying issues, navigate use of guidelines and simplify the reporting process.

Early release, published at www.cmaj.ca on March 7, 2016. Subject to revision.

CMAJ GUIDELINES

Recommendations on screening for lung cancer

Canadian Task Force on Preventive Health Care*

CMAJ Podcasts: author interview at https://soundcloud.com/cmajpodcasts/151421-guide

Lung cancer is the most common cause of cancer-related deaths and the most commonly diagnosed cancer among Canadians — an estimated 26 600 Canadians were diagnosed and 20 900 died from lung cancer in 2015.[1] In Canada, the incidence of lung cancer is currently higher in men than in women (although this gap is beginning to narrow), and more than 85% of cases are related to smoking tobacco. About 44% of Canadians (12.6 million) smoke or have quit smoking.[2] Those with a history of heavy smoking are at the greatest risk for lung cancer. Smoking history is often measured in pack-years, which is the product of the average number of packs smoked daily and the number of years of smoking (e.g., individuals who smoked one pack a day [20 cigarettes] for

ionizing radiation than usual CT scans, with chest radiography.[6] Ongoing trials of screening with low-dose CT[7–10] are expected to provide more evidence on the effectiveness of screening for lung cancer with low-dose CT. The current recommendations may be updated once these results are available or at least within five years.

Methods

The Canadian Task Force on Preventive Health Care is an independent panel of clinicians and methodologists that makes recommendations about clinical manoeuvres aimed at primary and secondary prevention (www.canadiantaskforce.ca). These recommendations were developed by a work group of six members of the task force

Competing interests: None declared.

This article has been peer reviewed.

*The authors of this article are listed at the end of the article, under "guideline writing group."

The complete list of current members of the Canadian Task Force on Preventive Health Care is available at www.canadiantaskforce.ca/members_eng.html

Correspondence to:
Canadian Task Force on Preventive Health Care,
info@canadiantaskforce.ca

CMAJ 2016. DOI:10.1503

Time to screen smokers for lung cancer

By Dr. Brian Goldman

(Courtesy of the American Cancer Society via Getty Images)

This year, more than 26 thousand Canadians will be diagnosed with lung cancer and close to 21 thousand will die of it. That's according to the **Canadian Cancer Society.** A controversial new set of screening guidelines **just published** in the Canadian Medical Association Journal say doctors should do more to save lives.

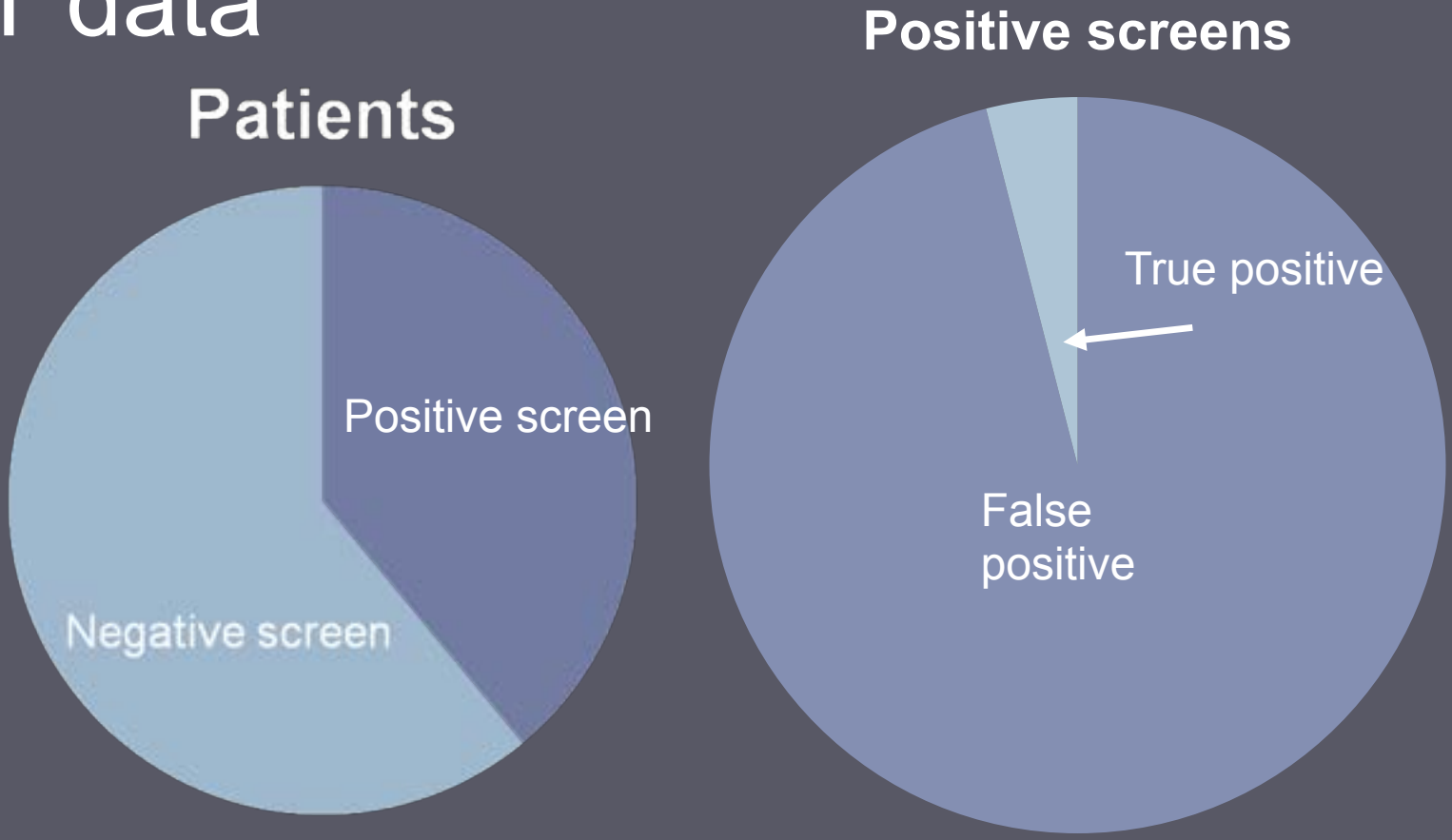
The guidelines say adults age 55 to 74 who are at high risk should be screened for lung cancer once a year for up to three years. By high risk, the guidelines mean men or women who are current heavy smokers or former heavy smokers who have quit within the past 15 years. Heavy smoking is defined as smoking on average a pack of cigarettes a day for at least 30 years.

The guidelines come from the Canadian Task Force on Preventive Health Care established by the Public Health Agency of Canada to develop guidelines to help prevent serious conditions like cancer and heart disease. The idea behind the guidelines is to detect lung cancers when they're tiny and perhaps more curable.

They say current or former heavy smokers should have a low dose CT scan of the chest once a year for up to

