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Request for coverage of LDCT by Medicare

Peter B. Bach, MD, MAPP
Memorial Sloan Kettering Cancer Center
bachp@mskcc.org

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Disclosures

- No Financial Conflicts of Interest
- I am a member of the MEDCAC
  - Here as a private citizen today
- I will discuss off label use of the CT scanner for screening:
  - FDA Label covers:
    - Diagnose disease, trauma or abnormality
    - Plan and guide interventional or therapeutic procedures
    - Monitor the effectiveness of therapy (e.g., cancer treatment)

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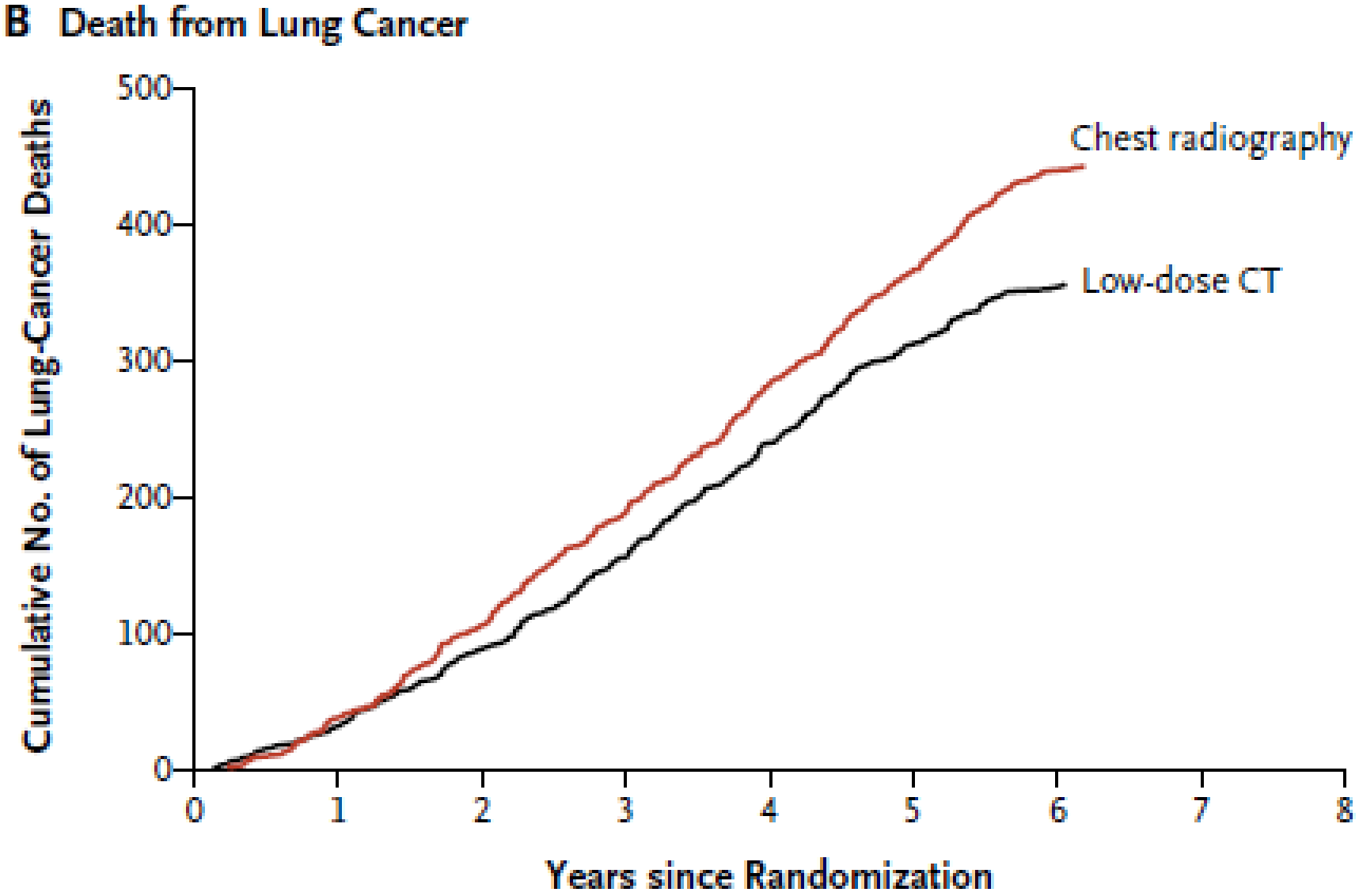
Outline

- Extrapolating the evidence from the NLST:
- What do we know about unstudied groups and interventions?
- What do we know about harm minimization?
  - False positives, incidental findings, centers of excellence
- Individualized decision making in the context of large risk variation

Extrapolating from the NLST

- Was group studied generalizable?
  - Do they represent lung cancer overall?
- Are findings generalizable?
  - Mortality
  - False positives
  - Adherence
- Is setting generalizable?
- Some things we need to know more about

NLST shows efficacy of LDCT screening for lung cancer in protocol driven study



Partial overlap with overall at-risk group: demographics

Table 6. Comparison of the National Lung Screening Trial (NLST) cohort with the NLST-eligible US population from the Tobacco Use Supplement (TUS) of the US Census Bureau Current Population Surveys*

Characteristic	NLST	TUS
Male, %	59.0	58.5
Age group, %		
55–59 y	42.8	35.2
60–64 y	30.6	29.3
65–69 y	17.8	20.8
70–74 y	8.8	14.7
Race/ethnicity, %		
Black	4.4	5.5
Hispanic or Latino, %	1.7	2.4
Education, %		
Less than high school	6.1	21.3
College degree or higher	31.5	14.4
Married, %	66.6	60.0
Current smoker, %	48.2	57.1
Median pack-years of cigarette smoking	48.0	47.0
US region, %		
Northeast	16.3	21.1
Midwest	39.2	28.8
South	23.9	33.0
West	20.6	17.2

Baseline Characteristics of Participants in the Randomized National Lung Screening Trial

