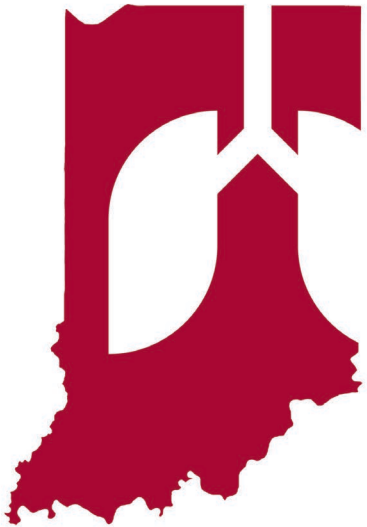

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Lung Cancer Screening - 2022

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11/4/2022

Disclosure Slide

1. Research and Programmatic Funding:
   - American Cancer Society, National Institutes of Health (NIH-NHLBI), Veterans Affairs BLR&D, VA-Office of Rural Health, Biodesix Inc.
2. Research/Scientific Consultant:
   - Bristol Myers Squibb
3. This presentation does not represent the views of the Department of Veterans Affairs of the United States Government.

Background and Overview

- Background
- Rationale for screening
- National Lung Screening Trial
- Lung screening recommendations
- Risks and Benefits
- Special Considerations of a Lung Cancer Screening Program
- Ongoing Questions and Needs

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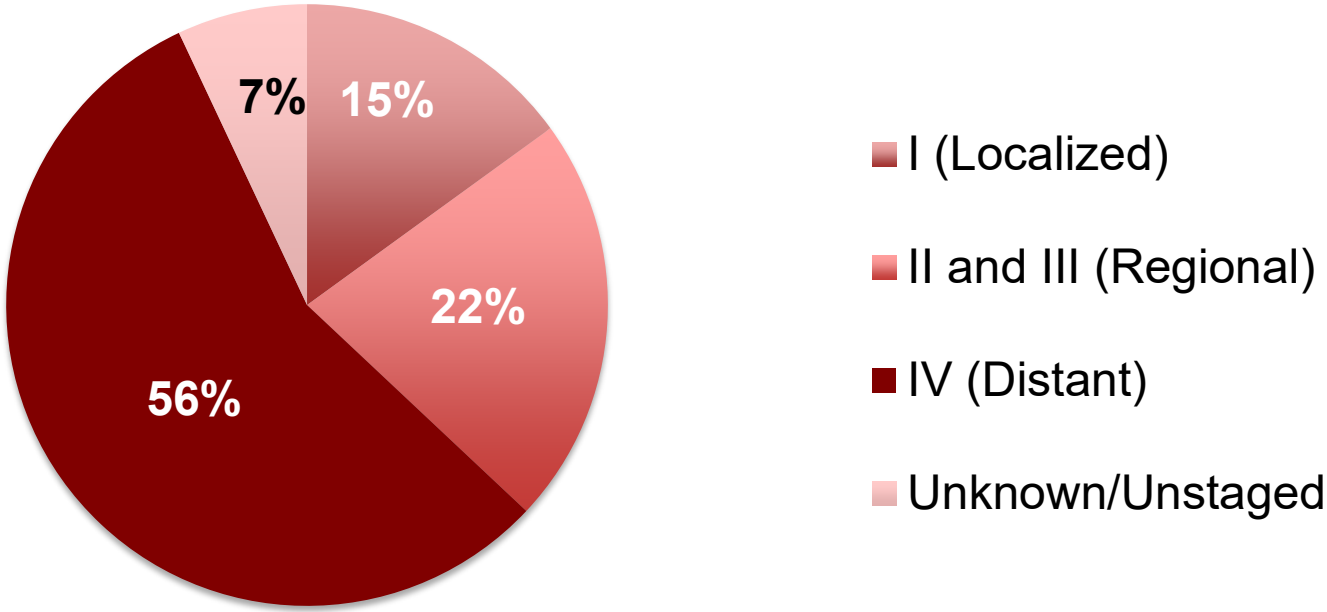
Lucas Oil Stadium Capacity 68,000	New Lung Cancer Cases 236,740	Lung Cancer Deaths 130,180

