AETC AIDS Education & Training Center Program Mountain West

Addressing the Increased Risk of Lung Cancer in People with HIV

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Disclosures

None.

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 the US

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

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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

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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)**

Hernandez-Ramirez, et.al. Lancet HIV 2017

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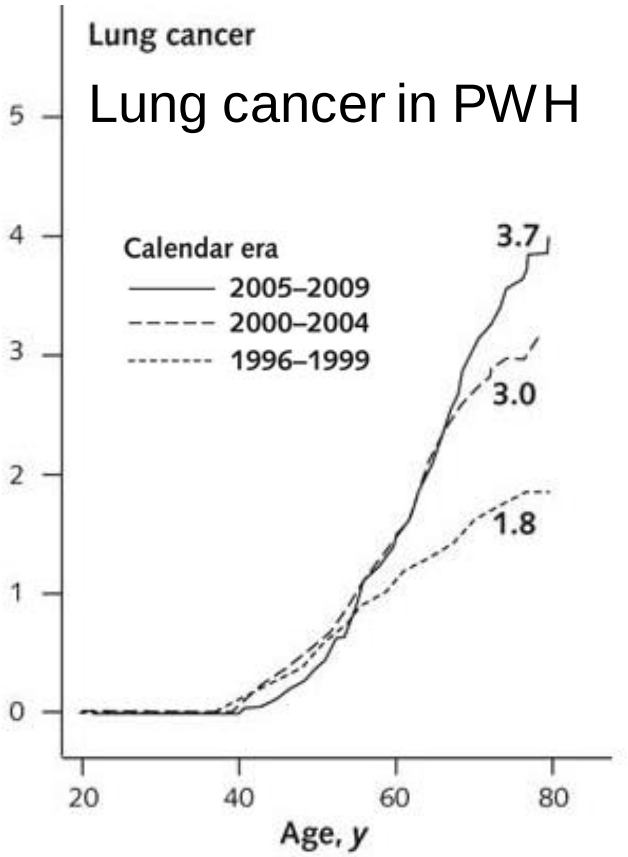
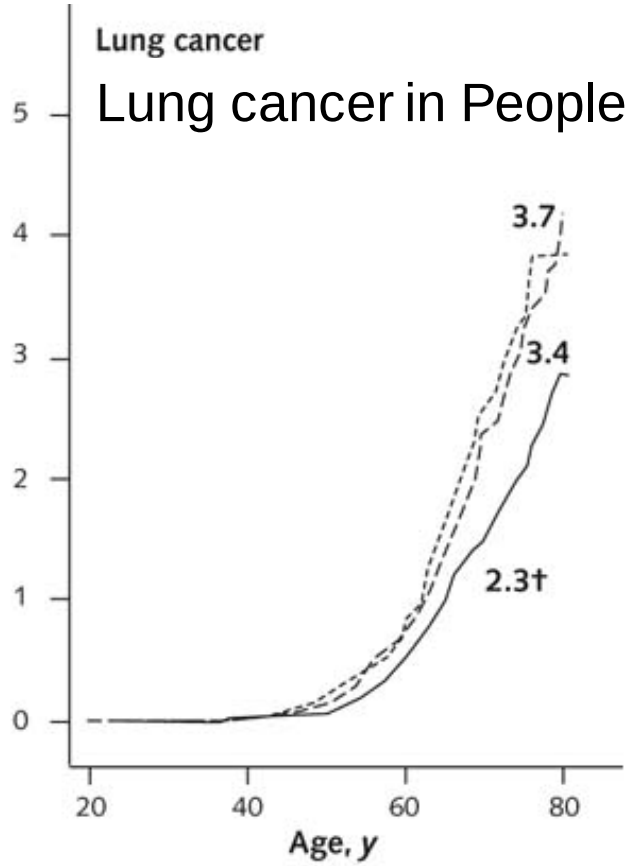
Incidence of lung cancer in PWH