Lung nodules are very common

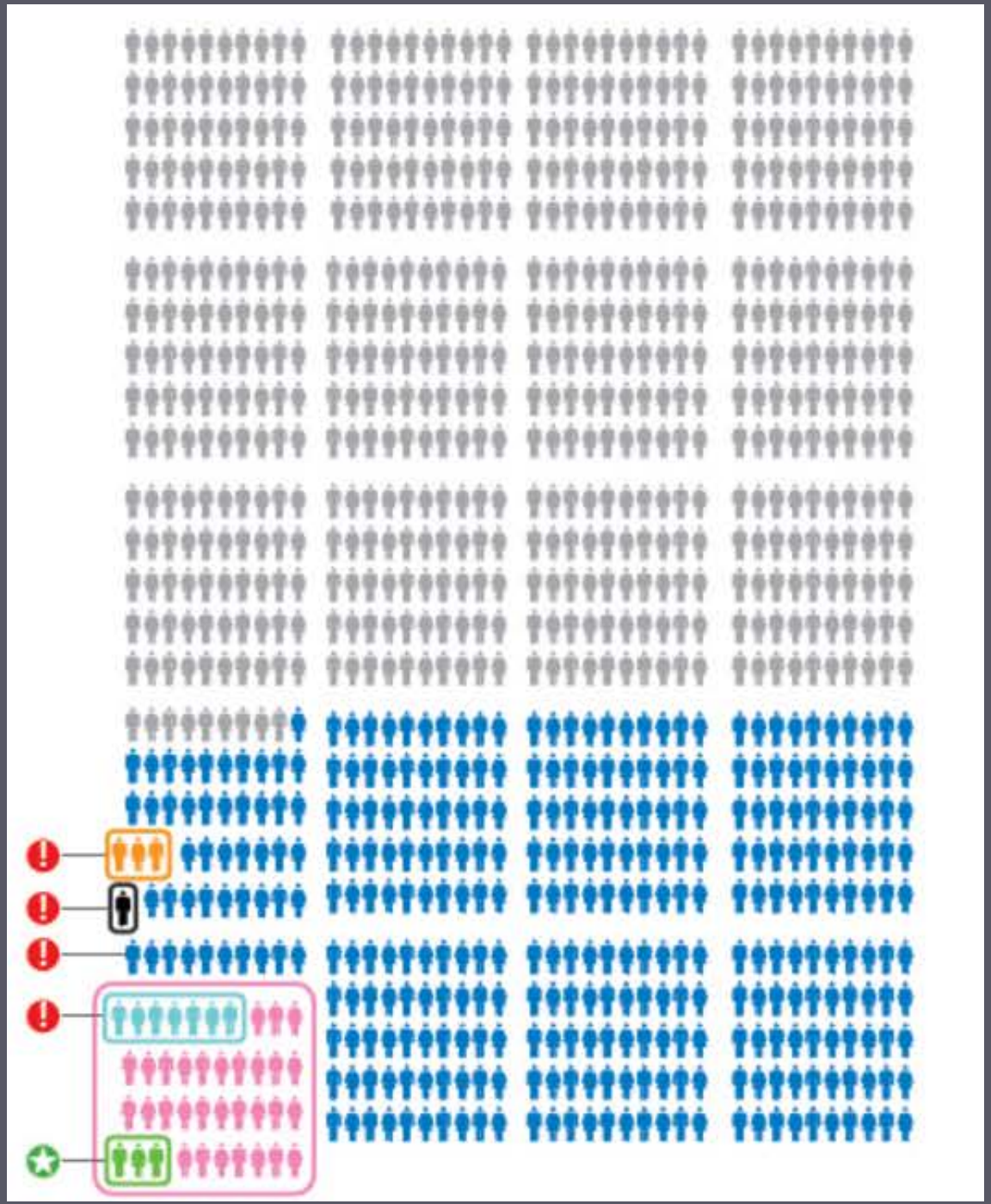
NLST data



Patients assume all nodules are cancer.

(Wiener. Chest 2013).

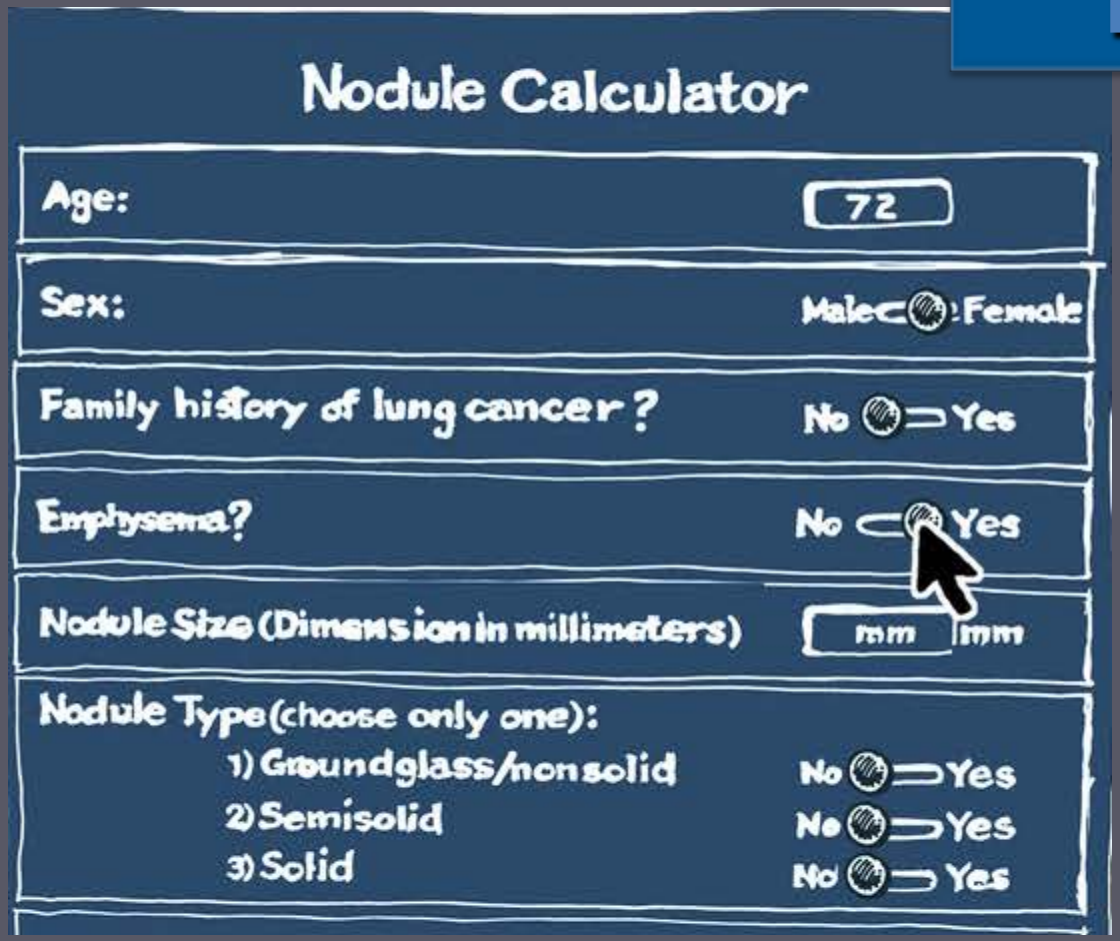
Be careful!



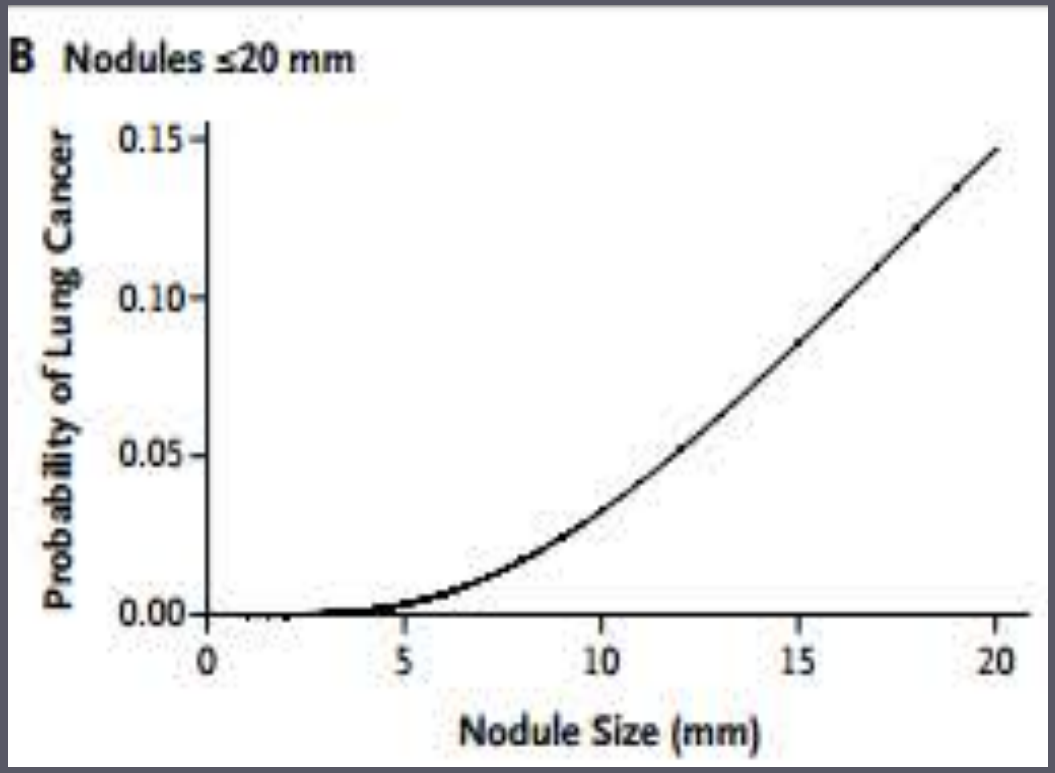
Canadian Task Force based on NLST data

Lung CT Screening Reporting and Data System (Lung-RADS™)

