

Addressing the Increased Risk of Lung Cancer in People with HIV

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Disclosures

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Objectives

1. Define both the risk and risk factors for lung cancer in people with HIV
2. Describe approaches to both primary and secondary prevention of lung cancer in people with HIV
3. Understand approaches to tailor smoking cessation and screening approaches for a population of people with HIV

Epidemiology of lung cancer in PWH

Impact of Lung Cancer

Common Types of Cancer	Estimated New Cases 2022	Estimated Deaths 2022
1. Breast Cancer (Female)	287,850	43,250
2. Prostate Cancer	268,490	34,500
3. Lung and Bronchus Cancer	236,740	130,180
4. Colorectal Cancer	151,030	52,580
5. Melanoma of the Skin	99,780	7,650
6. Bladder Cancer	81,180	17,100
7. Non-Hodgkin Lymphoma	80,470	20,250
8. Kidney and Renal Pelvis Cancer	79,000	13,920
9. Uterine Cancer	65,950	12,550
10. Pancreatic Cancer	62,210	49,830

Lung and bronchus cancer represents 12.3% of all new cancer cases in the U.S.



Lung cancer is by far the leading cause of cancer death in US

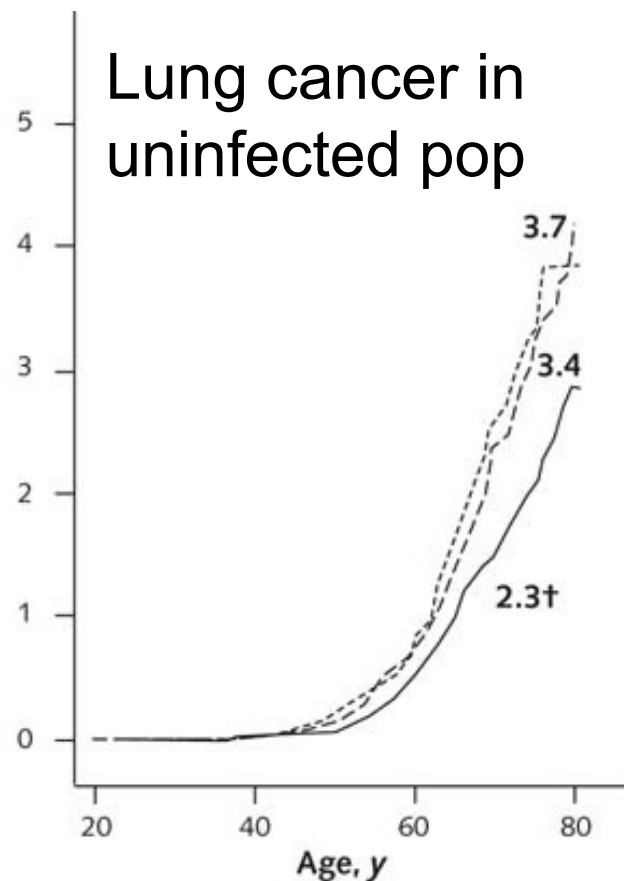
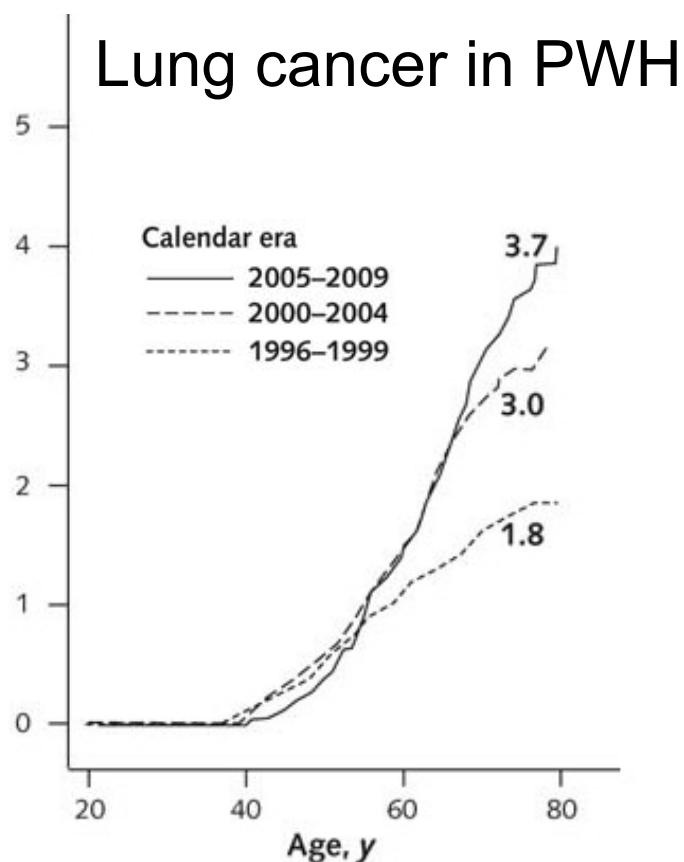
Impact of lung cancer in PWH

