Air pollution and lung health among people with HIV

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global health collaborative
MUST · Uganda

MASSACHUSETTS GENERAL HOSPITAL
GLOBAL HEALTH

HARVARD T.H. CHAN SCHOOL OF PUBLIC HEALTH

Outline

- Why HIV and lung disease, and why sub-Saharan Africa?
- 3 Research Questions:
    1. *What is the prevalence of lung dysfunction among PWH in sub-Saharan Africa?*
    2. *What is ambient air quality in rural Uganda?*
    3. *Do people with HIV have higher risk of air pollution-associated lung disease?*
- Ongoing work/next steps

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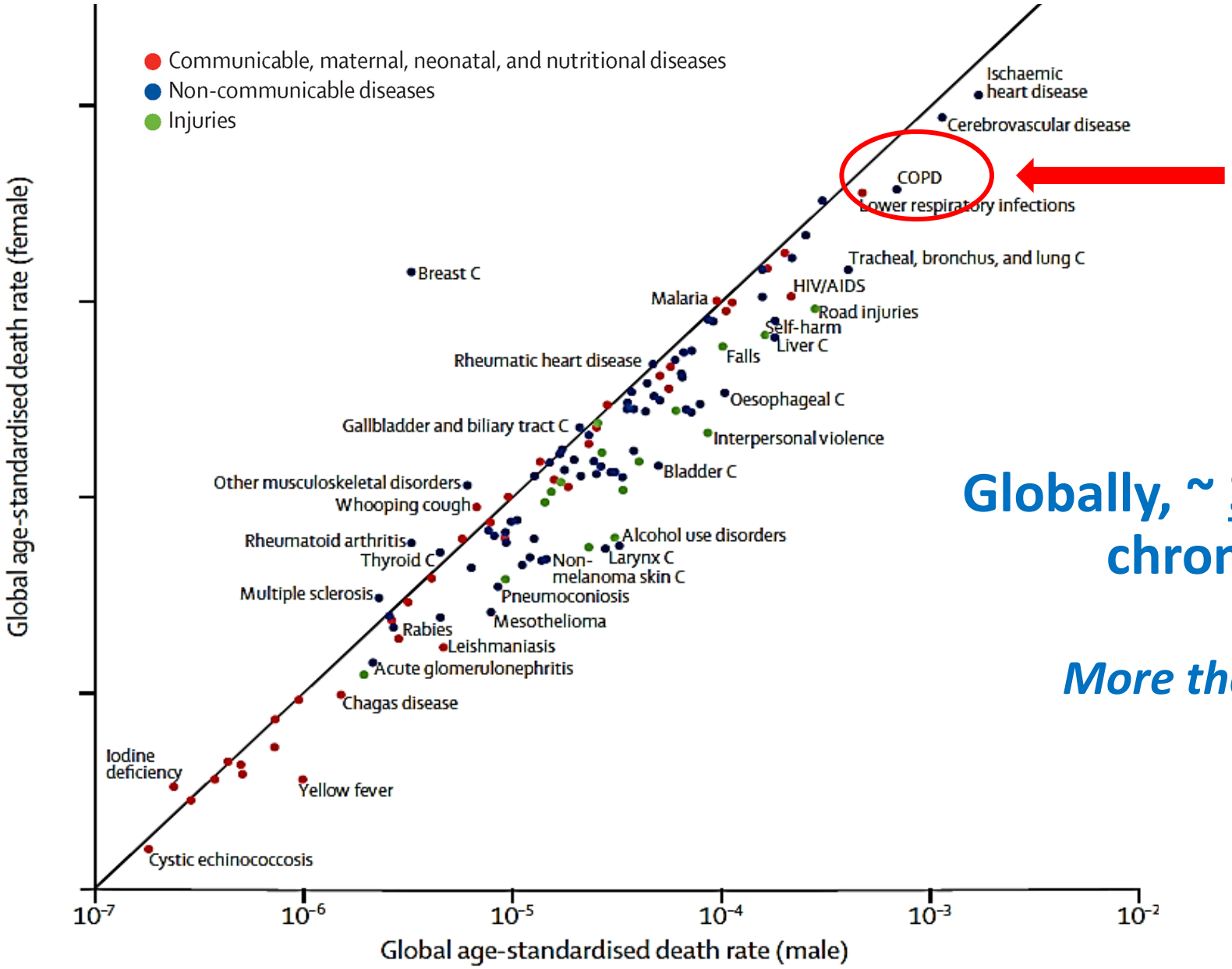
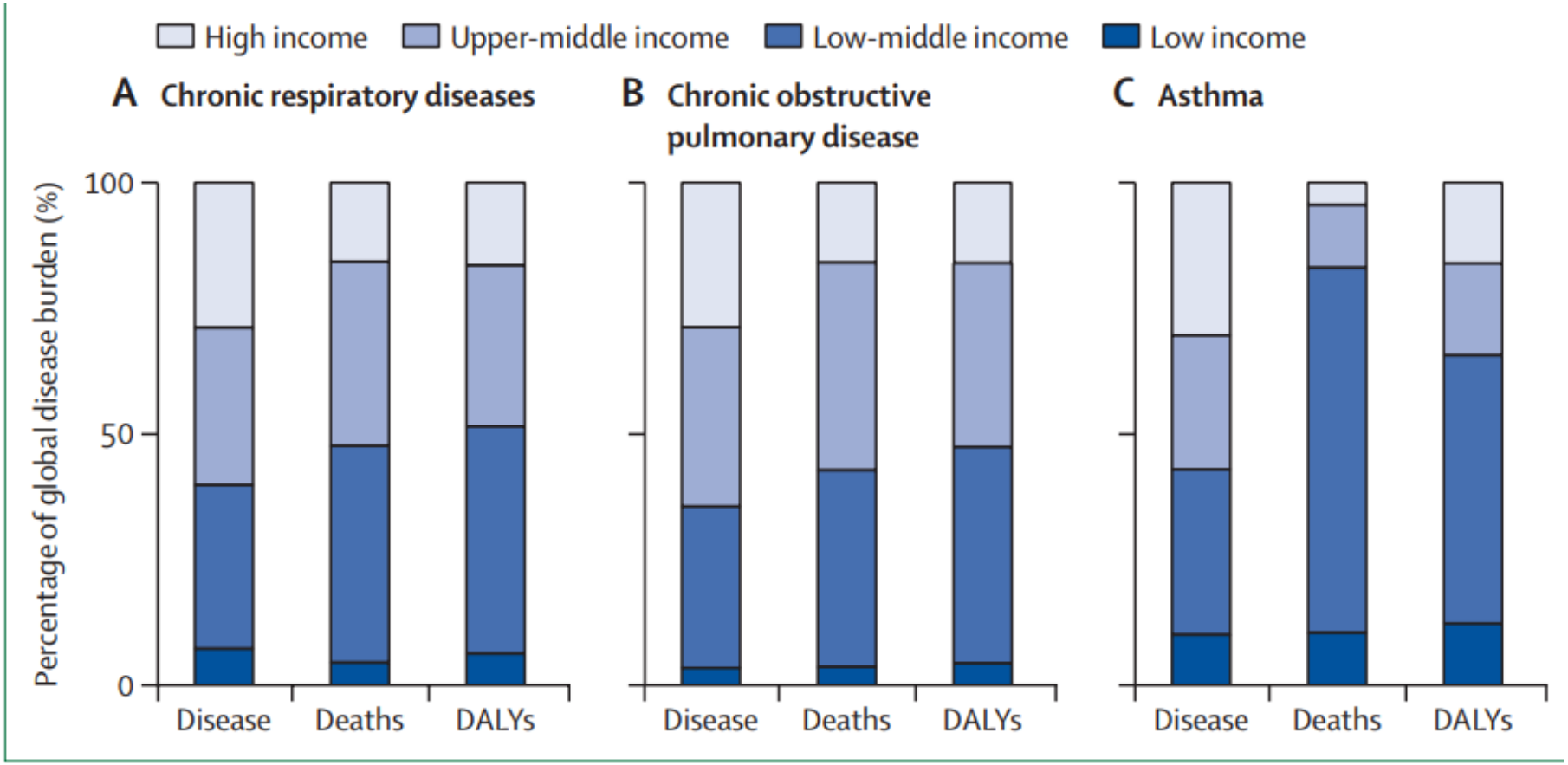


Globally, ~ 3.9 million deaths/year from chronic respiratory diseases

More than HIV/AIDS, TB and malaria combined

Lancet 2016;388:1459-1544
Lancet 2018; 392(10159):2052-90
Lancet Respir Med 2020;8:585--96

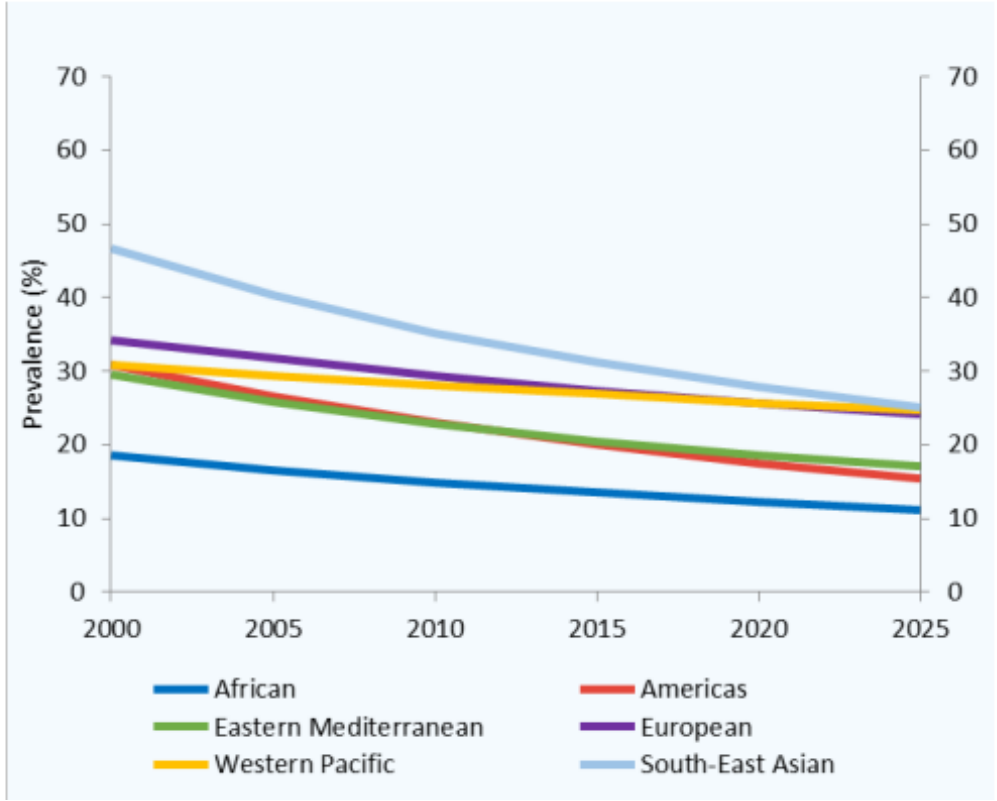
80% of lung disease morbidity and mortality occurs in low- and middle-income countries



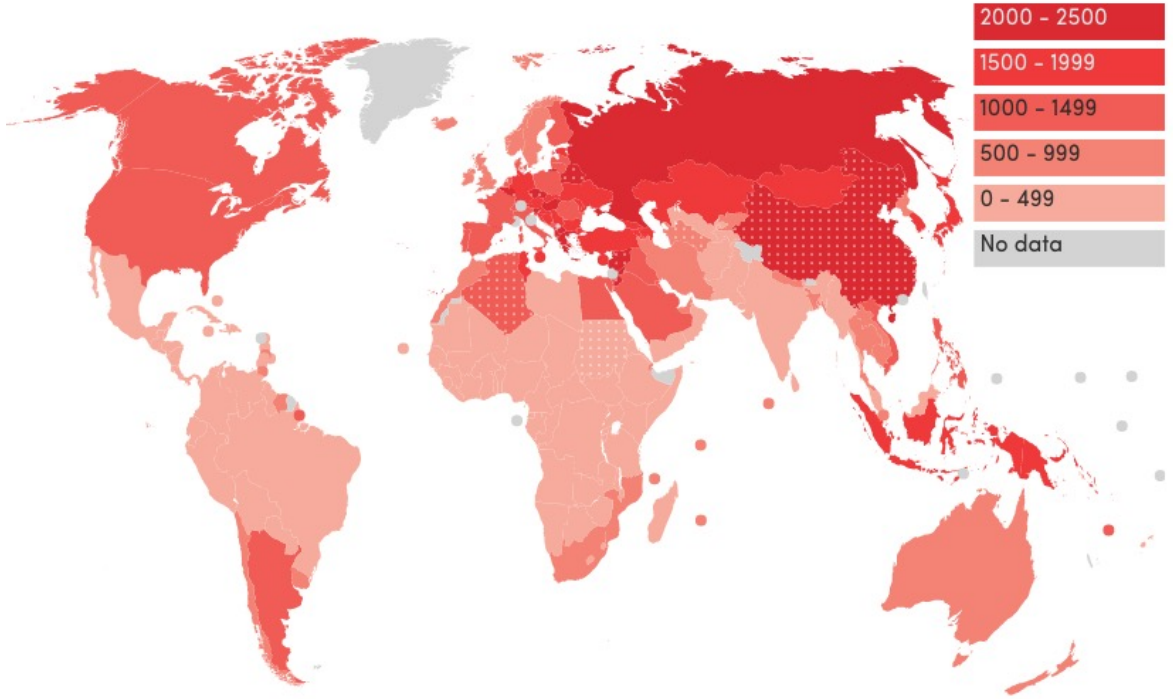
Meghji J *et al*. Lancet 2021;397:928-940