LURADS



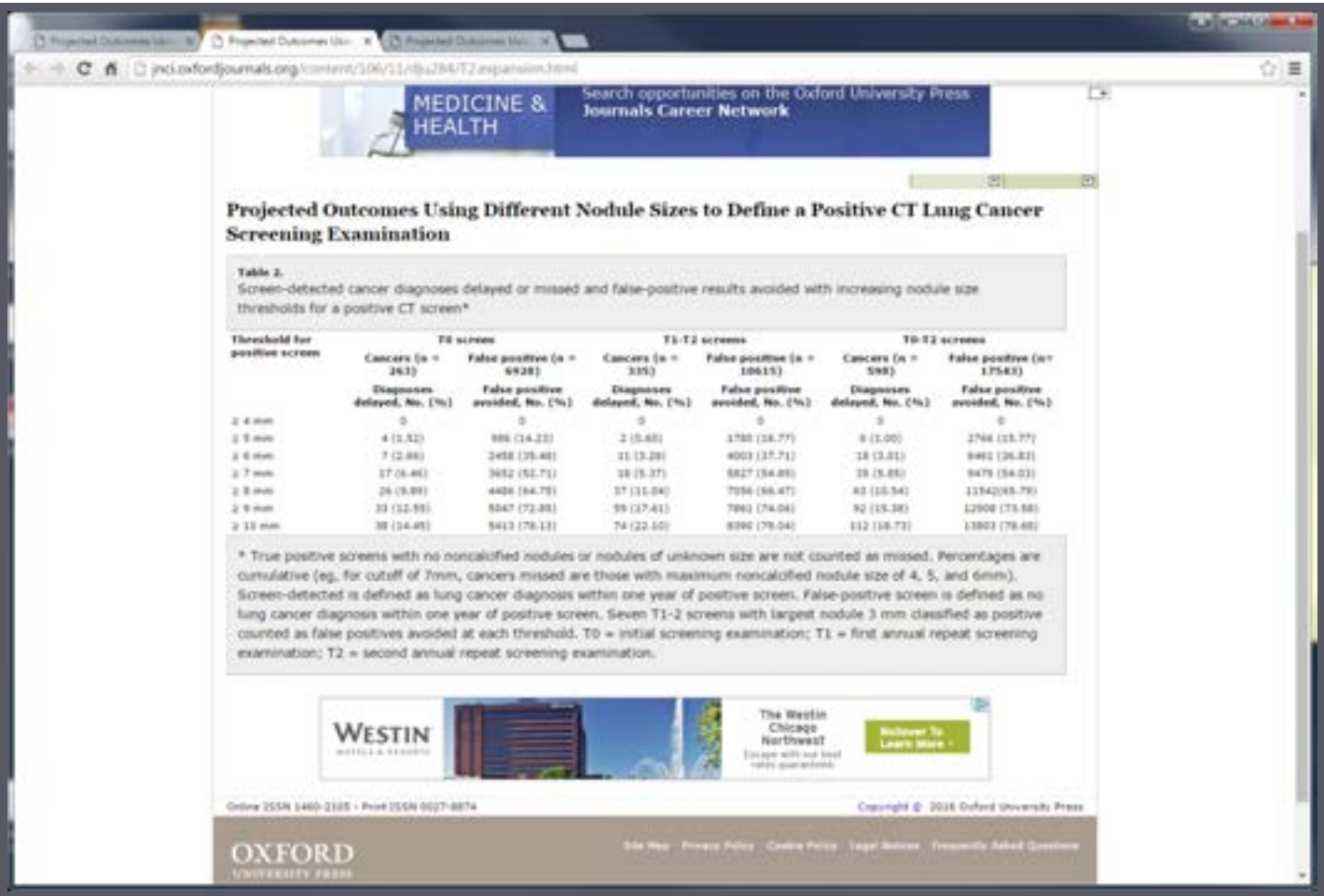
Change
Density
Size



4 mm 5r What about the missed cancers? 9mm

Based on NLST (total of 3 rounds screening)

Gierada, JNCI 2014



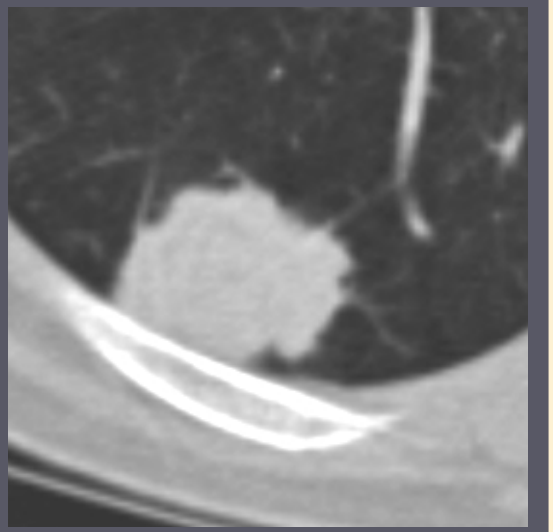
Projected Outcomes Using Different Nodule Sizes to Define a Positive CT Lung Cancer Screening Examination

Table 2.
Screen-detected cancer diagnoses delayed or missed and false-positive results avoided with increasing nodule size thresholds for a positive CT screen*

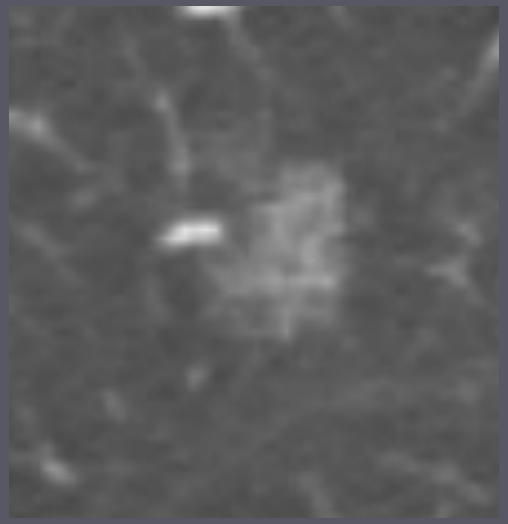
Threshold for positive screen	T0 screen		T1-T2 screens		T0-T2 screens	
	Cancers (n = 263)	False positive (n = 6928)	Cancers (n = 335)	False positive (n = 10615)	Cancers (n = 598)	False positive (n = 17543)
	Diagnoses delayed, No. (%)	False positive avoided, No. (%)	Diagnoses delayed, No. (%)	False positive avoided, No. (%)	Diagnoses delayed, No. (%)	False positive avoided, No. (%)
≥ 4 mm	0	0	0	0	0	0
≥ 5 mm	4 (1.52)	986 (14.23)	2 (0.60)	1788 (16.77)	6 (1.00)	2768 (15.77)
≥ 6 mm	7 (2.66)	2458 (35.48)	11 (3.28)	4003 (37.71)	18 (3.01)	6461 (36.83)
≥ 7 mm	17 (6.46)	3652 (52.71)	18 (5.37)	5827 (54.89)	35 (5.85)	9479 (54.03)
≥ 8 mm	26 (9.89)	4606 (66.79)	37 (11.04)	7056 (66.47)	63 (10.54)	11542(65.79)
≥ 9 mm	33 (12.55)	5047 (72.85)	59 (17.61)	7861 (74.04)	92 (15.38)	12908 (73.58)
≥ 10 mm	38 (14.45)	5413 (78.13)	74 (22.10)	8390 (79.04)	112 (18.73)	13803 (78.68)

* True positive screens with no noncalcified nodules or nodules of unknown size are not counted as missed. Percentages are cumulative (eg, for cutoff of 7mm, cancers missed are those with maximum noncalcified nodule size of 4, 5, and 6mm). Screen-detected is defined as lung cancer diagnosis within one year of positive screen. False-positive screen is defined as no lung cancer diagnosis within one year of positive screen. Seven T1-2 screens with largest nodule 3 mm classified as positive counted as false positives avoided at each threshold. T0 = initial screening examination; T1 = first annual repeat screening examination; T2 = second annual repeat screening examination.

