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***James L.
Mulshine, MD***

***Acting Dean,
Rush Graduate
College***



IT'S HOW MEDICINE

SHOULD BE

Status of US Prevention & Screening Implementation



Disclosures/ Learning Objective

- No disclosures
- No experimental uses with investigational tools or drugs

Learning Objectives

- Lung cancer remains a dominant global public health problem
- Early stage cancer can be detected and cured economically
- International collaboration is require to accelerate progress in making screening better, safer and cheaper

Lung Cancer & Tobacco Status

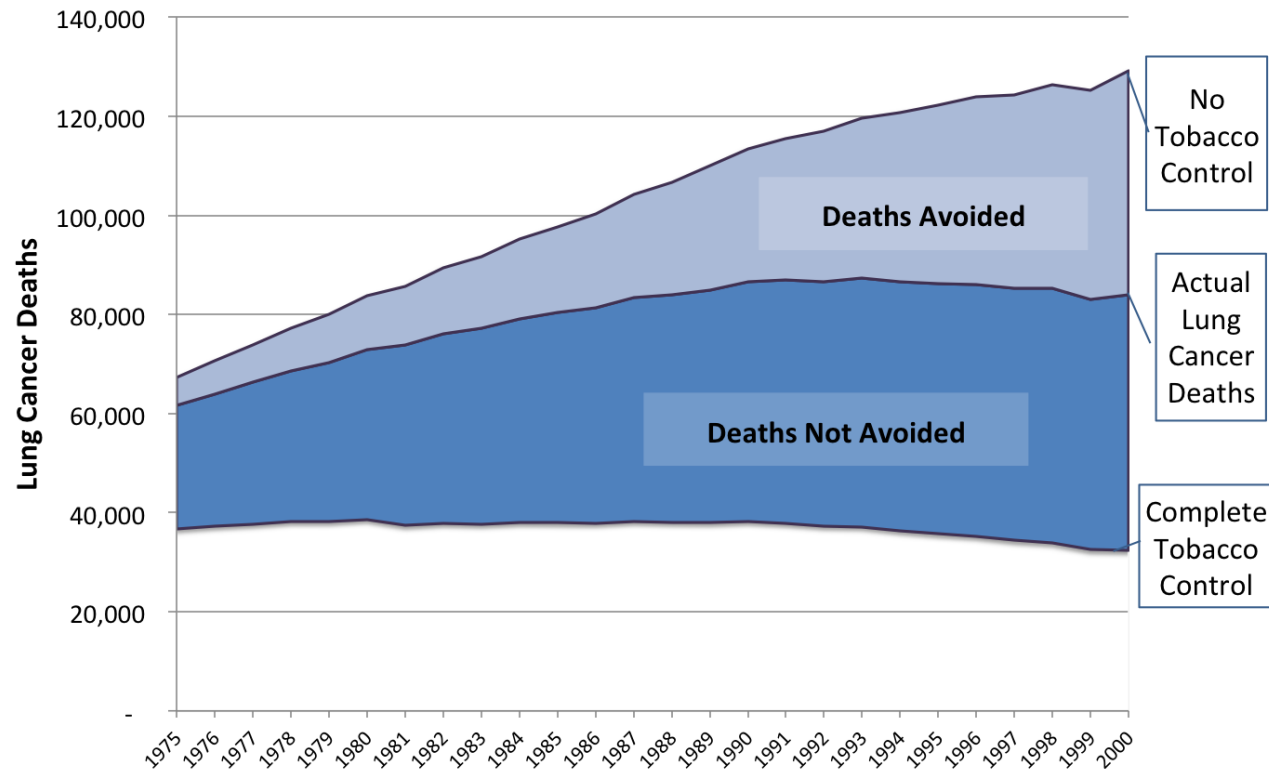
- Lung cancer remains the most common - and deadliest - cancer in the world, with an estimated 1.8 million new cases
- In 2012, 1.59 million deaths are expected in 2012 with more than 1/3 deaths in China
- There pollution will interact with tobacco exposures to further increase lung cancer rates
- As the world ages, lung cancer numbers will increase

What is Lung Cancer Screening?

- ***Screening is the pursuit of curable disease in asymptomatic populations***
- Proactive evaluation of a defined at-risk population
- Screening must advance the lung cancer diagnosis as reflected in eventual stage shift
- Advancing diagnosis extends sojourn time and effects the diagnostic approach (i.e. repeat scan in 6/12 months rather than do an immediate invasive diagnostic work-up)
- **Challenge is to maximize benefit while minimizing risk!**