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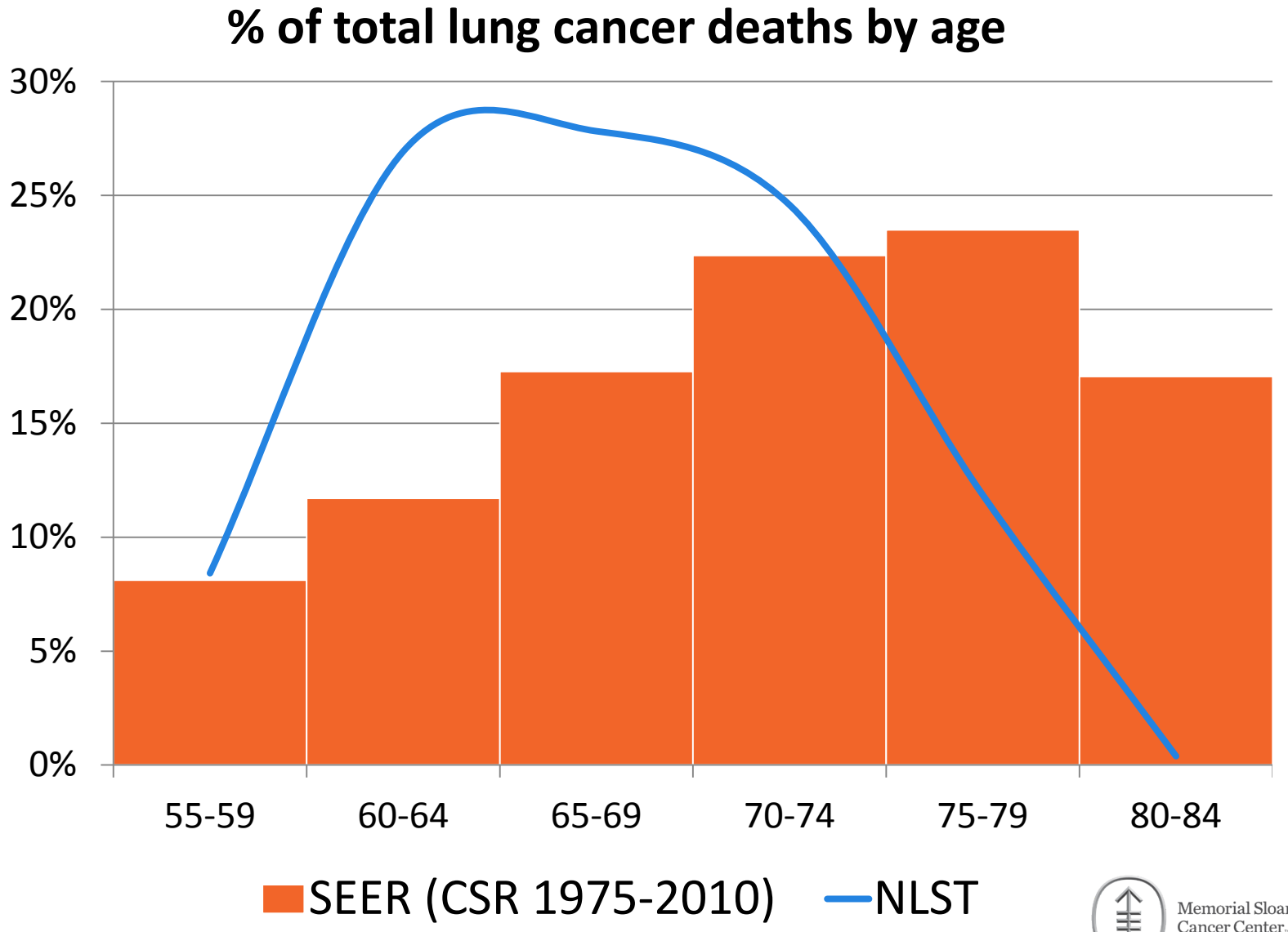
The National Lung Screening Trial Research Team

Modest overlap: Age when people die of lung cancer



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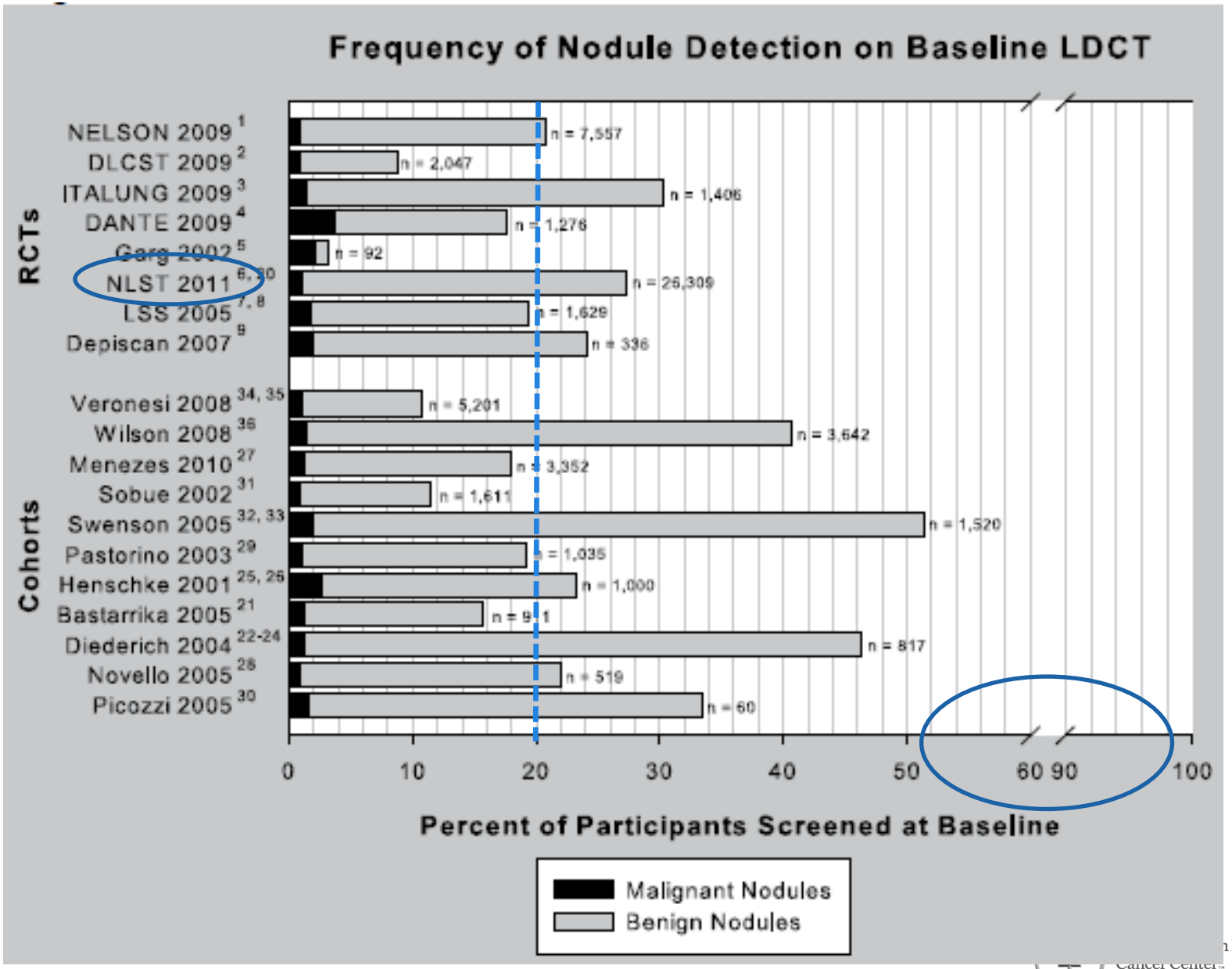
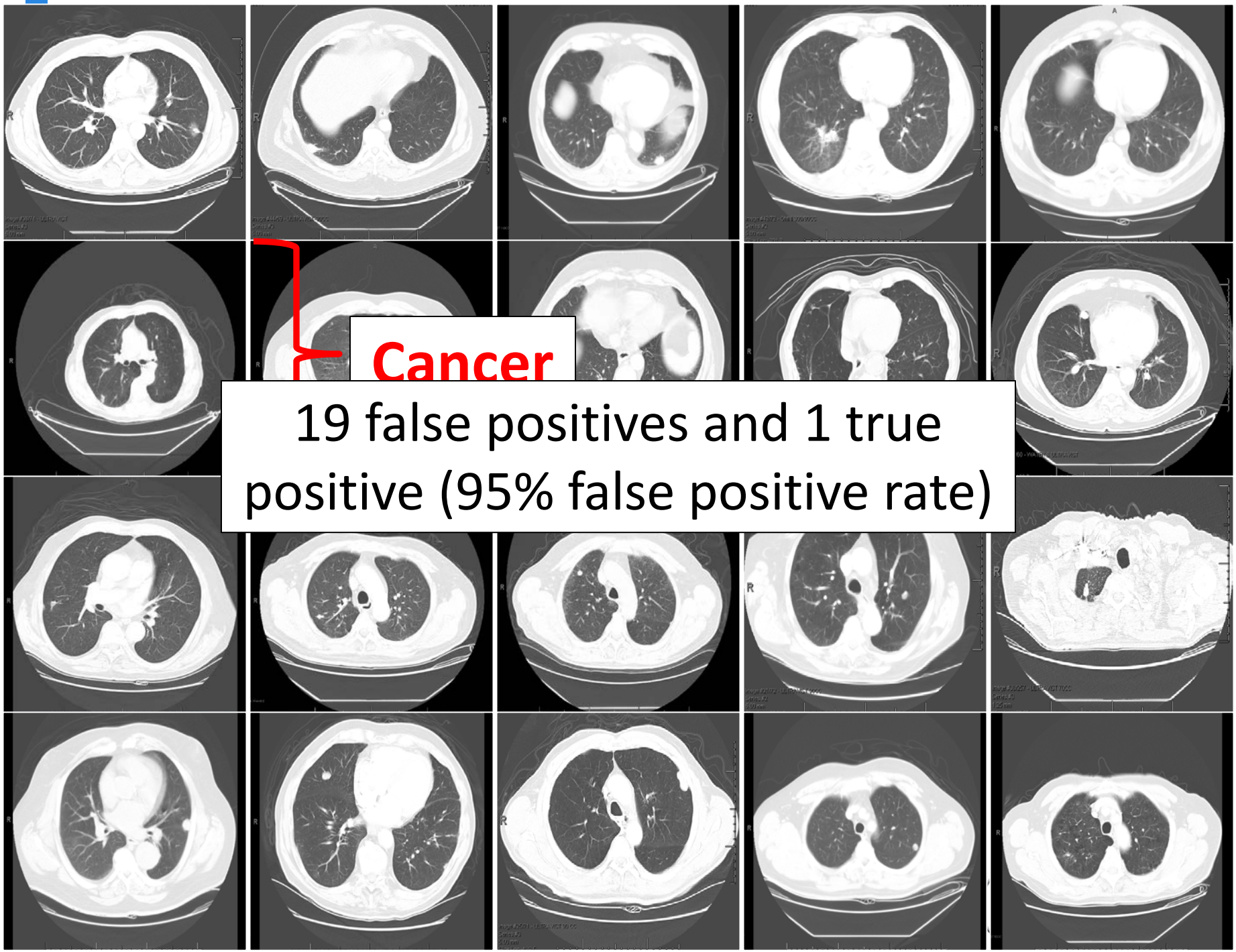
Care settings: not typical