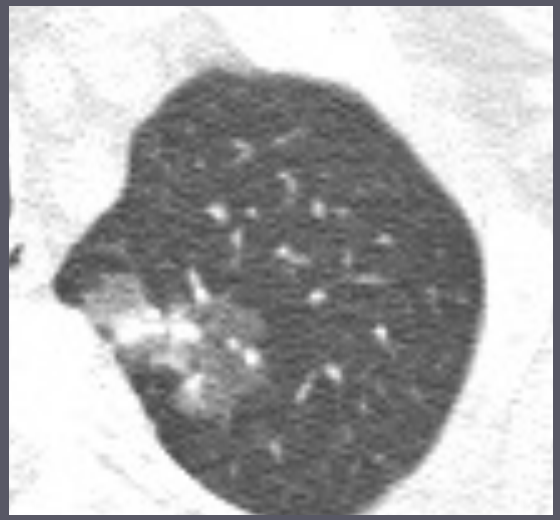
Density



Solid



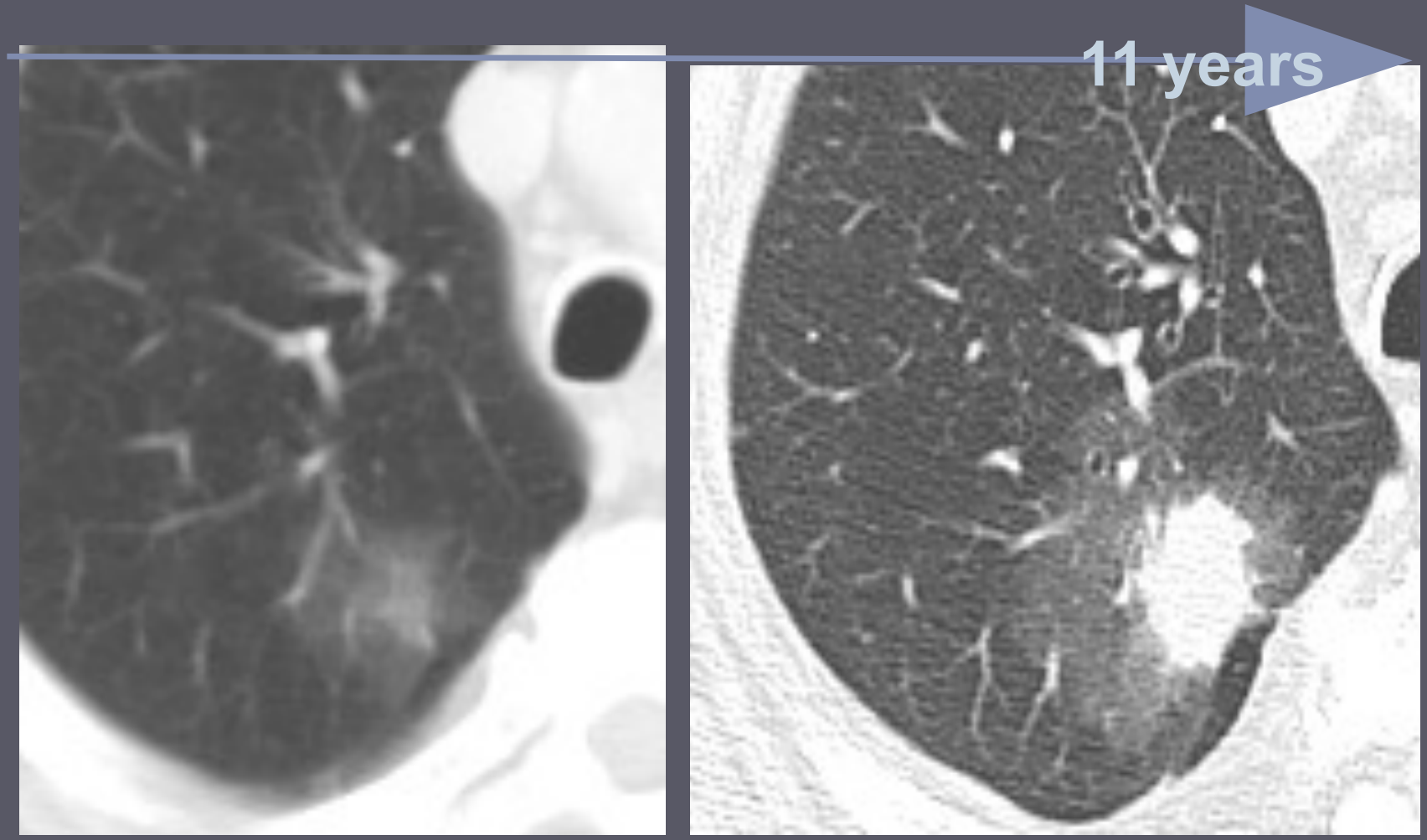
Ground glass



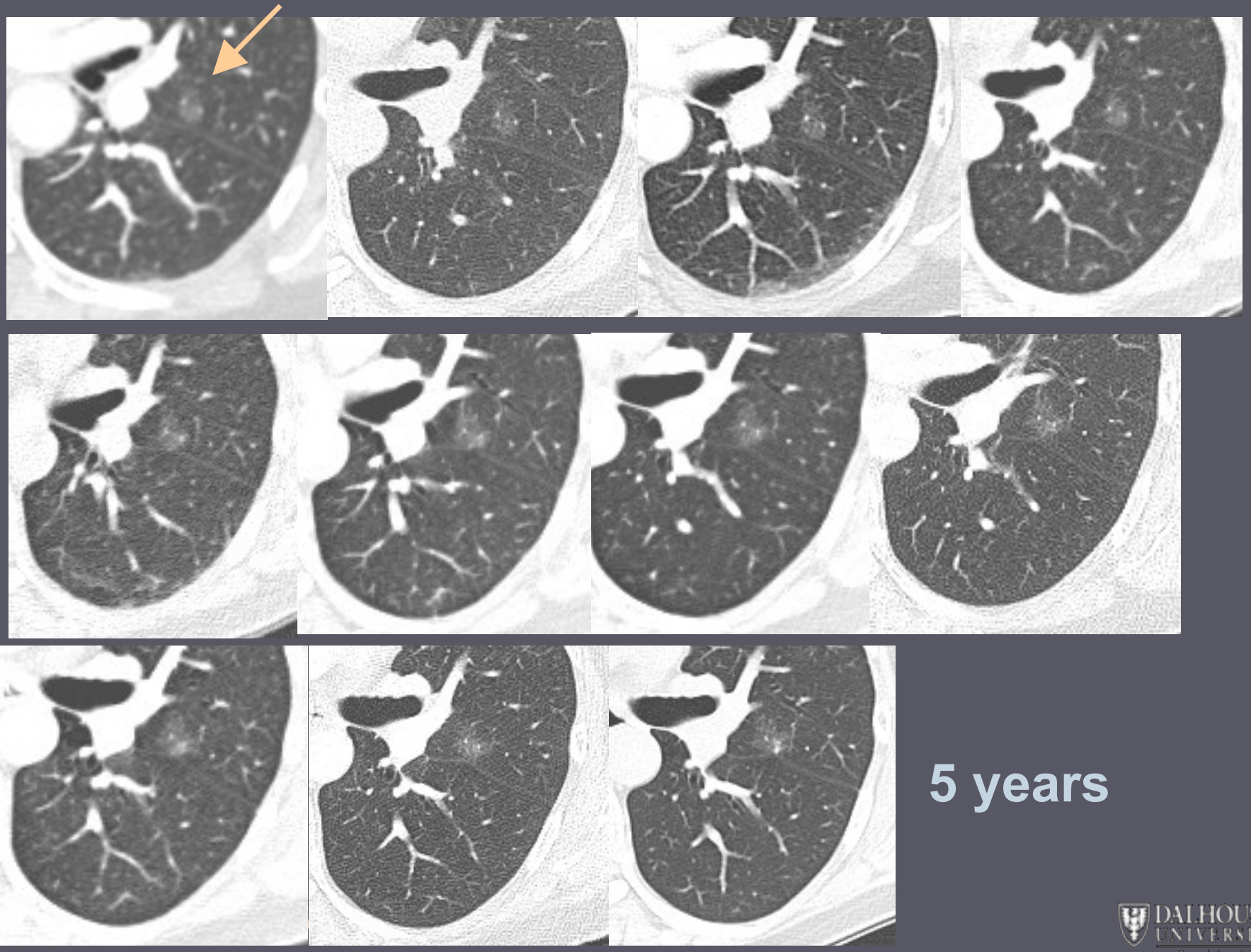
Part solid

Sub solid

Focal ground glass opacity can progress to invasive adenocarcinoma.



Well-differentiated lepidic adenocarcinoma



Baseline CT (size, density, others) + demographic information

	A	B	C	D	E	F
1	**Probability calculator estimating a pulmonary nodule being lung cancer.***			Version Tammemagi V1-2SEP13		
2	**Model: Full with spiculation.**					
3	**Instructions: In column B enter the values for the variable listed in column A. Ignore columns C through F.**					
4	**Variables**	**Enter Values**	**Transformation**	**Transfomed value**	**Beta coefficients**	**Calculated value**
5						
6	Age (years)	64	-62	2	0.0286687	0.0573
7	Sex (Male=0, Female=1)	0			0.6010727	0.0000
8	Family history of lung cancer (No=0, Yes=1)	0			0.296109	0.0000
9	Emphysema (No=0, Yes=1)	1			0.2953112	0.2953
10	Nodule size (in millimeters)	6.0		-0.2901	-5.385484	1.5626
11	Nodule type (choose only one from this category)					
12	Groundglass/nonsolid (No=0, Yes=1)	0			-0.1276173	0.0000
13	Semisolid/part-solid (No=0, Yes=1)	0			0.3769578	0.0000