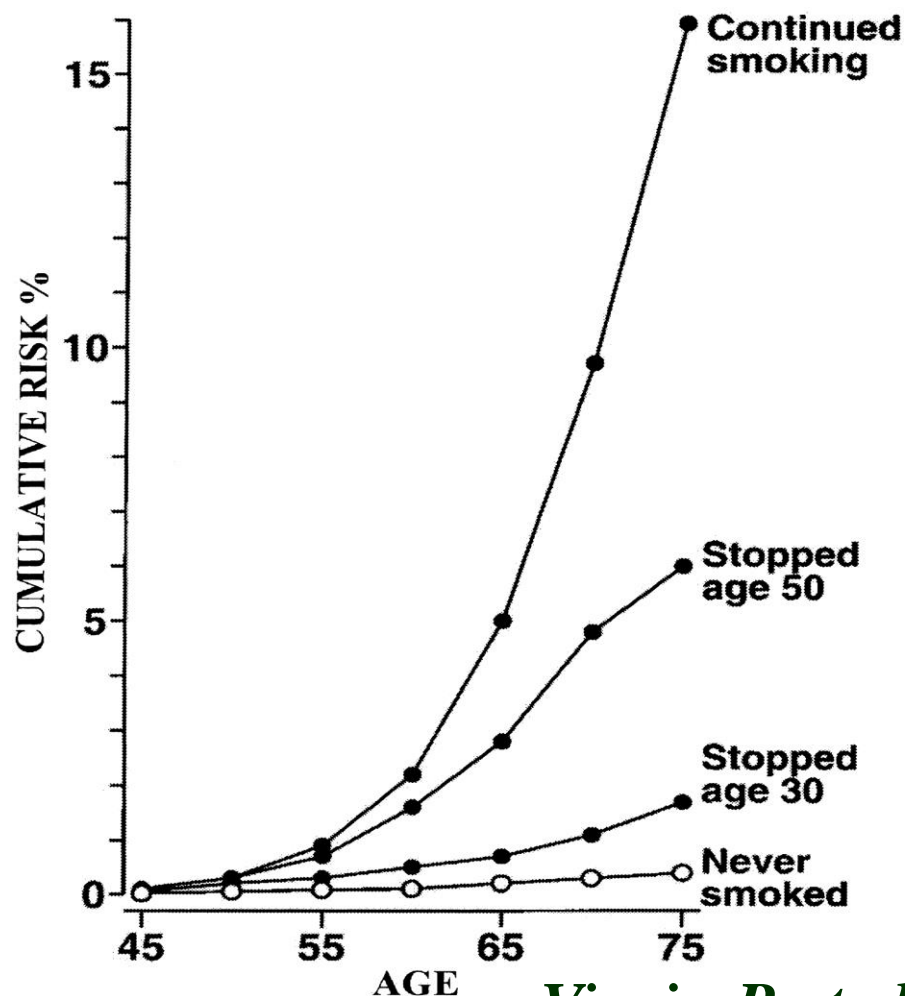
Progress Reducing Tobacco Mortality

Impact of Tobacco Control Efforts on Lung Cancer Deaths Among U.S. Males, 1975-2000



Why Lung Cancer Screening?

- **Symptom-detected lung cancer is lethal 90% of the time**
- **LDCT screening is a preventative service to detect lung cancer in asymptomatic, chronically tobacco-exposed populations in $\leq 1\%$, but then 60-80% of detected cases are Stage I**
- **Stage I is curable $\geq 70\%$ of the time**
- **Challenge is to enhance screening efficiency (i.e.- define favorable cohort, improve diagnostic w/u efficiency, improve safety of interventions, refine follow-up rates, integrate tobacco control, assess other thorax sites)**