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

- 2.8% in people without HIV

Silverberg, et.al. Ann Int Med 2015

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 adults without HIV
- HIV is an independent risk factor for lung cancer which has been confirmed in several studies

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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

Sigel, et.al. AIDS 2012

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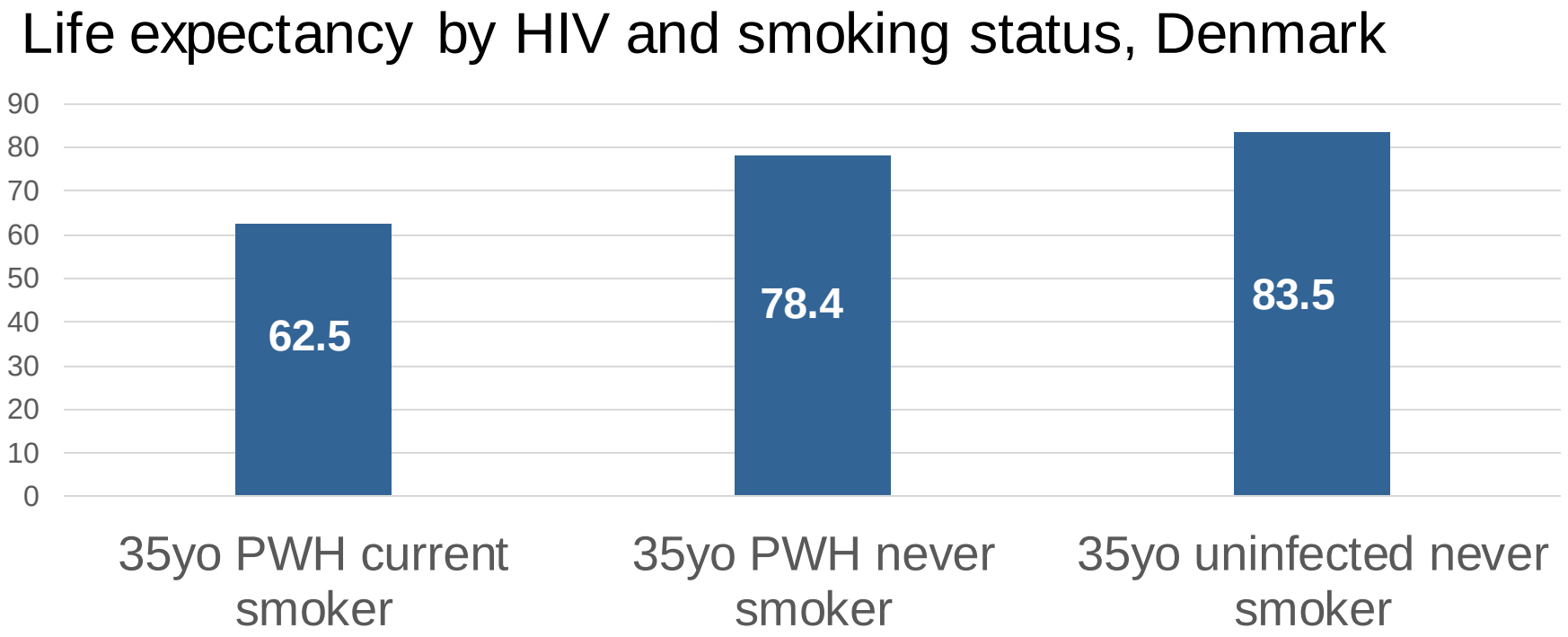
Primary Prevention: Smoking Cessation

