WHAT'S NEW IN LUNG CANCER SCREENING?

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Disclosures

- On the Speakers Bureau for AstraZeneca and Roche.

Lung Cancer Screening with LDCT

- Important recent updates
  - NELSON trial results
  - TALENT study
  - Changes in USPSTF recommendations
- Overcoming barriers to LDCT
- Liquid biopsy for early cancer detection

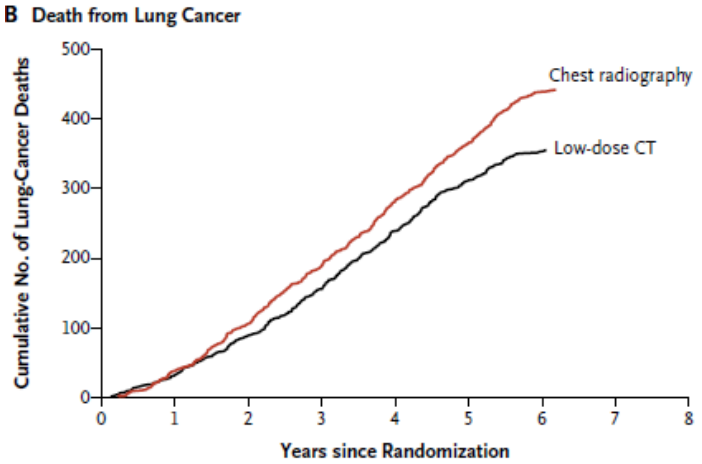
Lung Cancer Screening

- LDCT SCREENING SAVES LIVES
- CXR screening does not
- USPTF Recommended
- CMS approved
- Underutilized
  - National study estimated <5% of eligible patients are screened

NLST: Lung cancer CT screening

- Baseline + 2 yearly screens
- 20% relative reduction in lung cancer mortality
- 7% all cause mortality reduction
- 367/1060 lung cancers detected

diagnosed after screening phase



NELSON Trial

- 13,195 men and 2594 women age 50-74, ≥15pack-year, randomized 1:1 LDCT or observation (0,1,2,2.5 years)
- 24% mortality reduction at 10 years in men, 33% reduction at 10 years in women (59% reduction at 7 years)

TALENT study

- 12,011 never-smoking East Asians with other risk factors (family history, ETS, TB/COPD) underwent LDCT
- Baseline scans: Lung cancer in 3.2% of those with family history, 2.0% without
- 96.5% stage 0/1

Lung-RADS structured reporting

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	**Perifissural nodule(s)** *(See Footnote 11)* < 10 mm (524 mm^3) **Solid nodule(s):** < 6 mm (< 113 mm^3) new < 4 mm (< 34 mm^3) **Part solid nodule(s):** < 6 mm total diameter (< 113 mm^3) on baseline screening **Non solid nodule(s) (GGN):** <30 mm (<14137 mm^3) **OR** ≥ 30 mm (≥ 14137 mm^3) 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 (≥ 113 to < 268 mm^3) at baseline **OR** new 4 mm to < 6 mm (34 to < 113 mm^3) **Part solid nodule(s)** ≥ 6 mm total diameter (≥ 113 mm^3) with solid component < 6 mm (< 113 mm^3) **OR** new < 6 mm total diameter (< 113 mm^3) **Non solid nodule(s)** (GGN) ≥ 30 mm (≥ 14137 mm^3) on baseline CT or new	6 month LDCT	1-2%	5%
Suspicious Findings for which additional diagnostic testing is recommended	4A	**Solid nodule(s):** ≥ 8 to < 15 mm (≥ 268 to < 1767 mm^3) at baseline **OR** growing < 8 mm (< 268 mm^3) **OR** new 6 to < 8 mm (113 to < 268 mm^3) **Part solid nodule(s):** ≥ 6 mm (≥ 113 mm^3) with solid component ≥ 6 mm to < 8 mm (≥ 113 to < 268 mm^3) **OR** with a new or growing < 4 mm (< 34 mm^3) solid component **Endobronchial nodule**	3 month LDCT; PET/CT may be used when there is a ≥ 8 mm (≥ 268 mm^3) solid component	5-15%	2%
Very Suspicious Findings for which additional diagnostic testing and/or tissue sampling is recommended	4B	**Solid nodule(s)** ≥ 15 mm (≥ 1767 mm^3) **OR** new or growing, and ≥ 8 mm (≥ 268 mm^3) **Part solid nodule(s) with:** a solid component ≥ 8 mm (≥ 268 mm^3) **OR** a new or growing ≥ 4 mm (≥ 34 mm^3) 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 (≥ 268 mm^3) 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			