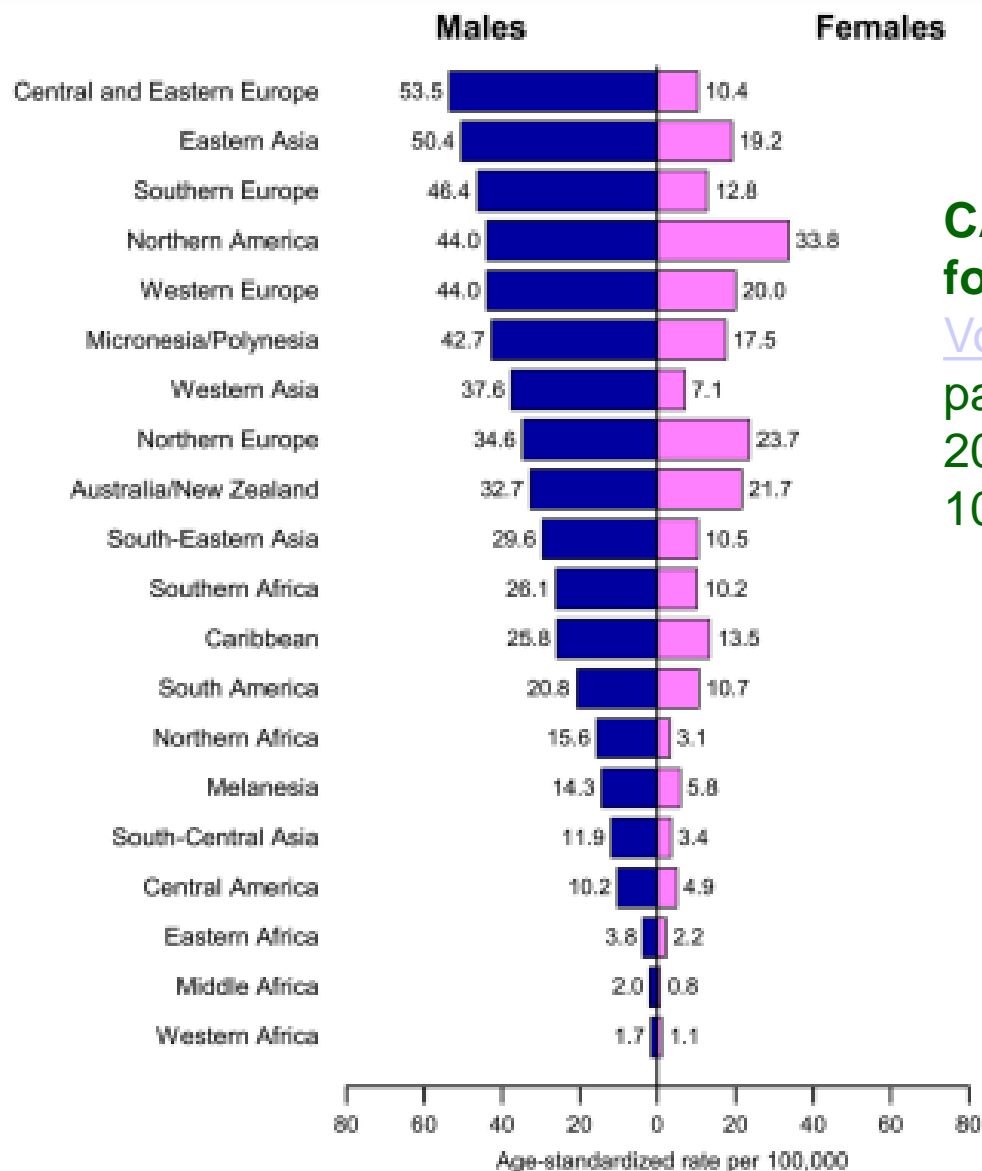


**Data from Sirs
Doll & Peto
unequivocally
demonstrates that
the risk of lung CA
after smoking
never returns to
normal**

Vineis, P. et al. JNCI 2004;96:99-106

- Cigarette smoking among adults, 18 & older who smoked 30 cigarettes or more a day went down significantly from 2005 -2012 – from 12.6- 7.0%
- Over 42 million American adults smoke cigarettes. (*CDC, Current cigarette smoking among adults – United States, 2005–2012, 2014*)
- From 2009-2012 US smoking-attributable economic annual costs were \$289-\$332.5 billion including \$132.5 to 175.9 billion for direct medical care of adults. (*US Surgeon General Report 2014*)

Lung Cancer Incidence Rates by Sex and World Area



**CA: A Cancer Journal
for Clinicians**

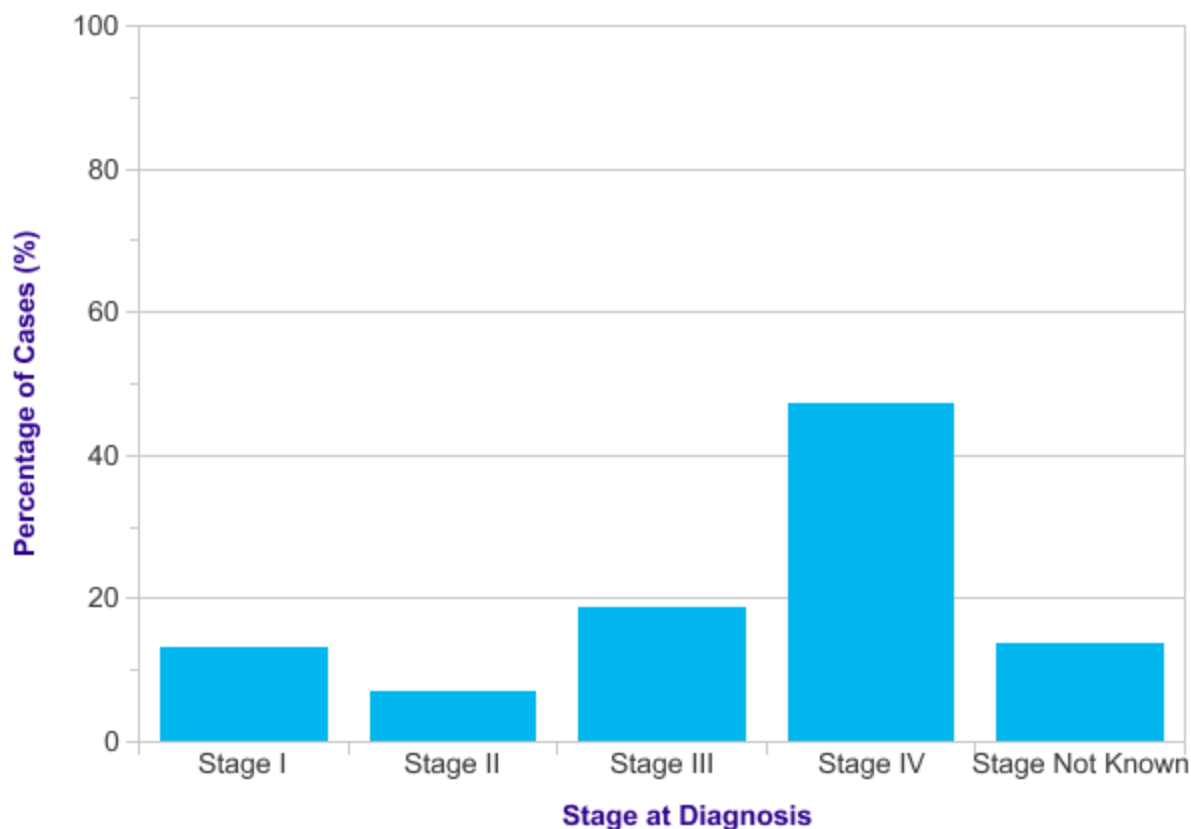
Volume 65, Issue 2,
pages 87-108, 4 FEB
2015 DOI:
10.3322/caac.21262

Rank Country: Lung Cancer Rate

• 1Hungary	51.6		
• 2Serbia	45.6		
• 3Korea	44.2	•Netherlands	37.2
• 4FYR Macedonia	40.8	•12Fr. Polynesia	37.1
• 5NewCaledonia	40.1	•13Belgium	36.8
• 6Montenegro	39.6	•14China	36.1
• 7Denmark	39.2		
• 8US	38.4		
• 9Poland	38.0		
• 10Canada	37.9		

CR-UK Lung Cancer By Stage

Proportion of Cancers Diagnosed at Each Stage, All Ages, England



Major Causes of Death

Spain*	United States#
Cancer	Heart Disease
Heart Disease	Cancer
Cerebrovascular Disease	Chronic Lower Respiratory Diseases
Chronic lower respiratory disease	Cerebrovascular Disease

*

STATISTICS 2013 MINISTRY OF HEALTH, SOCIAL SERVICES AND EQUALITY

Four leading causes account for 60% of deaths

National Vital Statistics Reports, CDC, 2013

Comparison NLST and NELSON Cancer Detection and Stage I Rates T0, T1

NLST

- ROUND 1 NO. OF CA/TOTAL SCREENED 168/24,715 (0.67%)
- ROUND 2 NO. OF CA/TOTAL SCREENED 211/24,102 (0.87%)
- Stage 1/All Cases T0- 104/165 (63%)