Smoking might *not* be the leading cause of lung disease in sub-Saharan Africa (…for now)

Figure 4. Trends in current tobacco use among people aged ≥15 years

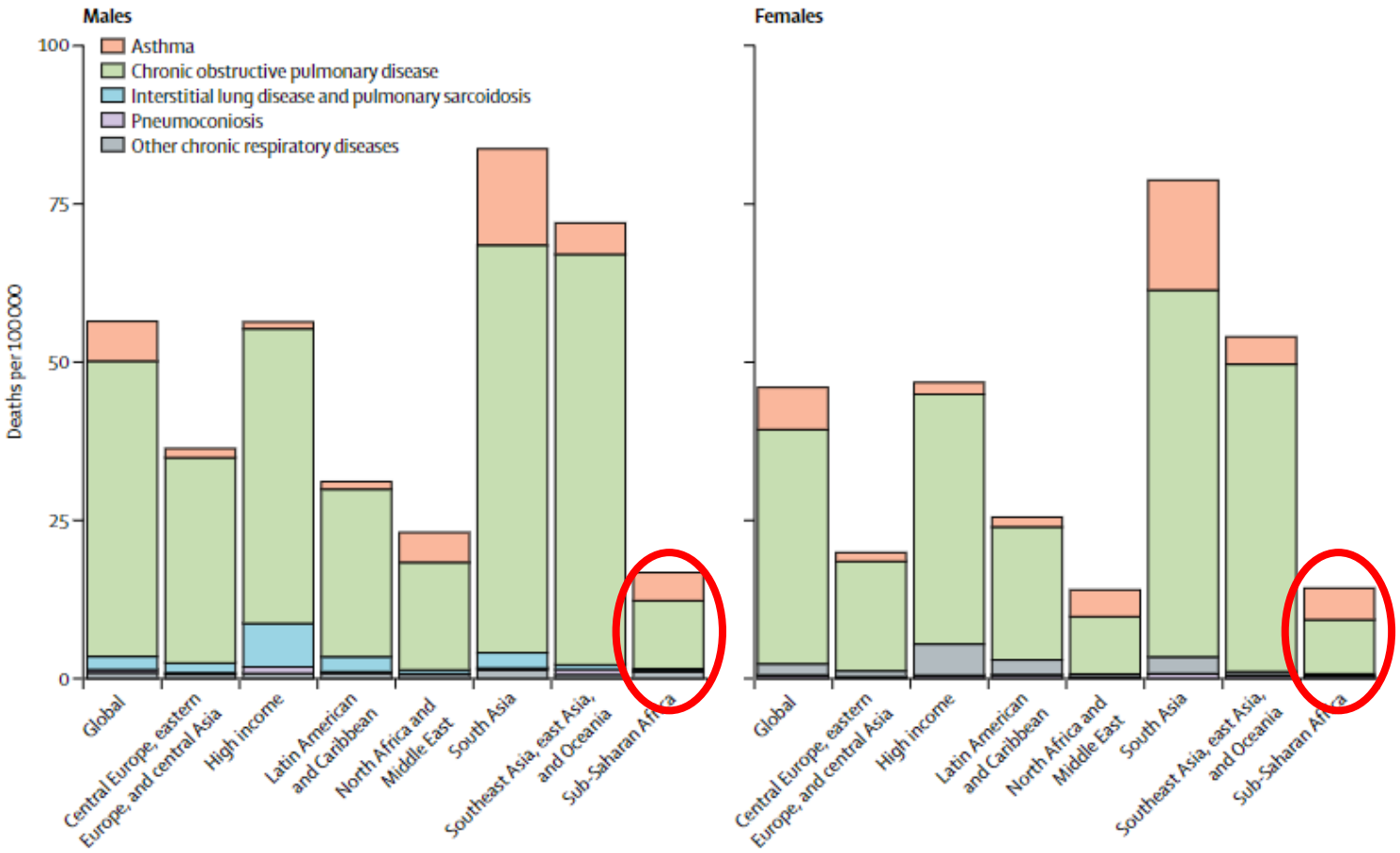


 # cigarettes smoked per person per year (2016)

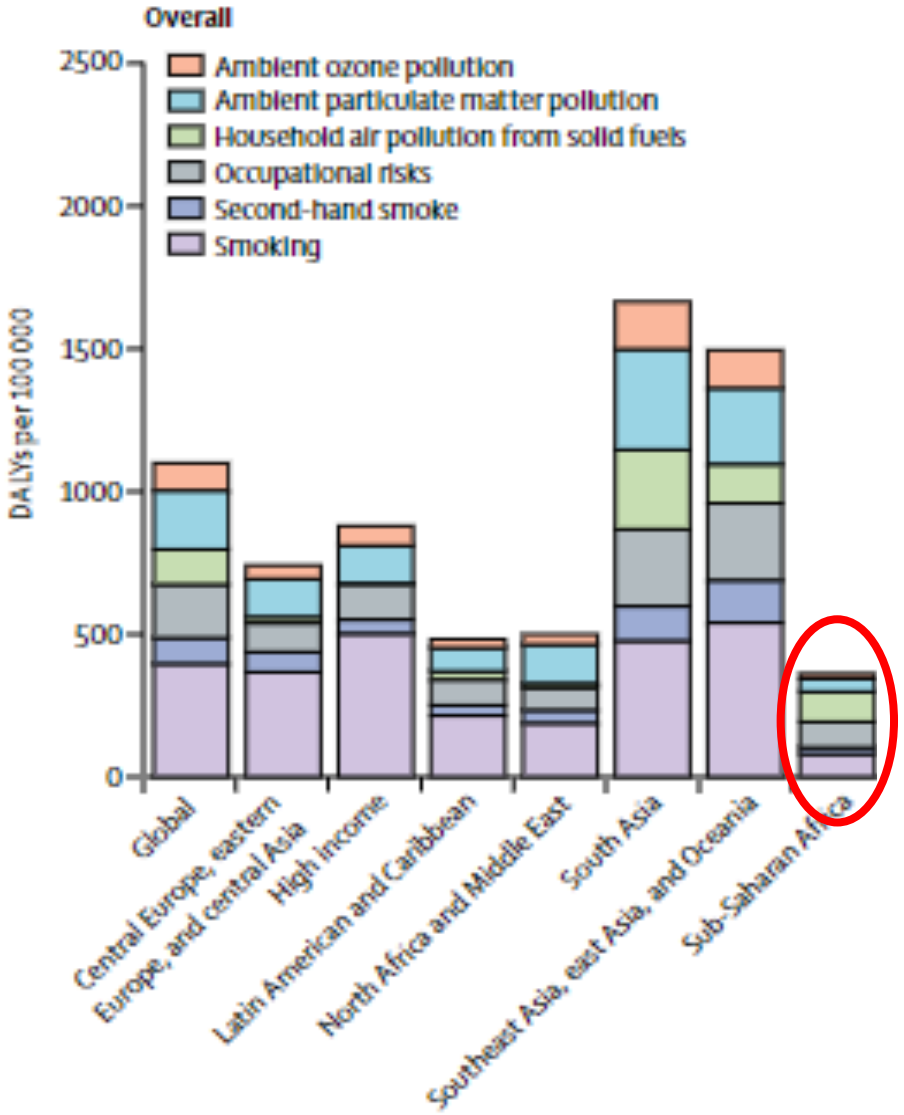


www.tobaccoatlas.org;
WHO global report on trends in prevalence of tobacco use 2000 - 2025

Global ***deaths*** from chronic lung disease



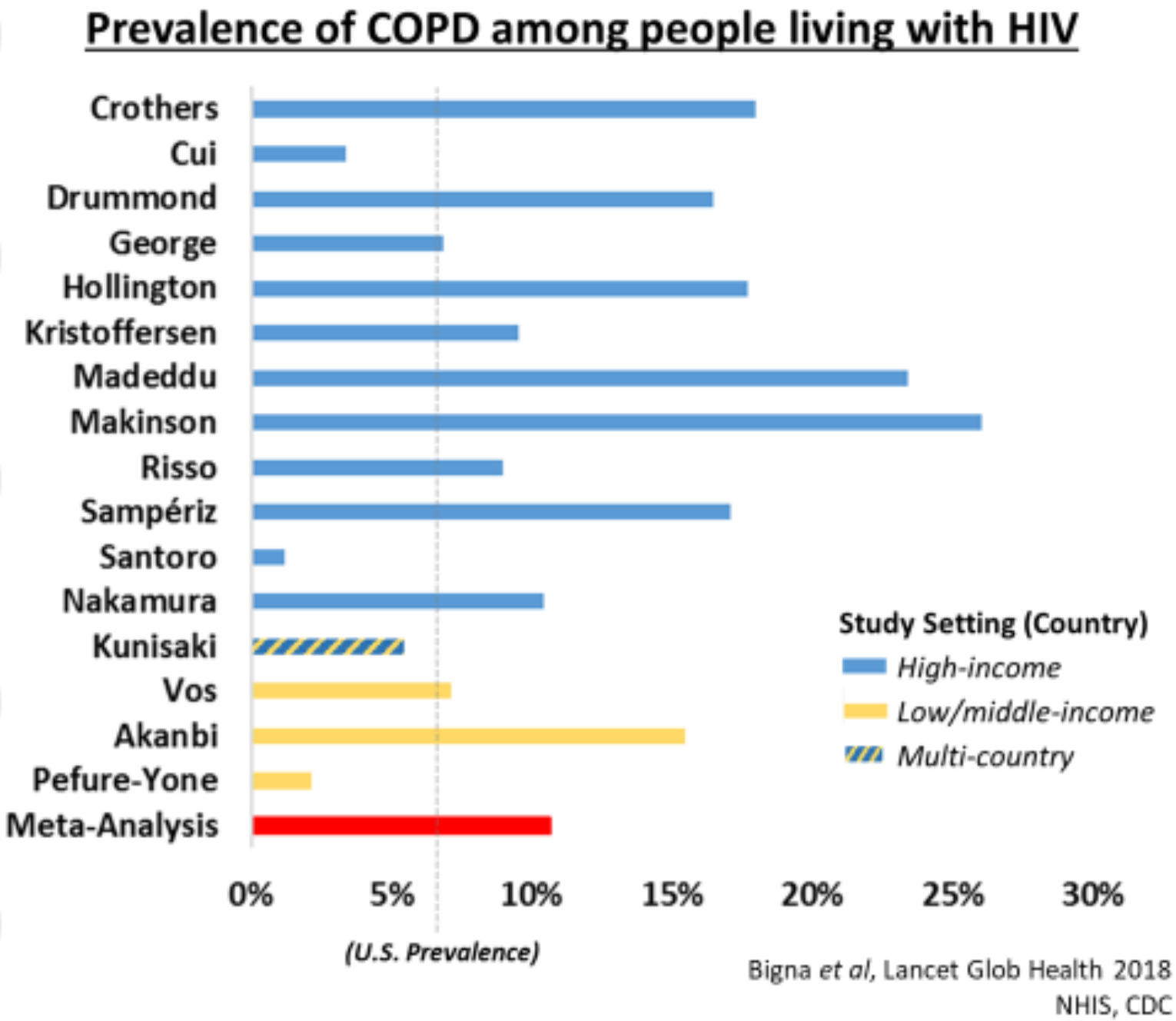
Global ***causes*** of chronic lung disease