- Lung cancer is the most common cause of NADC
- Leading cause of cancer death
- Leading cause of death in some populations
- Cumulative incidence has increased with improved HIV management*

Incidence of lung cancer in PWH

Cancer Type	Observed Cases	SIR (95% CI)
All cancers	21,294	1.69 (1.67-1.72)
AIDS-defining cancers	6,384	14.0 (13.6-14.3)
Non-AIDS-defining cancers	14,344	1.21 (1.19-1.23)
Virus-unrelated non-AIDS defining cancer	10,200	0.92 (0.90-0.94)
Lung cancer	2,475	1.97 (1.89-2.05)

Incidence of lung cancer in PWH



In 1996-2009 era, cumulative incidence is 3.4% by age of 75

- 2.8% in uninfected population

Risk of lung cancer in PWH

- Increased risk is largely driven by smoking behavior
 - An estimated 35-50% of PWH in Western countries currently smoke (~60% former)
 - Approximately 40% of PWH in US vs. 20% of uninfected adults
- HIV is an independent risk factor for lung cancer which has been confirmed in several studies

Risk of lung cancer in PWH

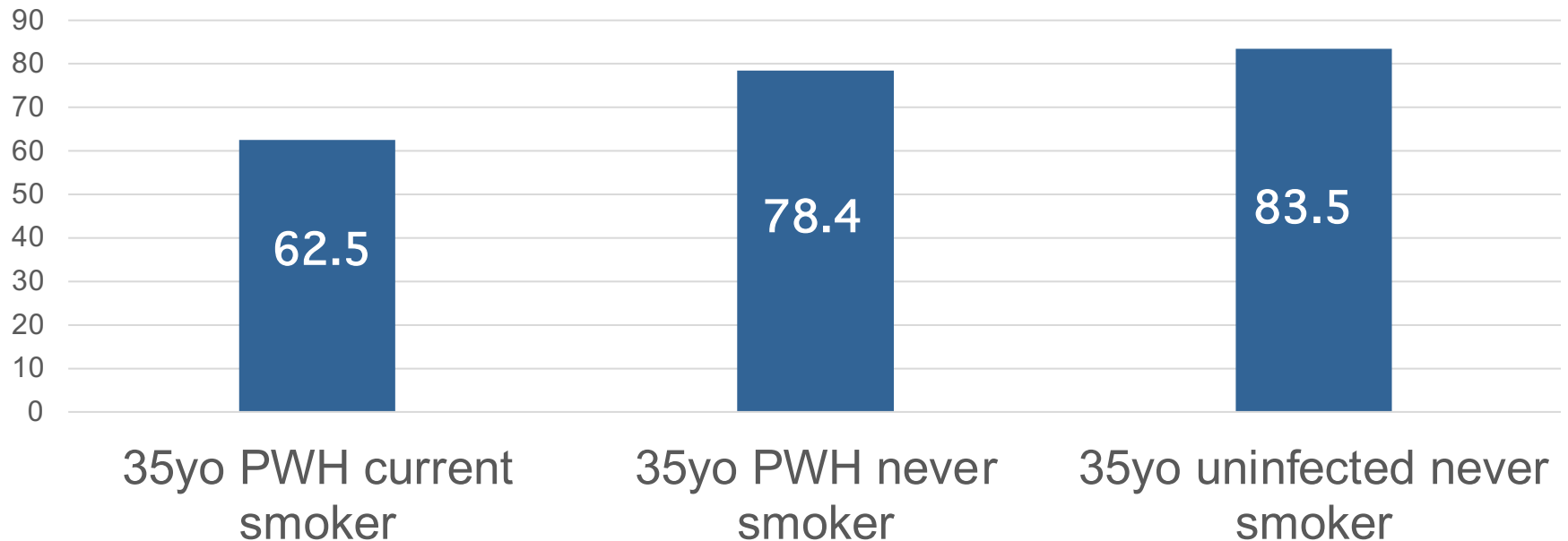
Adjusted IRR of lung cancer

Characteristic	IRR	95% CI
HIV Infection	1.7	1.5-1.9
Age (per 10-year increase)	2.3	2.2-2.5
Former smoker (compared to never)	3.0	2.2-4.1
Current smoker (compared to never)	6.3	4.7-8.4
COPD	1.9	1.5-2.3
Previous bacterial pneumonia	1.5	1.1-2.0