NELSON

- ROUND 1 STAGE I/ALL DETECTED CA 40/7289 (0.5%)
- ROUND 2 STAGE I/ALL DETECTED CA 57/7289 (0.8%)^a
- Stage 1/ All CA Cases T0- 42/57 (73.7%)

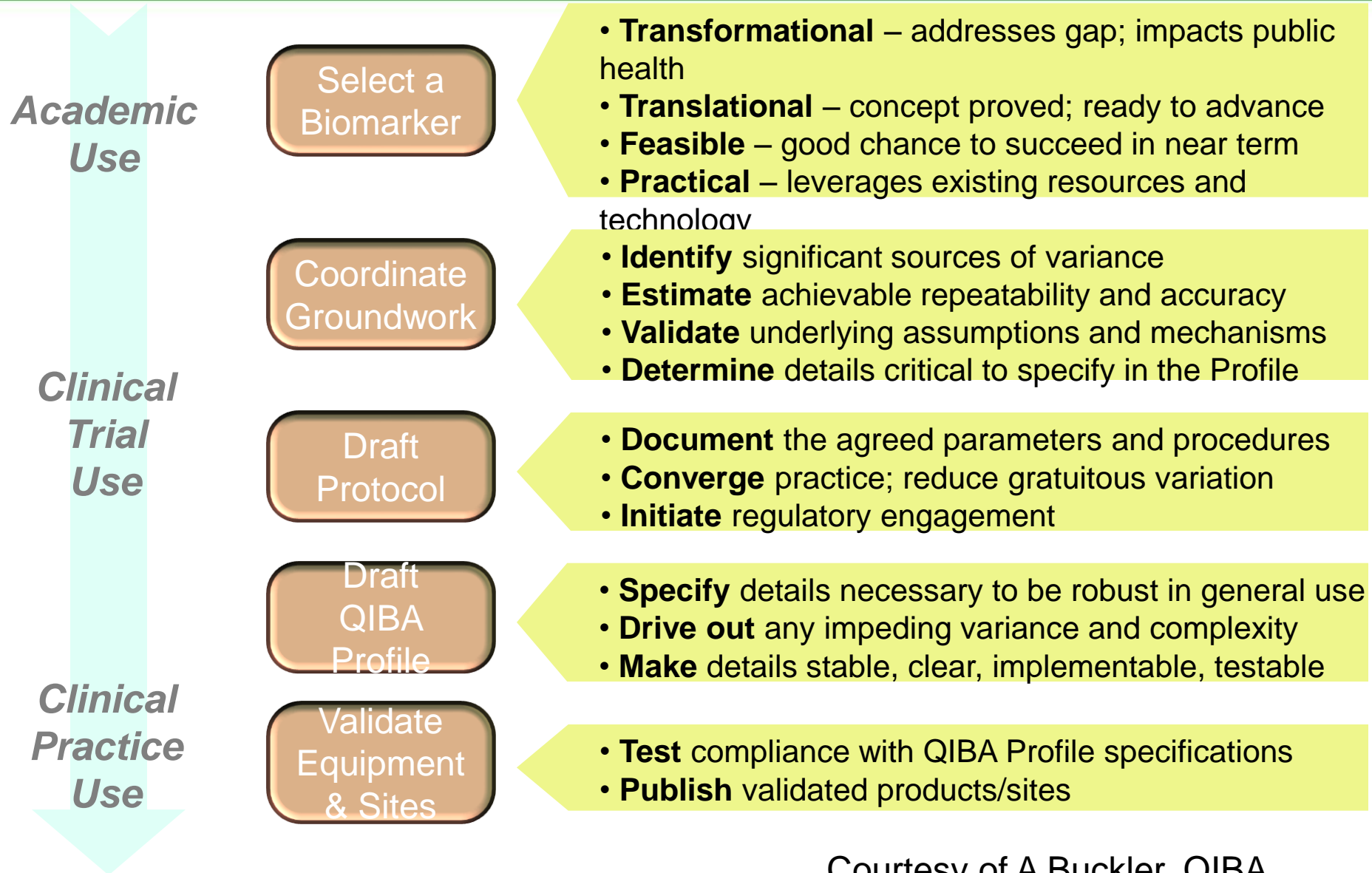
Mulshine, JL, D'Amico TA. Cancer J Clin: 2014 doi: 10.3322/caac.21239.
PMID: 24976072

Lung RADS Assessment Categories

Descriptor Primary Category	
Incomplete	- 0
Negative	-1
Benign Appearance or Behavior	
-2 Probably benign	-3
Suspicious	
6 month LDCT	-4A
3 month LDCT	-4B.
Significant - other	-S
Prior Lung Cancer	-C

