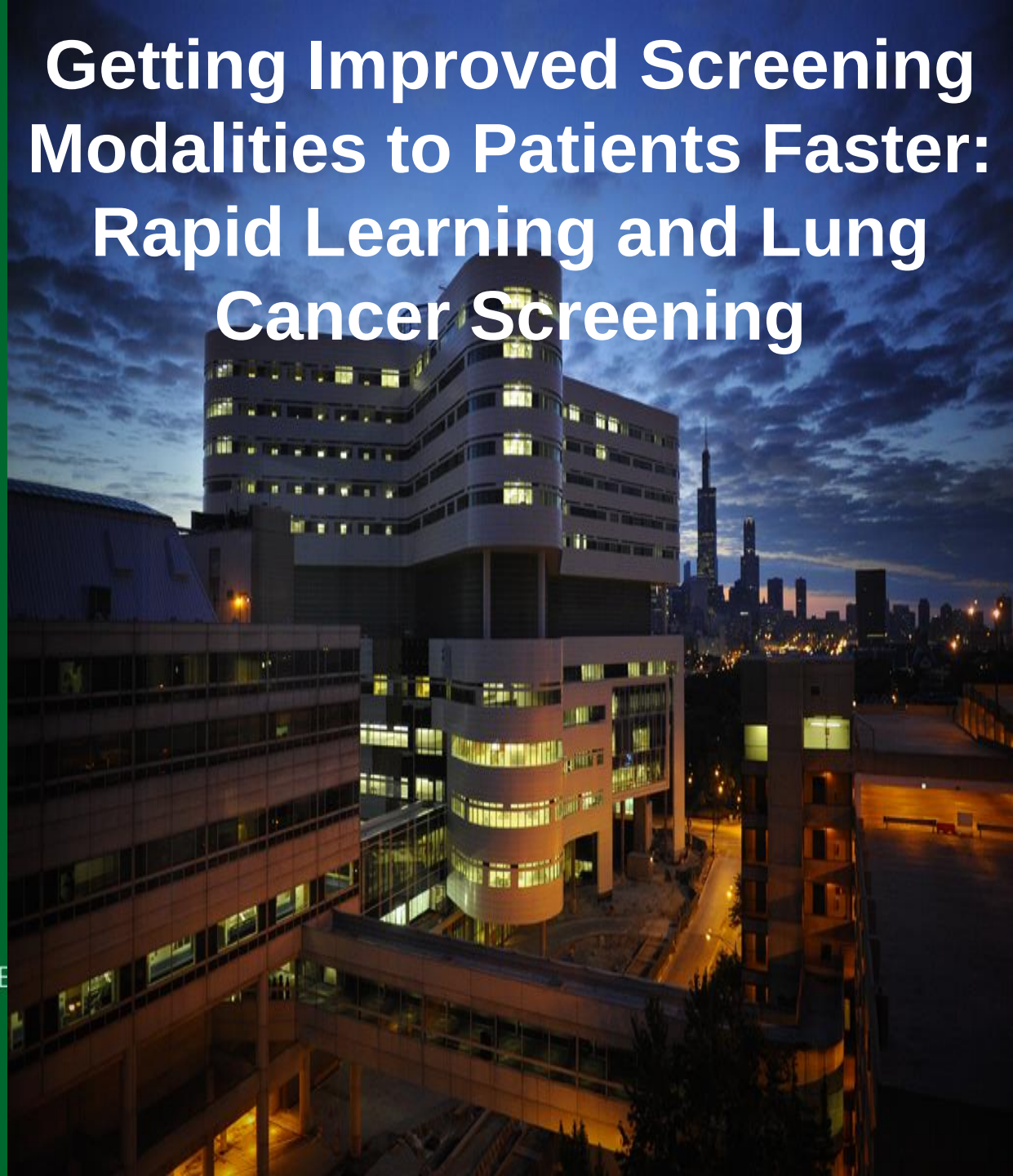
Getting Improved Screening Modalities to Patients Faster: Rapid Learning and Lung Cancer Screening