Primary Prevention: Smoking Cessation

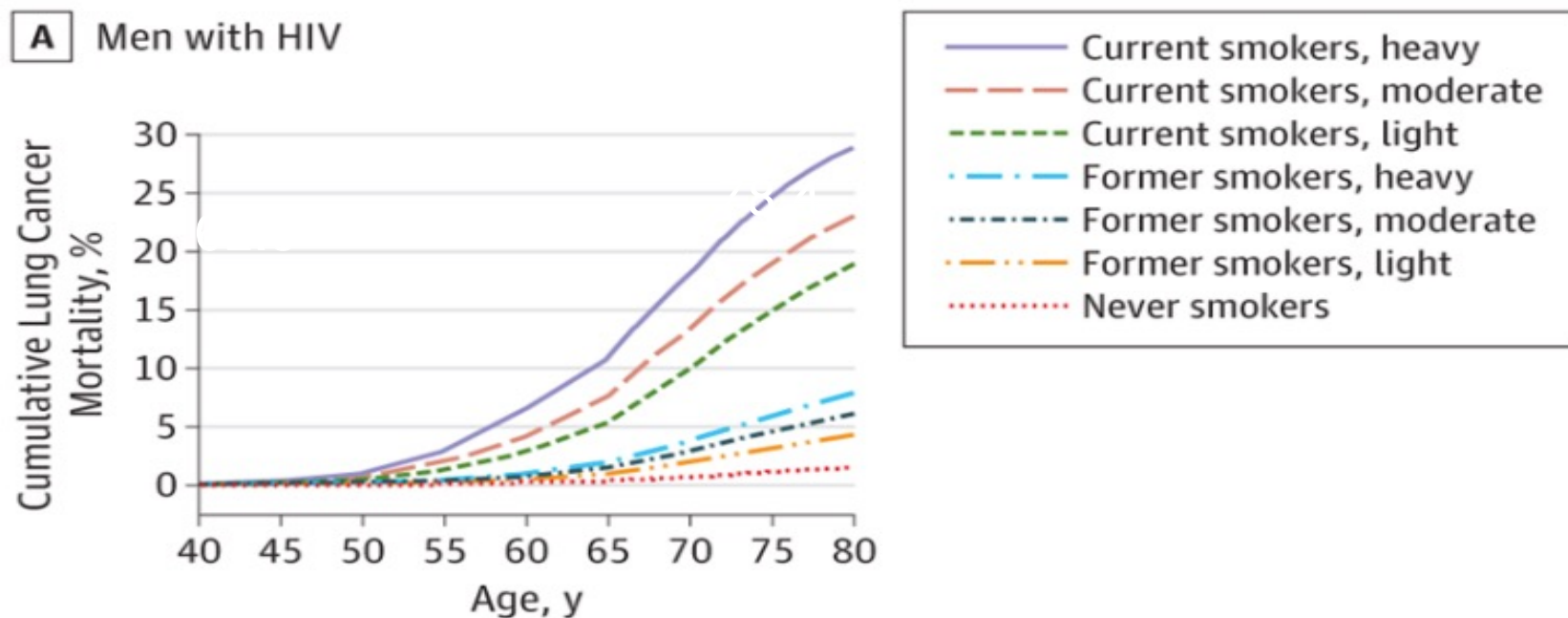
Impact of smoking in PWH

Life expectancy by HIV and smoking status, Denmark



Impact of smoking in PWH

Impact of cessation on lung cancer risk



Impact of smoking in PWH

- PWH who smoke are 6-13x more likely to die from lung cancer than AIDS-related causes
- Quitting by age 40 can result in drastic reduction in lung cancer mortality
 - 40yo heavy smoking man who continues to smoke has a 29% cumulative lung cancer mortality by age 80
 - Drops to 8% if he quits at age 40
- Of US PLWH, if 20% of current smokers quit, 6900 deaths (12% of total lung cancer deaths) could be avoided

Lessons from cessation studies in PWH

- Both standard pharmacologic therapies and NRT are safe and effective in PWH
 - Phase 3 trials of varenicline in US and France
- Limited studies of interventions specific to PWH
 - Improved efficacy of intensive interventions
 - Combining behavioral support and pharmacotherapy
 - Patient motivation likely a key component of cessation
- Increasing interest in “vaping” as a harm-reduction strategy
- Consider your patients unique identities, circumstances and motivations

Secondary Prevention: Lung Cancer Screening

Evidence for Lung Cancer Screening

Comparison of outcomes: National Lung Screening Trial

Trial Arm	Person Years (py)	Lung Cancer Deaths	Lung Cancer Mortality per 100,000 py	Reduction in Lung Cancer Mortality (%)	95% CI	p Value
LDCT	144,103	356	247	20.0	6.8 to 26.7	0.004
CXR	143,368	443	309			

Trial Arm	Person Years (py)	Deaths	All-cause Mortality per 100,000 py	Reduction in All-Cause Mortality (%)	95% CI	p Value
LDCT	167,389	1877	1121	6.7	1.2-13.6	0.02
CXR	166,382	2000	1202			