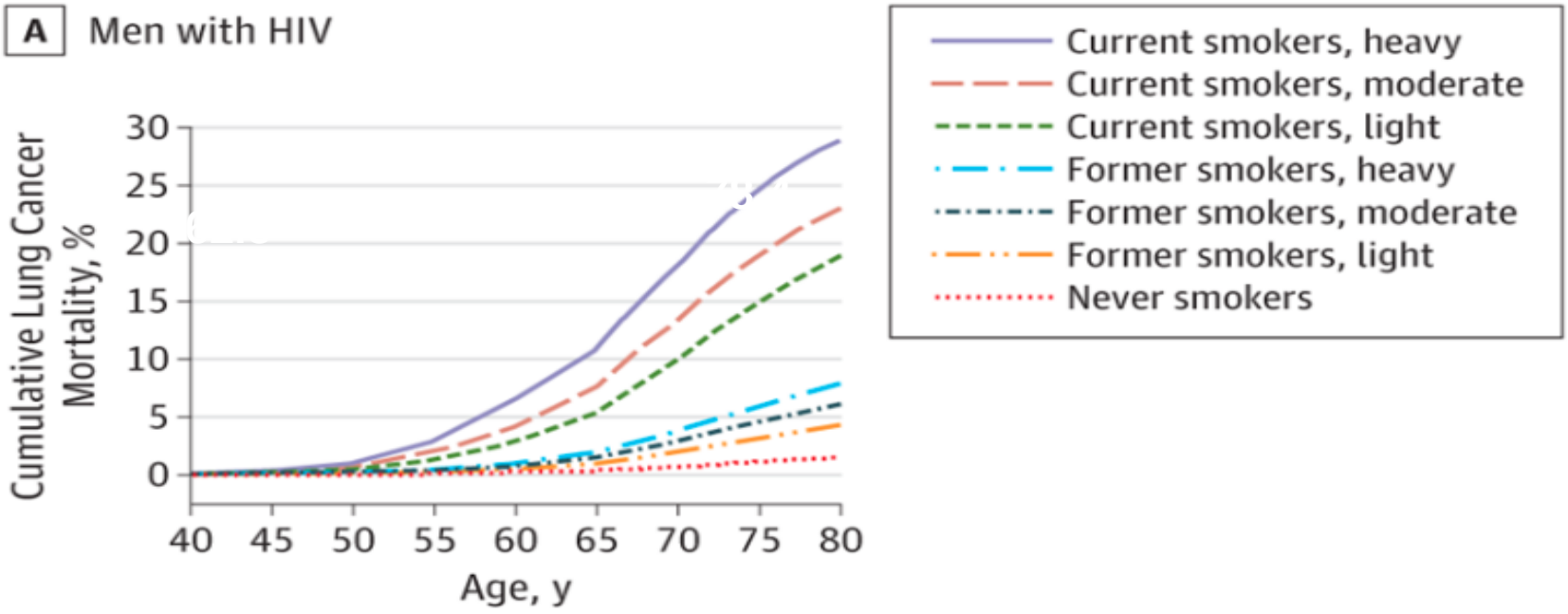
Impact of smoking in PWH



Sigel, et.al. AIDS 2012

Impact of smoking in PWH

Impact of cessation on lung cancer risk



Reddy et.al. JAMA Int Med 2017

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 PWH, if 20% of current smokers quit, 6900 deaths (12% of total lung cancer deaths) could be avoided

Ashare RL, et.al. Drug Alcohol Dependence. 2019.
Mercie P, et.al. Lancet HIV. 2018.

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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

Reddy et.al JAMA Int Med 2017

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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			

NLST, et.al. NEJM 2011

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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