March 20, 2014

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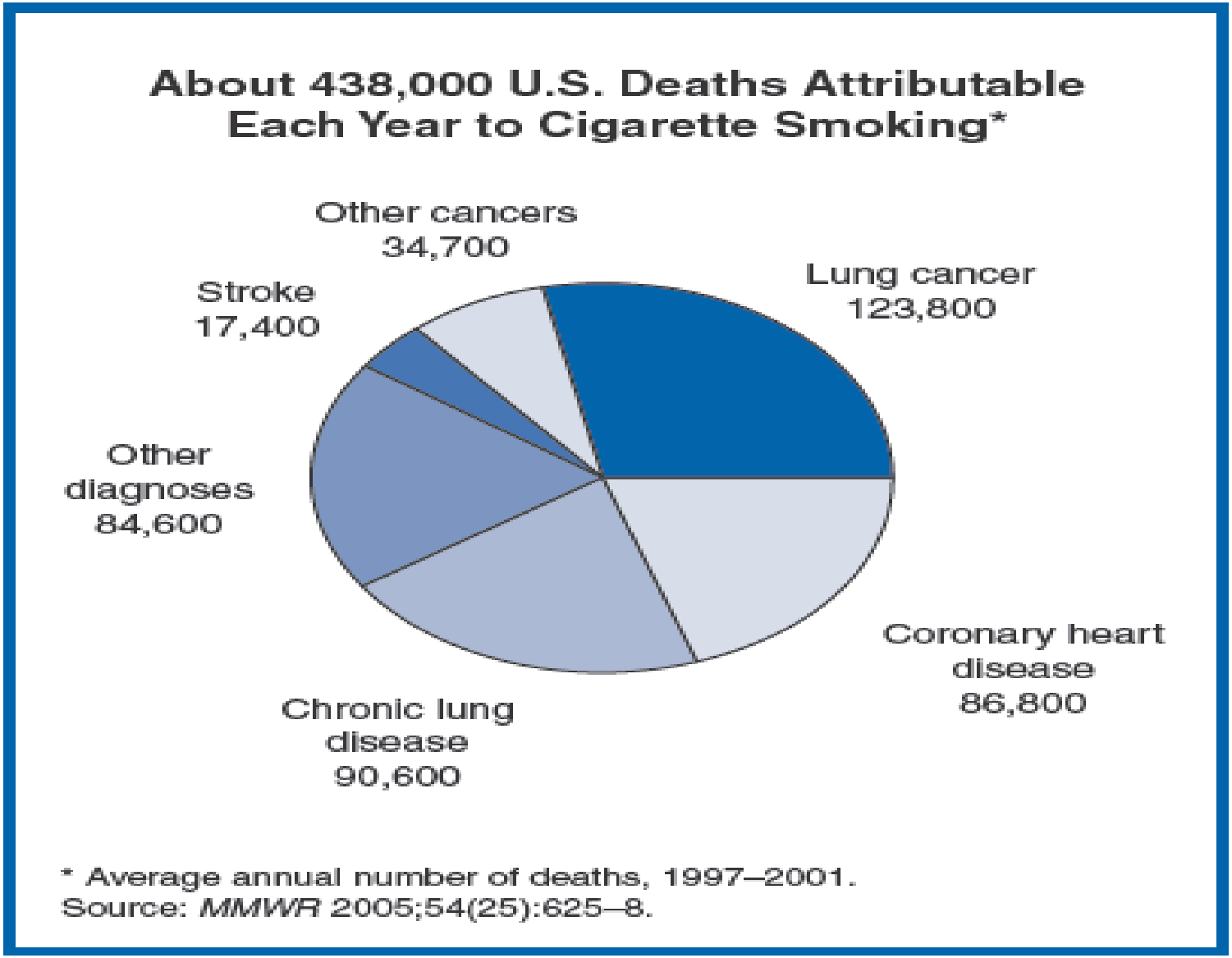