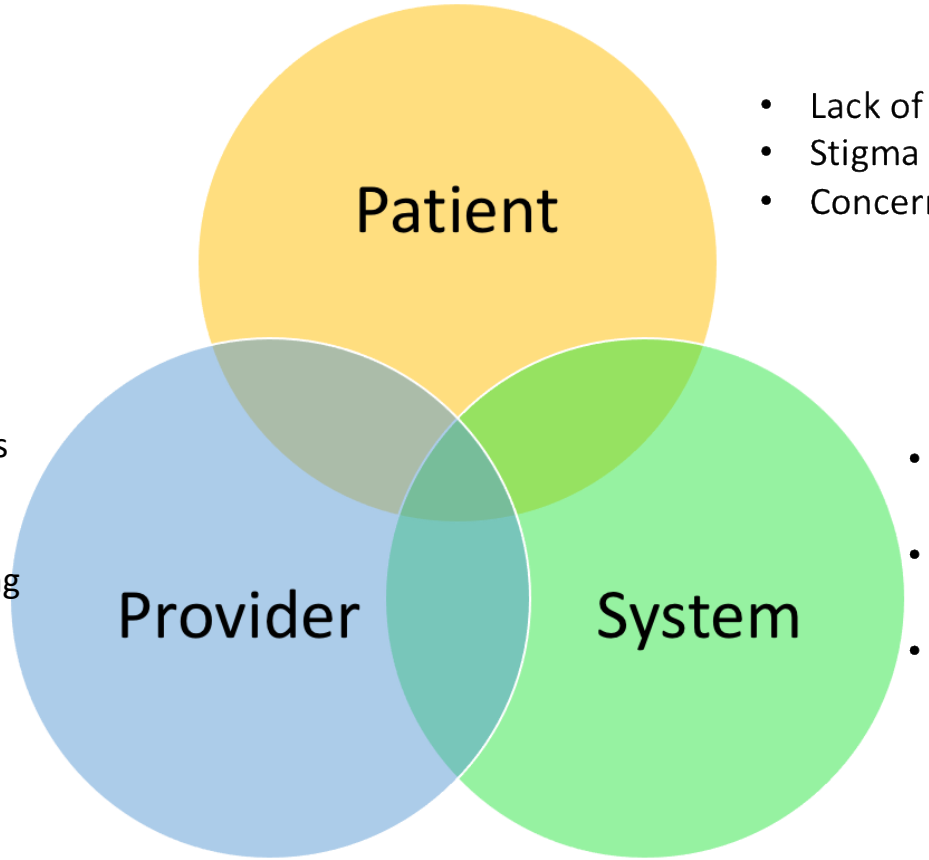
- Radiologist classifies findings with recommendations on next follow-up imaging
- Invasive testing is very uncommon with this approach (~2% of screened patients).
- Invasive testing is very uncommon in people without cancer

Recent USPSTF Changes

- Old: Age 55-80, >30 pack-years
- New: Age 50-80, >20 pack-years
- Maintains the 15-year quit rule

Note: All patients who may be candidates for treatment including surgery and radiation should be screened.

Barriers to Lung Cancer Screening



- Lack of knowledge about LCS
- Stigma related to smoking
- Concerns about costs

- Lack of knowledge of guidelines
- Lack of knowledge of benefits
- Misconceptions of cost
- Time for shared decision-making

- Lack of detailed tobacco use information to identify patients
- Shared decision-making requirement
- Lack of health system resources/ benchmarks for LCS

Raz et al. J Thorac Oncol 2016
Raz et al. Clin Lung Cancer 2018
Raz et al. Clin Lung Cancer 2019