NLST, et.al. NEJM 2011
Pinsky, et.al. Ann Int Med 2015

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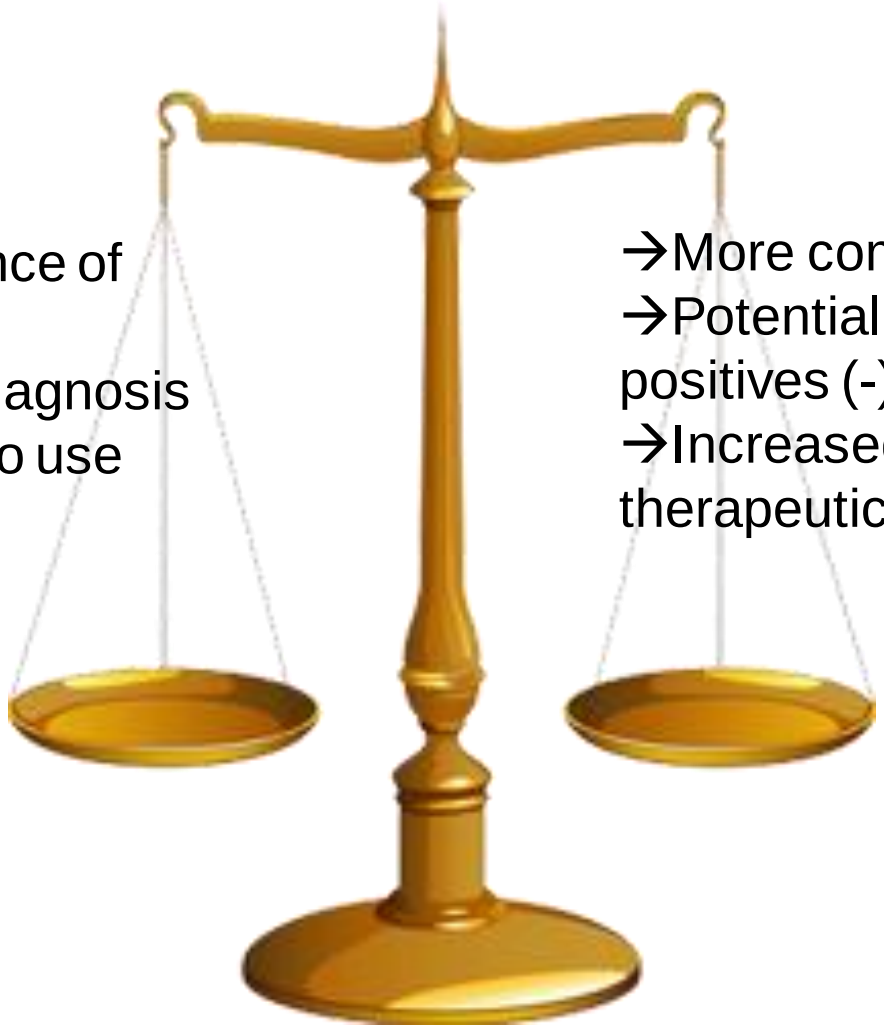
Benefits and Harms in PWH

→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 (-)

NLST, et.al. NEJM 2011
Pinsky, et.al. Ann Int Med 2015

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Screening Trials in PWH

Characteristic	JHU study	ARNS French study
Population	- 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
Intervention	- 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
Control	None	None
Outcomes		
Positive findings	48 (21%)	94 (21%)
Lung cancer cases	1	10
Other	Poor adherence to subsequent scans	18 diagnostic procedures with no AEs

Hulbert, et.al. JThor Onc 2014
Makinson, et.al. AIDS 2016

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False positives in PWH

Factors associated with non-calcified nodules

Predictor	Odds Ratio	95% CI
HIV status		
Without HIV	--	
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