14	Solid [referent group](No=0, Yes=1)	1			0	0.0000
15	Upper lobe location (No=0, Yes=1)	0			0.6581383	0.0000
16	Spiculation (No=0, Yes=1)	1			0.7729335	0.7729
17	Nodule count (number of nodules detected on screen)	3	-4	-1	-0.0824156	0.0824
18	Model constant (do not change)					-6.78917
19					xb =	-4.018604
20						
21				**Probability that nodule is lung cancer ** =**		**0.018**
22	* Reference: McWilliams A, Tammemagi M, Mayo J, Roberts H, Liu G, Soghrati K, Yasufuku K, Martel S, Laberge F. et al. Probability of cancer in pulmonary nodules detected on first screening computed tomography. New England Journal of Medicine 2013;369;10.					
23	** This is the probability that a nodule of this type and with these patient demographics & history would be diagnosable as cancer during standard follow-up monitoring for 2 to 4 yrs.					
24	Please send comments or issues with the calculator to martin.tammemagi@brocku.ca					

http://www.brocku.ca/lung-cancer-risk-calculator

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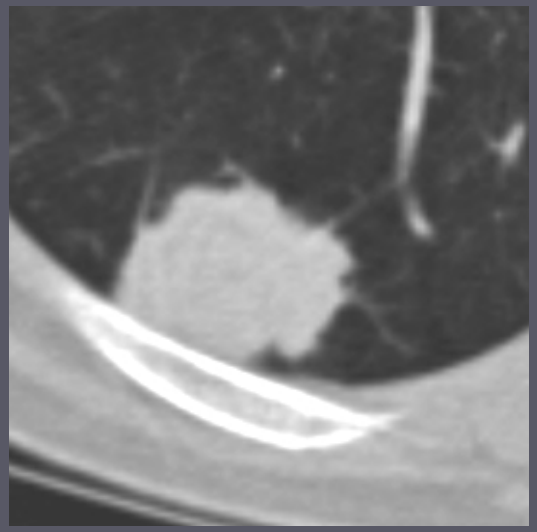
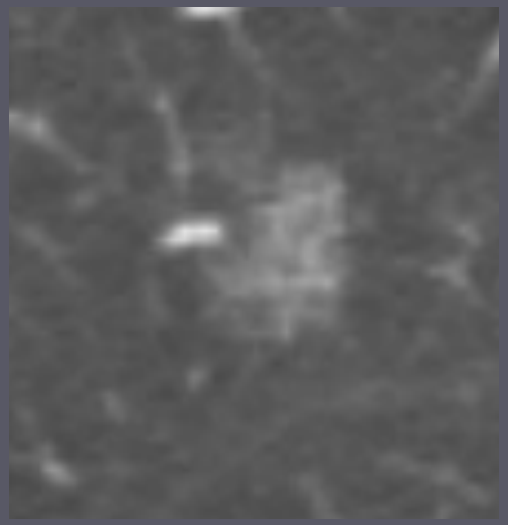
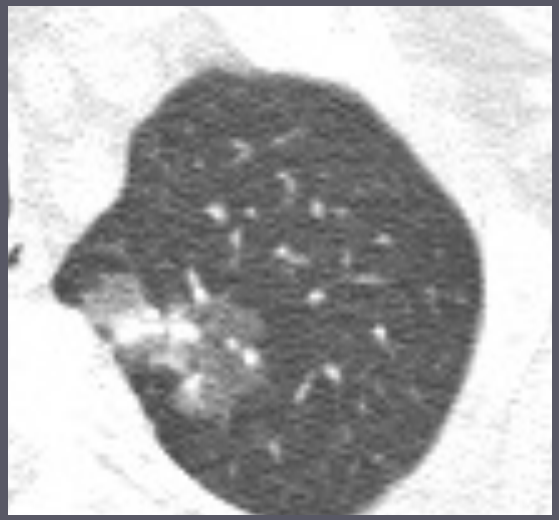
Change