eTable 3: Study Sites for the National Lung Screening Trial

Site	ACRIN/ LSS	Staffed Hospital Beds [18]	NCI Designated Cancer Center [19]	Academic Medical Center [18 b]
Jonnson Cancer Center at UCLA	ACRIN	450[a]	Yes	Yes
Beth Israel Deaconess Medical Center	ACRIN	582	Yes	Yes
University of Michigan Medical Center	ACRIN	915	Yes	Yes
Dartmouth-Hitchcock Medical Center	ACRIN	372	Yes	Yes
The Cancer Institute of New Jersey	ACRIN	610[a]	Yes	Yes
Wake Forest University	ACRIN	840	Yes	Yes
St. Elizabeth Health Center	ACRIN	128	No	No
Brown University, Rhode Island Hospital	ACRIN	699	No	Yes
The University of Texas M.D. Anderson Cancer Center	ACRIN	571	Yes	Yes
University of California, San Diego	ACRIN	527	Yes	Yes
Mayo Clinic, Jacksonville	ACRIN	214	No	Yes
Moffit Cancer Center, University of South Florida	ACRIN	206	Yes	Yes
Emory University	ACRIN	569	Yes	Yes
Northwestern University	ACRIN	848	Yes	Yes
University of Iowa	ACRIN	687	Yes	Yes
Jewish Hospital Rudd Heart and Lung Center	ACRIN	1,012[a]	No	Yes
Ochsner Medical Center	ACRIN	719	No	Yes
Johns Hopkins University	ACRIN	918	Yes	Yes
Mayo Clinic, Rochester	ACRIN	859	Yes	Yes
University of Pennsylvania	ACRIN	752	Yes	Yes
Medical University of South Carolina	ACRIN	696	Yes	Yes
Vanderbilt University	ACRIN	842	Yes	Yes
Brigham and Women's Hospital	ACRIN	763	Yes	Yes
University of Alabama at Birmingham	LSS	1097	Yes	Yes
University of Colorado Denver	LSS	395	Yes	Yes
Pacific Health Research and Education Institute	LSS	NA	No	No
Henry Ford Health System	LSS	799[a]	No	Yes
University of Minnesota School of Public Health	LSS	808	Yes	Yes
Washington University School of Medicine	LSS	1284	Yes	Yes
University of Pittsburgh Medical Center	LSS	1601	Yes	Yes
University of Utah Health Sciences Center	LSS	466	Yes	Yes
Georgetown University Medical Center	LSS	406	Yes	Yes
Marshfield Clinic Research Foundation	LSS	504[a]	No	Yes