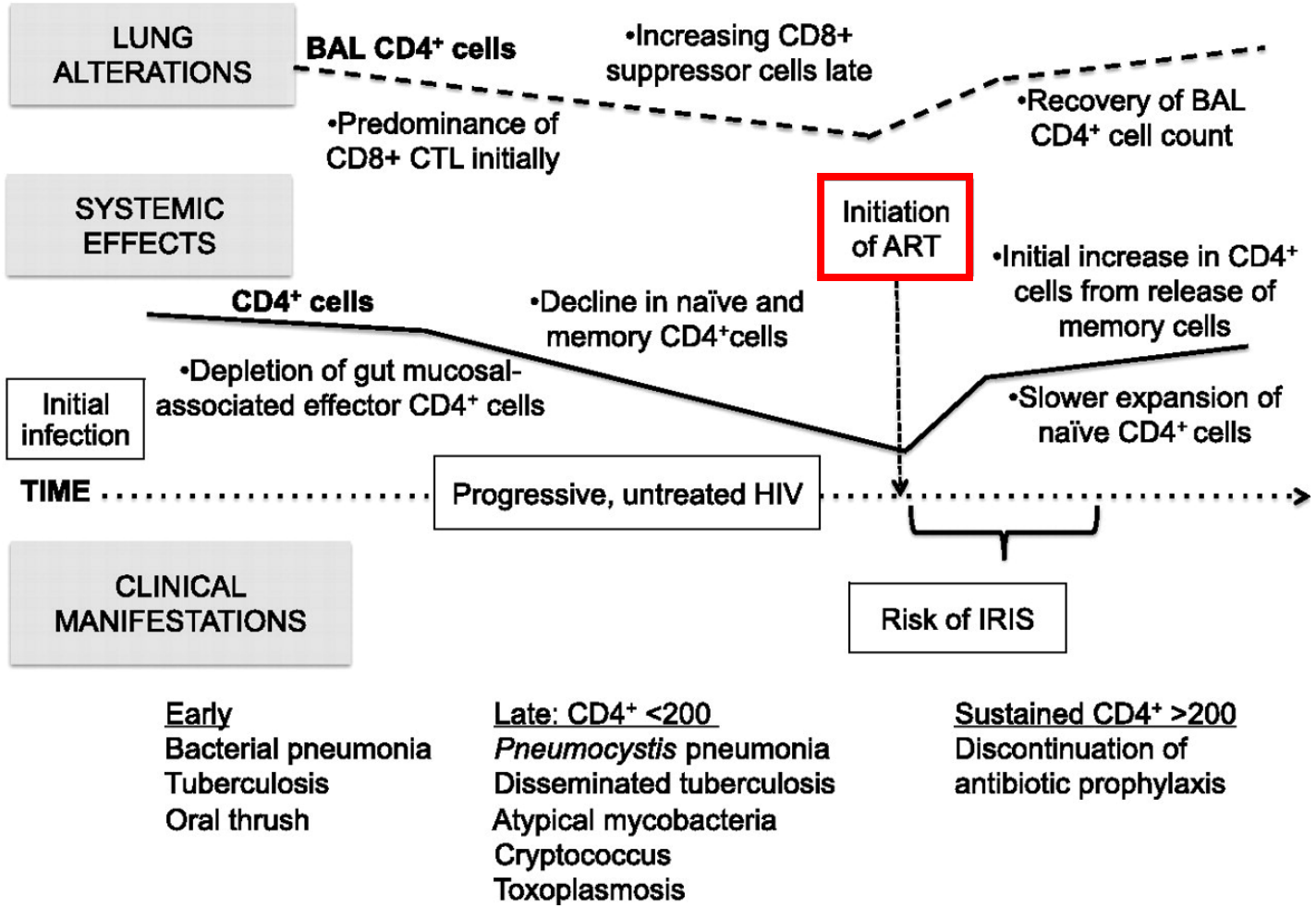
Lancet Respir Med 2020;8:585-596

In sub-Saharan Africa, HIV may be an underappreciated driver of chronic lung disease

People with HIV are at risk for chronic lung disease



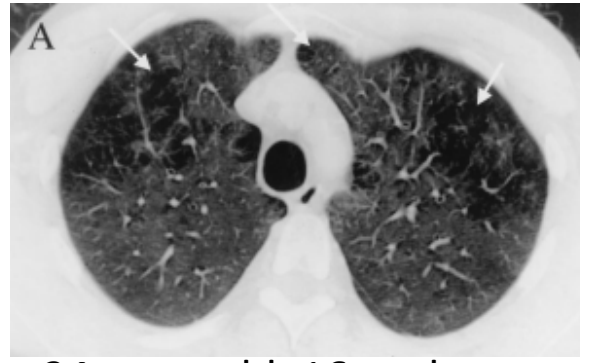
With ART, the epidemiology of lung disease among PWH has changed



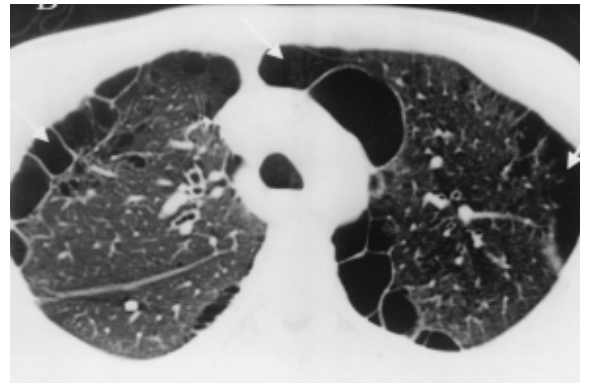
Crothers K *et al*. Proc Am Thorac Soc, 2011

Smoking and HIV

- Smoking is more prevalent among PWH
- However, despite similar smoking levels, PWH have:
  - Accelerated emphysematous lung destruction
  - More COPD
  - More lung cancer
- For PWH on ART, smoking reduces life expectancy more than HIV itself



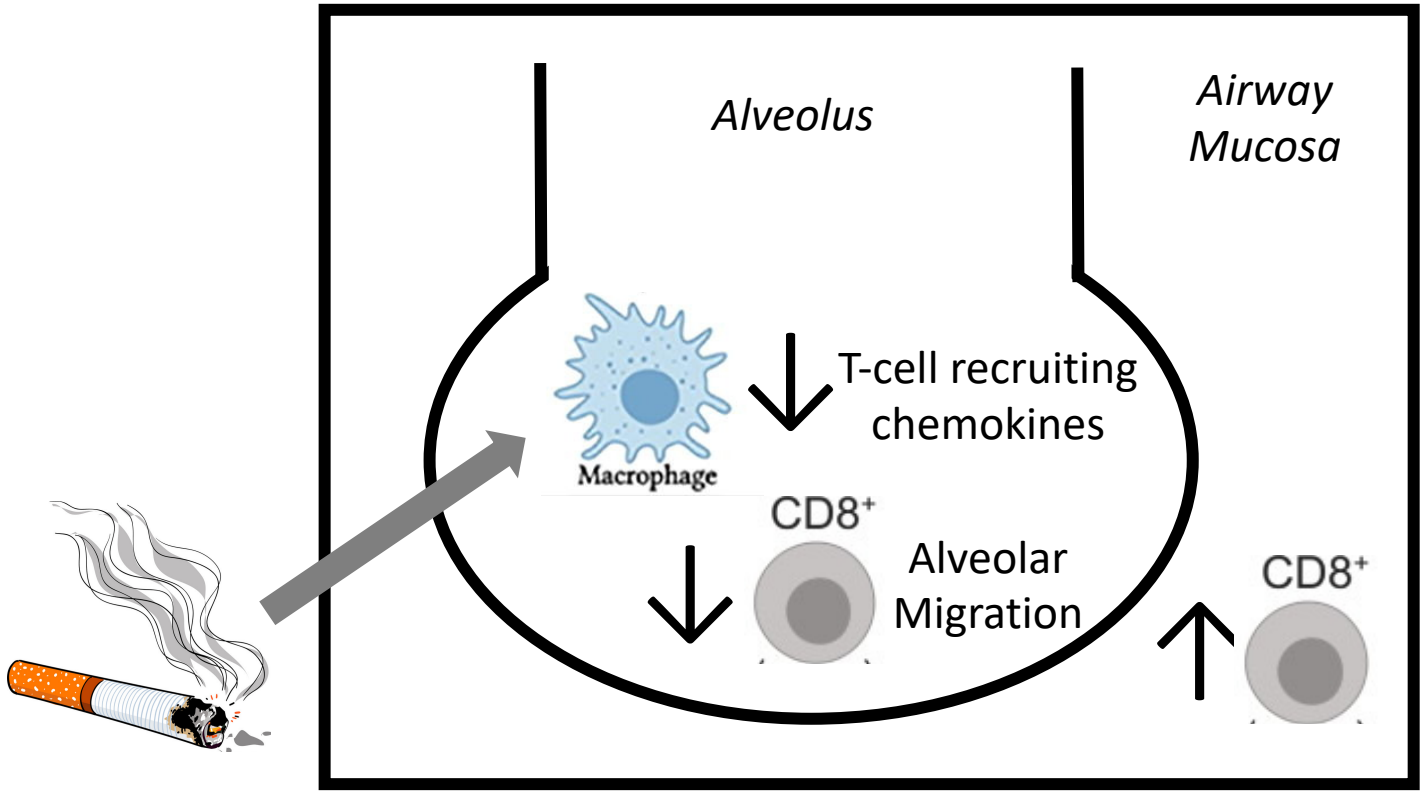
34 years old, 16 pack-years


30 years old, 9 pack-years

Mdege ND *et al*. Lancet Glob Health, 2017; Mutevedzi *et al.* PLoS One, 2013; Diaz PT *et al*. Ann Intern Med, 2000; Johnson PI *et al*. AIDS 2021; Crothers K *et al*. AJRCCM, 2011; Reddy KP *et al*. JID, 2016