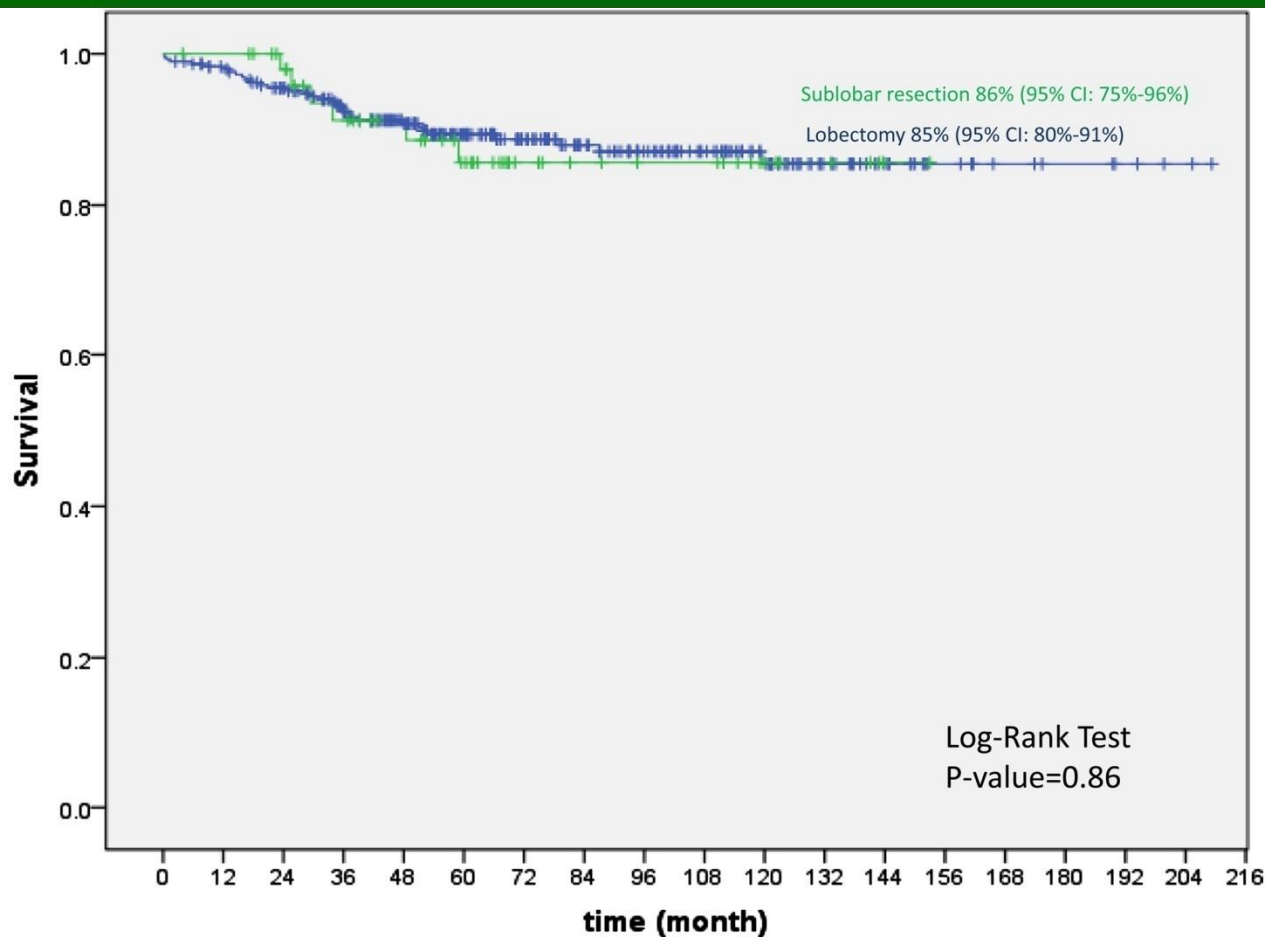
Lung-RADS™ Version 1.0 Assessment Categories Release date: April 28, 2014

QIBA Process – “Industrializing Biomarker Use”



Courtesy of A Buckler, QIBA

Lesser Surgery in Stage Ia Lung CA



No. at risk

Lobectomy	294	281	262	234	203	162	132	106	88	71	52	31	20	12	8	6	4	2	0
Sublobar resection	53	52	47	40	35	28	18	15	13	13	7	5	1	0	0	0	0	0	0

Altorki N et al (J Thorac Cardiovasc Surg 2014;147:754-64)

Outcomes with IA Solid NSCLC

Univariate and multivariate analyses for overall survival after sublobar resection

Variable	Univariate	Multivariate		
	<i>p</i> value*	Hazard ratio	95 % CI	<i>p</i> value*
Age (year)	0.3121			
Gender (female)	0.0404	0.384	0.105–1.400	0.1470
Pack-year smoking	0.7737			
Maximum tumor size (c-T1a)	0.0077	0.283	0.103–0.776	0.0141
Radiological part-solid tumor	0.0455	0.290	0.079–1.066	0.0623
Serum CEA level (CEA ≤3.0 ng/ml)	0.0032	0.303	0.096–0.961	0.0426
Operative mode (segmentectomy)	0.1949			
Histology (adenocarcinoma)	0.0218	0.588	0.211–1.644	0.3116

Hattori A et al. Gen Thor Cardiovasc Surg Online 10/20/15

Cost/LYS & Life Expect. Lung CA Screening (50-64yrs) Baseline Scenario

Impact from stage-shift model.

• Cumulative life-years saved	2,297,504
• Lead time adjustment	598,062
• True life years saved	1,699,442
• Cost per additional life-year	\$ 18,862
• Life expect. lung CA no screening	5.71 yrs
• Life expect. lung CA with screening	9.50 yrs

Goldberg et al. Popul Health Manag. 2010;13(1):33-46

Goal for Lung Cancer Screening

- Actuarial simulation model predicts over the next fifteen years 985,284 quality adjusted life years could be saved
- With the addition of smoking cessation to that screening process, the cost utility ratio of quality adjusted life years could be reduced from \$28,240 to \$16,198 per life year gained.

A. Vilanti et al PLOS One 8: e71379, 2013

- LDCT saved 51,000 QALY at an incremental cost-effectiveness ratio of \$52,000/QALY
- An adjunct smoking cessation program improving the quit rate by 22.5% improves the incremental cost-effectiveness ratio to \$24,000/QALY.

Goffin JR et al. Cost-effectiveness of Lung Cancer Screening in Canada. JAMA Oncol. 2015 Sep;1(6):807-13. doi: 10.1001/jamaoncol.2015.2472.

RIGHTS AND EXPECTATIONS

THE RIGHTS OF THE PEOPLE

- You have the right to know if you are at risk for lung cancer.
- You have the right to know that well-organized low-dose CT screening has been shown to significantly reduce the possibility of dying from lung cancer.
- You have the right to clear and unbiased information on the risks and benefits of CT screening.
- You have the right to fair and equitable access to medically appropriate CT screening.
- You have the right to timely and compassionate care if you are diagnosed with lung cancer.
- You have the right to donate your scans and biological specimens to lung cancer research to help find additional life-saving cures.
- You have the right to ask screening sites if they follow the Guiding Principles for Lung Cancer Screening Excellence and provide care in a multi-disciplinary continuum.