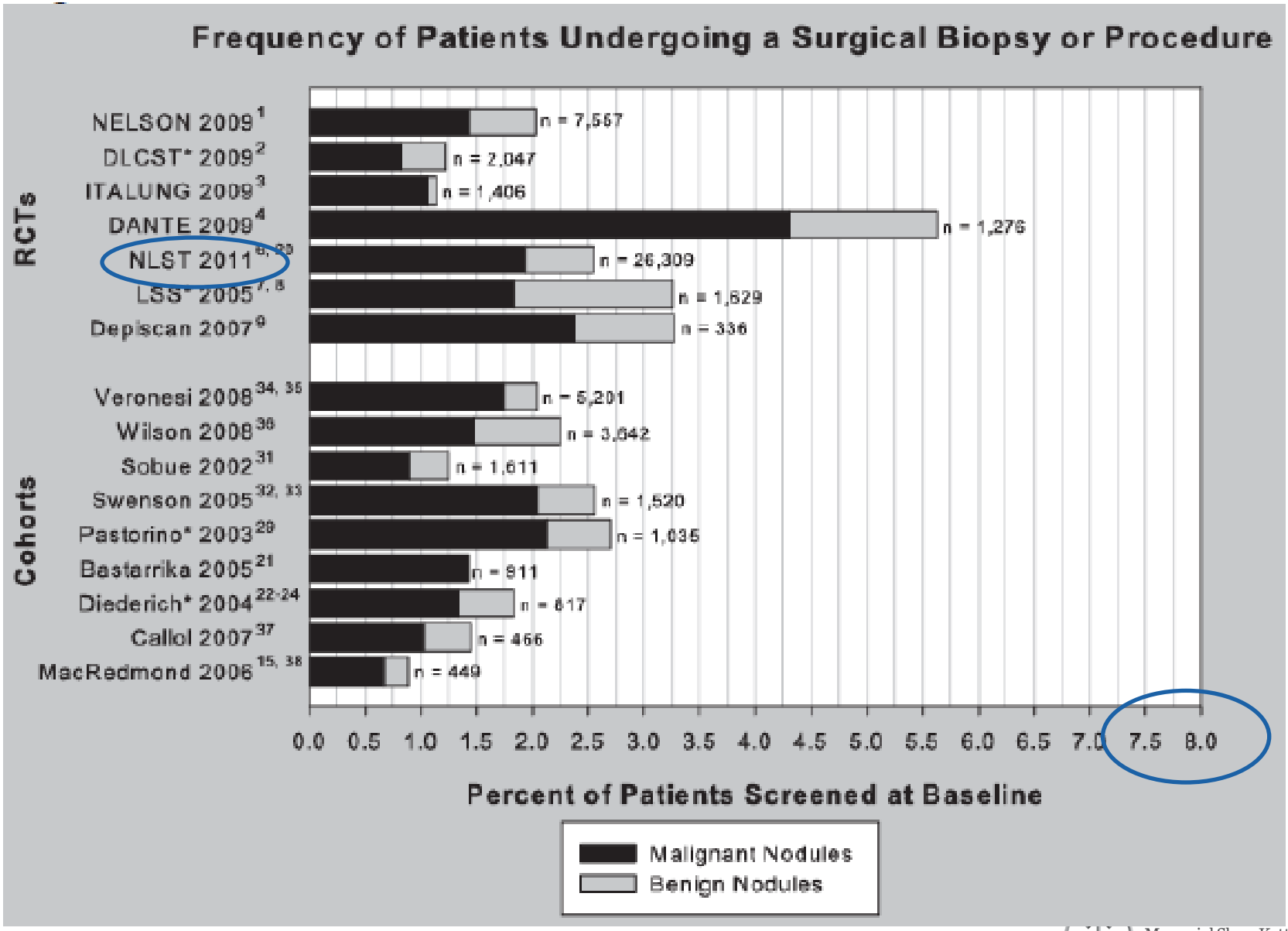
False positive rates: not consistent





19 false positives and 1 true positive (95% false positive rate)

Rate of invasive followup procedures: inconsistent



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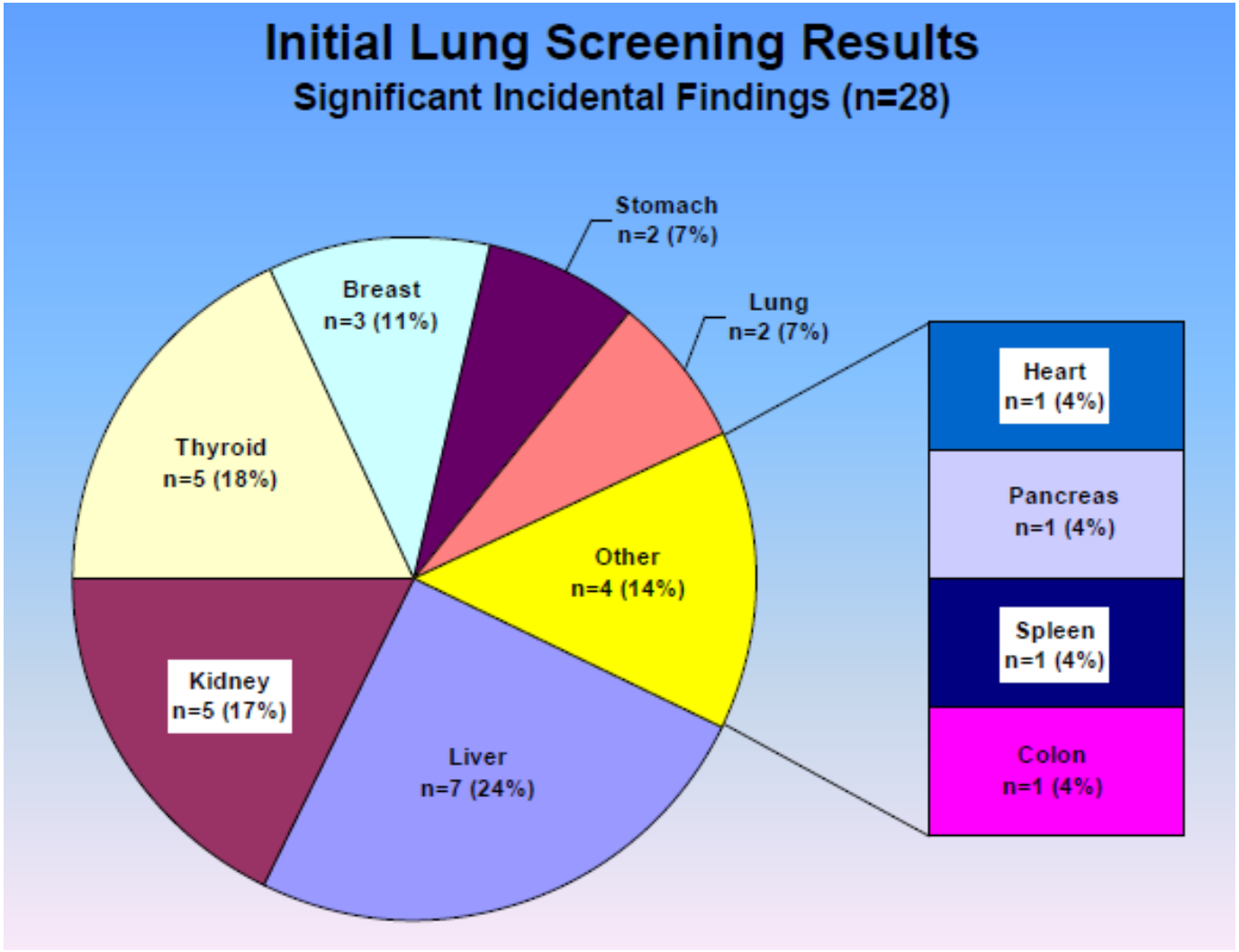
Reproducibility of lung cancer mortality reduction

Study	OR (< 1 favors CT)	95% CI lower bound	95% CI upper bound
DANTE	0.94	0.5	1.75
DLCST	1.37	0.63	2.98
MILD	2.5	0.98	6.36
NLST	**0.8**	**0.7**	**0.92**
Pooled (random effects)	1.09	0.7	1.68
Pooled (fixed effects)	0.84	0.74	0.96

Reproducibility of mortality from causes other than lung cancer

Study	OR (<1 favors CT)	95% CI lower bound	95% CI upper bound
DANTE	0.97	0.56	1.7
DLCST	1.49	0.94	2.37
MILD	2.13	1.05	4.34
NLST	**0.98**	**0.91**	**1.05**
Pooled (random effects)	1.21	0.87	1.67
Pooled (fixed effects	0.99	0.93	1.07

Need to know more about – Incidental Findings: Lahey Clinic experience



NLST: reproducibility of adherence

- NLST: Compliance with screening:
  - 98.5% - 92% - 90%
- DLSCT: 100% - 96% - 95%
- Pittsburgh study (PLUSS): 97% - 89%
- Menezes et al 2010 (I-ELCAP): 100% - 80% - 20%
- Mayo clinic study: 100% - 97%