Evidence for Lung Cancer Screening

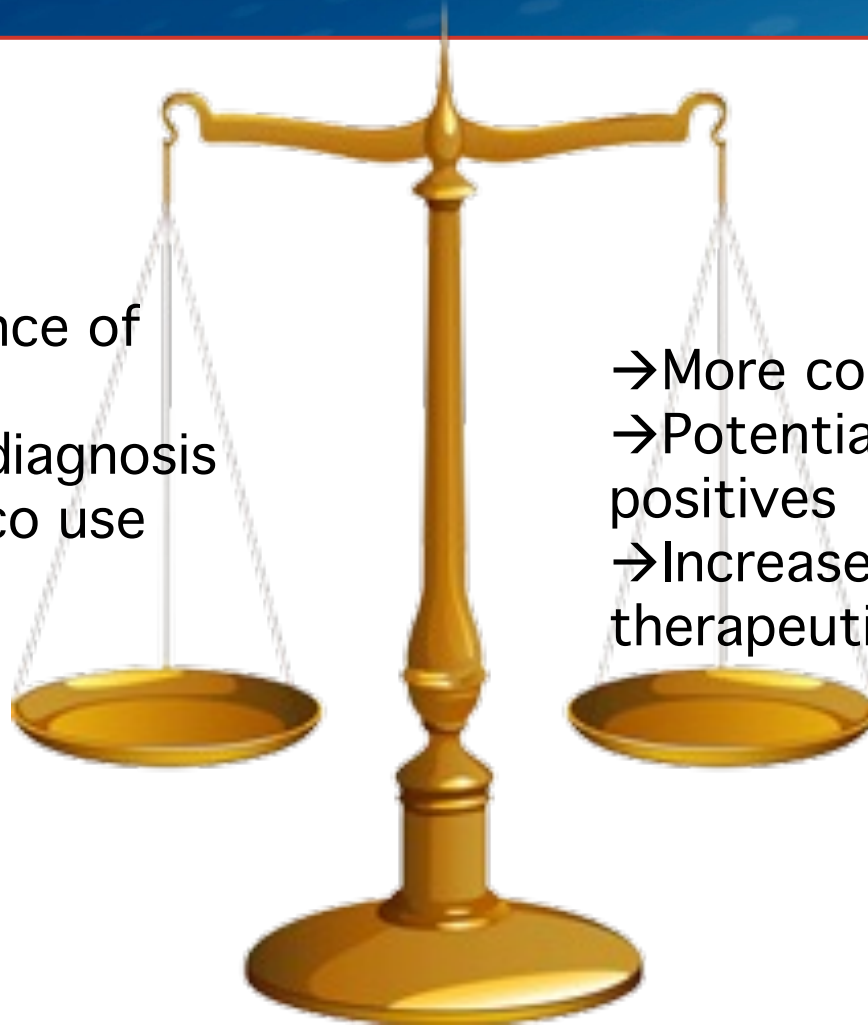
Comparison of outcomes: National Lung Screening Trial

	LDCT			CXR		
	Number Screened	Number Positive	Percent Positive	Number Screened	Number Positive	Percent Positive
Screening Round 1	26,309	7191	27.3	26,035	2387	9.2
Screening Round 2	24,715	6901	27.9	24,089	1482	6.2
Screening Round 3	24,102	4054	16.8	23,346	1174	5.0
All Screening Rounds	75,126	18,146	24.2	73,470	5043	6.9

Benefits and Harms in PWH

→ Increased incidence of lung cancer
→ Younger age at diagnosis
→ Increased tobacco use

→ More competing risks
→ Potential increase in false positives
→ Increased diagnostic and therapeutic harms