LUNG CANCER ALLIANCE COMMITTS TO THE FOLLOWING: WE WILL

ESTABLISH the Lung Cancer Screening Excellence Forum, an ongoing assembly of thought leaders to develop the mechanism for data and specimen collection, and for incorporating validated imaging and biomedical advances into screening and the continuum of care.

CONTINUE to provide responsible and timely information on lung screening and research advancements to the public.

CONTINUE to inform the public of those sites committed to providing lung cancer screening within a continuum of care following best practices.

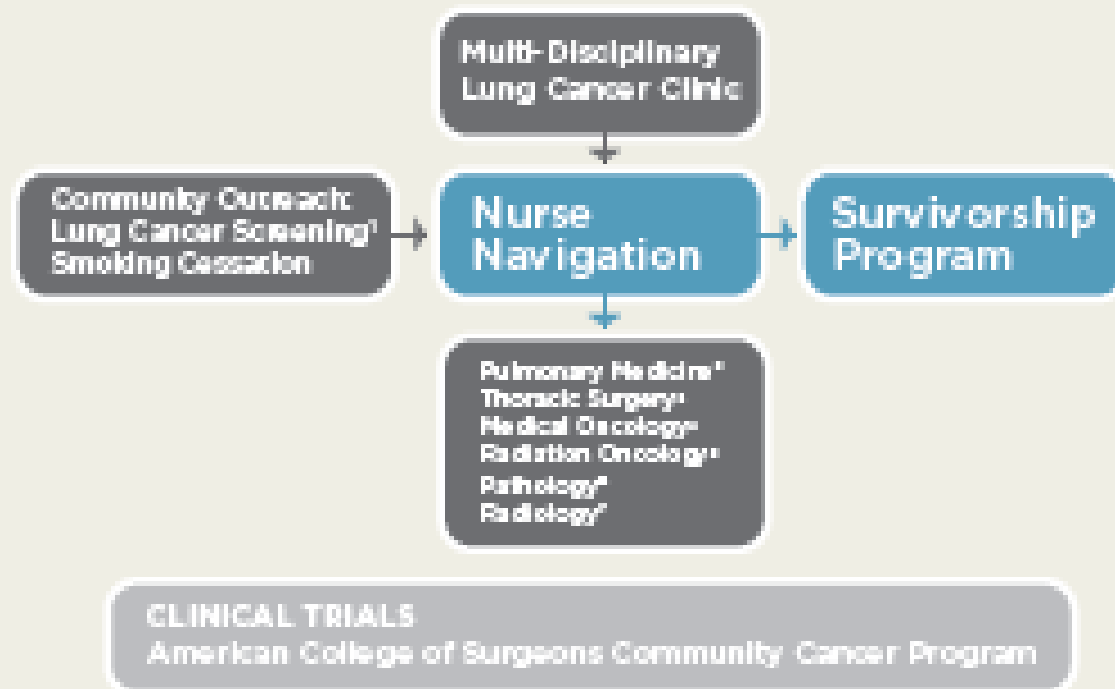
CONTINUE to work collaboratively with the medical community to provide the public and patient perspective.

CONTINUE to support research in imaging, targeted therapies and the molecular signatures of precancerous cellular environments, risk and malignancy for all types of lung cancers.

CONTINUE to work with all stakeholders to support measures to reduce tobacco exposure in our society, as well as to collaborate with partners to address issues contributing to the stigmatization of lung cancer and work to reduce disparities in the delivery of quality lung cancer screening services.