Utilization of LDCT is low

Physician practices (in past 12 months)	
Lung cancer screening tests ever ordered	
LDCT	129 (52%)
Chest radiograph	107 (43.1%)
Referred most or almost all high risk patients for	
LDCT for lung cancer screening	52 (21.1%)
Lung cancer screening program	20 (8.1%)
Ever initiated discussions about lung cancer screening with patients	177 (72%)
Primary care practice has a mechanism for reminders when a patient is due for lung cancer	79 (32.6%)

- Surveyed 250 PCPs in LA County

Raz et al. JTO 2016

Barriers to LCS among Primary Care Physicians

	N	Median Physician Response (IQR)	% of Physicians who Strongly or Somewhat Agree
Perception			
Lung cancer screening is not covered by insurance plans	248	2 (2-4)	54.4% (N=135)
I don't have time to discuss the risks and benefits of lung cancer screening**	250	5 (4-5)	9.2% (N=23)
The risks of lung cancer screening are too high	250	4 (3-5)	10% (N=25)
The benefits of lung cancer screening are not clear to me	248	4 (2-5)	29.8% (N=74)
Our affiliated imaging facilities don't offer LDCT	246	5 (3-5)	10.2% (N=25)
Lung cancer screening is too expensive for our health care system	249	3 (2-4)	25.3% (N=63)
Lung cancer screening may encourage smokers to continue to smoke	250	5 (3-5)	12.4% (N=31)

- Surveyed 250 PCPs in LA County

Raz et al. JTO 2016

PCP Knowledge of LCS Guidelines is Variable

Measure Knows that lung cancer screening with LDCT is recommended for high risk patients by		Family Practice N=107 N (%)	Internal Medicine N=135 N (%)	p-value
National Comprehensive Cancer Network (NCCN)	Yes	34 (32)	54 (41)	0.2871
	No	7 (7)	10 (8)	
	Not Sure	65 (61)	67 (51)	
United States Preventive Services Task Force (USPSTF)	Yes	53 (50)	61 (46)	0.8443
	No	21 (20)	28 (21)	
	Not Sure	32 (30)	43 (33)	
American Cancer Society (ACS)	Yes	48 (45)	72 (55)	0.2277
	No	10 (9)	14 (11)	
	Not Sure	48 (45)	45 (34)	

Raz et al. Clin Lung Cancer 2018

Smokers enrolled in smoking cessation counseling have little knowledge about LCS

- Surveyed 185 current smokers in group smoking cessation at Kaiser
- Top barriers (agree/strongly agree):
  - Lack of knowledge about the test (56%)
  - Worry about results (56%)
  - No family history of lung cancer (49%)
  - No symptoms of lung disease (45%)
  - Worry about feeling like social outcast for smoking (39%)
  - High cost (38%)
  - Worry about being blamed for having smoked (37%)

Raz et al. Clin Lung Cancer 2018

Educating current smokers enrolled in smoking cessation about LCS improves LCS utilization

Patients that watched the video and completed the survey			
	Completed Survey (n=136)	Controls (n=255)	p-value
Any chest CT within 6 months after survey or randomization	25 (18.4%)	22 (8.6%)	0.0047
LDCT within 6 months after survey or randomization	13 (9.6%)	11 (4.3%)	0.0396

Raz et al. Clin Lung Cancer 2021

It is feasible to train smoking cessation counselors to deliver LCS education

Trained smoking cessation counselors to provide LCS education during group smoking cessation counseling at 3 sites in Kaiser Permanente system

How much did the intervention help with your understanding of LCS (Median – IQR, range 1-5, higher=more understanding)	
Benefits of LCS	5 (5-5)
How LCS is done	5 (5-5)
Who is eligible for LCS	5 (5-5)
Harms of LCS	5 (5-5)
LCS coverage by insurance	5 (5-5)
Who to contact to learn more about LCS	5 (5-5)
Was the information provided about LCS	
Too little	2 (8%)
The right amount	23 (92%)
Too much	0