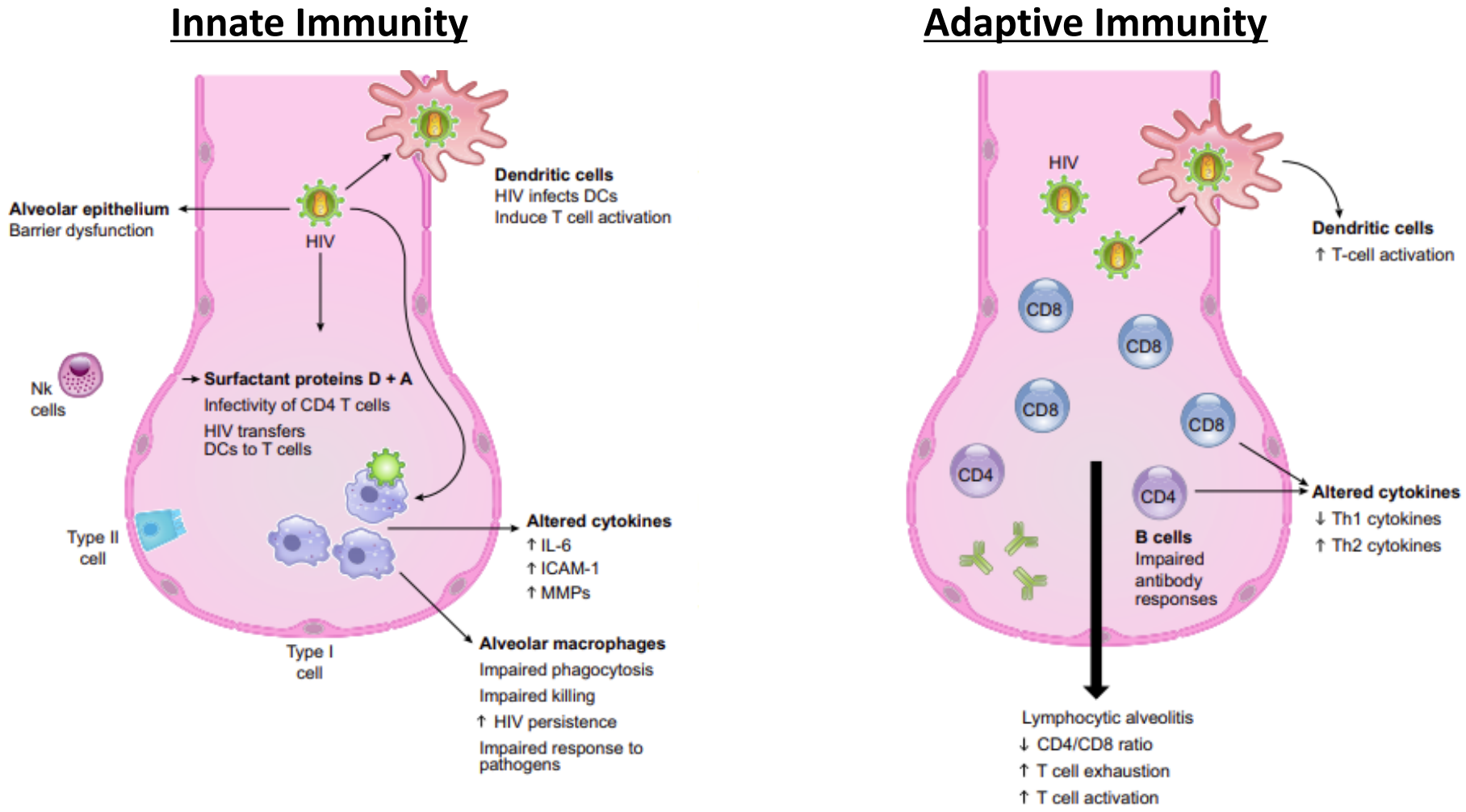
Smoking and HIV

HIV+ smokers exhibit more lung damage than HIV- smokers



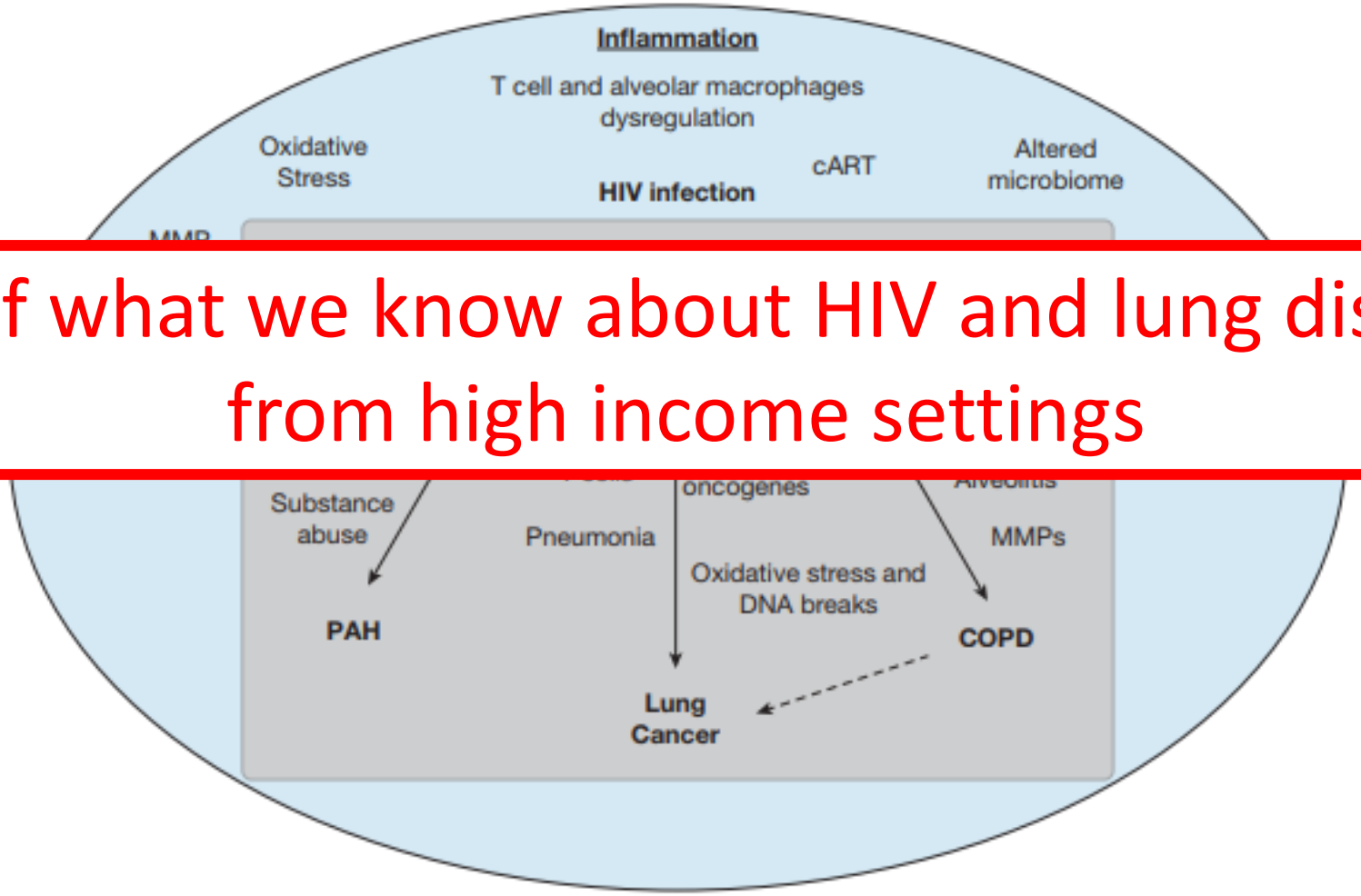
Corleis *et al.* AJRCMB 2021

HIV itself causes direct lung injury



Cribbs SK *et al*. Physiol Rev, 2020

People with HIV are at risk for chronic lung disease



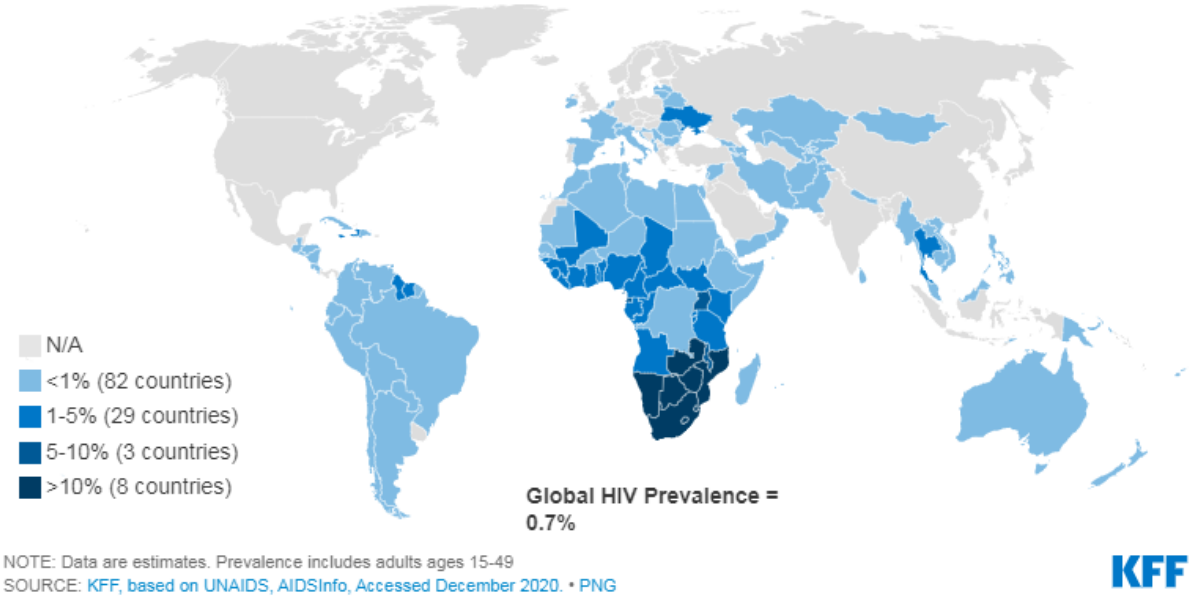
Most of what we know about HIV and lung disease is from high income settings

Presti RM *et al.* Chest 2017

Most people with HIV live in sub-Saharan Africa

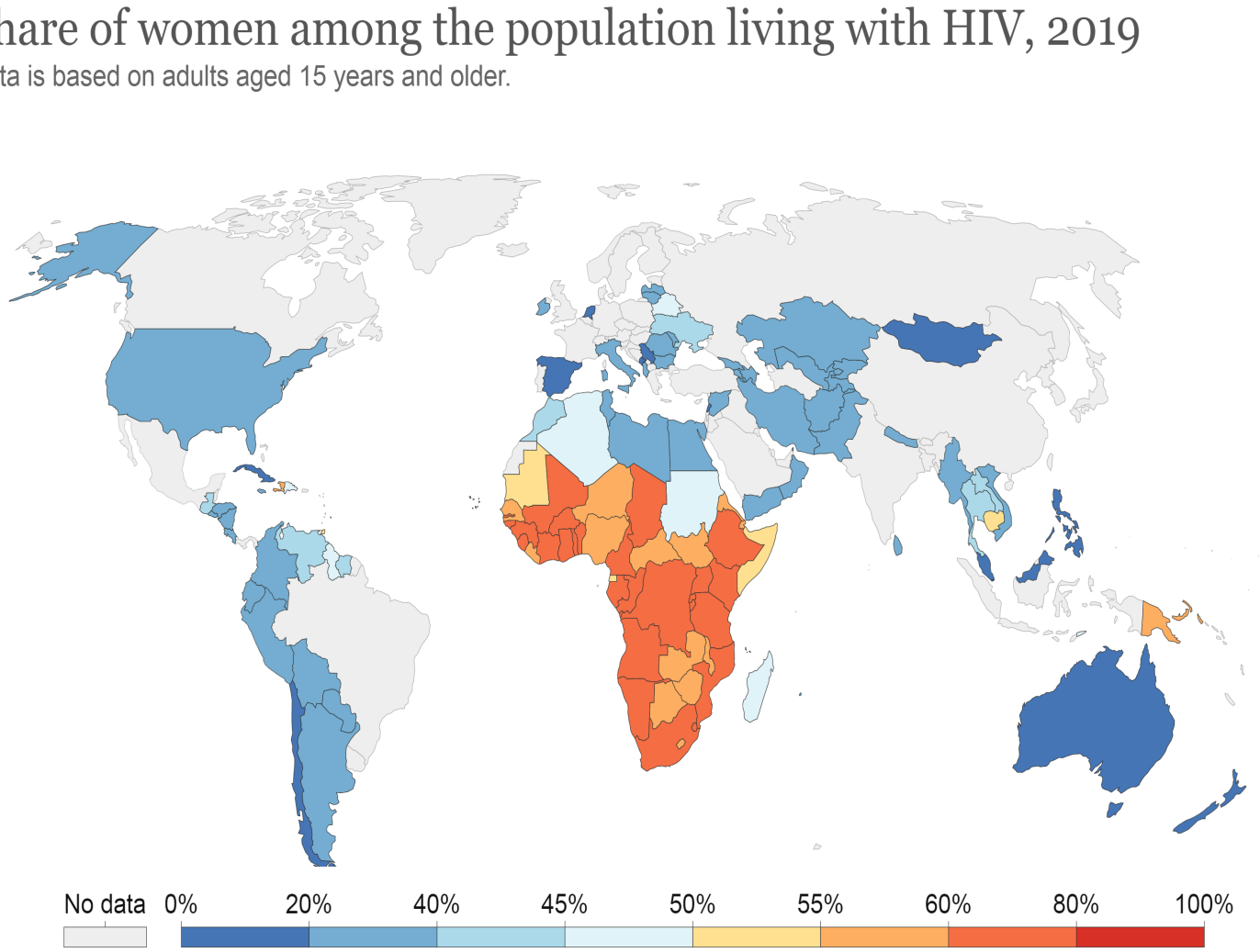
- Globally, 38 million people are living with HIV
- Sub-Saharan Africa is the epicenter
  - 2/3 of global population with HIV
  - 50% of new HIV diagnoses
- Non-communicable diseases are leading causes of morbidity and mortality among people with HIV on ART
- Lung disease risk factors (e.g., smoking, tuberculosis, air pollution) differ in SSA

HIV Prevalence, 2019



www.unaids.org
Johnson LF *et al.* PLoS Med 2013
Wandeler G *et al.* Curr Opin HIV AIDS, 2016
Nsanzimana S *et al.* Lancet Glob Heal 2015

Most people with HIV in SSA are women and girls



- 2/3 of new HIV diagnoses in SSA are among women and girls
- Data on lung disease among PLWH are from high income countries, where most PWH are men
- Many other lung diseases exhibit sex/gender differences, including COPD