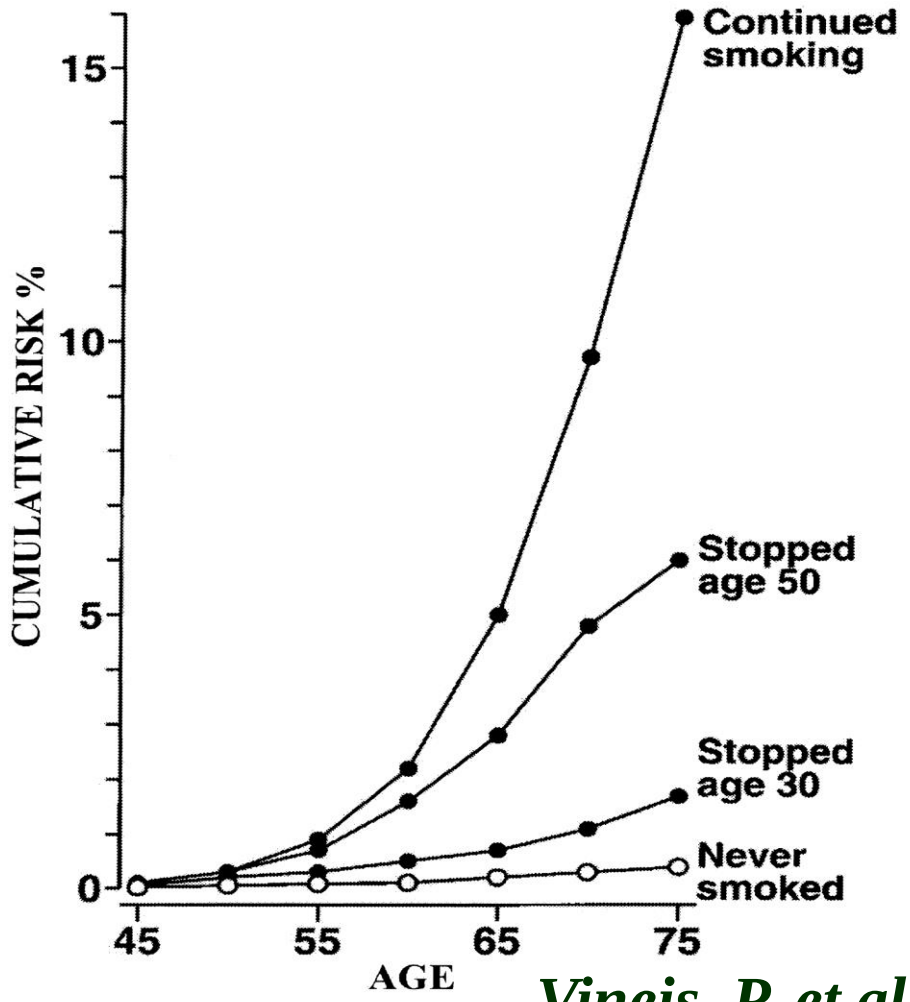
IT'S HOW MEDICINE SHOULD BE