Raz et al. Tob Prev Cess 2020

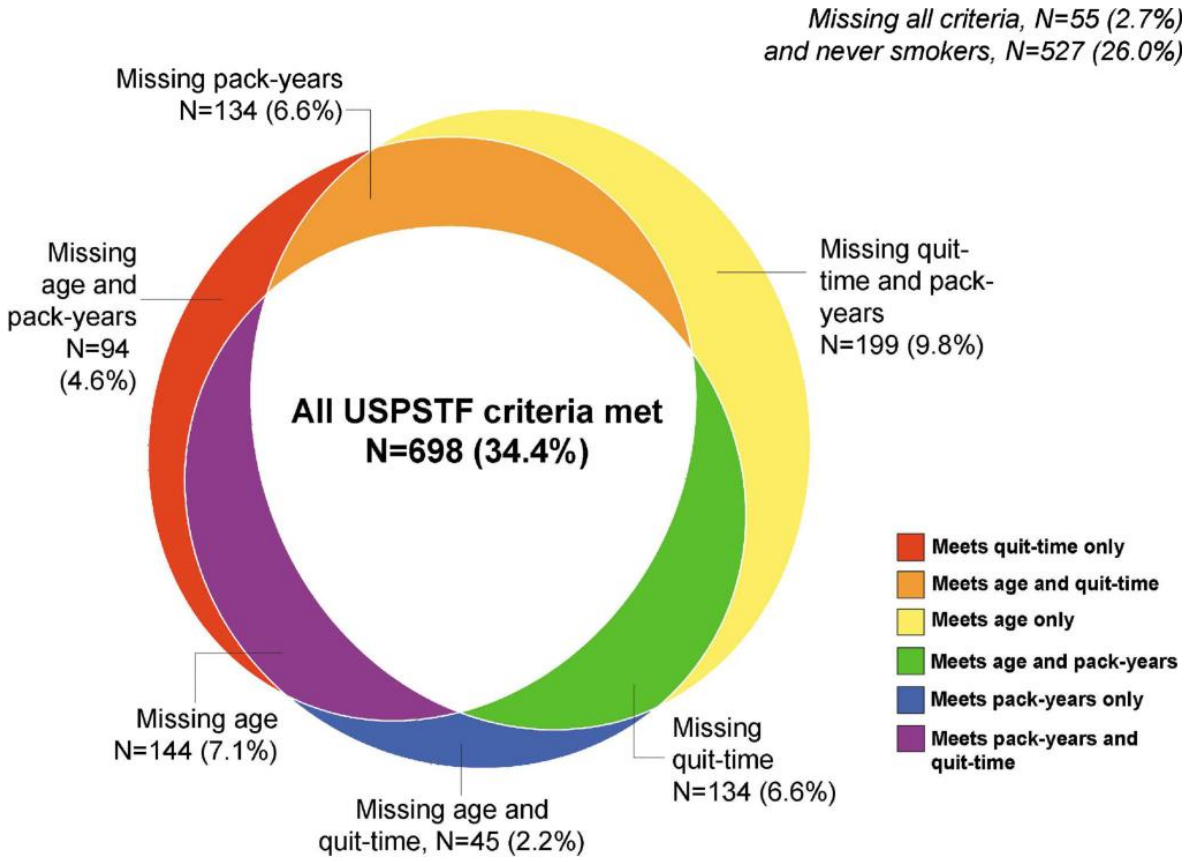
Patient follow-up with LDCT recommendations is low

- National Average for Follow-up with LDCT recommendations: ~55%
- Variability in adherence
- City of Hope program: 90% adherence
- One of the advantages of a LCS program vs standalone imaging center

Overcoming Barriers to LCS

- Educate/empower patients and family members
- PCP education
- EMR notifications
- Utilization of LCS programs
- Educate smoking cessation personnel
- Liquid biopsy (experimental)

Most who develop lung cancer are not eligible for LCS



- >65% of lung cancer patients not eligible for screening
- Disproportionately affects women, Asians, Latinx, African Americans

Wu and Raz, Clin Lung Cancer 2016

Risk Factors for Lung Cancer in Never and Light Smokers

Category	Examples
Environment	Secondhand smoke, radon, asbestos, pollution
Occupational	Rubber, painting, roofing
Disease	Infections, COPD
Genetic	Family history, germline mutations
Iatrogenic	Radiation
Sex	Female
Ethnicity	Asian, Latinx