UNAIDS, World Bank

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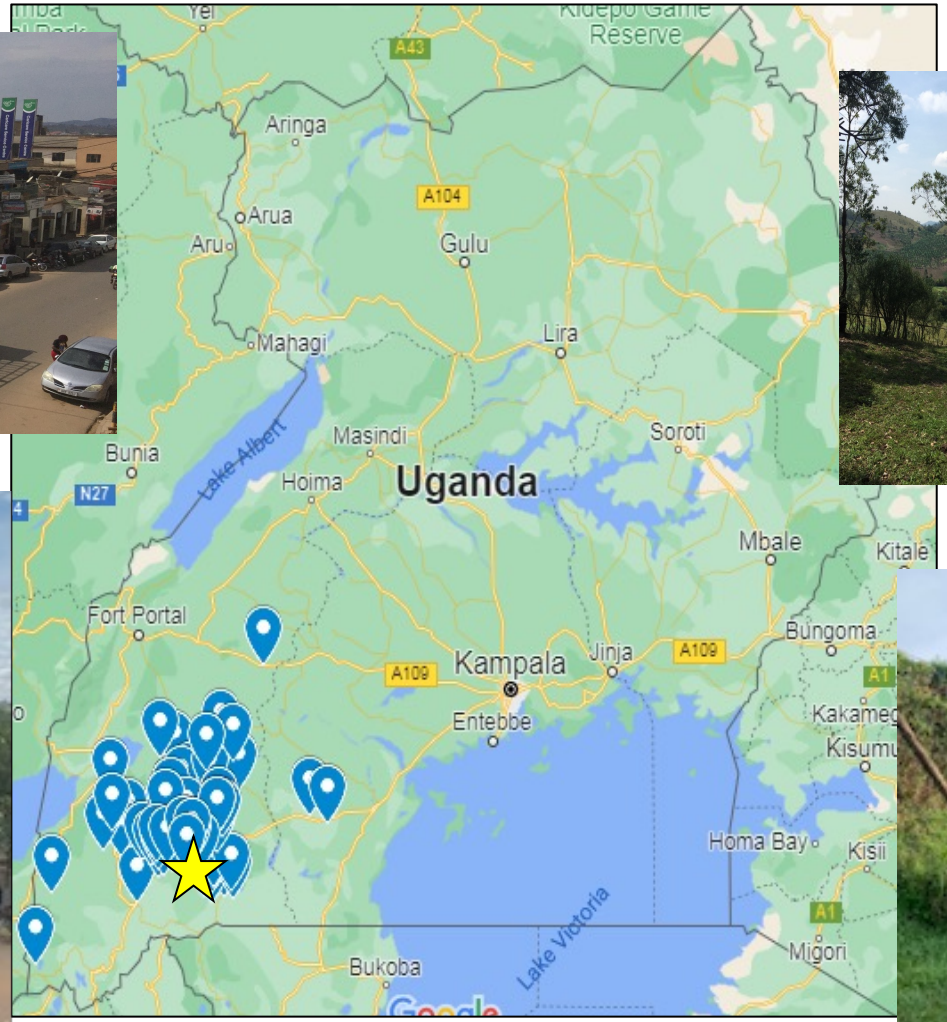
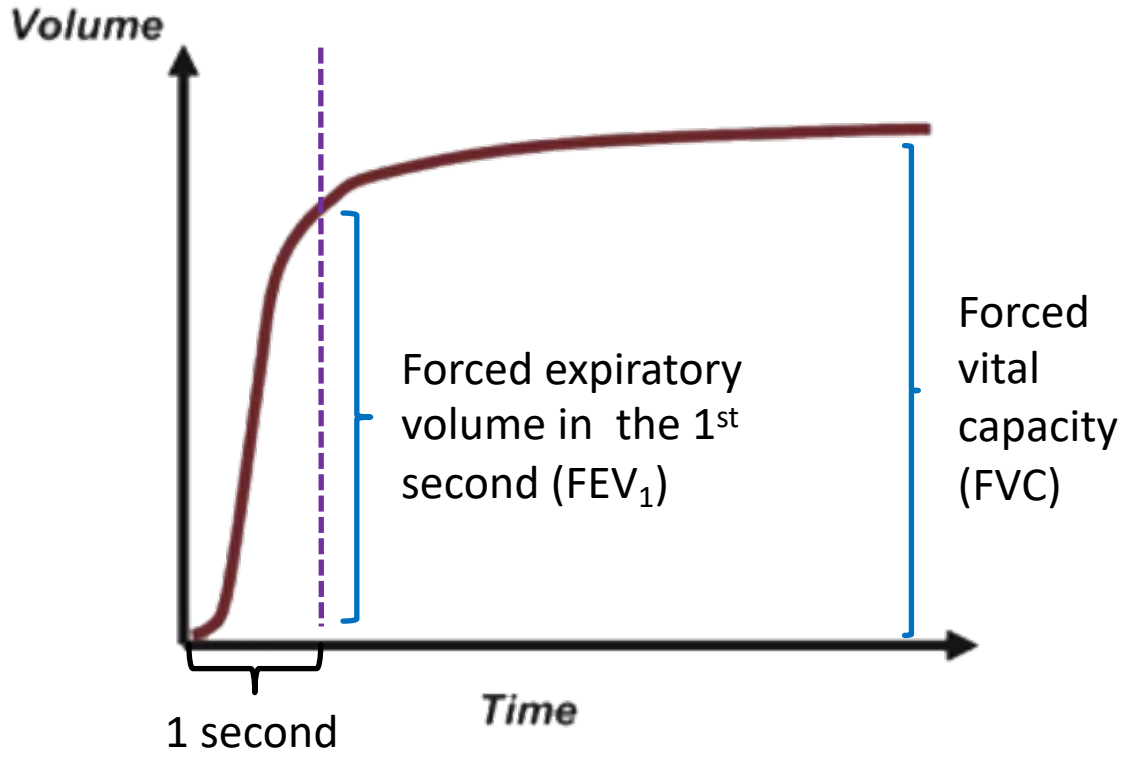
Where We Work: Mbarara, Uganda



The Study Cohort

- Age ≥ 40 years (n ~ 300)
- Two sub-groups:
  - HIV+ : In care, on ART ≥ 3 years
  - HIV - : Age/gender similar
- Since 2015, annual:
  - Respiratory symptom questionnaire
  - Pulmonary function testing
  - Personal air pollution measures
  - Blood samples
  - (recently) Induced sputum samples

Measuring Lung Function: Pulmonary Function Testing (spirometry)



Post-bronchodilator $FEV_1/FVC < 0.7$ = COPD

Figure 1. Study participants, 2015 through 2018

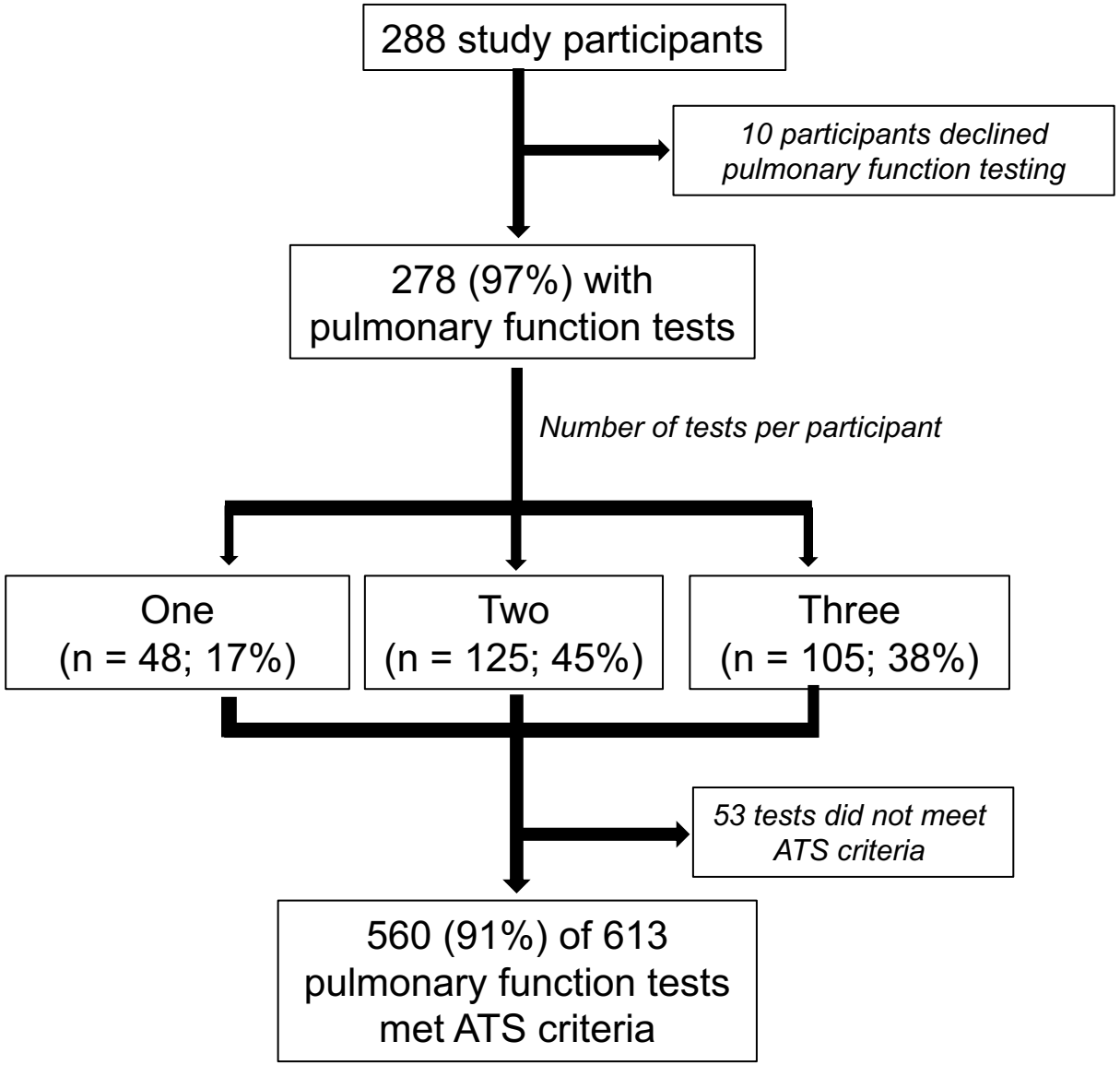


Table 1. Baseline Characteristics

	Total Cohort (n = 278)	HIV + (n = 145)	HIV - (n = 133)	*p* value
Demographics				
Age	52 [48, 55]	52 [49, 55]	52 [48, 55]	0.35
Women	130 (47)	68 (47)	62 (47)	0.96
Smoking history				0.004
Current	41 (15)	12 (8)	29 (22)	
Former	95 (34)	50 (34)	45 (34)	
Never	142 (51)	83 (57)	59 (44)	
Prior tuberculosis	17 (6)	17 (12)	0 (0)	< 0.001
Prior pneumonia	24 (9)	17 (12)	7 (5)	0.06
Biomass exposure				< 0.001
Charcoal	40 (14)	39 (27)	1 (1)	
Firewood	236 (86)	104 (73)	132 (99)	
HIV Characteristics				
Viral Load, copies/μL				
Undetectable		135 (94)		
Detectable, ≤ 10,000		6 (4)		
Detectable, > 10,000		2 (1)		
CD4 count, cells/mm^3				
100 – 349		26 (18)		
350 – 499		55 (38)		
≥ 500		64 (44)		
ART duration		9 [8, 10]		

McNeill J … North CM. Annals ATS 2022.

Most COPD diagnoses were among PWH

Table 2 Description of lung function and cardiovascular disease across cohort

Disease measure	Total cohort (n = 265)	HIV+ (n = 140)	HIV− (n = 125)	*p* value*
FEV_1 (L)	2.47 (2.07, 2.95)	2.40 (2.08, 2.95)	2.52 (2.04, 2.95)	0.853
FVC (L)	3.14 (2.66, 3.70)	3.09 (2.67, 3.76)	3.24 (2.66, 3.68)	0.936
FEV_1/FVC	0.80 (0.76, 0.83)	0.8 (0.75, 0.83)	0.8 (0.77, 0.83)	0.671
COPD (FEV_1/FVC < 0.7)	17 (6%)	13 (9%)	4 (3%)	0.044

Gilbert RF … North CM. BMC Pulm Med. 2022

Systemic inflammation is associated with ↓ lung function among PWH

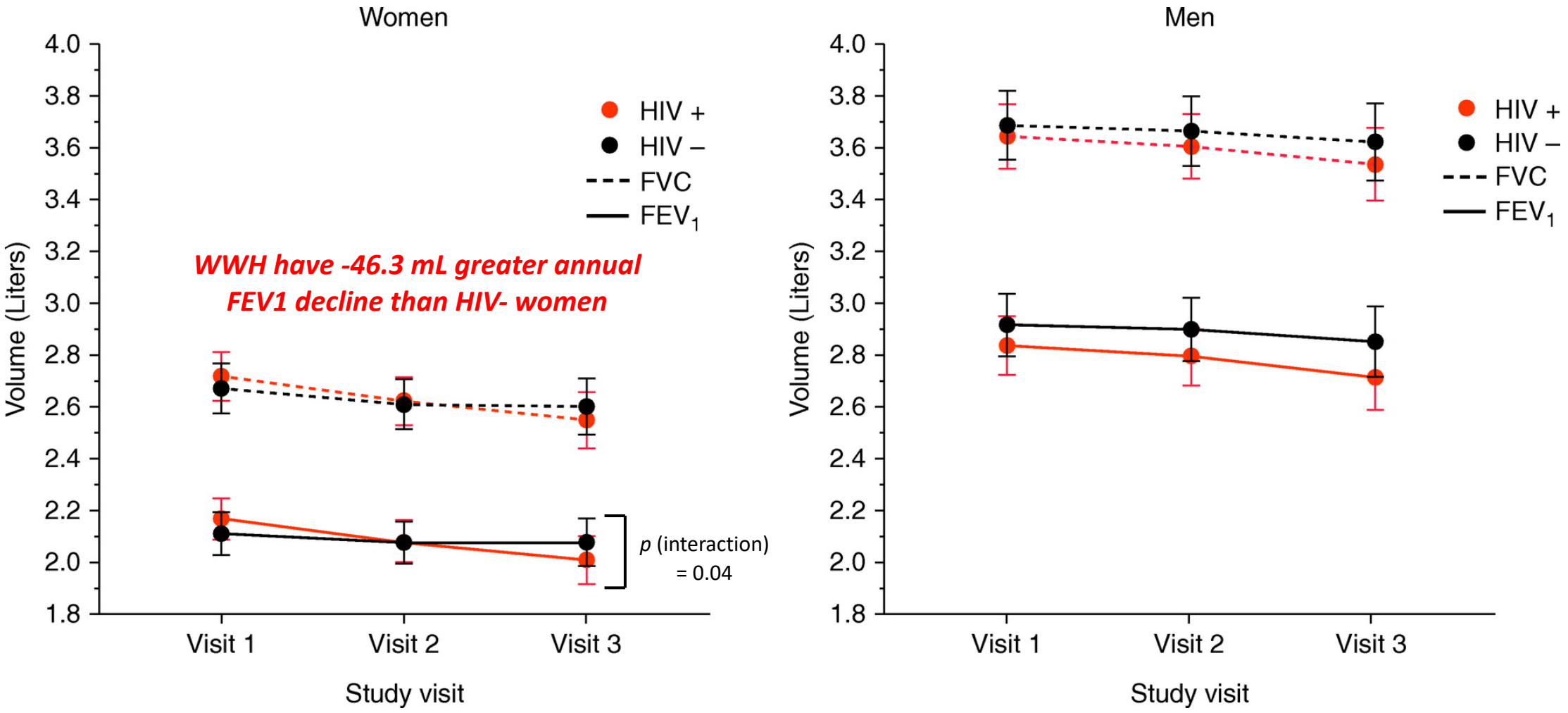
Table 1: Associations between lung function (mL) and serum biomarkers