Framework and Continuum of Care

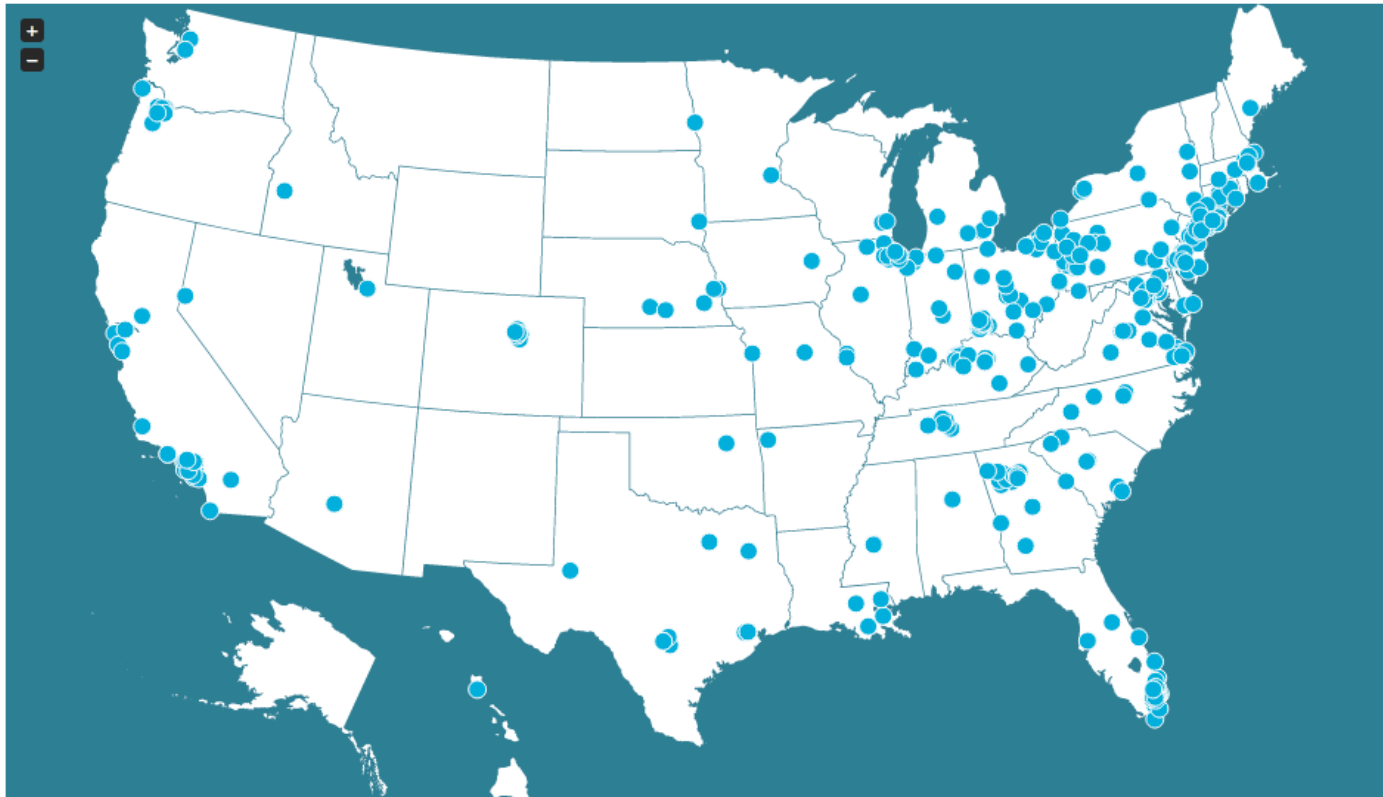
THE PATIENT EXPERIENCE



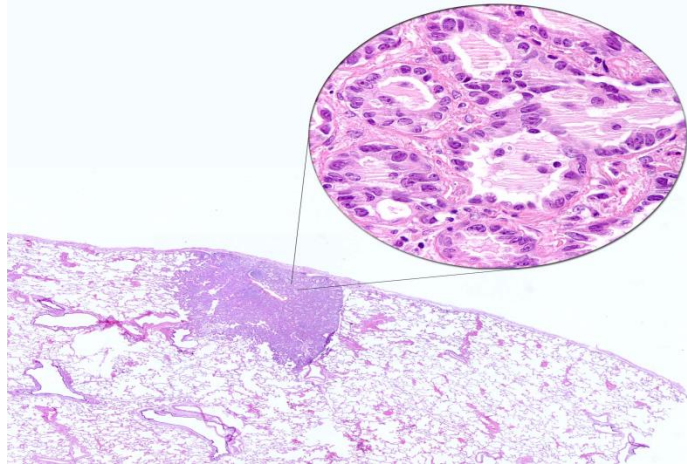
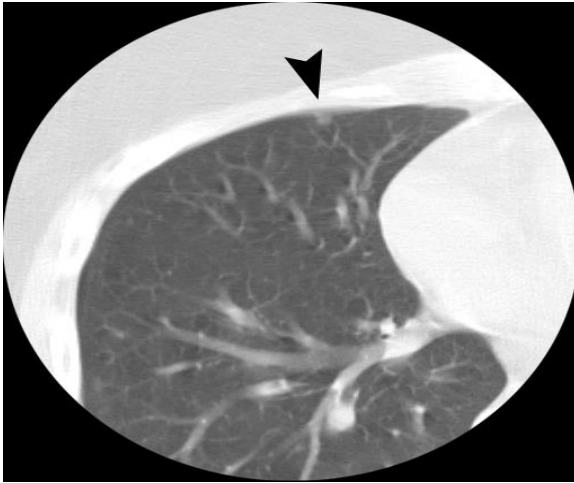
Percolation of Framework Sites

Screening Centers of Excellence

To see a listing of Screening Centers of Excellence near you, please click on your state or select from the list below. Use your mouse wheel to zoom in for a closer look at centers near you. You may also click and hold to drag the map to a new position.



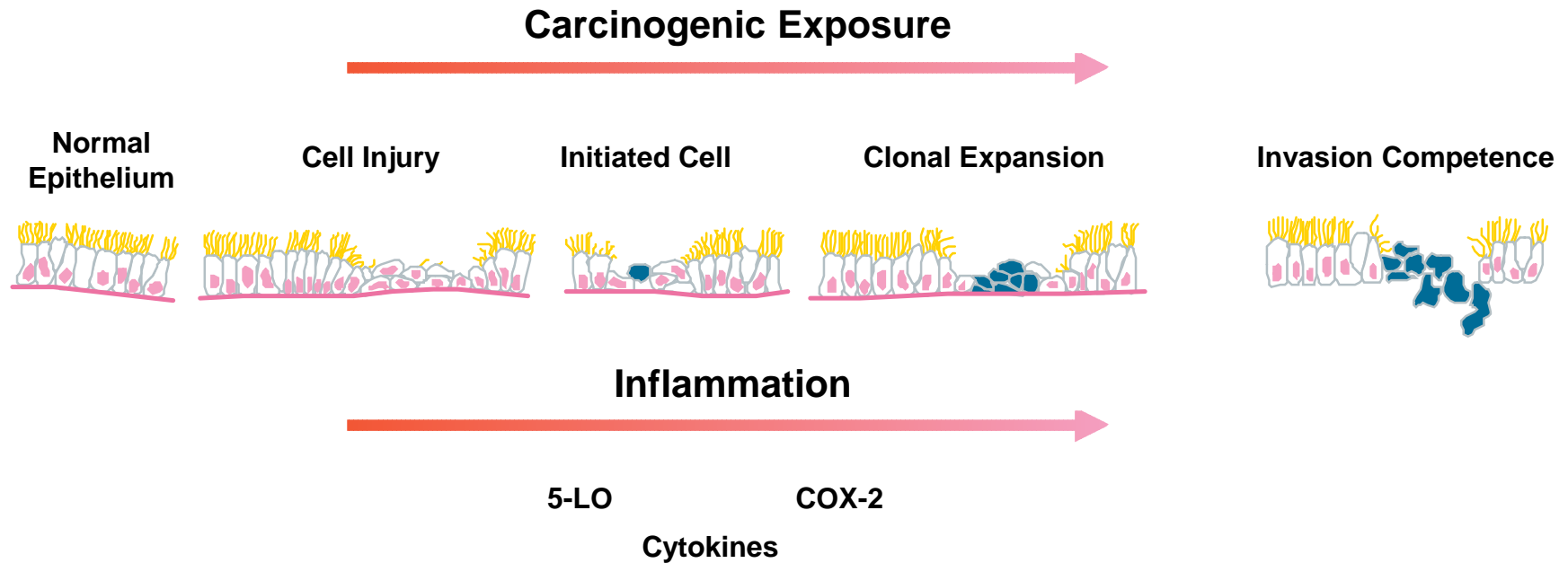
Imaging Pre-symptomatic Disease: Lung CA