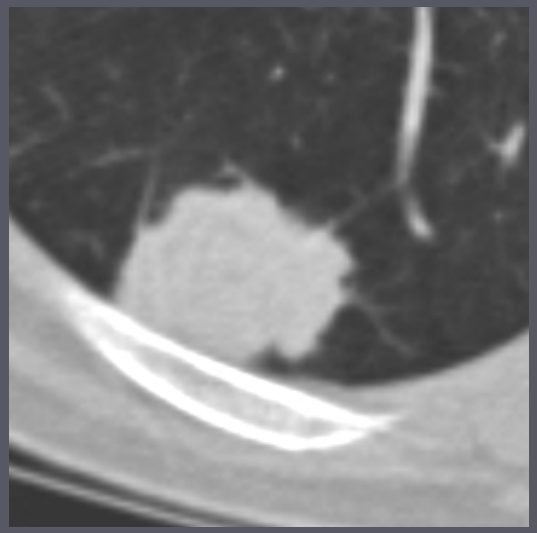


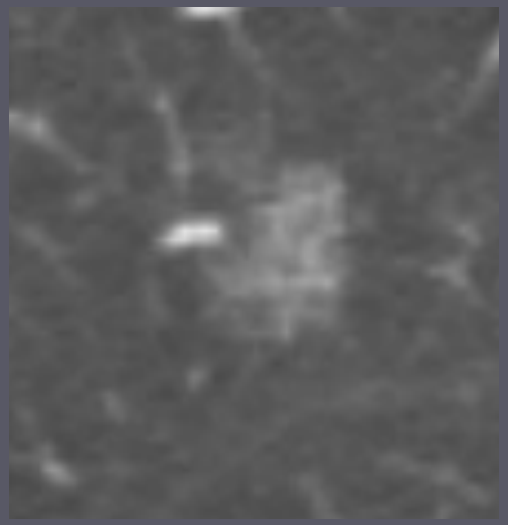
Baseline: up to 50% resolve

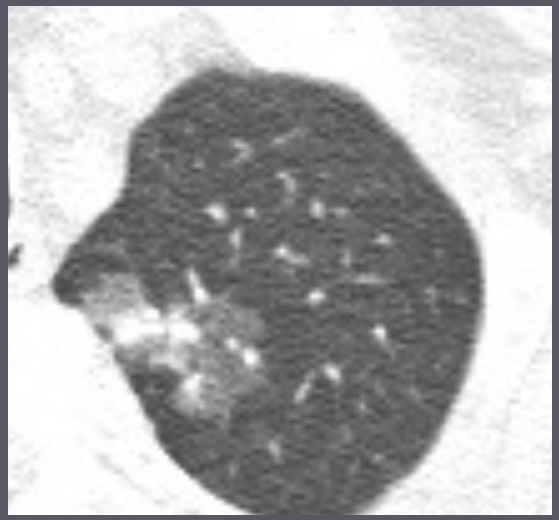
If persistent: adenocarcinoma spectrum.

Chang Chest 2013

Lee KJR 2007, Fan BJR 2012, Cho ATS 2013

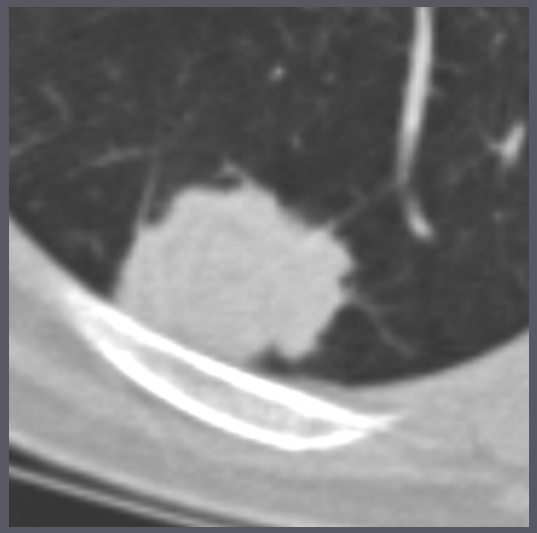


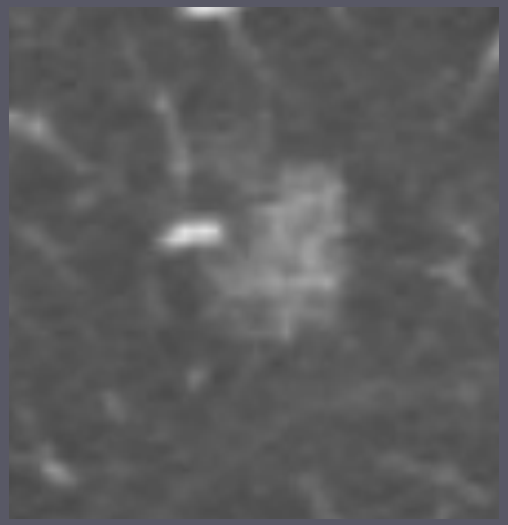


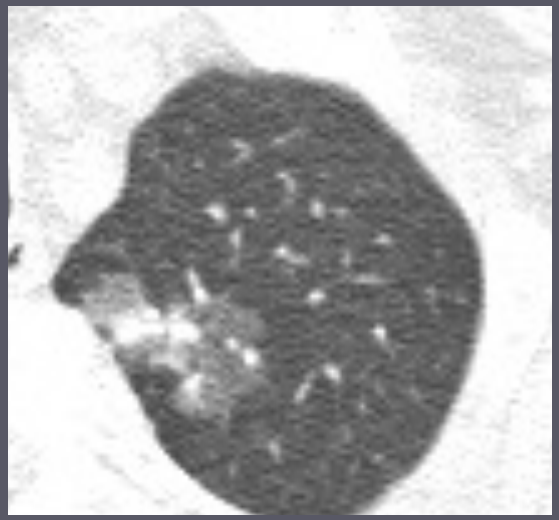


Aggressivity ⬆ with growth

Chang, Chest 2013; Kim JTO 2009; Lee Eur Rad 2009, Cho ATS 2013



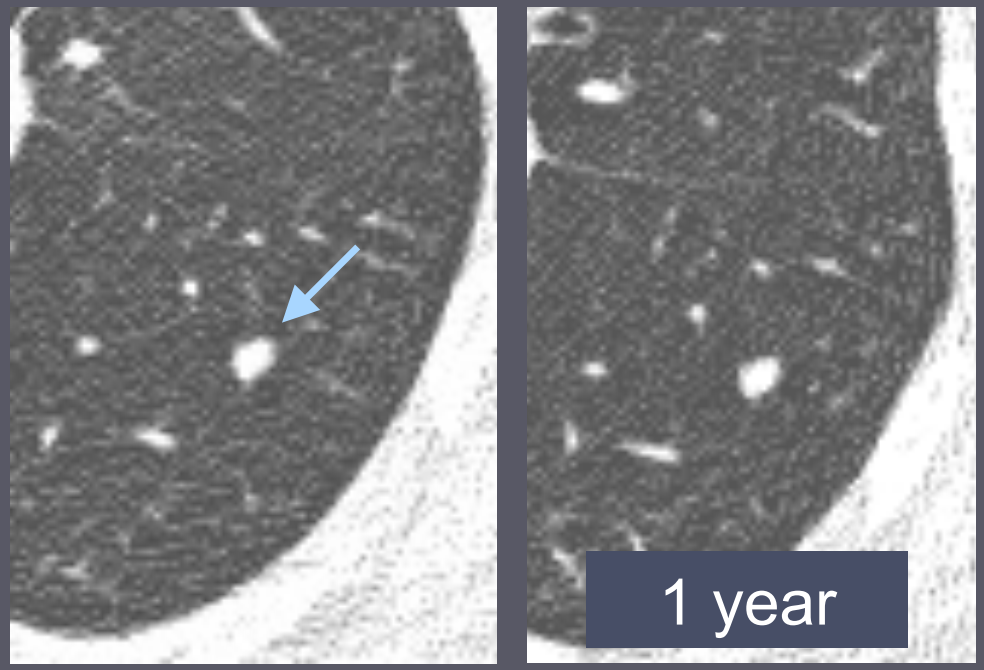




Aggressivity ⬆ with size
Aggressivity ⬆ with growth
Aggressivity ⬆ with density

Chang, Chest 2013; Kim JTO 2009; Lee Eur Rad 2009, Cho ATS 2013

Growth



- Slide on baseline versus annual
- - include discussion of new large nodules
- - or save this for disagreement slide

NLST protocol

Negative:

- Noncalcified <4mm

Positive:

- Non calcified ≥ 4 mm

No diagnostic algorithm.

I ELCAP protocol

Negative:

- no noncalcified nodule

Semipositive

- Baseline: < 6mm, all non solid
- Annual: <3mm, all non solid (new)

Positive

- Baseline: 6-14mm
- Annual: new ≥ 3mm, growing

Clear diagnostic algorithm.