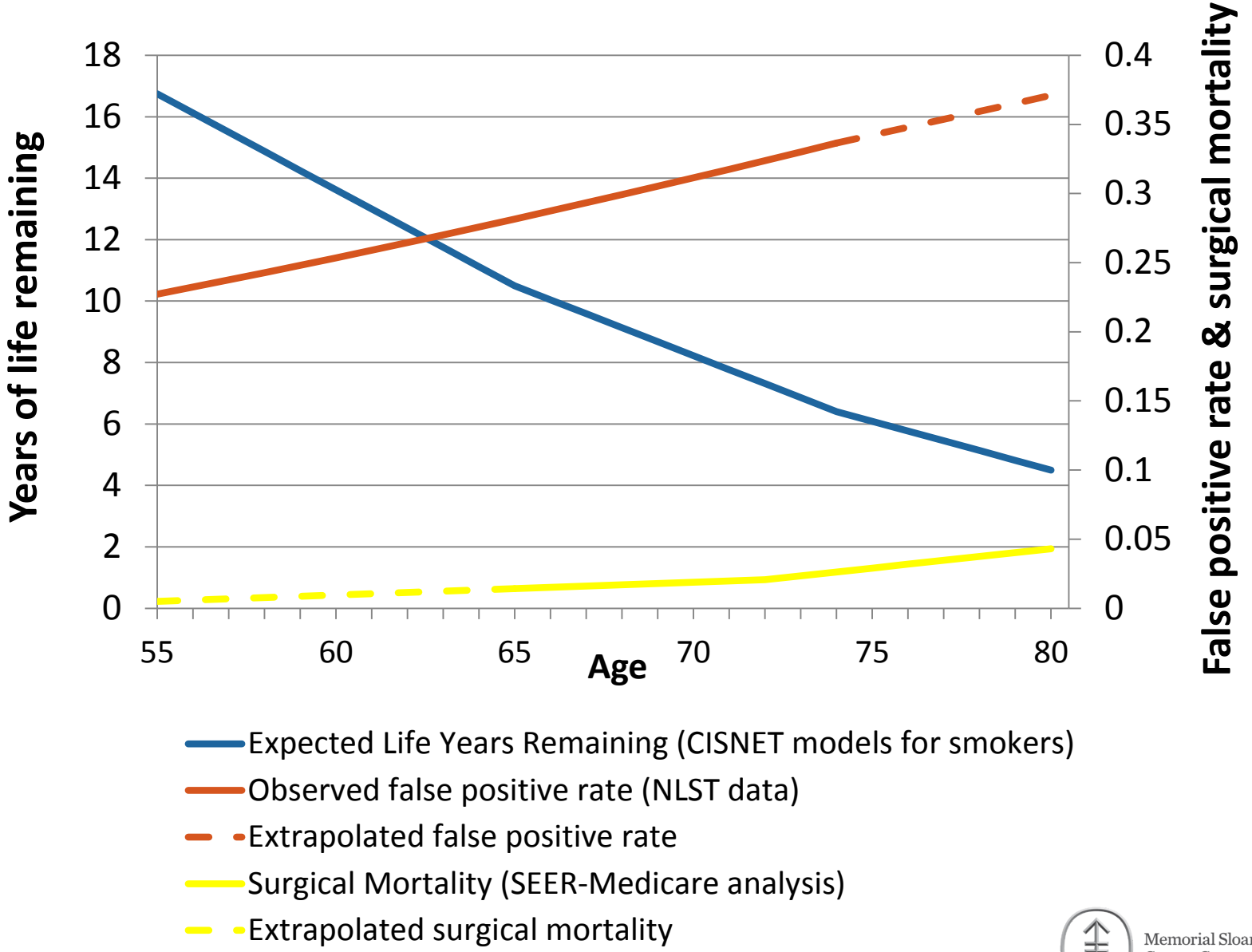
What to do about unstudied groups? Unstudied durations?

- Where we have no data:
  - Screening over 74
  - Screening for longer duration
  - Screening in 'real world' settings
- What can we infer?
- Can we trust the 'models' for extrapolating into future years?

Inference: older age groups

- NLST: fewer than 12% of subjects over age 70 at entry, none over 74
- Rising age and its tradeoffs:
  - Good: Risk of lung cancer rises (lowers number needed to screen)
    - Large differences: 80 yr old with 50 pyrs is at 11-times the 6-year risk of death from lung cancer compared to a 55 year old with 30 pyrs (4.5% vs 0.4%)
  - Bad:
    - Risk of false positives rises (more harm to those not benefitting)
    - Life expectancy falls (less benefit per 'saved life')
    - Risk of surgical death rises (reduces net benefit)

Bad trends with advancing age



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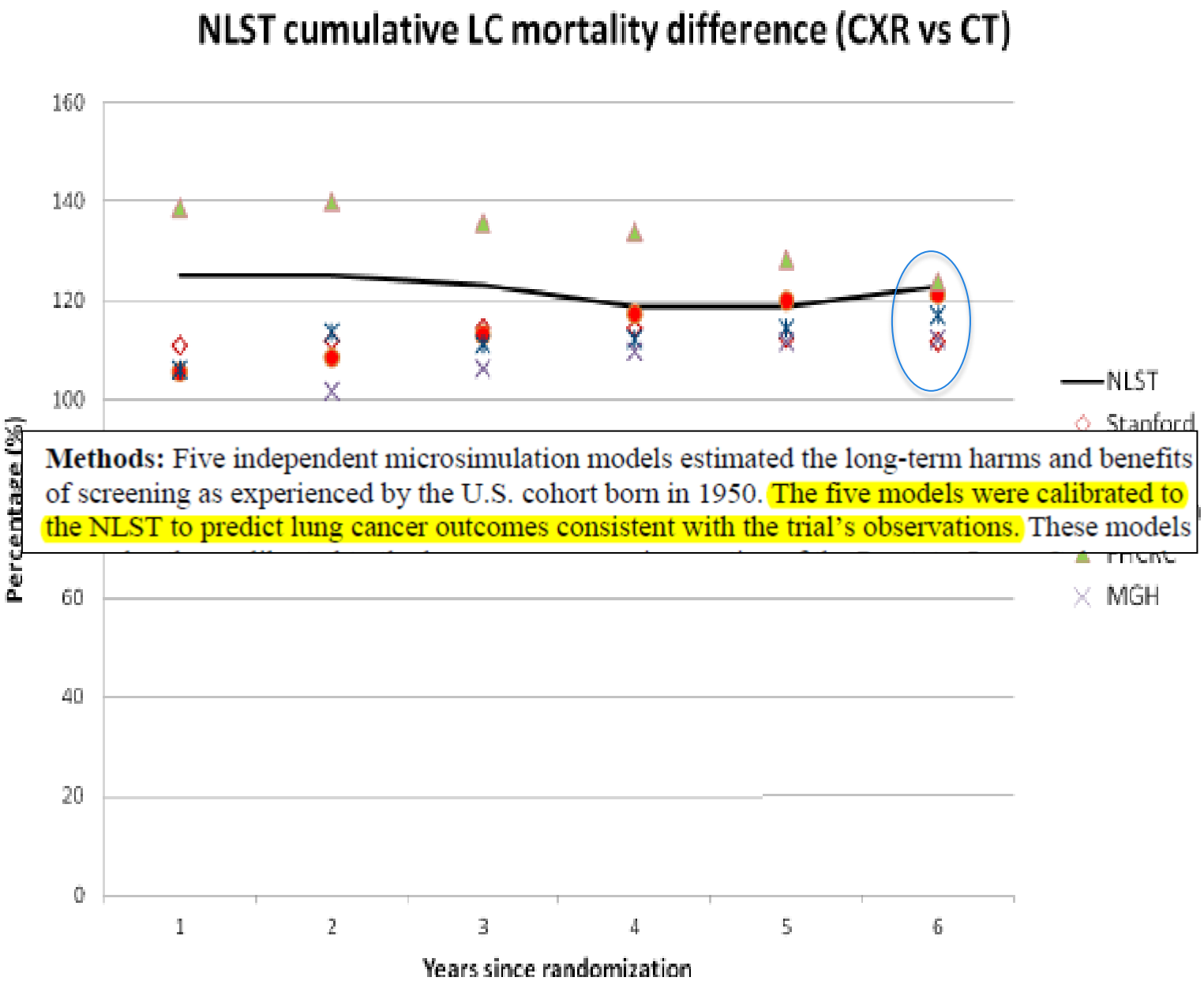
Screening for longer duration (relies on models)