Siegel et. al. Cancer Statistics, 2022, CA Cancer J Clin

Lung Cancer Stage at Diagnosis



http://seer.cancer.gov/statfacts/html/lungb.html

Significance of Early Diagnosis

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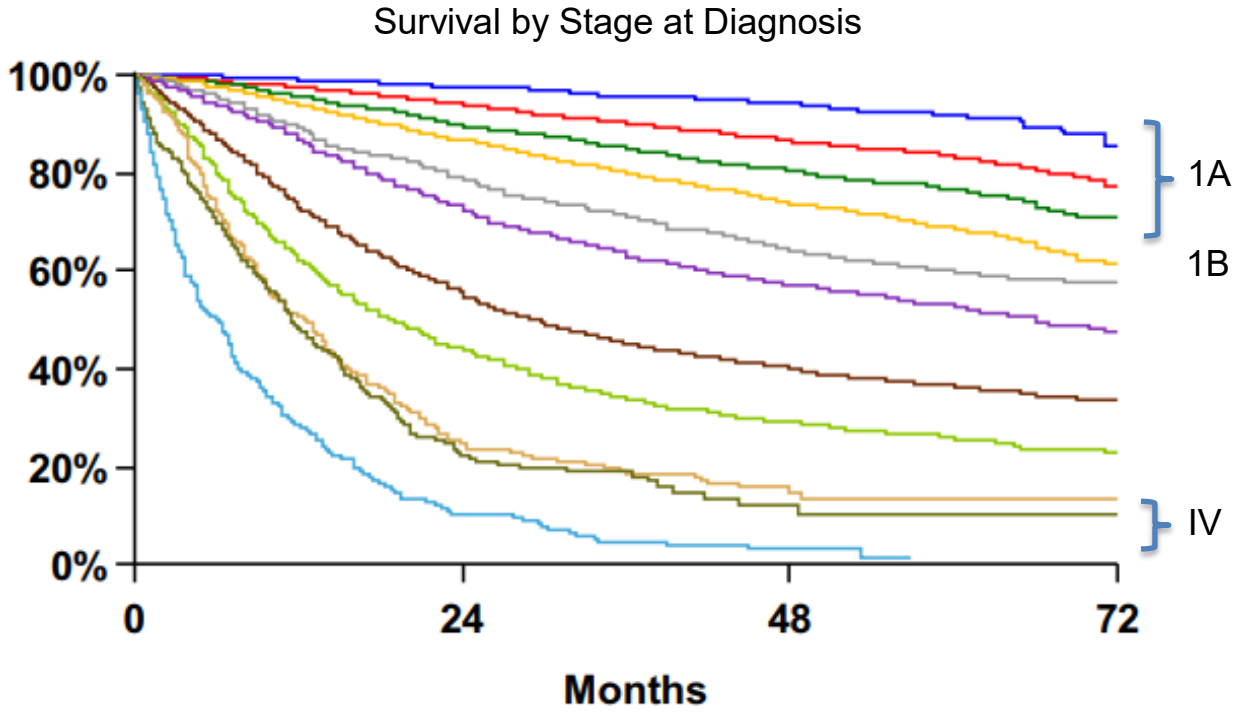
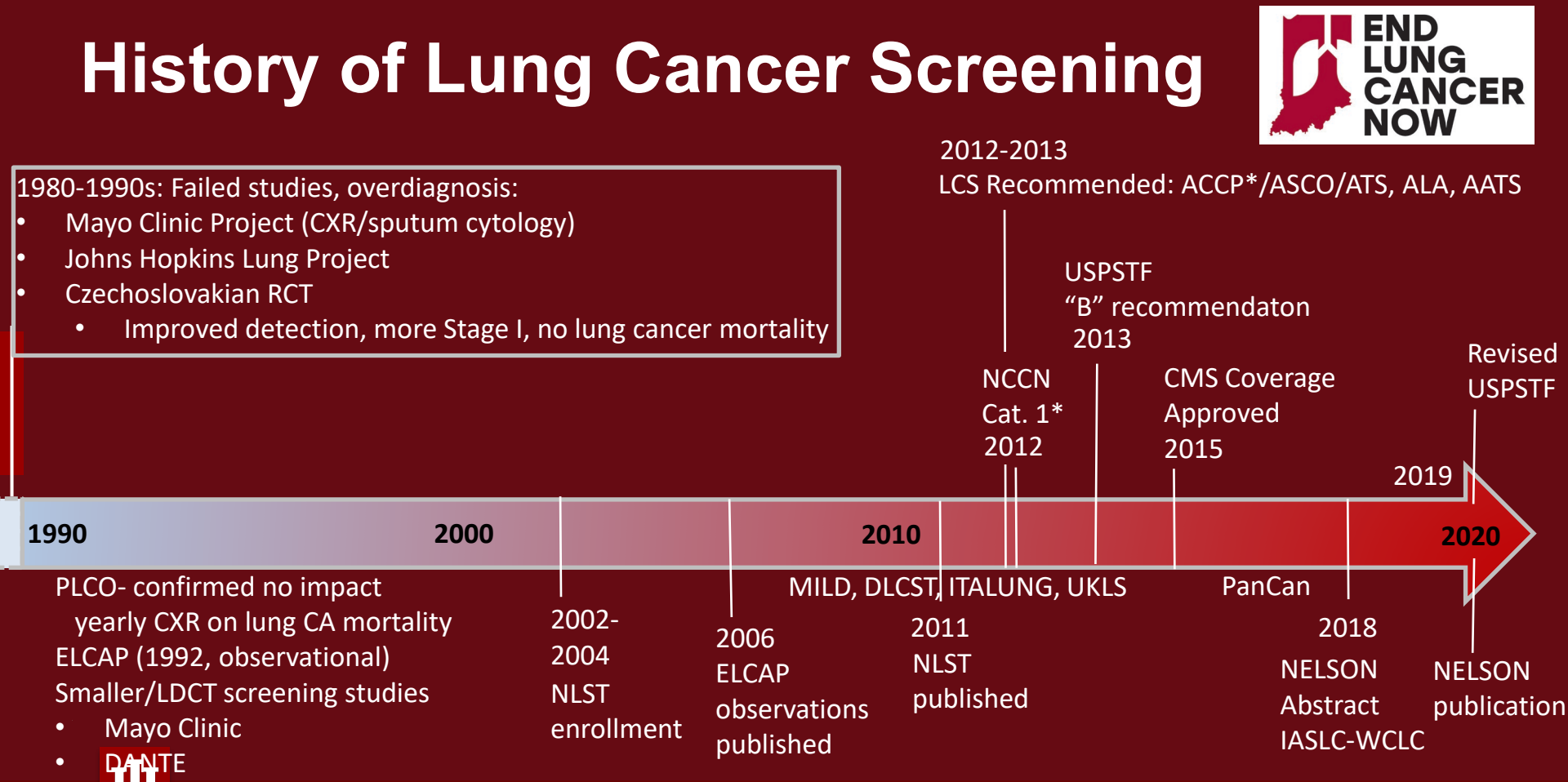


Goldstraw P et al. *J Thorac Oncol* 2015. 11(1):39-51

History of Lung Cancer Screening



NLST (National Lung Screening Trial)

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- Enrollment: 53,454 from 8/02-4/04
- Randomized to screening with low dose CT vs CXR
- Three annual screenings
- Median follow-up 6.5 yrs
- *Total adhererance 91%*

Aberle DR et al.; National Lung Screening Trial Research Team. *New Engl J Med.* 2011;365(5):395-409

The NEW ENGLAND JOURNAL of MEDICINE

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Inclusion	Exclusion
55-74 y/o	Previous lung or other cancer (5 years)
Tobacco ≥ 30 pack-yrs	CT chest ≤ 18 months
Quit ≤ 15 yrs	Hemoptysis Weight loss > 15 lbs/last yr
	Unable to undergo surgery

Table 5. Stage and Histologic Type of Lung Cancers in the Two Screening Groups, According to the Result of Screening.*