Screening Trials in PWH

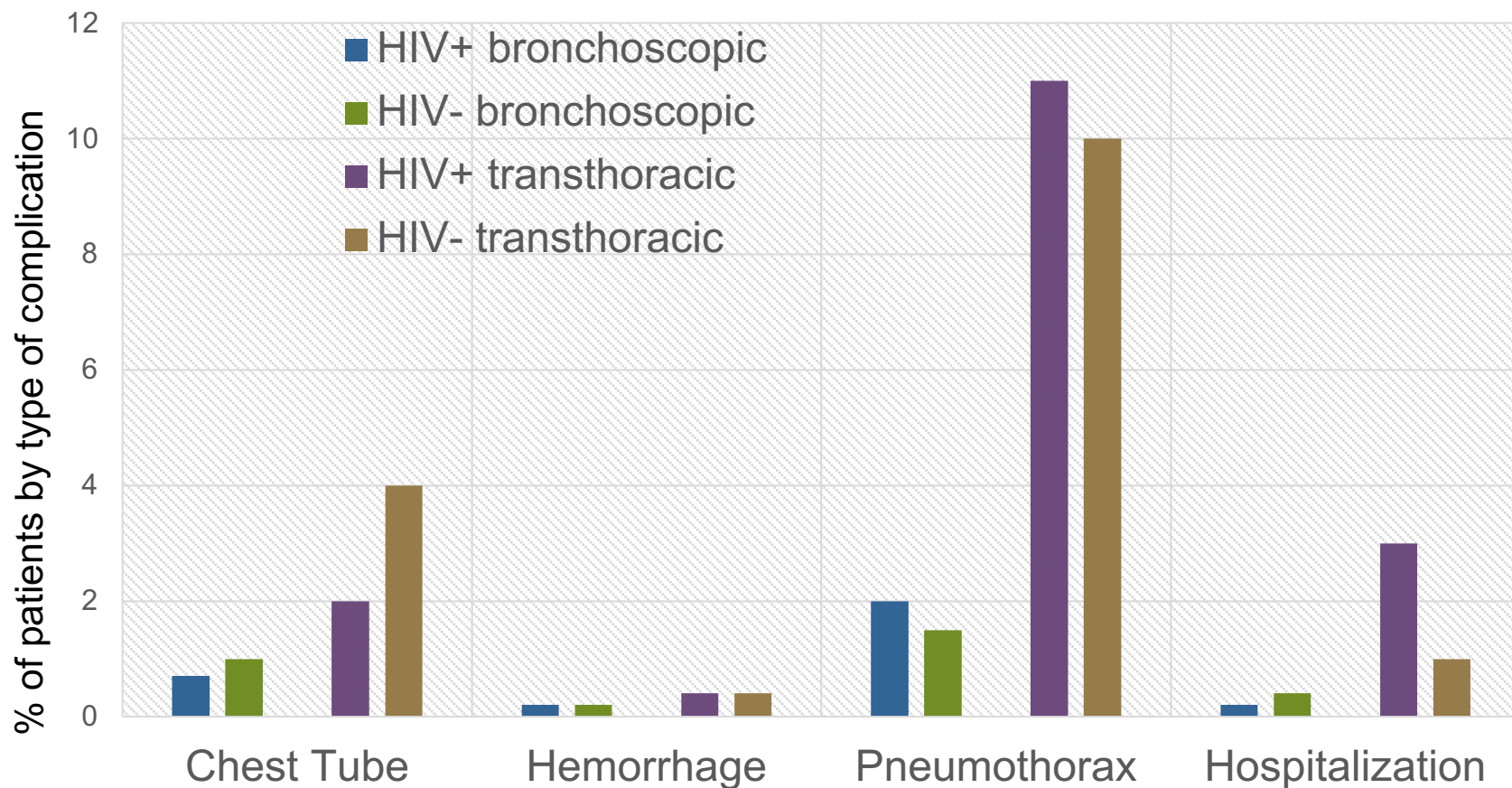
Characteristic	JHU study	ARNS French study
<u>Population</u>	-224 PWH: ≥ 25 years old current or former smokers ≥ 20 pack-years	-442 PWH: ≥ 40 years old current smokers (or quit in last 3 years) ≥ 20 pack-years current CD4 ≥ 100 cells/μL
<u>Intervention</u>	-5 annual rounds of screening with LDCT -algorithm for management of findings	-single chest CT with 2 years of follow-up (dosage in-between LDCT and diagnostic) -algorithm for management of findings
<u>Control</u>	None	None
<u>Outcomes</u>		
Positive findings	48 (21%)	94 (21%)
Lung cancer cases	1	10
Other	Poor adherence to subsequent scans	18 diagnostic procedures with no AEs

False positives in PWH

Factors associated with non-calcified nodules

Predictor	Odds Ratio	95% CI
HIV status		
Uninfected	--	
HIV+, CD4 <200	3.1	1.2-8.2
HIV+, CD4 ≥200	1.0	0.5-1.8
In PWH		
Soluble CD14, by quartiles	1.9	1.2-2.9
Emphysema	2.7	1.0-5.7