- CISNET models don't match each other, so which one is right (or most are wrong)
  - Life years gained per 100,000 persons ranges from 2,020 to 10,153
  - Number of persons overdiagnosed ranges from 72 to 426
- CISNET models don't mimic the 'present', so can't be relied on to forecast the 'future'

CISNET models don't predict shape of NLST benefit

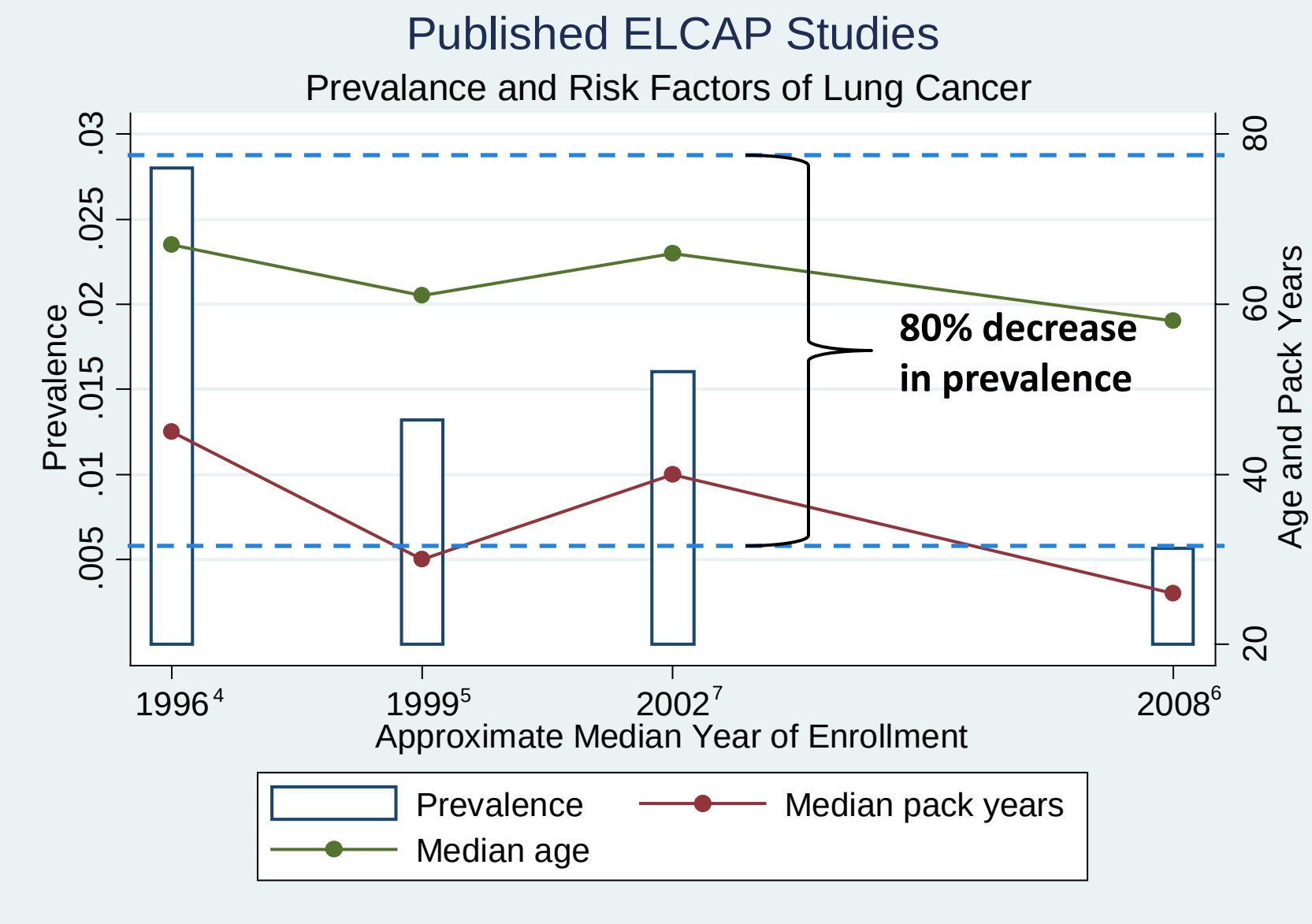


Methods: Five independent microsimulation models estimated the long-term harms and benefits of screening as experienced by the U.S. cohort born in 1950. The five models were calibrated to the NLST to predict lung cancer outcomes consistent with the trial's observations. These models

Harm minimization

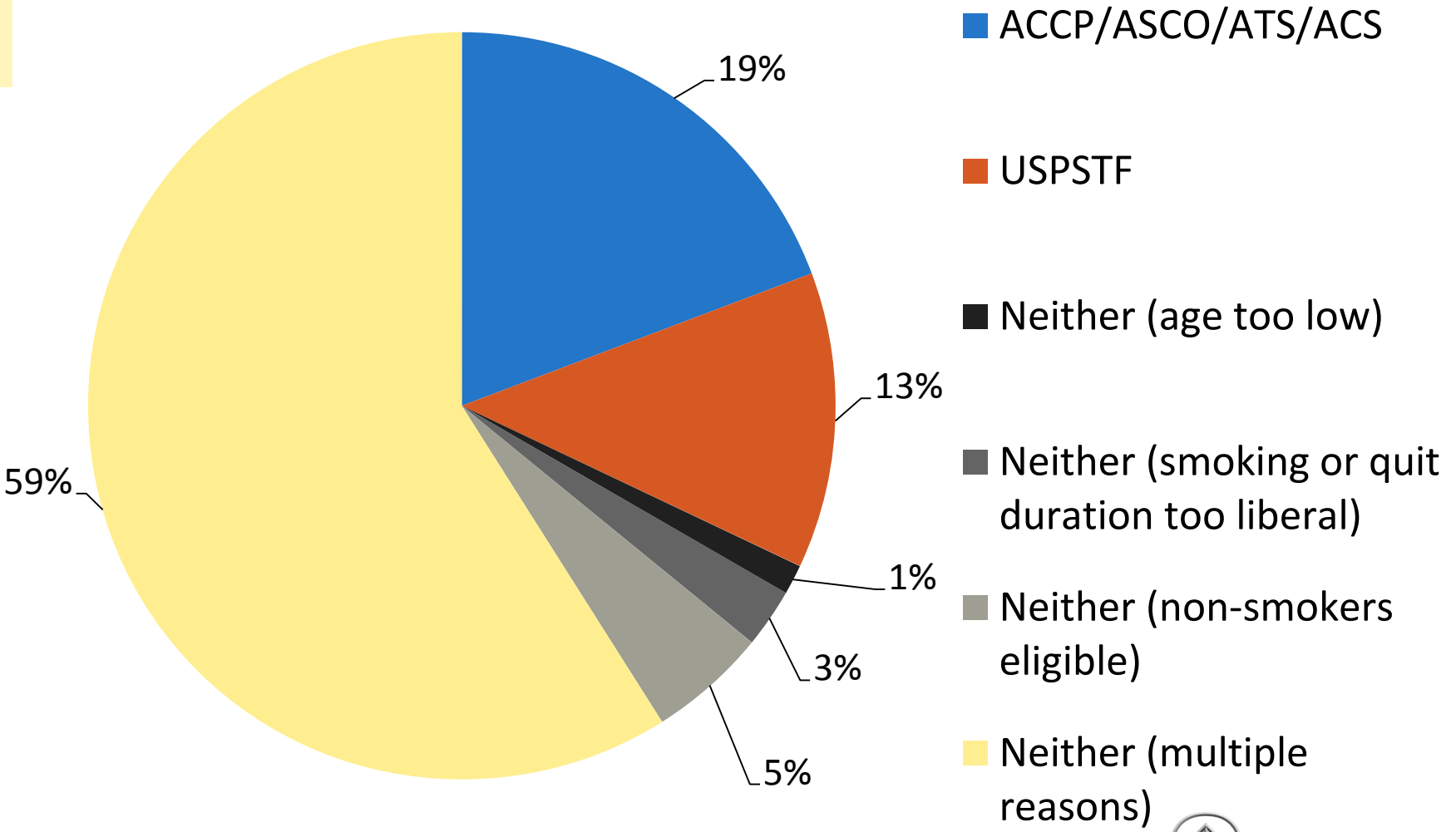
- Reasons for optimism:
  - Numerous efforts to codify approach to false positives ("LungRADS")
  - Efforts underway to create standards for follow-up and biopsies
- But some caution:
  - Statements that we can reduce 'false positives' may not accurately interpret data
  - 'Trusted lists of screening sites'??