Sigel, et.al. AIDS 2017
Triplette, et.al. AIDS 2018

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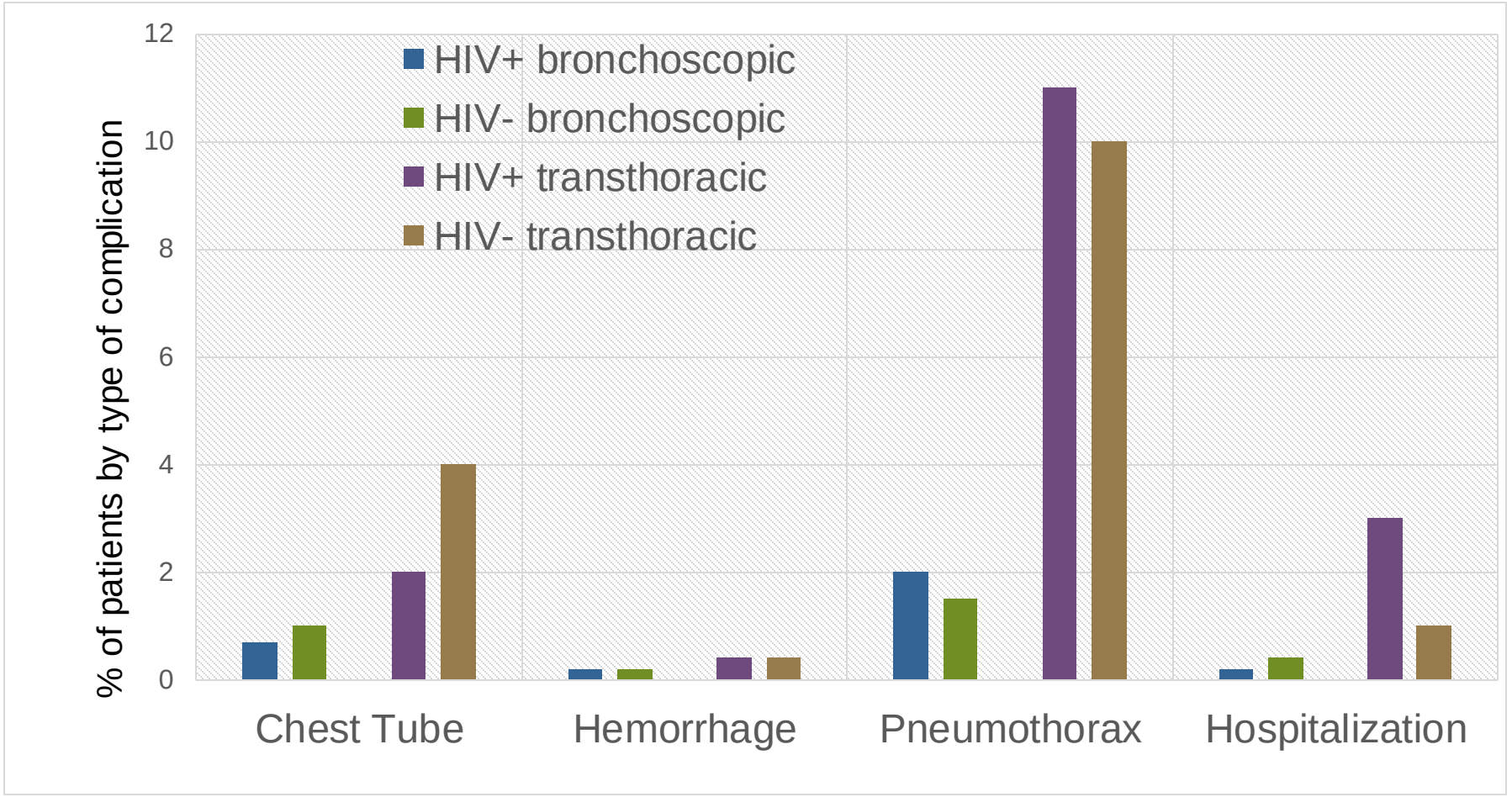
Screening harms in PWH