Liquid Biopsy for Early Detection

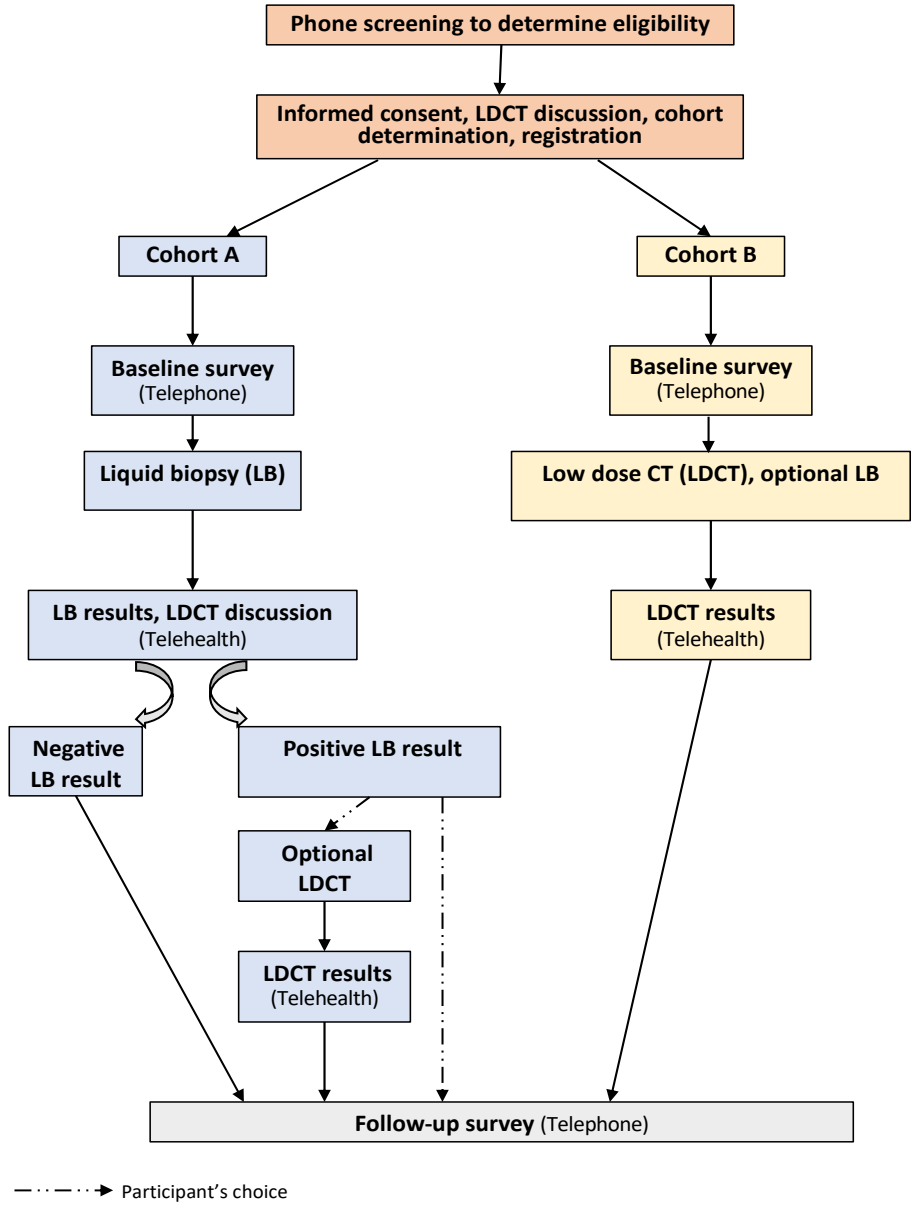
- Detects minute amounts of tumor DNA in blood
- Risk Factors +/- LB → LDCT
- Several in development
  - GRAIL (Galleri)
  - Thrive (CancerSEEK)
  - Quantgene (DEEPGEN)