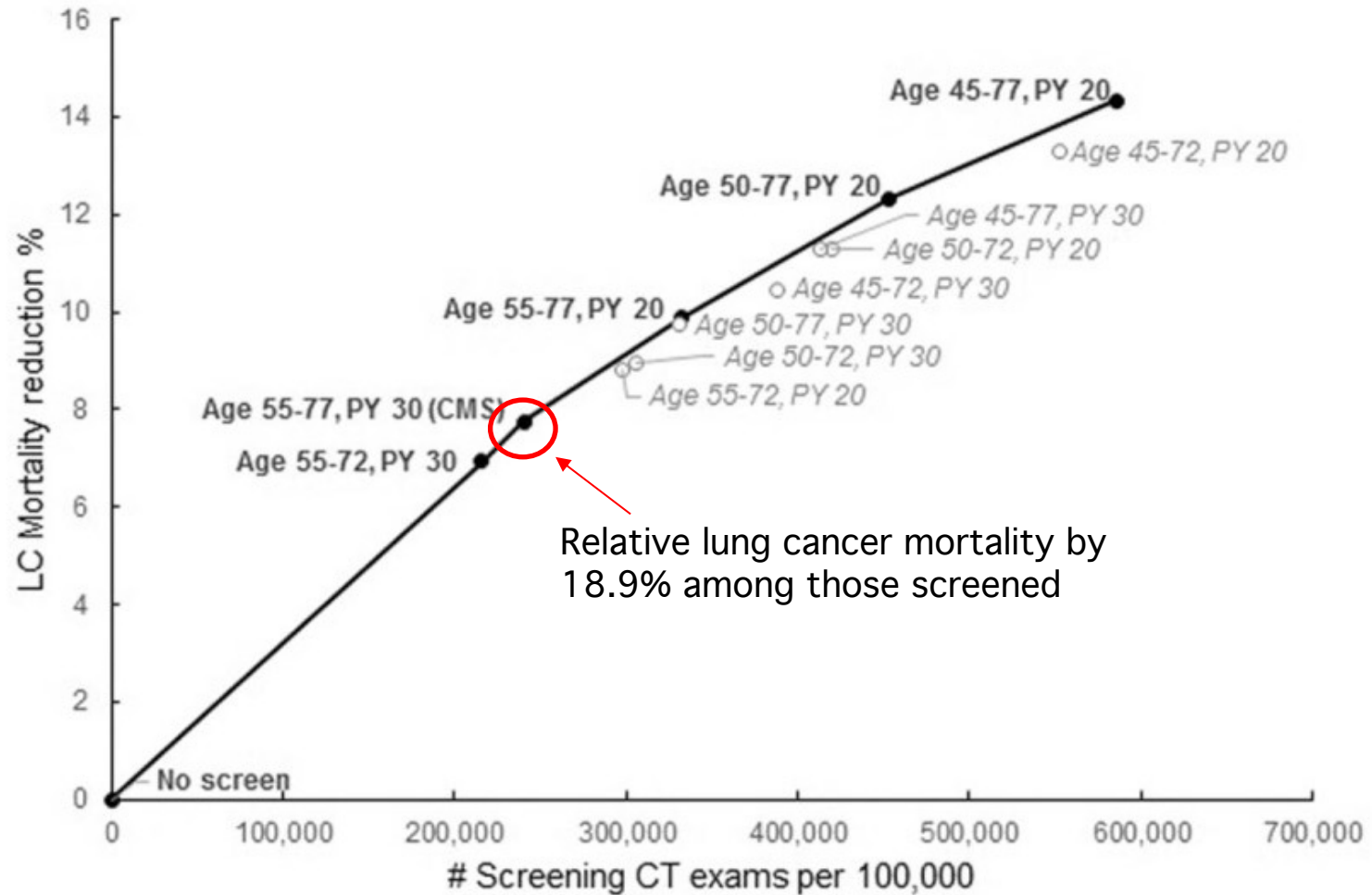
Screening harms in PWH



Modeling screening in PWH

- Adaptation of the Lung Cancer Policy Model
 - Monte Carlo microsimulation
 - Used to inform USPSTF guidelines
 - Included information from VACS cohort, SEER data and Kaiser Permanente Northern California HIV cohort
- Examined 12 combinations of screening criteria:
 - Age of initiation (45-55)
 - Age of termination (72 or 77)
 - Smoking pack-years (20 or 30)
- Excluded non-ART adherent PWH and CD4<500 cells/ μ L

Modeling screening in PWH



Recommending screening in PWH

- PWH are “covered” under current USPSTF and CMS guidelines for screening services
 - Age 50-80 (77 for CMS)
 - 20+ pack-years of cigarette use
 - Currently smoking or quit within 15 years
- Consider HIV control, competing risks of mortality, and patient preferences in decision making
- CMS mandated “Shared Decision Making” provides opportunity to discuss
 - Personalized benefits and harms of screening
 - Screening in context of overall medical care and goals
 - Emphasize smoking cessation and/or abstinence

Current state of lung cancer screening in PWH

- Uptake of screening is low
- 2 contemporary studies of LCS in usual care:
 - 14% of an eligible 104 patients in chart-review of a Midwestern academic HIV care practice
 - 2.7% of an eligible 476 in the DC COHORT, a cohort of PWH receiving care at one of 14 Washington, DC clinics
- Limited data on LCS interventions for PWH

The HIV-LCS study

- Overall objective: *Create a tailored shared decision-making tool to support LCS implementation for PWH*
- Aim 1 : Mixed-methods approach to understanding determinants of LCS behavior in PWH
 - Focus groups with LCS-eligible PWH
 - Interviews with providers
 - General discussion followed by iterative feedback on tools
- Aim 2: Single-arm pilot trial of SDM tool to prior to LCS
 - Evaluating improvement in LCS knowledge, decisional conflict, acceptability, feasibility