Stage and Histologic Type	Low-Dose CT				Chest Radiography			
	Positive Screening Test (N=649)	Negative Screening Test (N=44)†	No Screening Test (N=367)‡	Total (N=1060)	Positive Screening Test (N=279)	Negative Screening Test (N=137)†	No Screening Test (N=525)‡	Total (N=941)
	number/total number (percent)							
Stage								
IA	329/635 (51.8)	5/44 (11.4)	82/361 (22.7)		90/275 (32.7)	16/135 (11.9)	90/519 (17.3)	196/929 (21.1)
IB	71/635 (11.2)	2/44 (4.5)	31/361 (8.6)		41/275 (14.9)	6/135 (4.4)	46/519 (8.9)	93/929 (10.0)
IIA	26/635 (4.1)	2/44 (4.5)	7/361 (1.9)	35/1040 (3.4)	14/275 (5.1)	2/135 (1.5)	16/519 (3.1)	32/929 (3.4)
IIB	20/635 (3.1)	3/44 (6.8)	15/361 (4.2)	38/1040 (3.7)	11/275 (4.0)	6/135 (4.4)	25/519 (4.8)	42/929 (4.5)
IIIA	59/635 (9.3)	3/44 (6.8)	37/361 (10.2)	99/1040 (9.5)	35/275 (12.7)	21/135 (15.6)	53/519 (10.2)	109/929 (11.7)
IIIB	49/635 (7.7)	15/44 (34.1)	58/361 (16.1)	122/1040 (11.7)	27/275 (9.8)	24/135 (17.8)	71/519 (13.7)	
IV	81/635 (12.8)	14/44 (31.8)	131/361 (36.3)	226/1040 (21.7)	57/275 (20.7)	60/135 (44.4)	218/519 (42.0)	
Histologic type								
Bronchioloalveolar carcinoma	95/646 (14.7)	1/44 (2.3)	14/358 (3.9)	110/1048 (10.5)	13/276 (4.7)	1/135 (0.7)	21/520 (4.0)	35/931 (3.8)
Adenocarcinoma	258/646 (39.9)	8/44 (18.2)	114/358 (31.8)	380/1048 (36.3)	112/276 (40.6)	37/135 (27.4)	179/520 (34.4)	328/931 (35.2)
Squamous-cell carcinoma	136/646 (21.1)	13/44 (29.5)	94/358 (26.3)	243/1048 (23.2)	70/276 (25.4)	24/135 (17.8)	112/520 (21.5)	206/931 (22.1)
Large-cell carcinoma	28/646 (4.3)	3/44 (6.8)	10/358 (2.8)	41/1048 (3.9)	12/276 (4.3)	10/135 (7.4)	21/520 (4.0)	43/931 (4.6)
Non–small-cell carcinoma or other§	75/646 (11.6)	4/44 (9.1)	52/358 (14.5)	131/1048 (12.5)	40/276 (14.5)	30/135 (22.2)	88/520 (16.9)	158/931 (17.0)
Small-cell carcinoma	49/646 (7.6)	15/44 (34.1)	73/358 (20.4)	137/1048 (13.1)	28/276 (10.1)	32/135 (23.7)	99/520 (19.0)	159/931 (17.1)
Carcinoid	5/646 (0.8)	0	1/358 (0.3)	6/1048 (0.6)	1/276 (0.4)	1/135 (0.7)	0	2/931 (0.2)

50%

49%

Aberle DR et al.; National Lung Screening Trial Research Team. *New Engl J Med.* 2011;365(5):395-409

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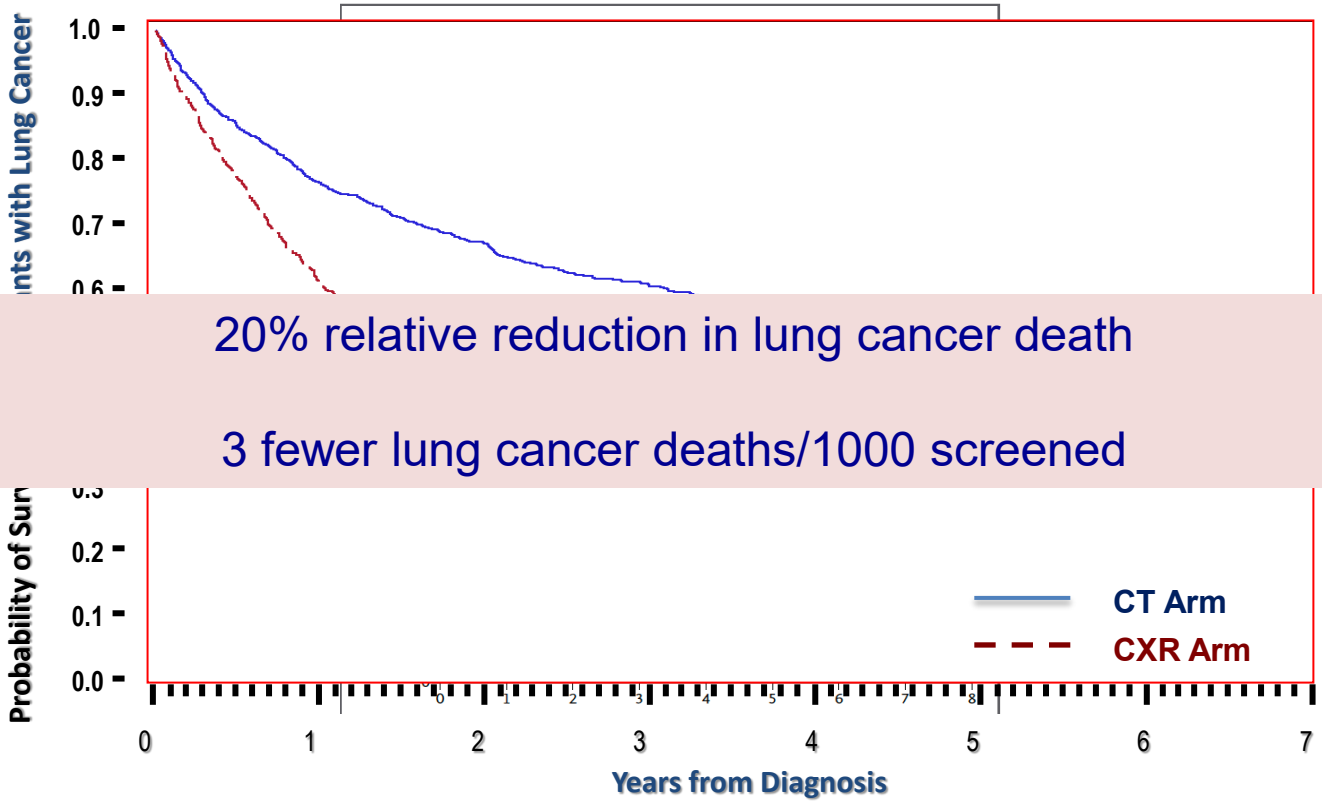

20% relative reduction in lung cancer death

3 fewer lung cancer deaths/1000 screened

Aberle DR et al.; National Lung Screening Trial Research Team. *New Engl J Med.* 2011;365(5):395-409

Lung Cancer Screening Trials

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TABLE 3] Summary of Design of Included Randomized Controlled Trials