Many things changing at once



Bach PB, Gould MK, Silvestri GA. Avoid False Positives in Low Risk Individuals by Not Screening Them. *Annals of Internal Medicine*. 2013. http://annals.org/article.aspx?articleid=1583810.

List of "trusted" sites (n=78)*
(Lung Cancer Alliance 2014)



***Sample was 1st half of listed US States**

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JOHN MUIR HEALTH

Lung Cancer Early Detection

John Muir Health is one of the country's leading institutes in researching early lung cancer detection techniques when the cancer is most treatable.

Through our participation in the I-ELCAP early lung cancer detection study, we have been able to detect a patient's lung cancer before symptoms develop. To be eligible for participation, you must:

- Be between 40-80 years old
- Have a long history of heavy smoking
- Or have an immediate family member with lung cancer
- Or have been exposed to radon gas or asbestos

http://www.johnmuirhealth.com/services/cancer-services/what-we-treat/lung-cancer-services/early-detection.html

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Risk and individual decision making

- Every guideline recommends shared decision making:
- Why? Risk varies predictably, so does benefit
- Decision tools are in development

Guidelines recommending shared decision making

cancer. The recommendations of the AATS task force are

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

pport individualized decision

Shared Decision Making

Shared decision making is important for persons within the population for whom screening is recommended. The benefit of screening varies with risk because

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tain. The decision to begin screening should be the result of a thorough discussion of the possible benefits, limita-

Findings from

rial established that lung cancer mortality in specific

screening. The choice to undergo lung cancer screening must be an individual one and the ALA should ensure that every patient has the information they need to make an informed decision. Patients should be informed beforehand about possible increased risk of radiation exposure, all possible follow-up procedures in the event of an abnormal finding, and the risks and costs of such procedures. Patients

smoke or have quit within the past 15 years. A process of informed and shared decision-making with a clinician related to the potential benefits, limitations, and harms associated with screening for lung cancer with low-dose computed tomography should occur before any decision is made to initiate lung cancer screening. Smoking cessation counseling remains a high priority for clinical attention in discussions with current smokers, who should be informed of their continuing risk of lung cancer. Screening should not be viewed as an alternative to smoking cessation. CA Cancer J Clin 2013;000:000-000. ©2013 American Cancer Society.

Remark 1

Counseling should include a complete description of potential benefits and harms (as outlined in the full guideline text) so the individual can decide whether to undergo LDCT screening.

Remark 6

The most effective duration or frequency of screening is not known.

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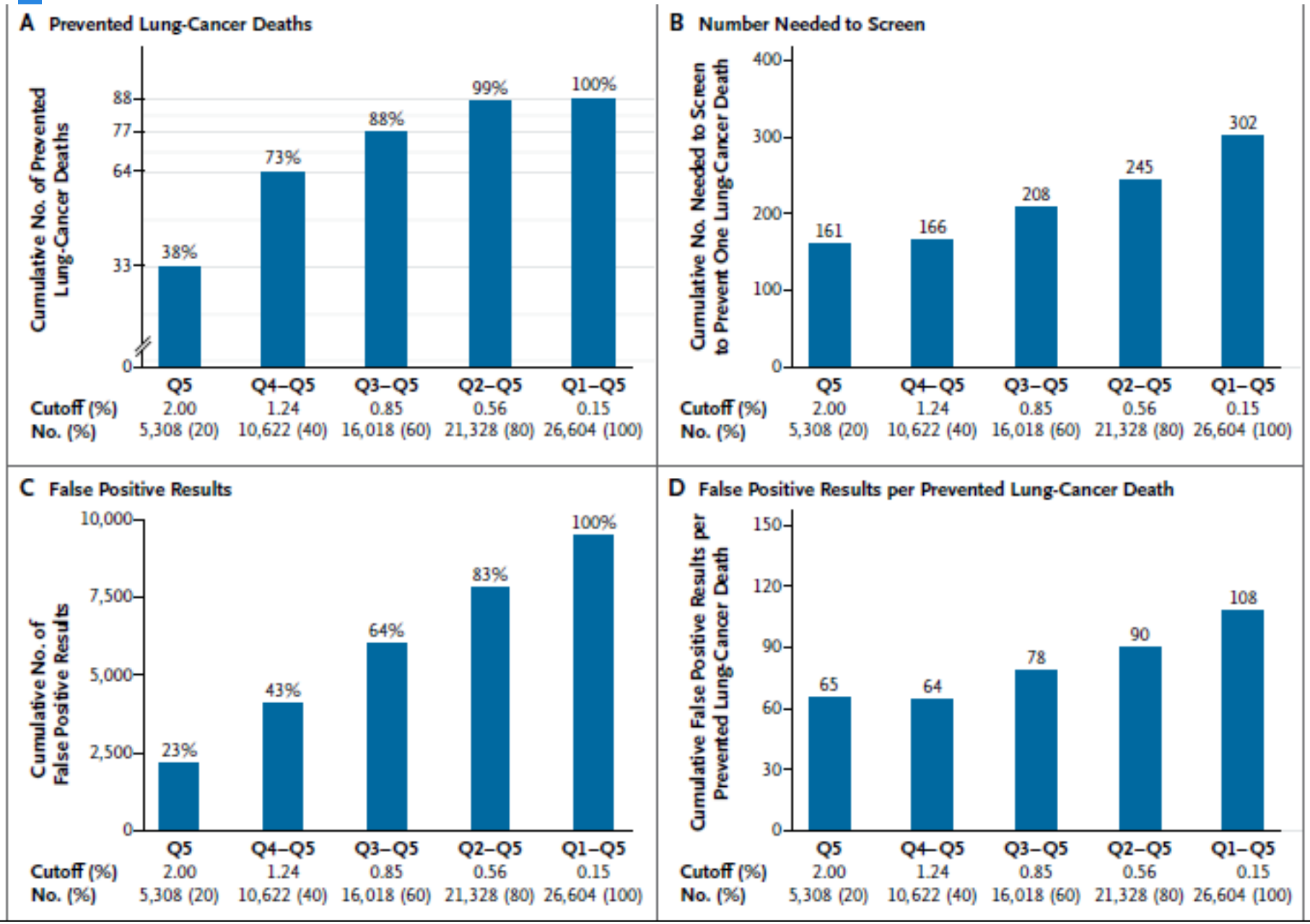
Risk variation in the NLST



Kovalchik SA, et al. Targeting of low-dose CT screening according to the risk of lung-cancer death. N Engl J Med. 2013;369(3):245-54.