The HIV-LCS study: participants

- Aim 1: 64 PWH-participants (and 11 HIV care providers)
 - 53% identified as a race/ethnicity other than NHW
 - 81% male; median age 59
 - 43% currently smoking; median pack-years was 35
 - 55% had annual income <\$30K
 - 41% received Medicaid insurance

 - 28% reported having a LCS exam before
 - 66% reported having other cancer screening

The HIV-LCS study: patient-provider themes

- Enthusiasm for prevention: High understanding of chronic disease risk in PWH and overall enthusiasm for health screenings
- Support for tailored care: Enthusiasm for dedicated or tailored screening interventions for PWH
- Impact of HIV on lung cancer: High awareness of high tobacco use and high lung cancer risk in PWH, less awareness of association between HIV and lung cancer independent of smoking
- Patient relationship to provider and health system: Screening decisions are often nested within trusting patient-provider relationships; though a few patients report medical skepticism rooted in HIV history
- Knowledge of LCS: Knowledge and experience with LCS is lower than other screening modalities among PWH and their providers
- Financial barriers: Issues of cost and coverage are identified as common barriers by patients and providers

“I gotta hear it from my doctor, and if they recommend that I don’t have it, then I don’t have it, if they recommend that I do then I will.”

“I think it just important for [PWH] in general to have checkups regularly, or screenings regularly, for things that are important, like lung cancer and other forms of cancer. Because we’re so susceptible.”

The HIV-LCS study: patient themes

- Impact of smoking cessation: For many PWH who had quit smoking, a “teachable moment” related to their health led to effective cessation
- Support for evidence: In supporting approaches to LCS in PWH, patients want an evidence-based and data-driven approach
- Importance of survivorship: Perceptions of survivorship at HIV diagnosis may have related to fatalism around tobacco use in the past, but narratives that support ongoing survival and health are important to health decisions in PWH

“I never thought I would turn 25, which is the reason that I drank and smoked and did a lot of the drugs, because I was for sure going to die, so the fact that I’m still here and I’ve been smoke free for eight years, you know, the life we have no idea.”

“I think we are much more aware of our health care needs, and concerns and are much more aware of how we are doing and what we need to worry about than most people.”

The HIV-LCS study: provider themes

- Barriers to prevention: Providers are not discussing lung cancer screening with all eligible patients; identified major barriers to all cancer screening and prevention include patients' acute issues, multimorbidity, mental health issues and other substance abuse
- Specific LCS barriers: Providers noted additional barriers to lung cancer screening scheduling, access, complexities of eligibility and the requirement for providers to perform shared decision making
- LCS prioritization: Providers have an overall positive view of LCS and its importance, though it falls below the priority of acute and primary prevention efforts around cardiovascular disease or active smoking.

”You know people have only so much bandwidth and if they’re busy going to multiple doctors appointments to manage their diabetes or their substance abuse or their mental health...it’s a little tough to say ‘Well you know, why don’t you also get lung cancer screening.’”

The HIV-LCS study: Tailoring a tool

- Create a facile and easy-to-use tool that could both be embedded in the EHR and pull existing data from the EHR
- Tailor both risk of lung cancer and competing risks to PWH
- Make level of detail customizable to the patient
- Provide a screening recommendation when appropriate
- Use figures and pictures to emphasize survival
- Tool that can be used in-office and reviewed at home

The HIV-LCS study: Tailoring a tool

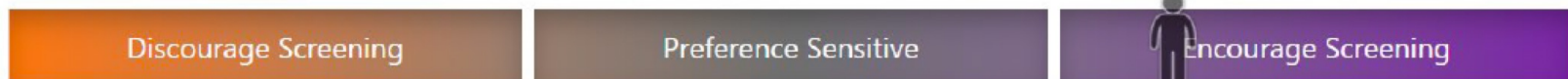
PERSONALIZED LUNG CANCER RISK ASSESSMENT

Screening benefits likely outweigh harms.

You are eligible for lung cancer screening.

Among eligible patients, your risk of developing lung cancer is higher than average.

You are at low risk of screening harm.



The benefits of lung cancer screening must be balanced against the potential harms including:

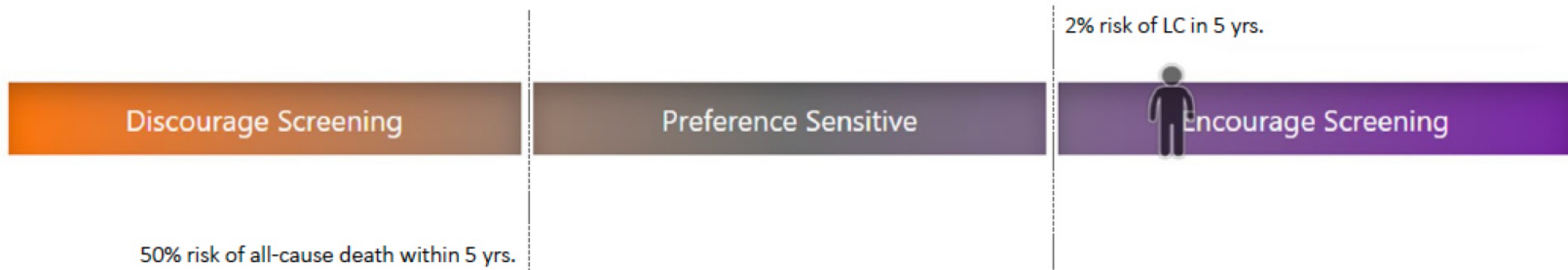
- false-positive findings
- unnecessary procedures
- finding a cancer that never would have hurt you