Study	Sample Size	Age (y)	Smoking History	Smoking Cessation (Years Since Quit)	Screening Interval and Duration	Follow-up (y)	Definition of Positive Result[a]	% Male	Lung Cancer Mortality (RR)
LDCT vs CXR								59%	0.85
NLST[12,13]	53,454	55-74	≥ 30 pack-years	≤ 15	3 annual screens	6.5 (median)	≥ 4 mm		
Depiscan[14]	765	50-75	≥ 15 cigarettes/d for ≥ 20 y	< 15	3 annual screens	NR	> 5 mm	71%	*
LDCT vs usual care (no screening)									
DANTE[15-17]	2,472 males	60-74	≥ 20 pack-years	< 10	5 annual screens; baseline CXR for both study arms	8	> 5 mm	100%	1.01*
DLCST[18-21]	4,104	50-70	≥ 20 pack-years	< 10	5 annual screens	10	> 15 mm or rapid growing 5- to 15-mm nodules (> 25% increase in volume on 3-mo repeat CT)	55%	1.03*
NELSON[22,23]	15,822	50-75	≥ 15 cigarettes/d for ≥ 25 y or ≥ 10 cigarettes/d for ≥ 30 y	< 10	4 screening rounds; interval after baseline: 1 y, 2 y, and 2.5 y	7	Volume > 500 mm^3 or volume 50-500 mm^3 with VDT < 400 d on 3-mo repeat CT	84%	0.76
ITALUNG[24-26]	3,206	55-69	≥ 20 pack-years	≤ 10	4 annual screens	6	≥ 5 mm solid nodule, a ground-glass nodule ≥ 10 mm, or any part-solid nodule	64%	0.70*
MILD[27-29]	4,099	≥ 49	≥ 20 pack-years	< 10	Two study arms: 5 annual screens; or 3 biennial screens	5	Volume > 250 mm^3 or rapid growing 60-250 mm^3 (> 25% increase in volume on 3-mo repeat CT)	68,69%	Annual: 2.48* Biennial: 1.24*
LUSI[30,31]	4,052	50-69	≥ 15 cigarettes/d for ≥ 25 y or ≥ 10 cigarettes/d for ≥ 30 y	< 10	4 annual screens	3	≥ 5 mm	66%	*
UKLS[32-34]	4,055	50-75	LLPv2 risk ≥ 5%		One screening	10	Volume > 500 mm^3 or volume 50-500 mm^3 with VDT < 400 d on 3-mo repeat CT	75%	*
LSS[35,36]	3,318	55-74	≥ 30 pack-years	< 10	One screening	1	≥ 4 mm	58%	*

Mazzone et al. CHEST. 2018

Current Screening Criteria?

Criteria according to:	US Preventative Services Task Force (2021)	Centers for Medicare & Medicaid Services
Insurance:	Private health insurance	Medicare beneficiaries
Age (years):	50-80	**50**-77
Smoking History:	20 pack-years or more	**20** pack-years or more
Smoking Status:	Current smoker or quit within 15 years	
Health Requirement	Asymptomatic of lung cancer	
Screening Frequency	Annually	
When to stop LCS	**When any of the below conditions occur:** 1. Exceeds upper age criterion 2. Has not smoked for > 15 years 3. Comorbidity that substantially limits life expectancy 4. Unable or unwilling to have curative surgery/treatment or follow-up	

Components of Lung Cancer Screening

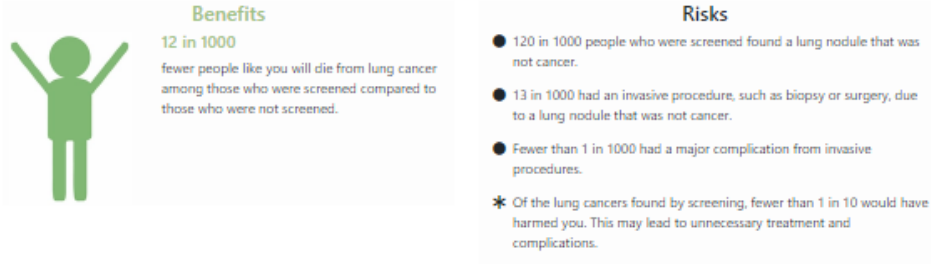
Shared Decision Making Visit

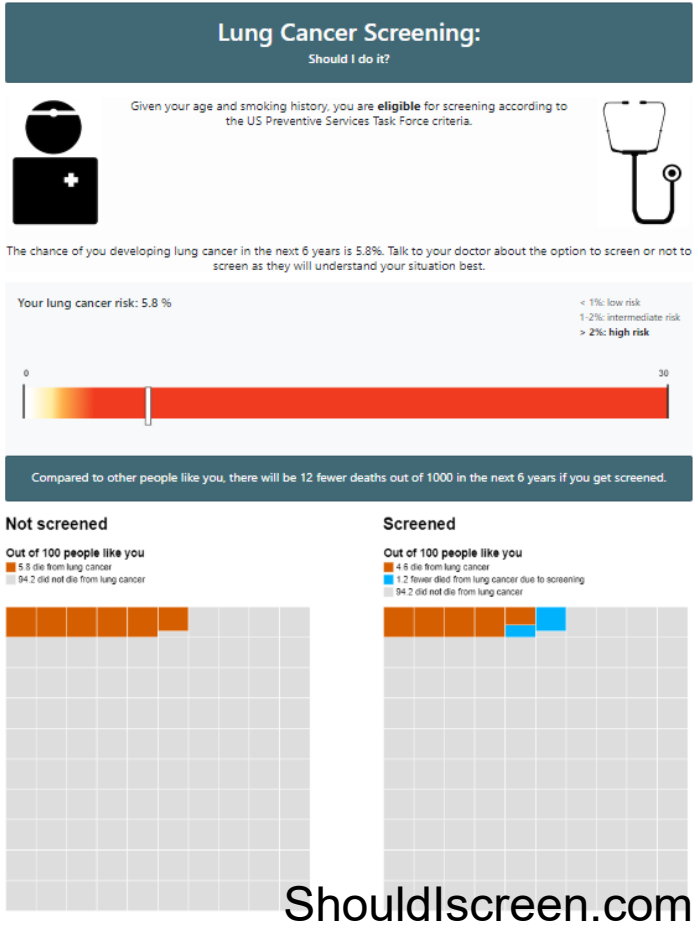
Review medical history, habits, current health

Review **personalized** risks and benefits

Review the program, communications and referrals, yearly screening & answer questions