Lung Cancer & Tobacco Mortality



Lifelong Risk of Lung CA Post Smoking



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

NLST Trial Result

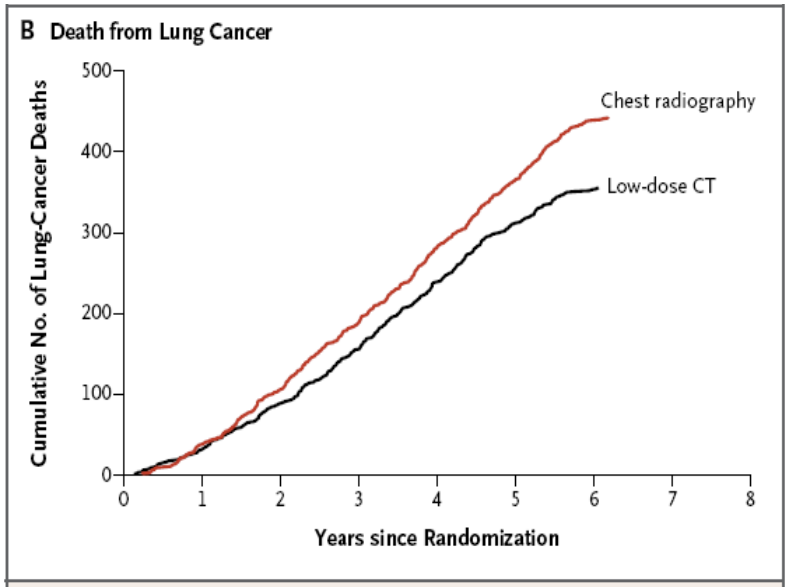


Figure 1. Cumulative Numbers of Lung Cancers and of Deaths from Lung Cancer.

The number of lung cancers (Panel A) includes lung cancers that were diagnosed from the date of randomization through December 31, 2009. The number of deaths from lung cancer (Panel B) includes deaths that occurred from the date of randomization through January 15, 2009.

- NLST 53K person trial
- Study took 9 yrs to complete with budget over $200 M
- NLST provides many answer but many more questions exist
- Enthusiasm to invest that amount of dollars in a new LDCT trial is low

N Engl J Med 2011;365:395-409.

USPSTF LDCT Screening Recommendation

Annals of Internal Medicine

U.S. Preventive Services TASK FORCE
www.USPreventiveServicesTaskForce.org

SCREENING FOR LUNG CANCER
CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Asymptomatic adults aged 55 to 80 y who have a 30 pack-year smoking history and currently smoke or have quit smoking within the past 15 y
Recommendation	Screen annually for lung cancer with low-dose computed tomography. Discontinue screening when the patient has not smoked for 15 y. Grade: B

Risk Assessment	Age, total cumulative exposure to tobacco smoke, and years since quitting smoking are the most important risk factors for lung cancer. Other risk factors include specific occupational exposures, radon exposure, family history, and history of pulmonary fibrosis or chronic obstructive lung disease.
Screening Tests	Low-dose computed tomography has high sensitivity and acceptable specificity for detecting lung cancer in high-risk persons and is the only currently recommended screening test for lung cancer.
Treatment	Non–small cell lung cancer is treated with surgical resection when possible and also with radiation and chemotherapy.
Balance of Benefits and Harms	Annual screening for lung cancer with low-dose computed tomography is of moderate net benefit in asymptomatic persons who are at high risk for lung cancer based on age, total cumulative exposure to tobacco smoke, and years since quitting smoking.
Other Relevant USPSTF Recommendations	The USPSTF has made recommendations on counseling and interventions to prevent tobacco use and tobacco-caused disease. These recommendations are available at www.uspreventiveservicestaskforce.org.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to www.uspreventiveservicestaskforce.org.

USPSTF sponsored CISNET Modeling Result

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

Ann Intern Med. 2013;():. doi:10.7326/M13-2771

Table. Screening Scenarios From CISNET Models*

Screening Scenario†				Benefit		Harm‡			CT Screens per Lung Cancer Death Averted, *n*
Minimum Pack-Years at Screening, *n*	Minimum Age at Which to Begin Screening, *y*	Time Since Last Cigarette, *y*	Population Ever Screened, %	Lung Cancer Deaths Averted, %	Lung Cancer Deaths Averted, *n*	Total CT Screens, *n*	Radiation-Induced Lung Cancer Deaths, *n*	Overdiagnosis, %§	
40	60	25	13.0	11.0	410	171 924	17	11.2	437
40	55	25	13.9	12.3	458	221 606	20	11.1	506
30	60	25	18.8	13.3	495	253 095	21	11.9	534
30	**55**	**15**	**19.3**	**14.0**	**521**	**286 813**	**24**	**9.9**	**577**
20	60	25	24.8	15.4	573	327 024	25	9.8	597
30	55	25	20.4	15.8	588	342 880	25	10.0	609
20	55	25	27.4	17.9	664	455 381	31	10.4	719
10	55	25	36.0	19.4	721	561 744	35	9.5	819

CISNET = Cancer Intervention and Surveillance Modeling Network; CT = computed tomography.