	HIV+ (n=122†)		HIV- (n=108†)	
	FEV_1	FVC	FEV_1	FVC
IL-6, per IQR increase	**-18.1 (-29.1 to -7.1)****	**-17.1 (-28.2 to -5.9)****	-6.2 (-16.0 – 3.5)	-8.7 (-20.8 – 3.5)
sCD14, per IQR increase	2.3 (-11.7 – 16.3)	7.0 (-6.9 – 21.0)	6.2 (-4.3 – 16.6)	8.9 (-4.1 – 21.8)
sCD163, per IQR increase	-11.4 (-24.0 – 1.2)	**-14.3 (-26.9 to -1.7)***	-3.7 (-13.8 – 6.3)	-6.5 (-19.0 – 6.1)
hsCRP, >3mg/L vs. <1mg/L	**-39.3 (-61.7 to -16.9)****	**-44.0 (-48.4 to -6.4)*****	**-37.9 (-63.2 to -12.6)****	**-58.0 (-88.4 to -27.5)*****

*p < 0.05, **p < 0.01, ***p<0.001; † hsCRP model sample sizes: n=120 (HIV+) & n=107 (HIV-); ‡ p values for HIV*biomarker interaction terms

North CM *et al.* JAIDS 2018.

HIV serostatus is associated with faster lung function decline among women (but not men)



McNeill J … North CM. Annals ATS 2022.

Why? 3 Working Hypotheses

Differences in:

1. Air pollution exposure and/or influence on lung health
2. HIV-associated systemic inflammation
3. Advanced reproductive aging

Are women with HIV just exposed to more air pollution? Maybe.

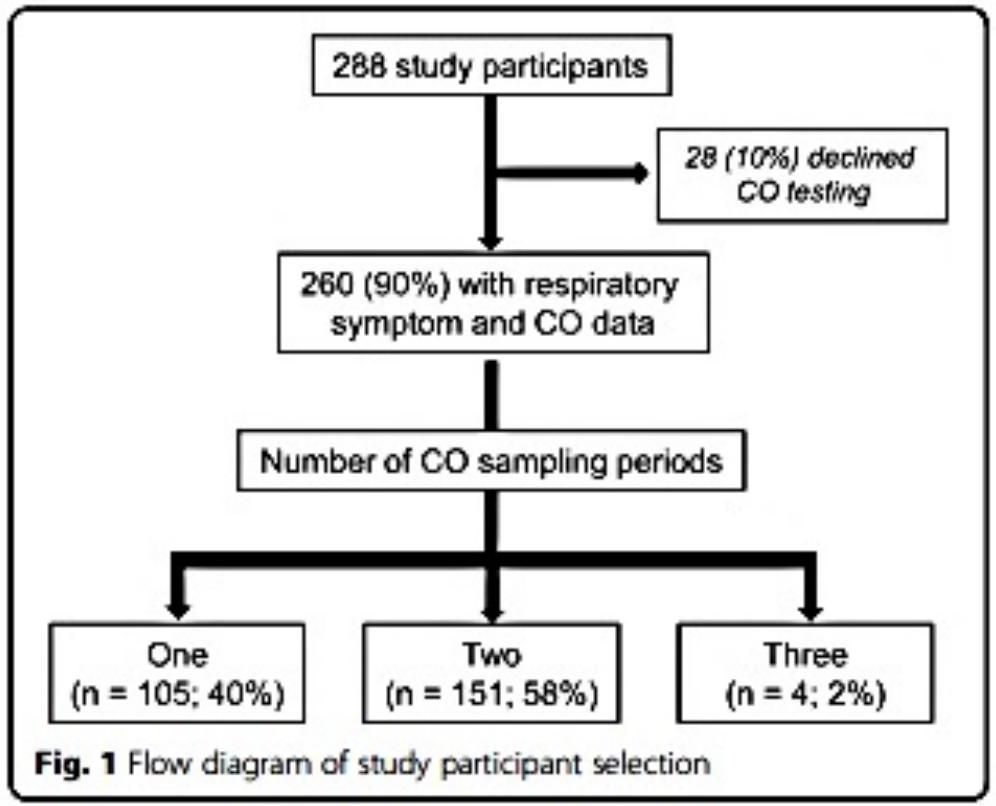
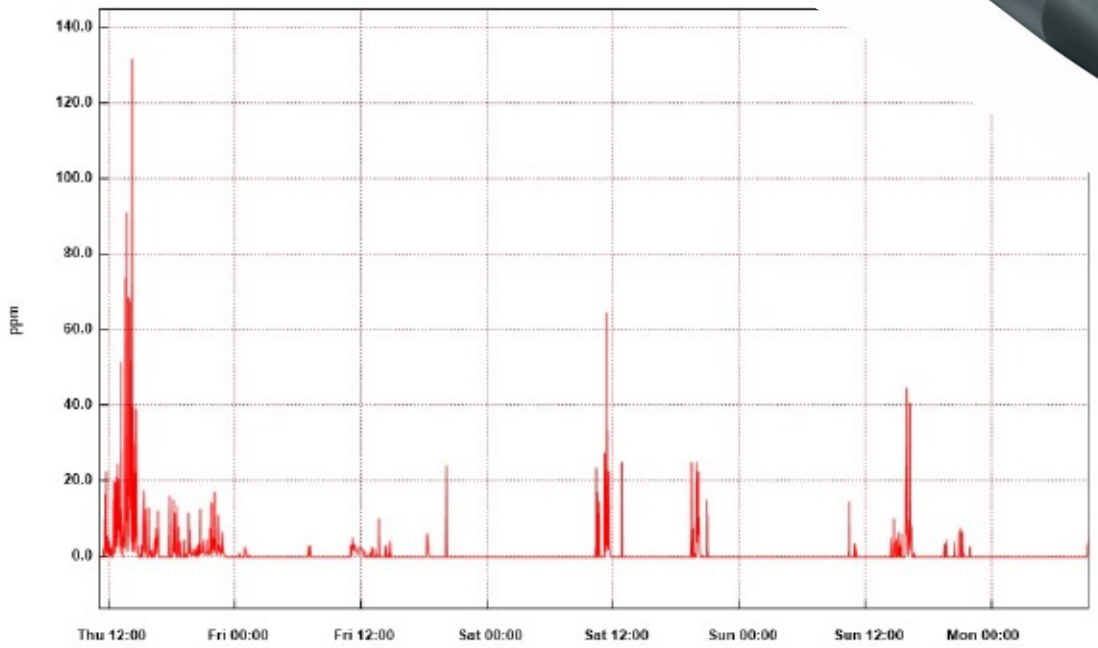


Fig. 1 Flow diagram of study participant selection

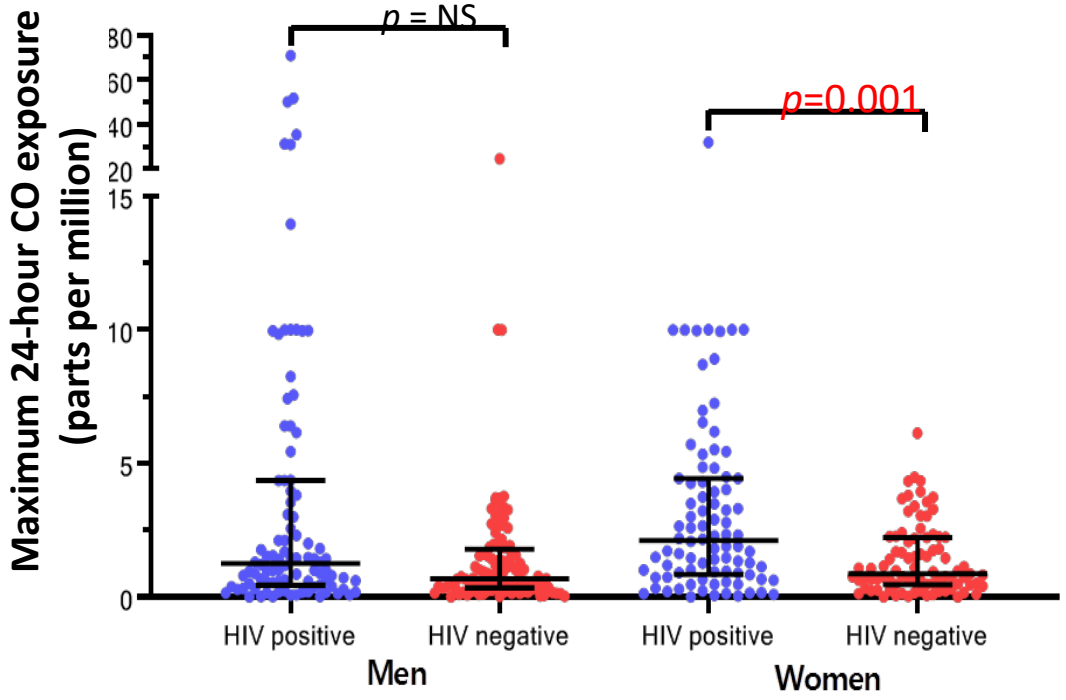
Example of ambulatory carbon monoxide levels over time



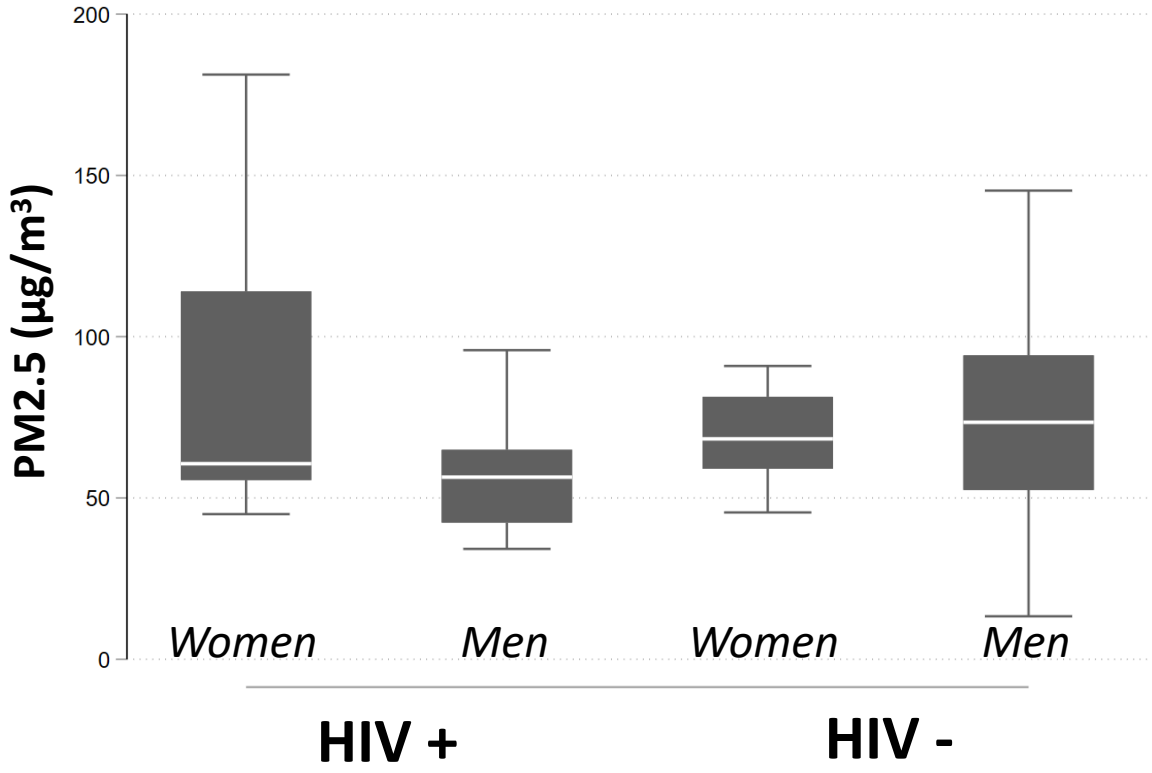
North CM *et al*. Environ Health, 2019

Are women with HIV just exposed to more air pollution? Maybe.