Tobacco Treatment Counseling





ShouldIscreen.com

Benefits vs harms

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False positives

False negatives

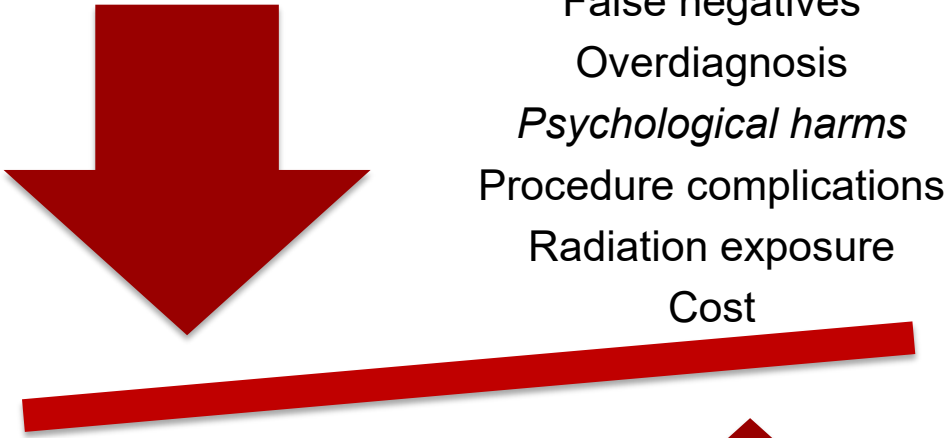
Overdiagnosis

Psychological harms

Procedure complications

Radiation exposure

Cost



Decreased mortality

20-26% decrease lung cancer death

7% decrease all cause

Teachable moment for cigarette smoking cessation

Causes of Lung Nodules

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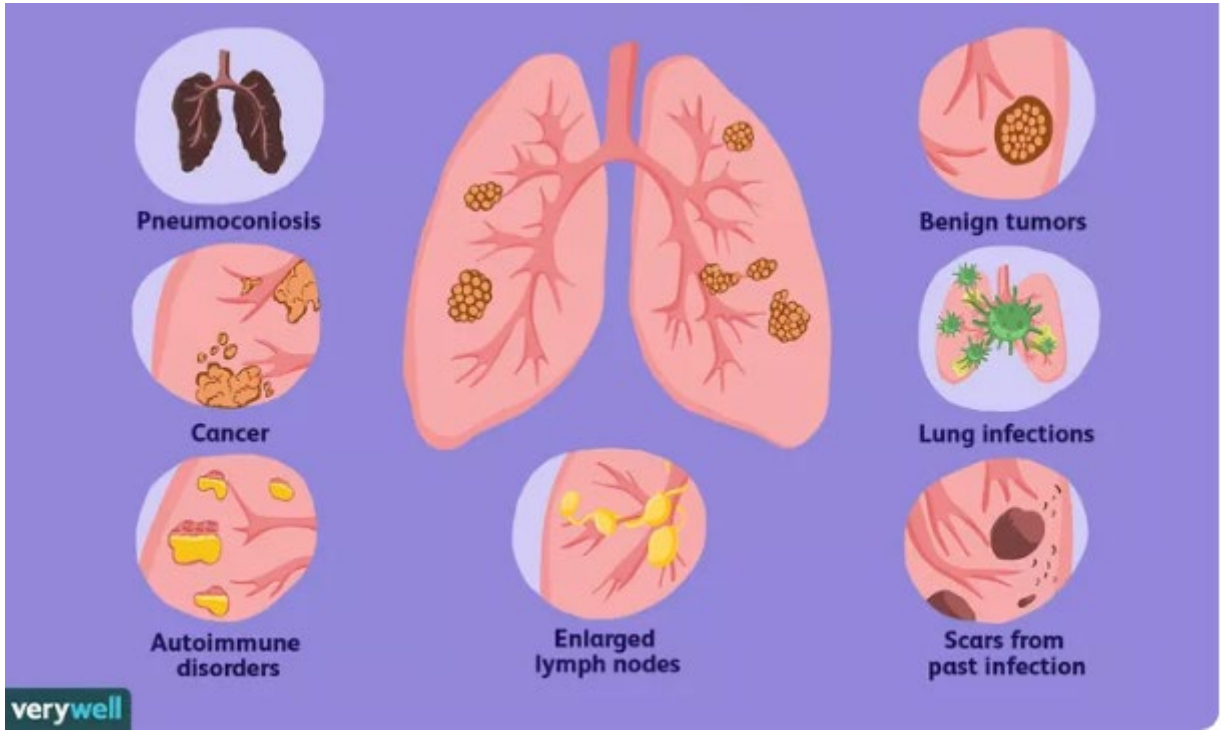
26-60%
LDCTs



96%
Benign

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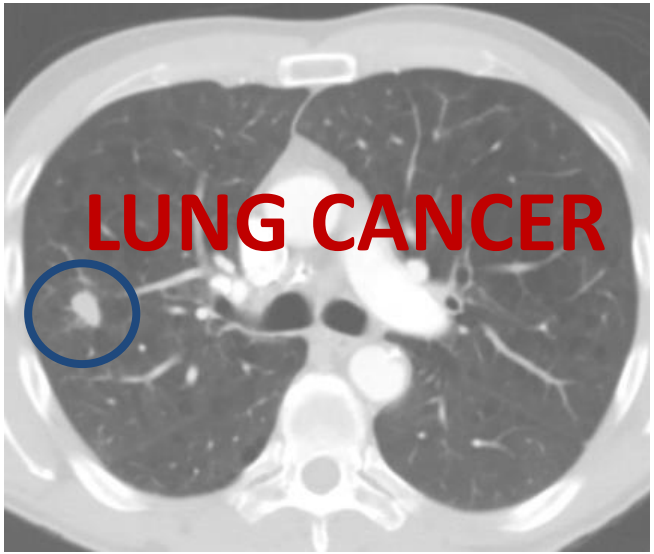
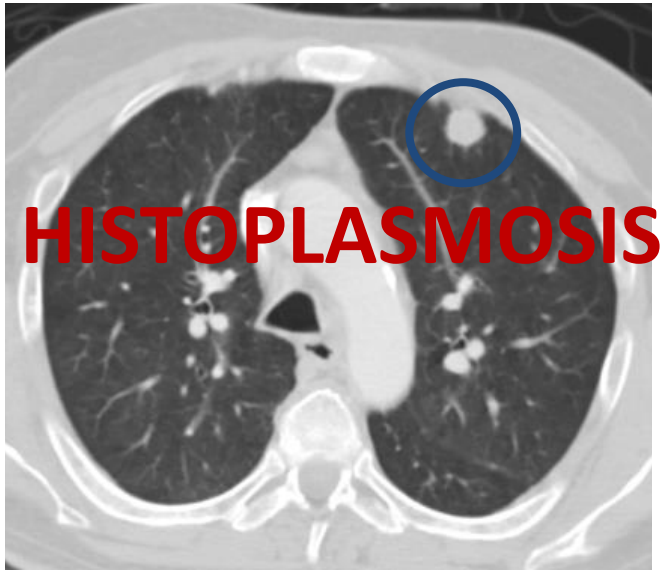
62 Year Old Male Smoker