Sensitivity and Specificity of Liquid Biopsy for Early Lung Cancer Detection

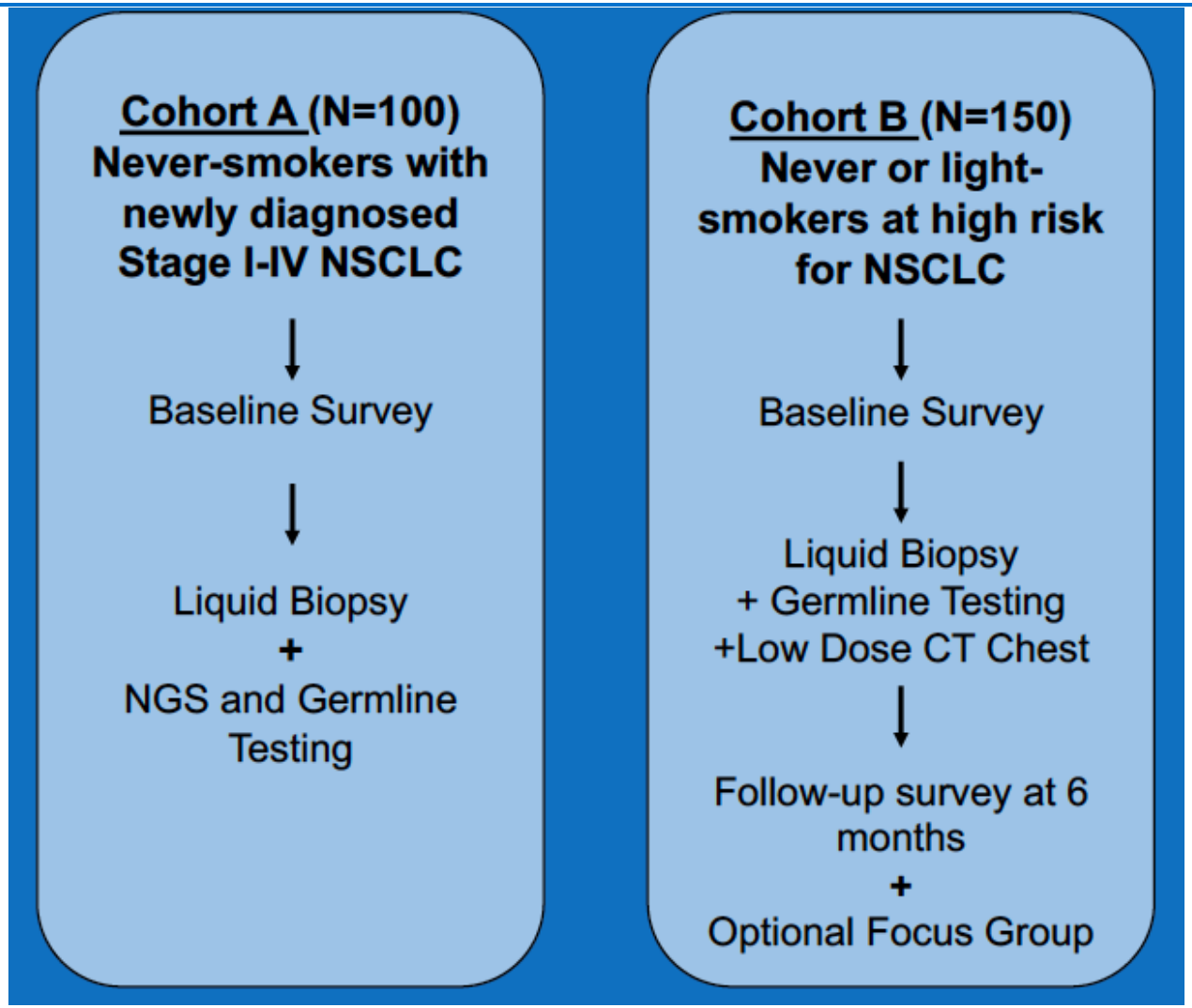
- GRAIL: Sensitivity 99%, Specificity (early stage lung cancer): 21%
- Thrive: Sensitivity 99%, Specificity (early stage lung cancer): 22%
- Quantgene: Sensivity 99%, Specificity (early stage lung cancer): 52%

Note: Studies performed in predominantly non-Hispanic White participants (82% of participants overall, ~5% Blacks, ~5% Asian)