Ambulatory carbon monoxide exposure is highest in women with HIV



Ambulatory $PM_{2.5}$ exposure is not different by sex or HIV serostatus



North CM. *Unpublished data*.

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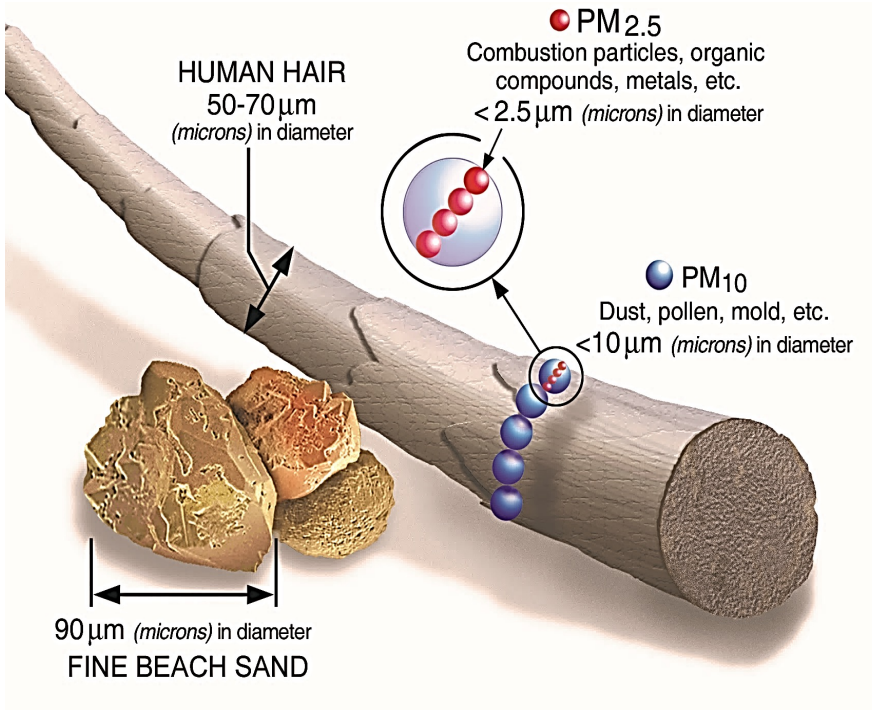
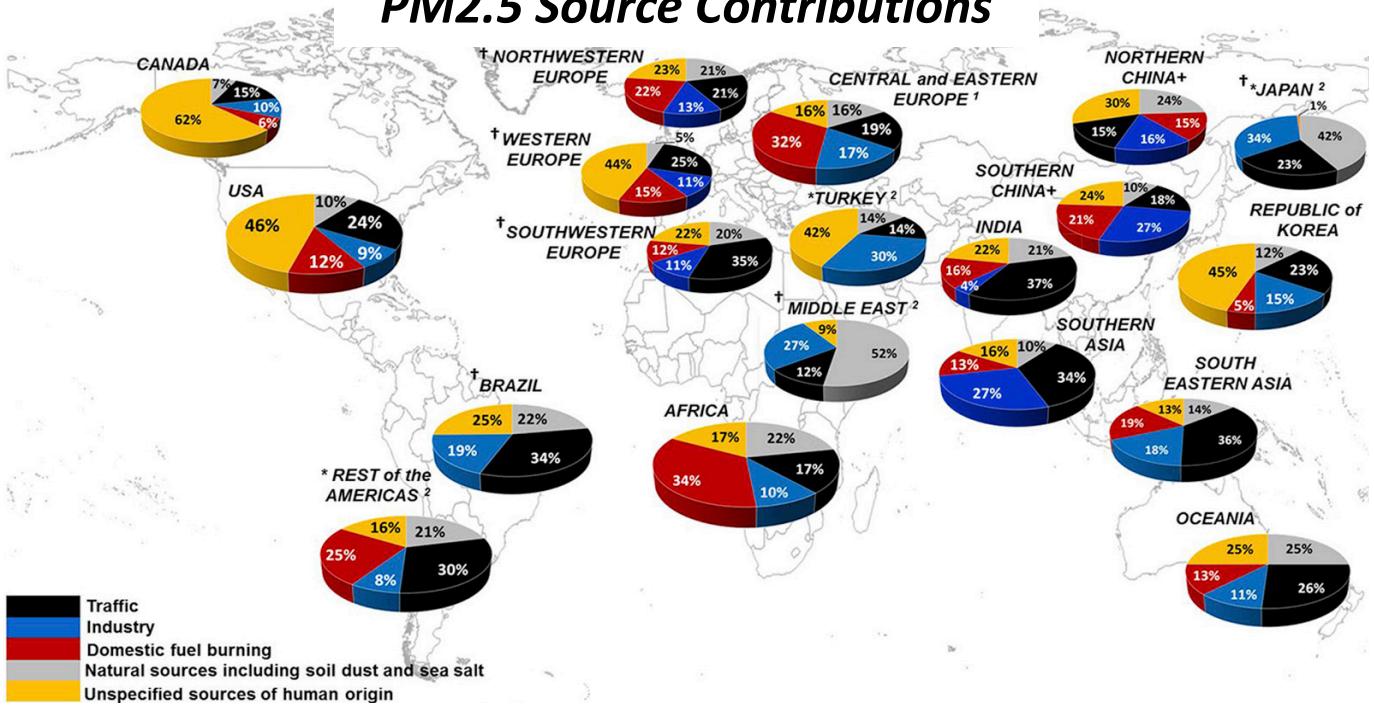
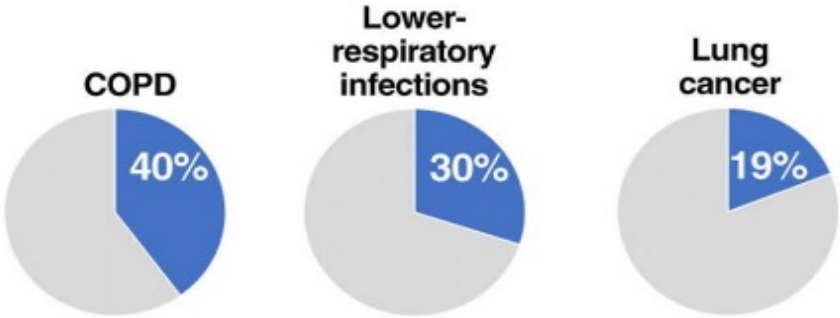
Ambient air pollution: Particulate matter (PM)



PM2.5 Source Contributions



Percentage of global deaths from specific causes attributable to total air pollution