54 Year Old Male Smoker



Minimizing risks of radiation exposure

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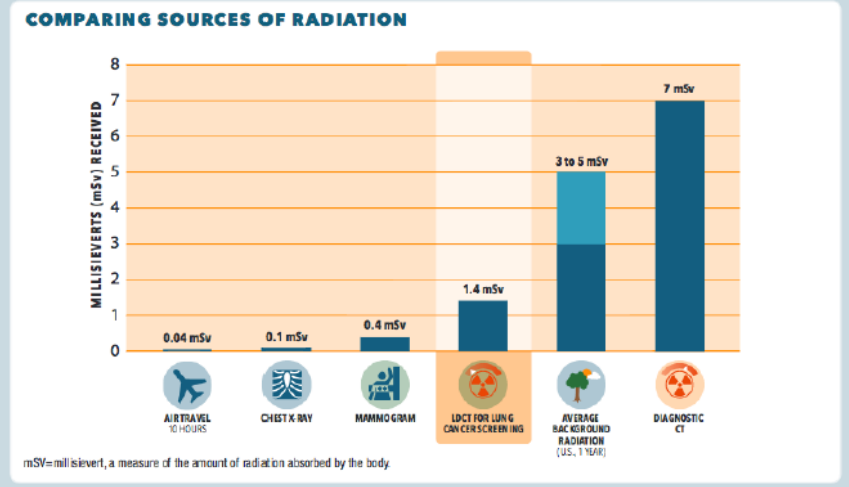
Avg. NLST participant = 8mSv

~ 1 death per 2500 screened patients

 # needed to screen to prevent 1 death:
320 (3 years)
130 (10 years)

HARM: Radiation exposure

Exposure to radiation increases a person's chance of developing cancer. LDCT screening for lung cancer exposes a person to radiation. If the screening test is positive, additional testing may involve higher doses of radiation. Researchers do not know how being exposed to radiation from LDCT scans and additional diagnostic imaging tests may affect people. The figure below shows the amount of radiation from one LDCT scan compared with other sources of radiation.



https://effectivehealthcare.ahrq.gov/ehc/assets/File/lung-cancer-screening-decision-aid-160323.pdf

Bach et al. JAMA (2012). Aberle et al (2011). deKoning et al. (2020)

Components of Lung Cancer Screening

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Low Dose Computed Tomography of Chest (Low Dose CT Chest)

- Low Radiation Dose
- Quick (~ 3-5 minutes)
- Non-contrasted (no needles!)
- Protocolized Interpretation and Management Plan

Lung cancer survivor Mr. Bobby Richardson receives follow-up care at the Richard L. Roudebush VA Medical Center in Indianapolis. *(Photo by Mark Turney, Richard L. Roudebush VA Medical Center.)*

Components of Lung Cancer Screening

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Protocolized Follow-up

- Standardized Reporting System
- Review of Imaging/Results ("Nodule" board)
- Streamline Referral and Diagnostic Procedures
- Management of Incidental Findings
- Patient tracking and yearly follow-up

Standardized Interpretation of Imaging and Management of Findings

Lung-RADS™ Version 1.1

Assessment Categories Release date: 2019

Category Descriptor	Lung-RADS Score	Findings	Management	Risk of Malignancy	Est. Population Prevalence
Incomplete	0	Prior chest CT examination(s) being located for comparison Part or all of lungs cannot be evaluated	Additional lung cancer screening CT images and/or comparison to prior chest CT examinations is needed	n/a	1%
Negative No nodules and definitely benign nodules	1	No lung nodules Nodule(s) with specific calcifications: complete, central, popcorn, concentric rings and fat containing nodules	Continue annual screening with LDCT in 12 months	< 1%	90%
Benign Appearance or Behavior Nodules with a very low likelihood of becoming a clinically active cancer due to size or lack of growth	2	**Solid nodule(s):** < 6 mm new < 4 mm **Part solid nodule(s):** < 6 mm total diameter on baseline screening **Non solid nodule(s) (GGN):** <30 mm **OR** ≥ 30 mm and unchanged or slowly growing **Category 3 or 4 nodules unchanged for ≥ 3 months**			
Probably Benign Probably benign finding(s) - short term follow up suggested; includes nodules with a low likelihood of becoming a clinically active cancer	3	**Solid nodule(s):** ≥ 6 to < 8 mm at baseline **OR** new 4 mm to < 6 mm **Part solid nodule(s)** ≥ 6 mm total diameter with solid component < 6 mm **OR** new < 6 mm total diameter **Non solid nodule(s)** (GGN) ≥ 30 mm on baseline CT or new	6 month LDCT	1-2%	5%
Probably Suspicious Findings for which additional diagnostic testing is recommended	4A	**Solid nodule(s):** ≥ 8 to < 15 mm at baseline **OR** growing < 8 mm **OR** new 6 to < 8 mm **Part solid nodule(s:** ≥ 6 mm with solid component ≥ 6 mm to < 8 mm **OR** with a new or growing < 4 mm solid component **Endobronchial nodule**	3 month LDCT; PET/CT may be used when there is a ≥ 8 mm solid component	5-15%	2%
Suspicious Findings for which additional diagnostic testing and/or tissue sampling is recommended	4B	**Solid nodule(s)** ≥ 15 mm **OR** new or growing, and ≥ 8 mm **Part solid nodule(s) with:** a solid component ≥ 8 mm **OR** a new or growing ≥ 4 mm solid component	Chest CT with or without contrast, PET/CT and/or tissue sampling depending on the *probability of malignancy and comorbidities. PET/CT may be used when there is a ≥ 8 mm solid component. *For new large nodules that develop on an annual repeat screening CT, a 1 month LDCT may be recommended to address potentially infectious or inflammatory conditions*	> 15%	2%
	4X	Category 3 or 4 nodules with additional features or imaging findings that increases the suspicion of malignancy			
Other Clinically Significant or Potentially Clinically Significant Findings (non lung cancer)	S	**Modifier - may add on to category 0-4 coding**	As appropriate to the specific finding	n/a	10%
Volumetric measurements		1.5 mm = 1.8 mm^3 4 mm = 33.5 mm^3 6 mm = 113.1 mm^3 8 mm = 268.1 mm^3	10 mm = 523.6 mm^3 15 mm = 1767.1 mm^3 20 mm = 4188.8 mm^3 30 mm = 14137.2 mm^3		