* All scenarios model the results of following a cohort of 100 000 persons from age 45 to 90 y or until death from any cause, with a varying number of smokers and former smokers screened on the basis of smoking history, age, and years since stopping smoking. Bold text indicates the screening scenario with a reasonable balance of benefits and harms and that is recommended by the U.S. Preventive Services Task Force.

† In all scenarios, screening is continued through age 80 y.

‡ Number of CT screenings is a measure of harm because it relates to the number of patients who will have risk for overdiagnosis and potential consequences from false-positive results.

§ Percentage of screen-detected cancer that is overdiagnosis; that is, cancer that would not have been diagnosed in the patient's lifetime without screening.

Improve Diagnostic Work-up

- **NELSON published diagnostic work up efficiency in NEJM and found a sensitivity of 95%, specificity of 99% using a Siemens Lung Care volume measurement tool***
- **I-ELCAP and NELSON use a nodule growth criteria to separate clinically significant from non-malignant behaving nodules using quantitative imaging (filter for overdiagnosis)^**
- **RSNA (QIBA) is defining imaging protocols and QC/QS criteria to ensure robust measurements**

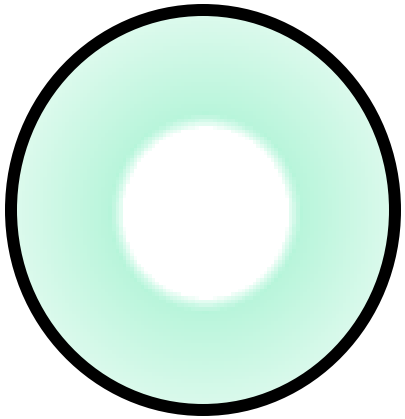
*van Klaveren RJ et al NEJM, 2009 ^Wagnetz et al AJR, 2012

Improving Efficiency/Cost of LDCT Screening

- **Better define risk strata to determine which population yields best screening outcome**
- **Refine diagnostic work up algorithm to find screening-detected cases with minimal morbidity**
- **Improve intervention to remove or ablate detected primary lung cancer with minimal mortality**
- **Establish rational basis for frequency of screening follow up**
- **Validate candidates and targets for adjuvant therapy for more aggressive screen-detected cancers**