- CT resolution doubling every two yrs for > decade
- Improved microprocessor capabilities
- Image processing capabilities evolving rapidly
- Capability to image and resolve smaller critical nodules (contribution of LIDC & RIDER Databases)
- Imaging progress drives changes in clinical care

Courtesy of I-ELCAP, NEJM, 352, 2005

Contribution of the Inflammatory Response in Chronic Injury to Lung CA



Ballaz et al. Clin Lung Ca 5:46, 2003

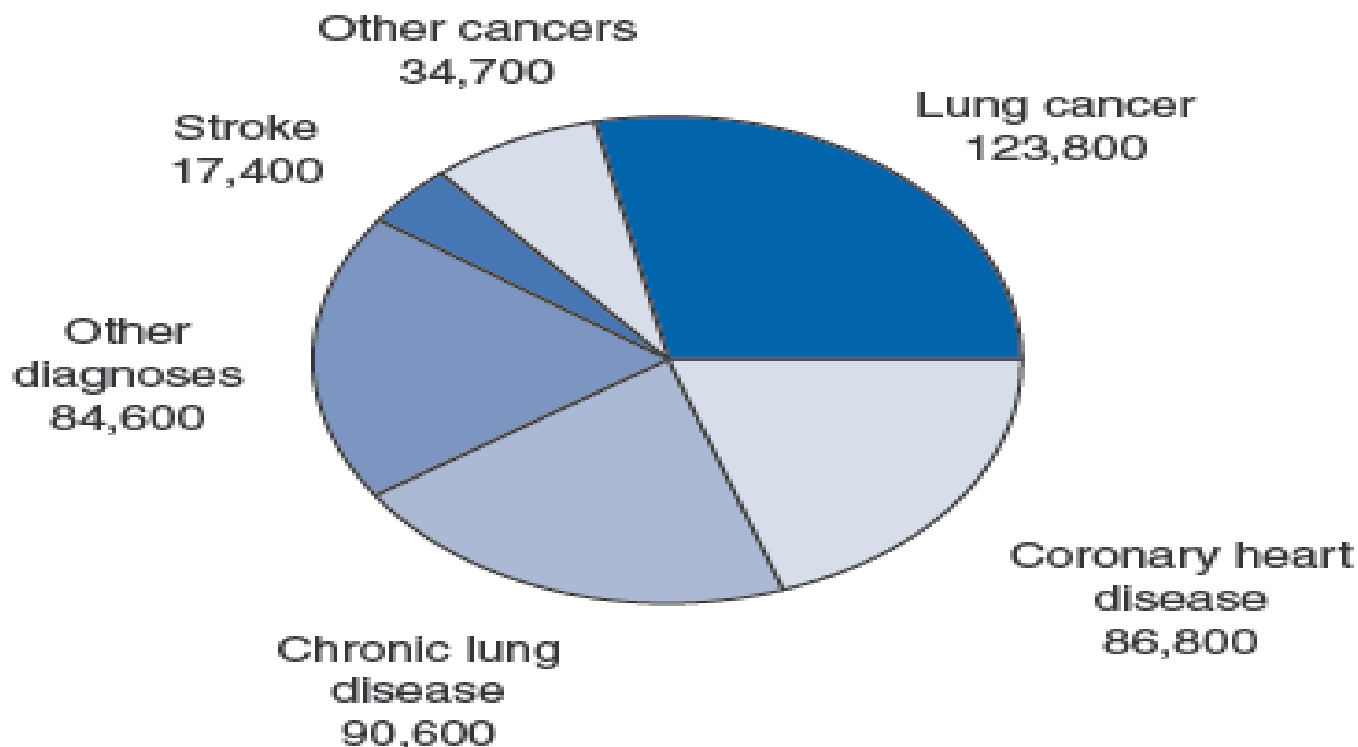
Biomarkers to Stratify Stage I Pts

- Practical, quantitative-PCR-based assay reliably identified patients with early-stage non-squamous NSCLC at high risk for mortality after surgical resection.

Kratz JR et al. A practical molecular assay to predict survival in resected ... Lancet. 2012;379:823. 2012

Context for LDCT Management

**About 438,000 U.S. Deaths Attributable
Each Year to Cigarette Smoking***



* Average annual number of deaths, 1997–2001.
Source: *MMWR* 2005;54(25):625–8.

Evolution of CT Screening?

- Implement lung cancer screening as proposed by the LCA “Framework”
- Use optimized imaging protocol for LDCT
 - Assess for aggressive CAs
 - Assess COPD
 - Assess Coronary calcium scores
- Develop pilot trials for targeted lung cancer adjuvant RX; specific life style interventions for COPD or high CAC scores as well as pragmatic trials (i.e. statins, ASA, aerosolized steroids) to manage full tobacco injury

Improving CT Process Can Reduce Harms and Costs

- Earlier lung cancer may be less frequently metastatic
- Management of smaller, earlier lung cancer may be safer with less recovery time
- International collaborative data sharing may catalyze screening management improvement
- Integration of Smoking Cessation and other Tobacco-induced Thoracic Diseases can greatly increase productivity of LDCT screening