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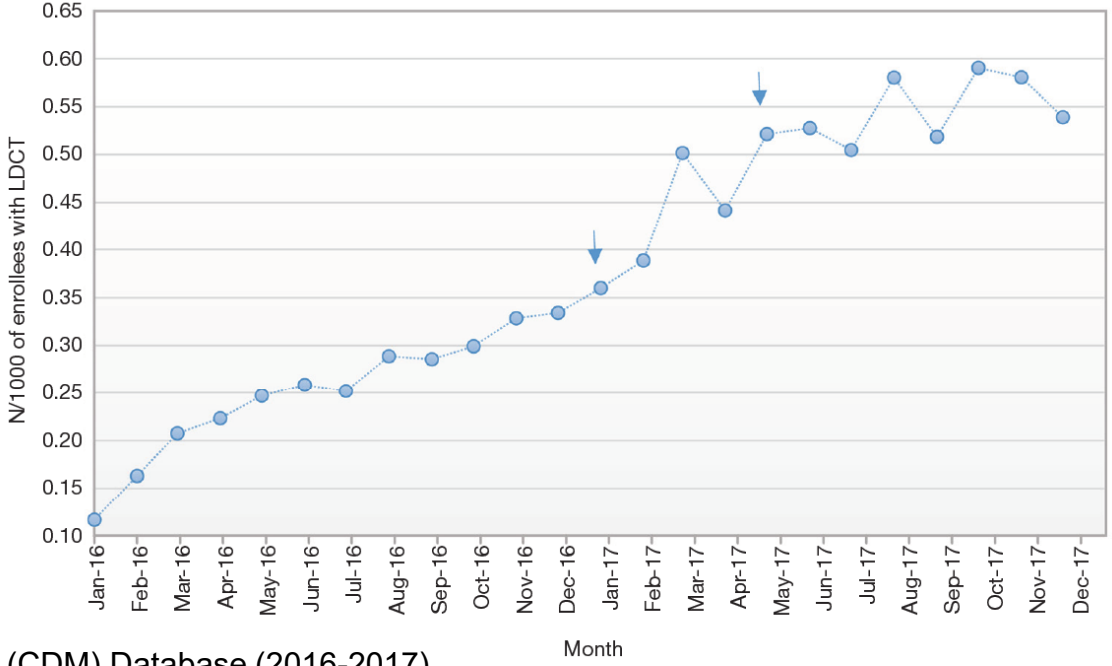
- **Lung-RADS**
- I-ELCAP
- LU-RADS
- Others

Ongoing Challenges/Needs in Lung Cancer Screening

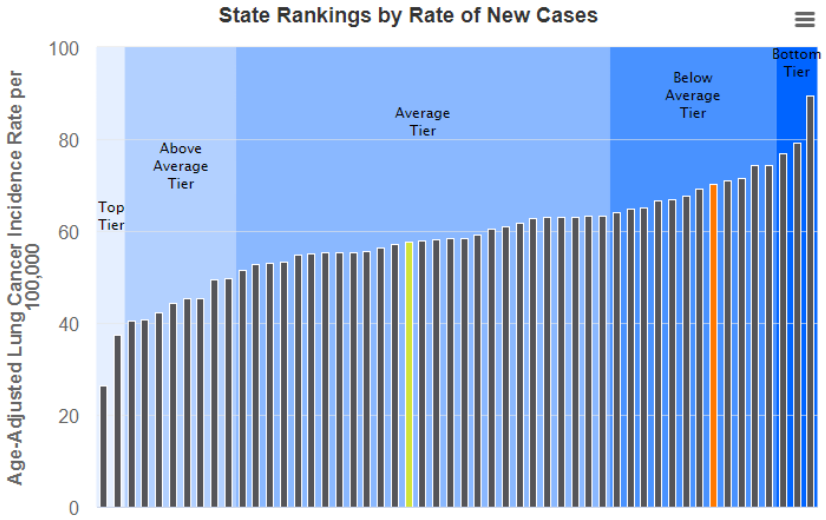
LCS Uptake is Increasing.. But still Lo…



Clinformatics Data Mart (CDM) Database (2016-2017)

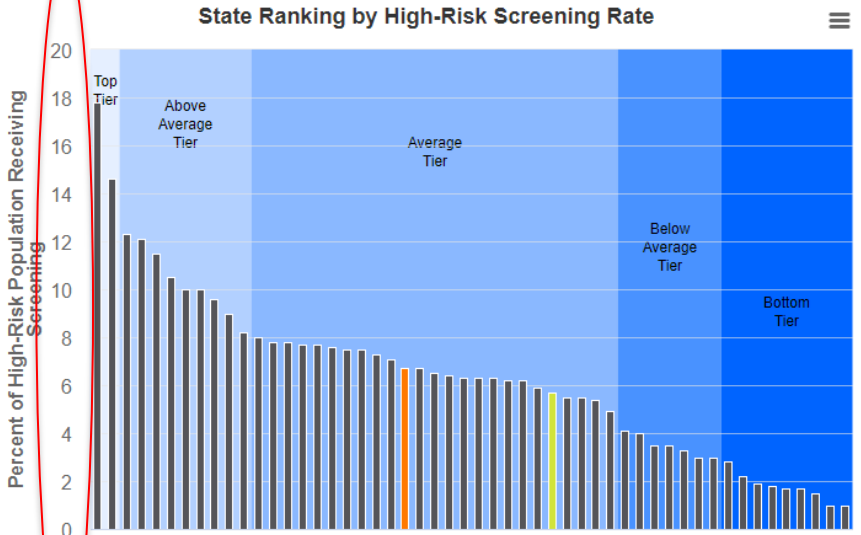
Okereke et al. J Thorac Dis. 2019
Zahnd and Eberth. Am J Prevent Med. 2020