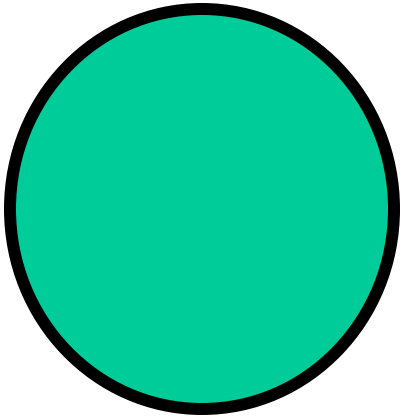
Distribution of Lung Cancer Risk

Cohort Status

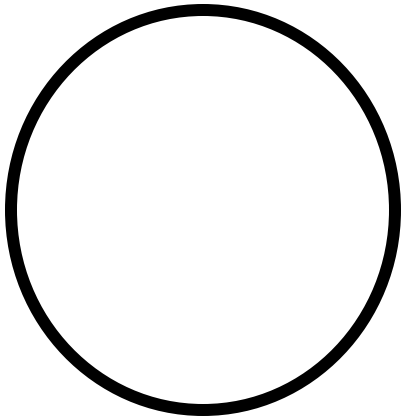


High Risk

Individual Status



Disease Present

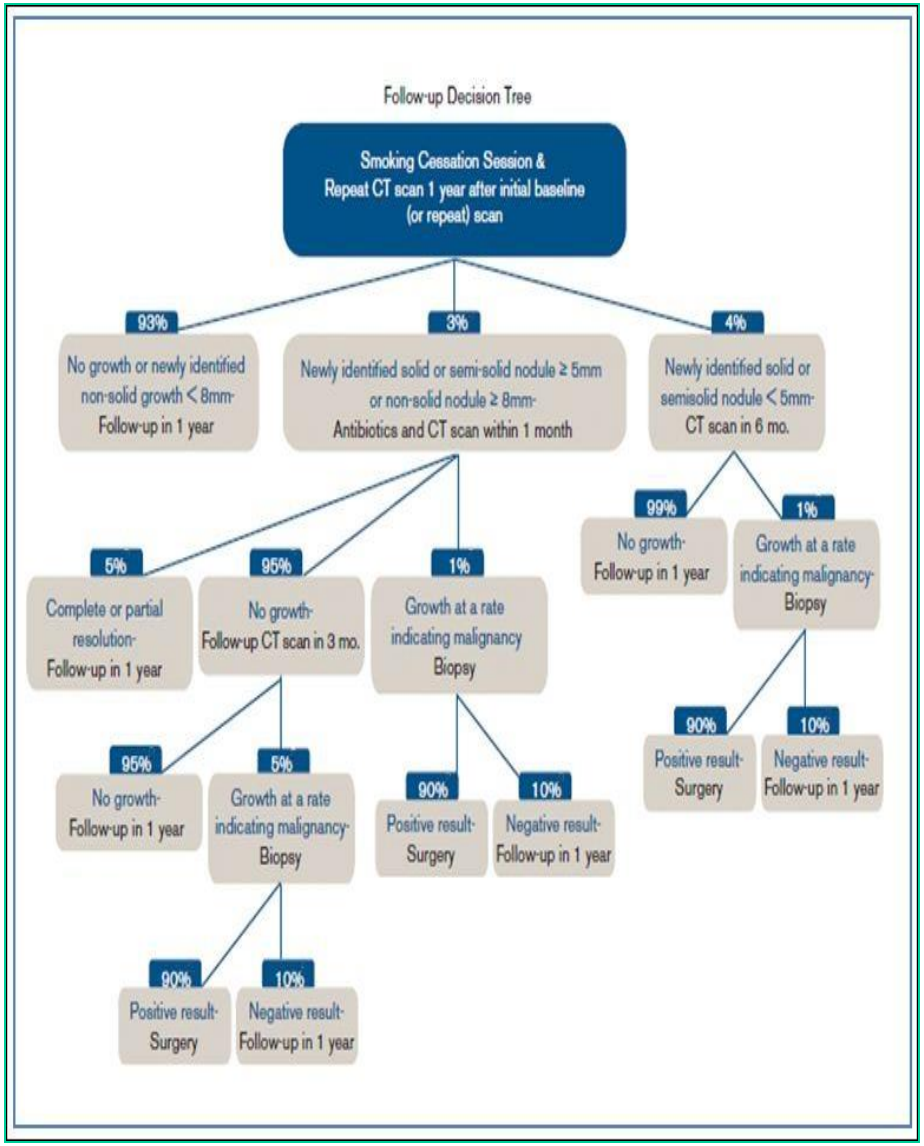


Disease Absent

Moving To Rapid Learning

- Institute of Medicine (IOM) Roundtable on Evidence-based Medicine from the National Academy of Science suggested that a “new clinical paradigm be developed that takes better advantage of data generated in the course of healthcare delivery which would speed and improve the development of evidence for real-world decision making.”

Can We Apply Rapid Learning?