Crothers, et.al. ATS 2019

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/µL

Kong et.al. AIDS 2018

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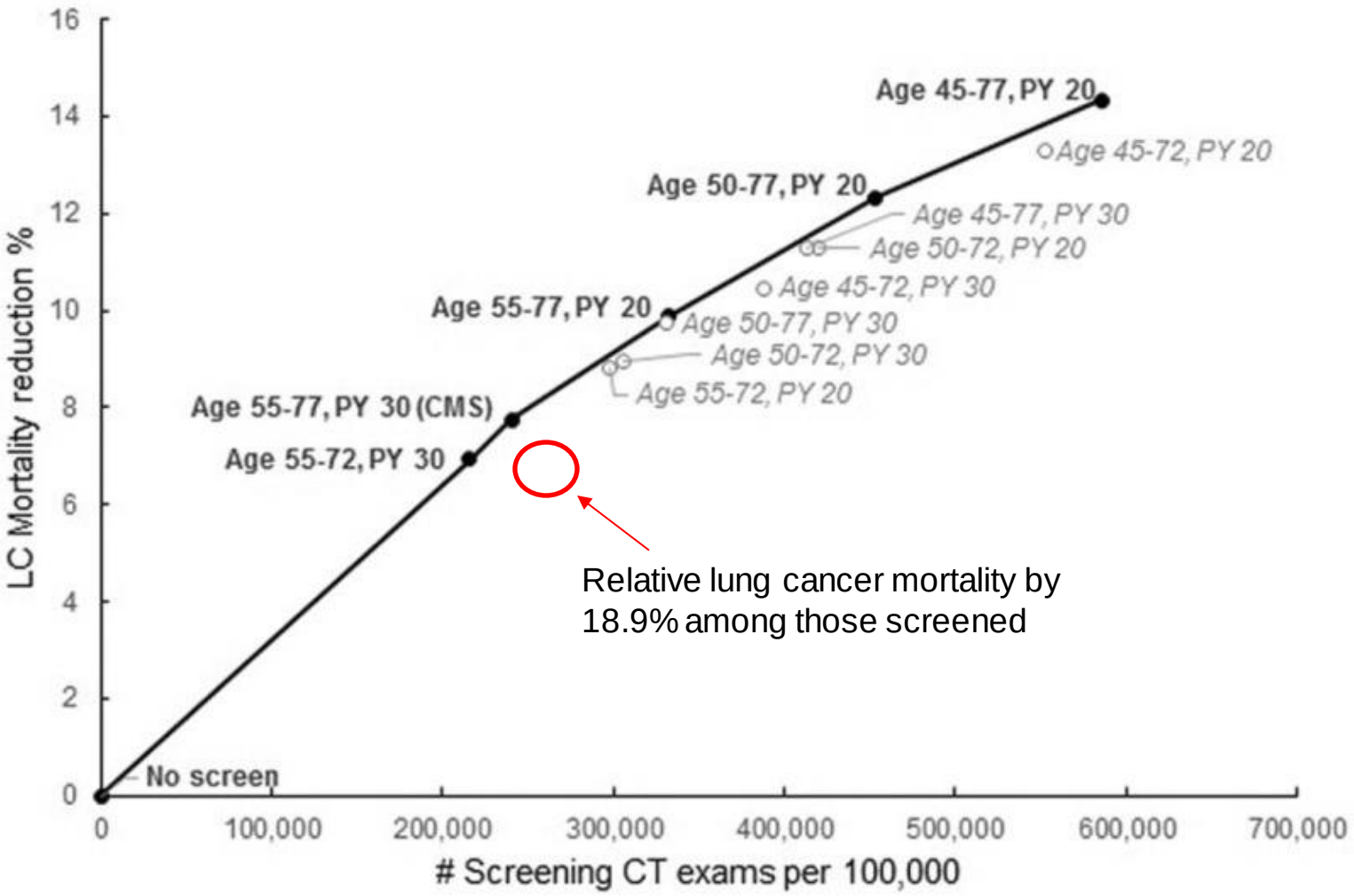
Modeling screening in PWH



Kong et.al. AIDS 2018

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

Kong et.al. AIDS 2018

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Conclusions

- Lung cancer is a substantial cause of morbidity and mortality in PWH
- Among PWH currently smoking, successful cessation can vastly expand life expectancy
- Traditional methods of cessation are safe and effective in PWH
- Lung cancer screening is an effective tool for lung cancer-specific mortality reduction
- Main harm to consider in PWH is competing risks
- We need more design and evaluation (implementation) studies to support tailored methods for cessation and screening in PWH

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