Lung Cancer Screening in Indiana



44th in new lung cancer diagnosis

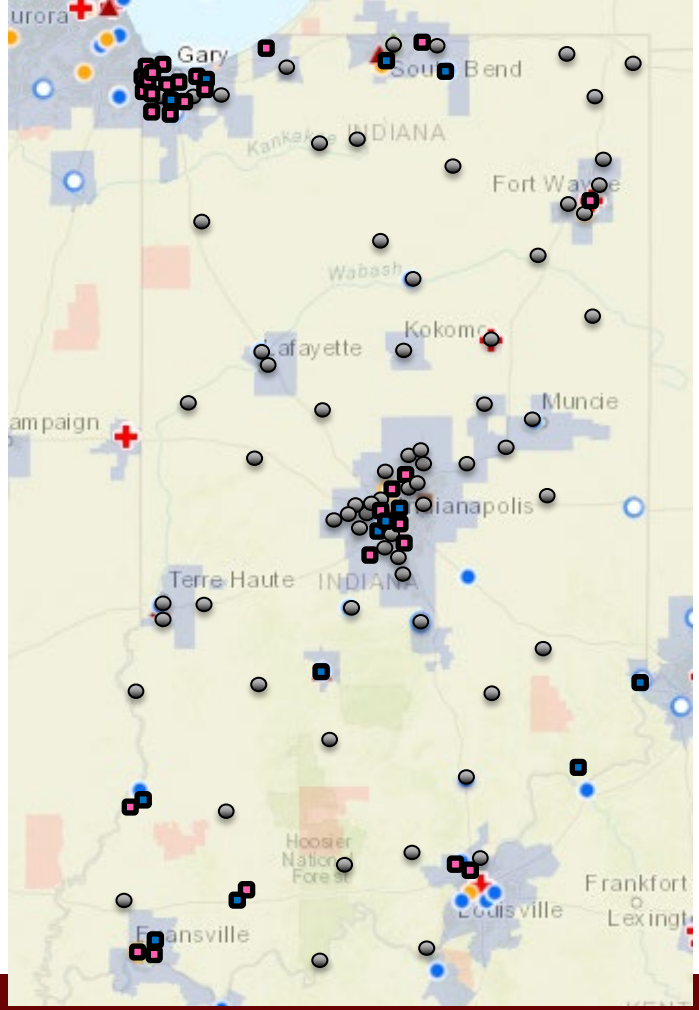
19% smoking rate in Indiana



22nd in lung cancer screening

American Lung Association. State of Lung Cancer 2021. Indiana. https://www.lung.org/research/state-of-lung-cancer/states/Indiana/ Accessed 10/17/22

Location, location, location…



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Pink

Blue

GO2 FOUNDATION FOR LUNG CANCER CENTER OF EXCELLENCE SCREENING
Delivering Excellence in Responsible Screening

DESIGNATED Lung Cancer Screening Center AMERICAN COLLEGE OF RADIOLOGY

Gray = minimal equipment for LCS

Yearly Compliance

1. *Yearly compliance is low*: 46% (T1), 38% (T2) and 28% (T3)
2. Compliance with Lung-RADS recommended follow-up increased:
   - Older (65-73 years) compared to younger (50-64 years) patients
   - Concerning Nodule (LungRADS 4 > 3 > 2 compared to LungRADS 1)
   - Hiring a dedicated program coordinator and active reminders
   - Former smokers > Current smokers
3. **System Barriers**: patient communication, failure to order scan or follow-up, misunderstanding (program vs scan), tracking system
4. **Patient Barriers**: transportation, communication, asymptomatic, fear, other medical, financial costs
5. ***Highlights the need for systematic dedication to adequate resources and patient tracking.***

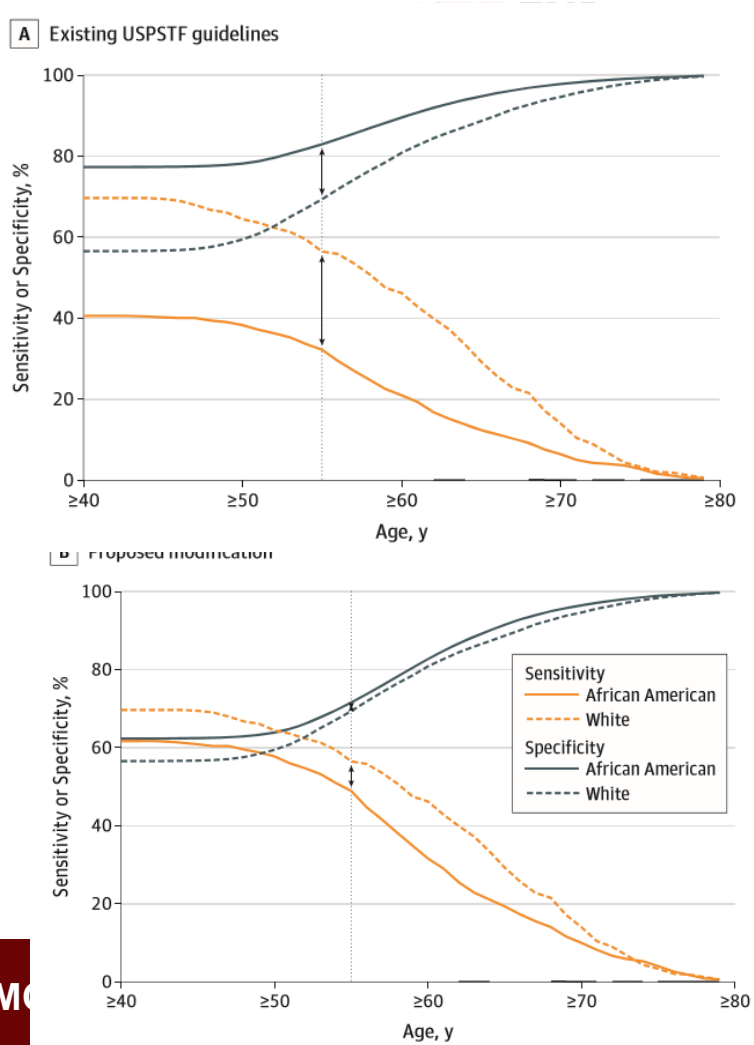
Lin et al. J Thorac Onc. 25 Sept 2021

Disparities and missed high-risk populations

Screening Inclusion/Barriers

- Rural and urban (vs low-resource urban)
- Minority groups
- Social and economically disadvantaged Resource-poor environments
- Other high-risk exposures (radon, radiation, coal/tar pitch, 2nd-hand smoke)
- Other high-risk groups (EGFR)

Aldrich et al. JAMA Oncol 2019.



Pulmonary oncologist Dr. Catherine R. Sears meets with VALOR clinical trial participant Mr. Bobby Richardson. *(Photo by Mark Turney, Richard L. Roudebush VA Medical Center.)*

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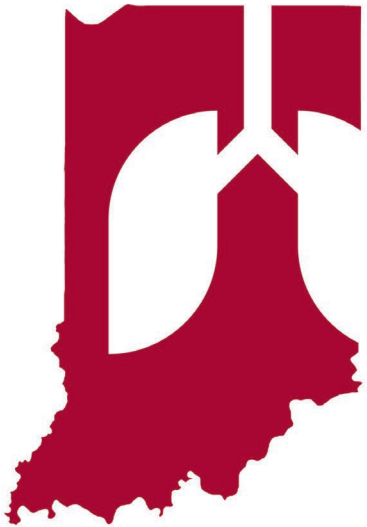
Minimizing Barriers

- Risk prediction models
- Biomarkers
- Radiomics
- Outreach/Advocacy
  - focused clinical
  - diversity research
- Resources
- Cross-institutional collaborations



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