NLST

Negative:

Non calcified < 4mm

Positive:

Non calcified ≥ 4 mm

No diagnostic algorithm

I ELCAP (baseline)

Negative:

no noncalcified nodule

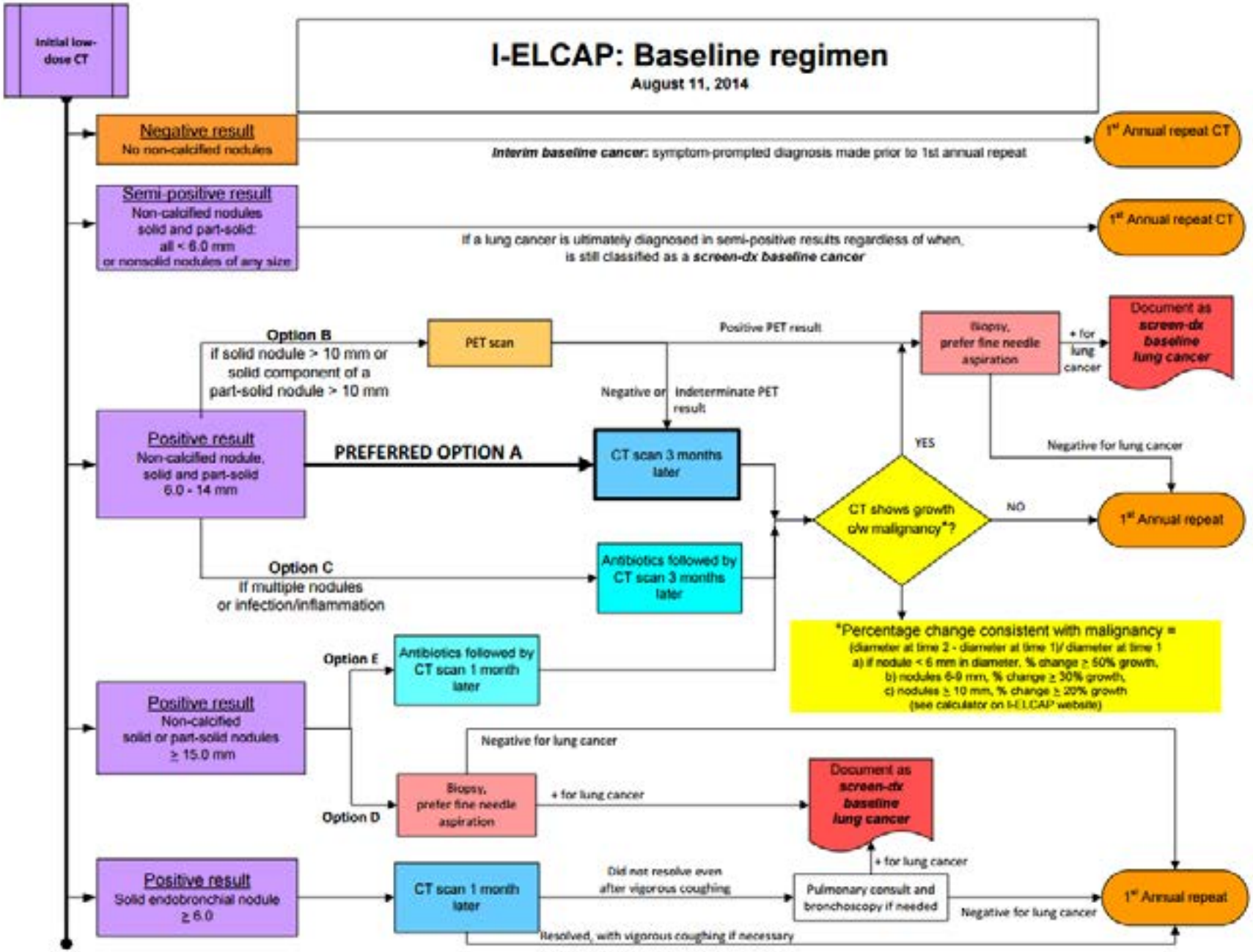
Semipositive

Solid, PS < 6mm, any size NS

Positive

Solid or PS ≥ 6mm

Clear diagnostic algorithm


Initial low-dose CT
I-ELCAP: Baseline regimen
August 11, 2014
Negative result
No non-calcified nodules
Interim baseline cancer: symptom-prompted diagnosis made prior to 1st annual repeat
1st Annual repeat CT
Semi-positive result
Non-calcified nodules
solid and part-solid:
all < 6.0 mm
or nonsolid nodules of any size
If a lung cancer is ultimately diagnosed in semi-positive results regardless of when,
is still classified as a screen-dx baseline cancer
1st Annual repeat CT
Option B
if solid nodule > 10 mm or
solid component of a
part-solid nodule > 10 mm
PET scan
Positive PET result
Biopsy,
prefer fine needle
aspiration
+ for
lung
cancer
Document as
screen-dx
baseline
lung cancer
Negative or Indeterminate PET
result
Positive result
Non-calcified nodule,
solid and part-solid
6.0 - 14 mm
PREFERRED OPTION A
CT scan 3 months
later
YES
Negative for lung cancer
CT shows growth
c/w malignancy*?
NO
1st Annual repeat
Option C
If multiple nodules
or infection/inflammation
Antibiotics followed by
CT scan 3 months
later
*Percentage change consistent with malignancy =
(diameter at time 2 - diameter at time 1)/ diameter at time 1
a) if nodule < 6 mm in diameter, % change ≥ 50% growth,
b) nodules 6-9 mm, % change ≥ 30% growth,
c) nodules ≥ 10 mm, % change ≥ 20% growth
(see calculator on I-ELCAP website)
Option E
Antibiotics followed by
CT scan 1 month
later
Positive result
Non-calcified
solid or part-solid nodules
≥ 15.0 mm
Negative for lung cancer
Biopsy,
prefer fine needle
aspiration
+ for lung cancer
Document as
screen-dx
baseline
lung cancer
Option D
Positive result
Solid endobronchial nodule
≥ 6.0
CT scan 1 month
later
Did not resolve even
after vigorous coughing
Pulmonary consult and
bronchoscopy if needed
+ for lung cancer
Negative for lung cancer
1st Annual repeat
Resolved, with vigorous coughing if necessary

Lung-RADS and LU-RADS

- Lung-RADS: American College of Radiology
  - Webpage available April 28 2014

- LU-RADS: Canadian radiologists (I-ELCAP, Pan Canadian Early Detection Study)
  - Published online ahead of print April 21 2014
  - Open access in the CARJ

ngs and fat containing nodules	
olid nodule(s): < 6 mm new < 4 mm	Continue annual screening with LDCT in 12 months
art solid nodule(s): < 6 mm total diameter on baseline screening	
on solid nodule(s) (GGN): < 20 mm OR ≥ 20 mm and unchanged or slowly growing	
ategory 3 or 4 nodules unchanged for ≥ 3 months	
olid nodule(s): ≥ 6 to < 8 mm at baseline OR new 4 mm to < 6 mm	6 month LDCT
art solid nodule(s)	
≥ 6 mm total diameter with solid component < 6 mm OR new < 6 mm total diameter	
on solid nodule(s) (GGN) ≥ 20 mm on baseline CT or new	
olid nodule(s): ≥ 8 to < 15 mm at baseline OR growing < 8 mm OR new 6 to < 8 mm	3 month LDCT; PET/CT may be used when there is a ≥ 8 mm solid component
art solid nodule(s: ≥ 6 mm with solid component ≥ 6 mm to < 8 mm OR with a new or growing < 4 mm solid component	
ndobronchial nodule	
olid nodule(s) ≥ 15 mm OR	

LOW RISK - NEGATIVE

Return to screening

Lung-RADS	LU-RADS
Specific benign features	
< 6mm solid or part solid	< 5mm
< 4 mm new solid	
< 20mm ground glass Can grow slowly	
Nodule stable for ≥ 3 mos	Stable for ≥ 2 or 5 years

- Limitation to 3 screens (baseline and 2 annual):
  - What does this mean for the definition of a "negative" screen?
    - Negative (really negative) OR
    - Negative but you must come back in a year
  - Tiny new nodules are not really negative.
  - Ground glass slowly growing nodules are not really negative.