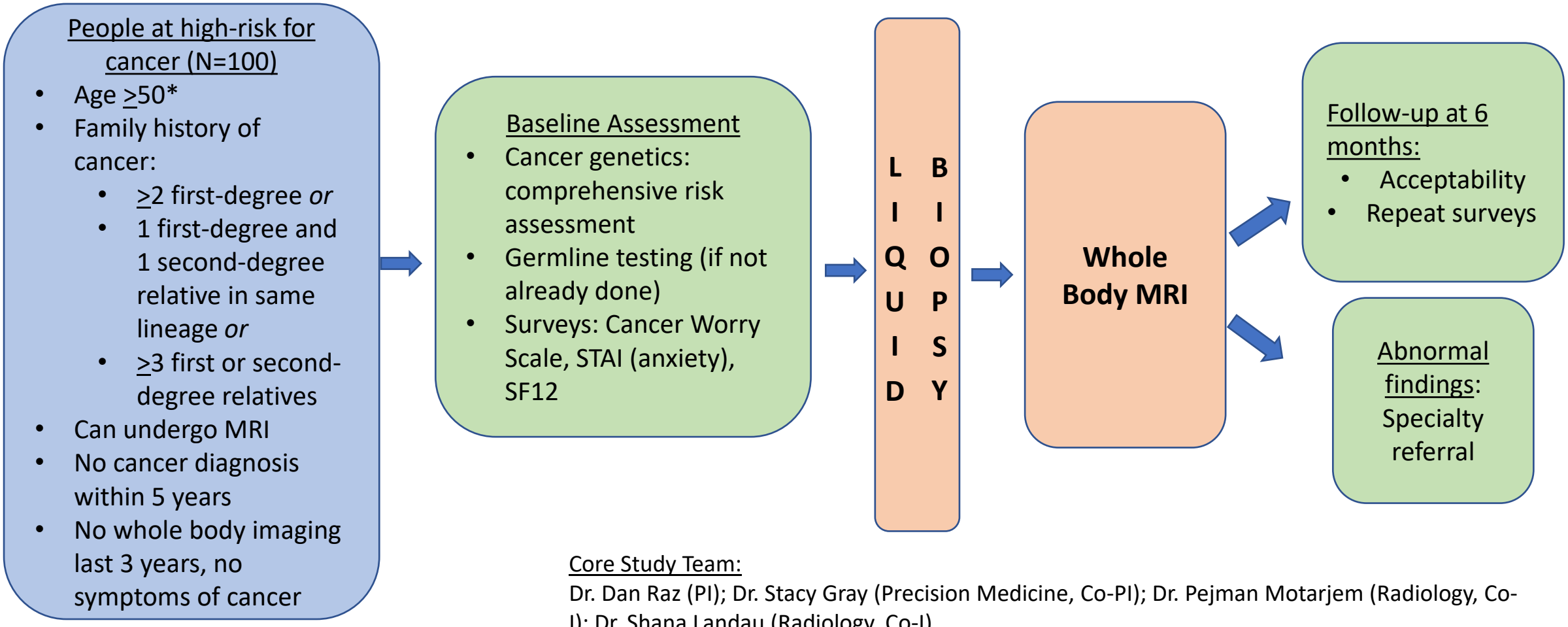
Liquid Biopsy at Home: An option to increase utilization of LDCT?



Study: Liquid Biopsy for Lung Cancer Screening in Light- and Never-smokers



Whole Body MRI and liquid biopsy for early cancer detection: feasibility trial



*Patients also eligible at age <10 years of affected first degree relative

Core Study Team:

Dr. Dan Raz (PI); Dr. Stacy Gray (Precision Medicine, Co-PI); Dr. Pejman Motarjem (Radiology, Co-I); Dr. Shana Landau (Radiology, Co-I)

City of Hope

Summary

- Lung Cancer Screening with LDCT saves lives
- LDCT is severely underutilized due to a number of barriers
- Patient and PCP education needed about benefit of LCS
- Strategies for LCS in people outside of USPSTF criteria needed

Contact information and resources

Dan Raz, MD: draz@coh.org

Sophia Yeung (Lung cancer screening coordinator): syeung@coh.org

COH Lung Cancer Screening Sites:
City of Hope, Duarte
Newport Beach (Newport Diagnostic Center)
Lancaster/Antelope Valley (AVOIC)
City of Hope Corona (coming soon)

Other Lung Cancer Screening Centers of Excellence:
https://go2foundation.org/risk-early-detection/screening-centers/