Benefit travels with risk of disease

Table. Projected Likelihood Over 6 Years of Lung Cancer Death With or Without Screening per 1000 Persons Screened*

Participant	Risk Factors	Deaths From Lung Cancer (Without Screening) per 1000 Persons, *n*	Deaths From Lung Cancer (With Screening) per 1000 Persons, *n*	Lung Cancer Deaths Averted per 1000 Persons, *n*	Persons Needed to Be Screened Annually for 3 y to Prevent 1 Death From Lung Cancer Over 6 y, *n*
"Typical" participant in the NLST	62-year-old male current 1.5-PPD smoker for 35 y	19.5	15.6	3.9	256
Minimum eligible participant in the NLST	55-year-old female former 1-PPD smoker for 30 y who just quit	4.0	3.2	0.8	1236
High-risk participant eligible for the NLST	70-year-old current 2-PPD smoker for 55 y	60.9	48.7	12.2	82
Minimum eligible participant by NCCN guidelines	50-year-old male former 1-PPD smoker for 20 y who quit 10 y ago with an occupational asbestos exposure history	1.6	1.3	0.3	3180
Low-risk eligible participant for Sequoia Hospital lung screening program	40-year-old female former 1-PPD smoker for 10 y who quit 15 y ago	0.10	0.08	0.02	35 186

NCCN = National Comprehensive Cancer Network; NLST = National Lung Screening Trial; PPD = packs per day.
* Assuming the program includes 3 annual y of screening.

When the Average Applies to No One: Personalized Decision Making About Potential Benefits of Lung Cancer Screening

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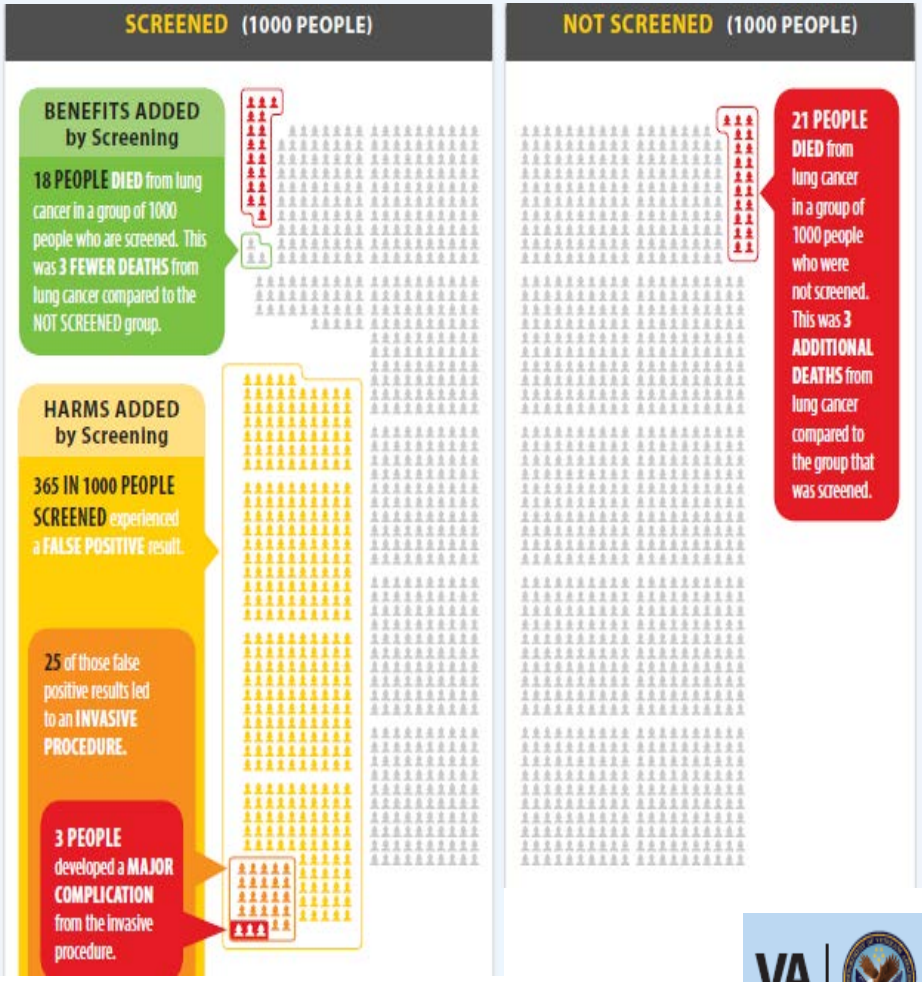
Peter B. Bach, MD, MAPP, and Michael K. Gould, MD, MS

Decision tools under piloting

Benefits and Harms Experienced by People Ages 55–74 Who Were Screened for Lung Cancer With Low-Dose CT Scans Once a Year for 3 Years as Compared to Those Who Were Not Screened*



pcori | Patient-Centered Outcomes Research Institute

Promoting Informed Decisions about Lung Cancer Screening

Principal Investigator

Robert J. Volk, PhD

Organization

University of Texas MD Anderson Cancer Center

Funding Announcement

Assessment of Prevention, Diagnosis, and Treatment Options

Lung screening assessment for 1,000 people like you over the next 6 years	
Out of 1,000 people like you who are NOT screened, number who will be diagnosed with and die from lung cancer	5.1
Out of 1,000 people like you who ARE screened, number who will die from lung cancer	4.1
Out of 1,000 people like you who ARE screened, the number of lives that will be saved	1.0
Number of people like you that would need to be screened in order for ONE of you to benefit	975

VA

Some thoughts on your questions

- Question 1: Do benefits outweigh harms in Medicare population:
  - Benefits and harms vary by individual based on risk factors, life expectancy, preferences
  - What about:
    - High risk adults over 74 years of age?
      - No empiric data, minimal empiric data over 70
    - Annual screening beyond 3 annual LDCT screens
      - No empiric data, models not reliable or in agreement
    - Outside a clinical study improves health outcomes
      - No outcome data, reasons for concern about selecting setting

MEDCAC Voting Questions

- Harm minimization
  - Some good things happening: Amer College of Radiology efforts on BiRADS type approach
  - Serious concerns that coverage will lead to explosion of inappropriate activities, driven by a mix of good intentions and unrestrained entrepreneurialism

MEDCAC Voting Questions

- How confident are you that clinically significant evidence gaps remain regarding the use of LDCT (average effective dose of 1.5mSv) for lung cancer screening in the Medicare population outside a clinical trial?
  - Large groups of potentially eligible patients not studied
  - Tend to be populations who may derive less benefit, be harmed more (elderly, less well educated)

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Thank you

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