Re-analysis of I-ELCAP data from 2006 to 2010

- Reviewed 21,136 baseline screenings
  - 57% had at least a nodule
  - 16% had a positive result
  - Could reduce w/u frequency by changing cut-point from 5-8mm

Annals of Internal Medicine
Established in 1927 by the American College of Physicians

From: Definition of a Positive Test Result in Computed Tomography Screening for Lung Cancer: A Cohort Study

Ann Intern Med. 2013;158(4):246-252. doi:10.7326/0003-4819-158-4-201302190-00004

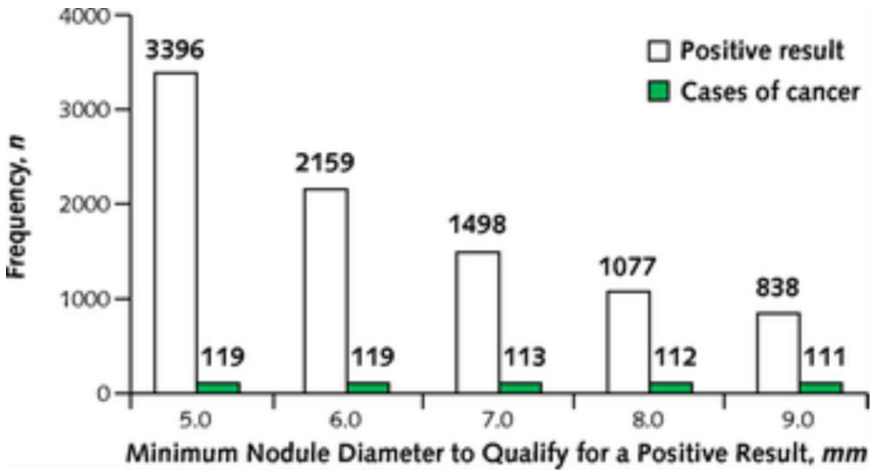


Figure Legend:

Frequency of a positive result and cases of lung cancer diagnosed within 12 mo of baseline enrollment.

I-ELCAP: 73 Institutions with 60,869 Participants and 131,942 CT scans

Ann Intern Med. 2013;158(4):246-252

Comparison of CA Screening Qualys

Intervention	Original value	Year	$/QALY saved (2012 USD)	$/QALY saved (2012 USD, sensitivity analysis)	Consistent with USPSTF guidelines	Reference
Lung cancer screening with LDCT in high risk population						
Annual screening over 15 years, aged 50–64	$28,240–$47,115	2012 USD	$28,240–$47,115	-	Under review	
Other preventive health interventions						
Colonoscopy every 10 years, ages 50–75	$4,870	2008 CAN	$8,552	$9,625	Yes	[44]
Annual fecal occult blood screening for colorectal cancer, ages 50–75	$15,991–$18,595	2008 CAN	$28,080–$32,652$31, 604–$36,750	Yes	[44]	
Papanicolaou (Pap) test for cervical cancer, every 3 years in women aged 20–65	$11,835	2000 USD	$18,662	$28,940	Yes	[45]
Biennial mammography and clinical breast exam in women, aged 50–75 years	$34,000	2000 USD	$53,611	$83,139	Yes	[46]
Type 2 diabetes screening, ages 25+	$56,649	1995 USD	$105,650	$192,741	No	[47]
Annual HIV testing in high risk population	$100,000	2001 USD	$150,745	$223,909	Yes	[48]
In-center dialysis vs. no renal replacement therapy	$129,200	2000 USD	$203,724	$315,928	Yes	[49]
Cholesterol-lowering medication (statin) vs. Step I diet[a]	$130,000–$260,000	1997 USD	$227,878–$455,755	$391,442–$782,883	-	[50]

USD, U.S. dollars; CAN, Canadian dollars.
[a]Among men with LDL> = 160 mg/dL.
doi:10.1371/journal.pone.0071379.t004

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

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

LC Screening as an Exemplar of System Change: Implementation Framework

- Only best practices for screening, evaluation, follow-up, smoking cessation
- Outcomes measured with rapid learning approaches & published
- Credential high quality, low cost providers
- Keep pace with computational & through-put revolution in imaging
  - Reduce costs thru higher efficiency

Rights and Expectations for Excellence in Lung Cancer Screening and Continuum of Care.
http://www.screenforlungcancer.org/national-framework/