The HIV-LCS study: Tailoring a tool

PERSONALIZED LUNG CANCER RISK ASSESSMENT

Screening benefits likely outweigh harms.

4.2% risk of developing lung cancer in 5 years
27.4% predicted risk of dying from all-causes within 5 years
Number Needed to Screen: ~167 similar patients to avoid 1 lung cancer death



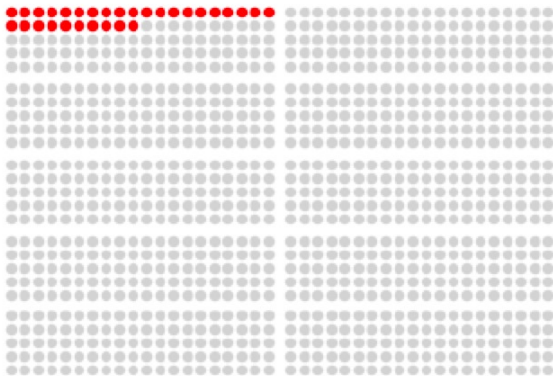
The benefits of lung cancer screening must be balanced against the potential harms including:

- false-positive findings
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The HIV-LCS study: Tailoring a tool

Among 1000 people like you...

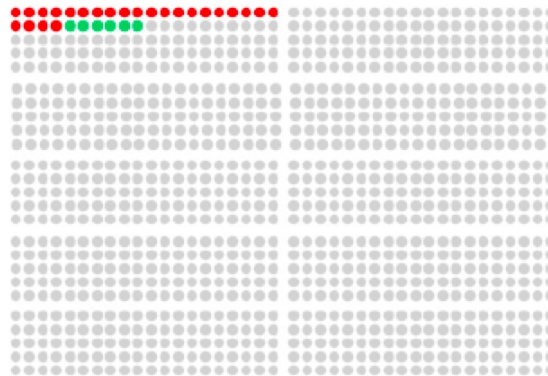
Not screened



Legend:

People who died from Lung Cancer ● 30

Screened



Legend:

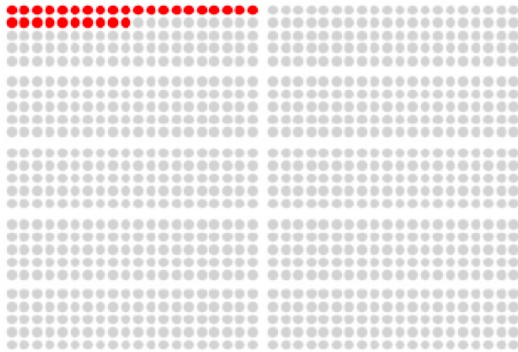
People who died from Lung Cancer ● 24

Lives saved from Lung Cancer because they were screened ● 6

The HIV-LCS study: Tailoring a tool

Among 1000 people like you...

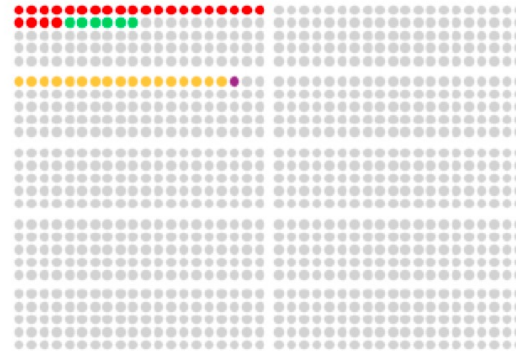
Not screened



Legend:

People who died from Lung Cancer ● 30

Screened



Legend:

People who died from Lung Cancer ● 24

Lives saved from Lung Cancer because they were screened ● 6

Many people need a repeat CT scan due to false-positive findings*

People who had an invasive test following a false alarm** ● 17

People who had complications following invasive tests ● 1

Conclusions

- People with HIV (PWH) are at 1.5-3 fold higher risk of lung cancer than the general population
- Risk largely reflects higher rates of smoking in PWH and increased efforts should be directed at evidence-based smoking cessation
- Lung cancer screening *can be* an effective tool to reduce lung cancer mortality in PWH
- Tailored and streamlined approaches to both primary and secondary prevention *will* increase the real-world effectiveness of both smoking cessation and lung cancer screening

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