PROBABLY BENIGN / INDETERMINATE

Surveillance CT

Lung-RADS

Solid:

- 6-8 mm baseline
- 4-6 mm if new

Part solid:

- If solid part < 6mm
- New < 6mm

Non solid:

- ≥ 20 mm

LU-RADS

3 small:

- 5-9 mm nodule not enlarging

3 large:

- ≥ 10mm AND
- Inflammatory features

Surveillance +

Lung-RADS

4A:

- Solid
  - 8-15 mm baseline
  - New 6-8 mm
  - Growing < 8 mm
- PS
  - with solid 6-8 mm,
  - New or ▲ Solid <4mm

LU-RADS

4A: Low risk but not definitive

4B: Likely AIS or MIA (persistent NS ≥ 10mm)

WORRISOME

Work up

Lung-RADS

4B:

- Solid
  - ≥ 15mm
  - Growing ≥ 8mm
  - New ≥ 8mm

PS with solid ≥ 8mm

with new or growing solid ≥ 4mm

LU-RADS

Negative work up would be discordant

4C: Likely malignant:

- worrisome persistence
  - subsolid ≥ 10mm not resolving (solid part ≥ 5mm)
- worrisome change
  - malignant growth rate
- worrisome baseline
  - ≥ 10 mm solid no inflammatory CT or clinical features

MALIGNANT

Lung-RADS

4x

Additional features or imaging findings that increase the suspicion of malignancy

LU-RADS

5

Invasion or chest wall or mediastinum

Discrepancy

Ground glass nodules ≥ 10mm

LungRADS 2 if <20mm or
LungRADS 3 if ≥ 20mm

No recommendation apart from LDCT

Lu-RADS 4B if persistent

- Refer
- If conservative – annual screen
- PET + biopsy not usually appropriate

- Most persistent pure GGO = AAH, AIS.
- Risk of AIS increases with size over 5mm.
- Risk of invasive cancer increases with size.
- Resected pure GGO
  - 100% adenocarcinoma in situ or invasive adeno

Fan BJR 2012, Cho ATS 2013, Chang CHEST 2013

- Long term natural his
  understood.
- Management of Pers
  comorbidities and ag

CHEST

DIAGNOSIS A

Executive Summar

Diagnosis and Manager
3rd ed: American Colleg
Evidence-Based Clinica

Frank C. Detterbeck, MD, FCCP; Sar
Doreen J. Addrizzo-Harris, MD, FCC

Nonsolid (Pure Ground Glass) Nodules

6.5.1. In the individual with a nonsolid (pure ground glass) nodule measuring ≤5 mm in diameter, we suggest no further evaluation (Grade 2C).

6.5.2. In the individual with a nonsolid (pure ground glass) nodule measuring >5 mm in diameter, we suggest annual surveillance with chest CT for at least 3 years (Grade 2C).

Remark: CT surveillance of nonsolid nodules should use noncontrast techniques with thin sections through the nodule of interest.

Remark: Nonsolid nodules that grow or develop a solid component are often malignant, prompting further evaluation and/or consideration of resection.

Remark: Early follow-up at 3 months may be indicated for nonsolid nodules measuring >10 mm (followed by nonsurgical biopsy and/or surgical resection for nodules that persist).

Remark: Limited duration or no follow-up may be preferred by individuals with life-limiting comorbidities in whom a low-grade malignancy would be of little consequence or by others who place a high value on avoiding treatment of possibly indolent lung cancer.

Discrepancy

Large new nodules – not present previous year

LungRADS 4B

Chest Ct +/- contrast,

PET/CT or

tissue sampling

depending on the probability of malignancy and comorbidities

Lu-RADS 3

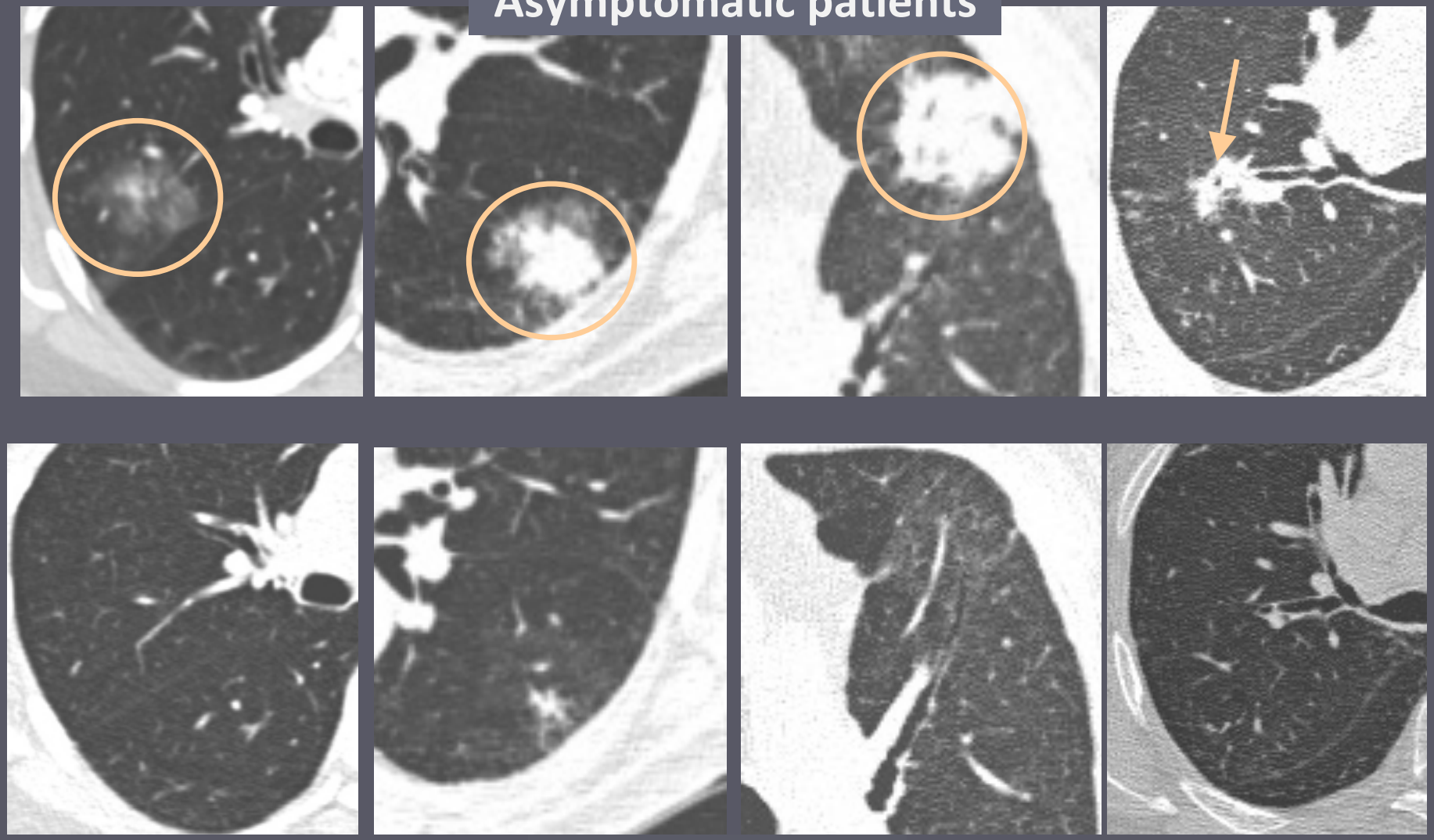
Short interval CT

If any inflammatory features including ANY gg component

Must be able to review images of most recent prior CT.

LU-RADS 3 – requires surveillance CT

Asymptomatic patients



Follow up CTs

- 2000 participants:
  - New nodules on annual screen much more likely to resolve than nodules on baseline screen.
  - (Possibly inflammatory nodules; 74% versus 29%)

- 321 participants
  - 11 new nodules ≥ 1 cm on annual repeat screen.
  - 100% resolved.

Libby Chest 2006;
Nova Scotia subset of Pan Canadian data, 2015

What to do?

- Do not use NLST – too many positive scans
- I ELCAP very prescriptive – need coordinated team
- Current online risk calculator useful for clinicians but limited use for radiologists in my opinion
  - – valid for baseline only
- Read the LU-RADS paper as a summary of the issues. (open access CARJ)
- Multidisciplinary approach essential.
  - You must be able to identify discordant results and have the ability to discuss.

If assign a LU-RADS or Lung-RADS classification, also give descriptive impression:

at minimum:

"normal/negative/low risk"

"indeterminate" – need surveillance

"positive" or "concerning"

is referral indicated?

THANK YOU

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