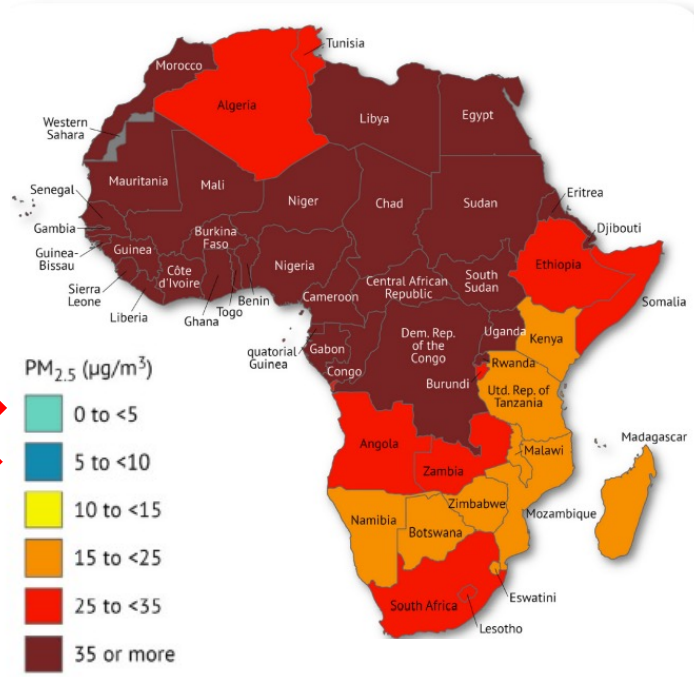


www.epa.gov

Karagulian F *et al.* Atmos Environ 2015

Ambient air quality is poor across SSA, but data are sparse

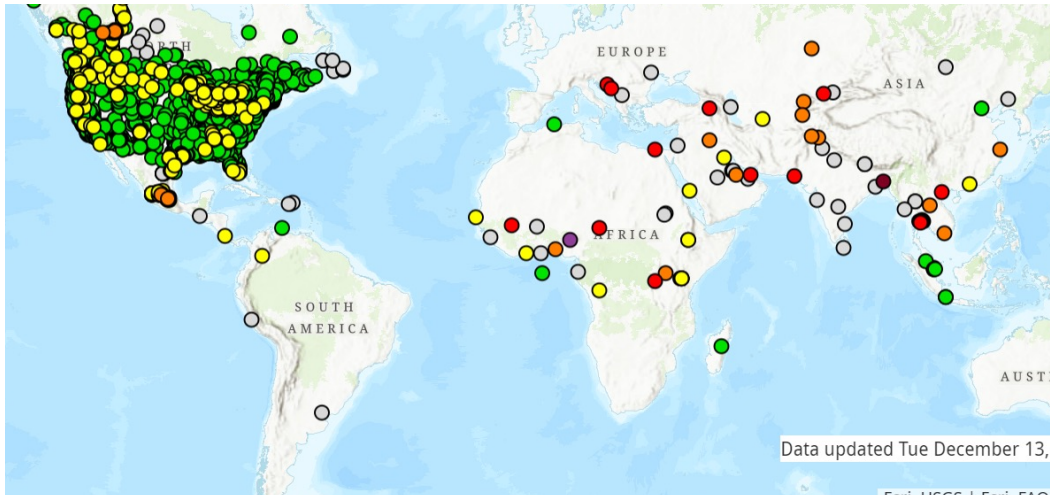
Annual PM2.5 Levels



EPA ➡
U.S. ➡

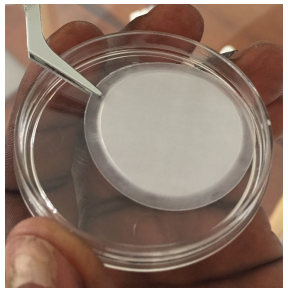
Source Data

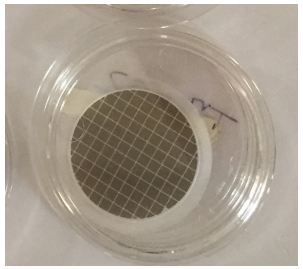
Air pollution monitoring stations

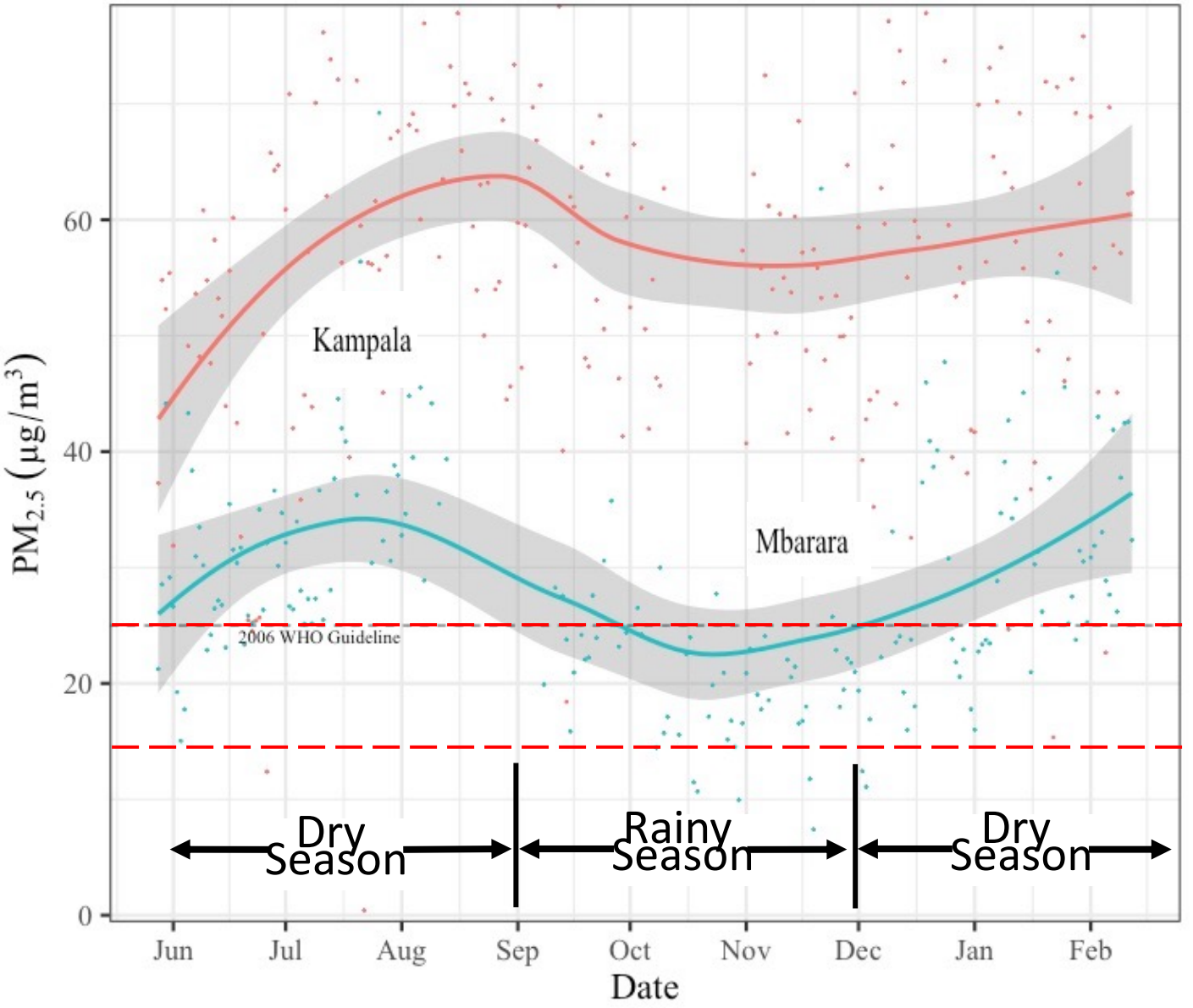


www.airnow.gov
The State of Air Quality and Health Impacts in Africa, HEI 2022

Ambient $PM_{2.5}$ levels in Mbarara





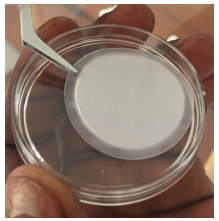


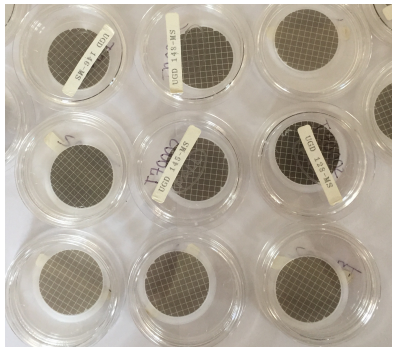
2006 Air quality standard

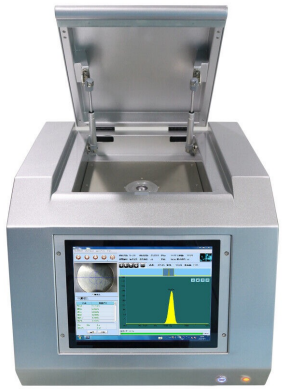
2021 Air quality standard

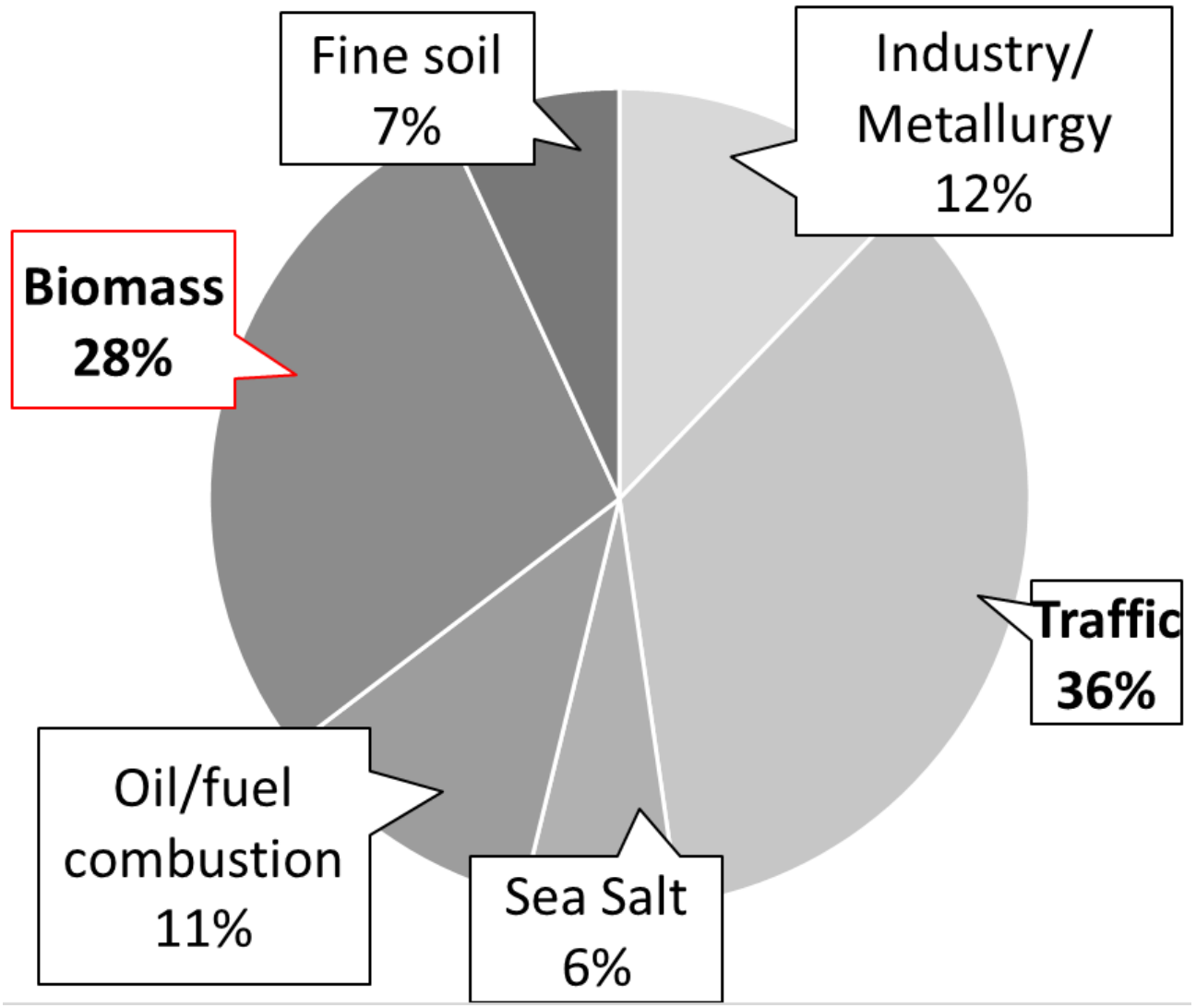
Onyango S, North CM. *Under Review*

Ambient $PM_{2.5}$ sources in Mbarara









Onyango S, North CM. *Under Review*

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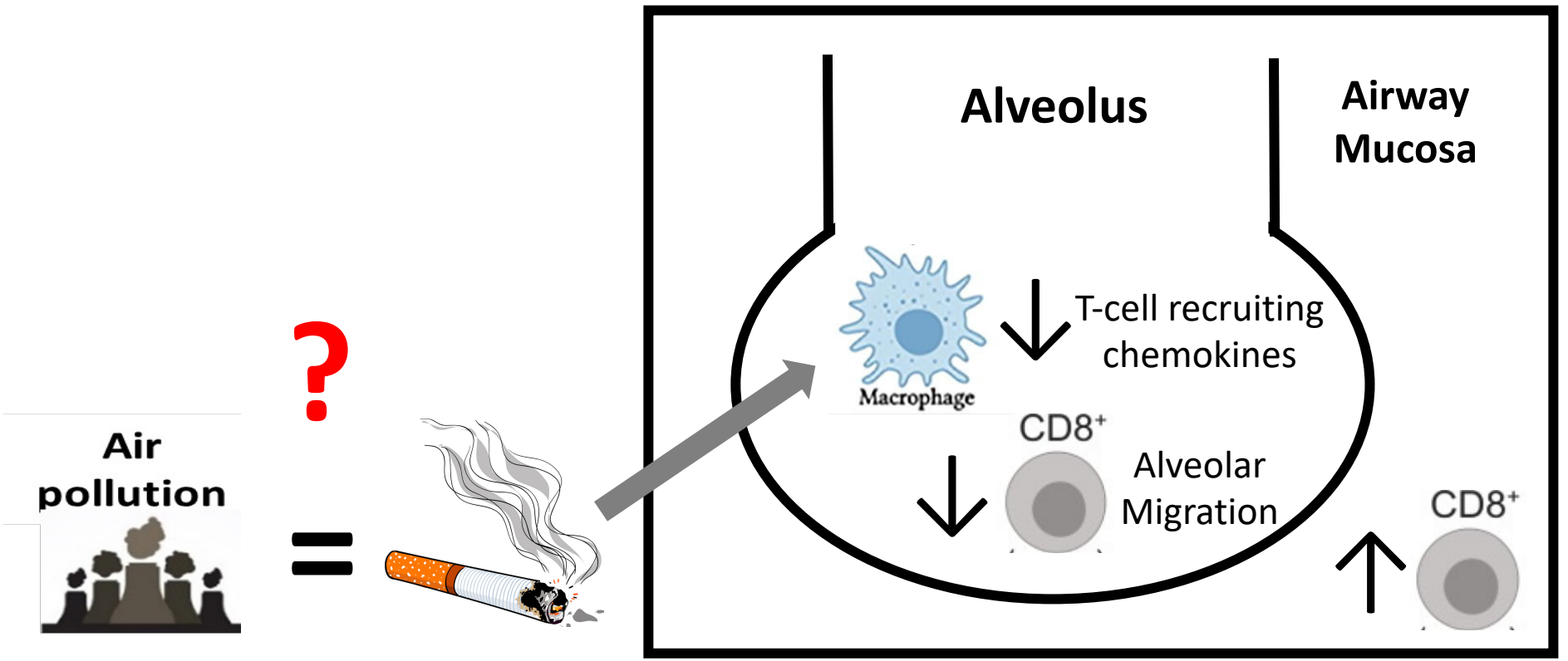
Among PWH, does air pollution act like smoking?



Corleis *et al.* AJRCMB 2021

At similar air pollution exposure levels, people with HIV have ↑ odds of resp symptoms

Table 6 Correlates of self-reported respiratory symptoms, stratified by HIV serostatus

Characteristic	HIV Positive *(202 sampling periods)*		HIV Negative *(218 sampling periods)*	
	Adjusted OR	95% CI	Adjusted OR	95% CI
Female sex	1.9	0.8, 4.3	11.2***	3.3, 38.0
1-h CO > 35 ppm	2.5*	1.0, 6.0	1.4	0.1, 14.4
Smoking status				
Current	2.6	0.6, 11.3	0.9	0.1, 5.0
Former	0.8	0.3, 2.0	1.3	0.6, 3.2

North CM *et al*. Environ Health, 2019

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Work in Progress – LUNG Study

✓ Visit 1

Resp symptom questionnaire

TB history, PPD

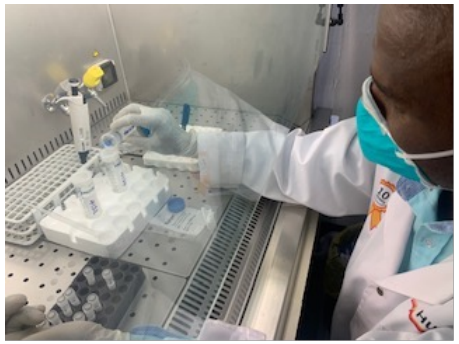
Ambulatory $PM_{2.5}$

✓ Visit 2

CT chest

PFTs

Induced sputum



Phlebotomy (Biomarkers)

[Visit 3]

[Bronchoscopy with BAL]

Funding Sources:
K23HL154863 (PI: North)
R01HL141053 (PI: Siedner)
Harvard CFAR (PI: North)

Work in Progress – Air Quality Study

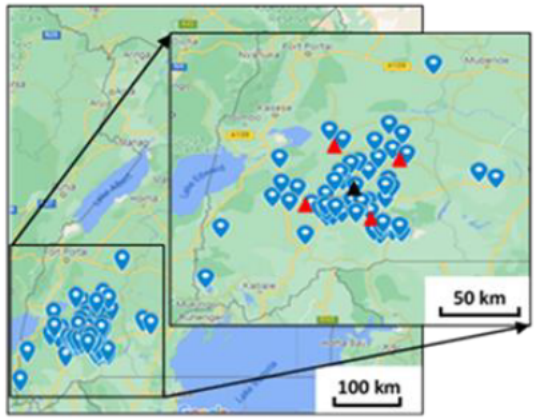
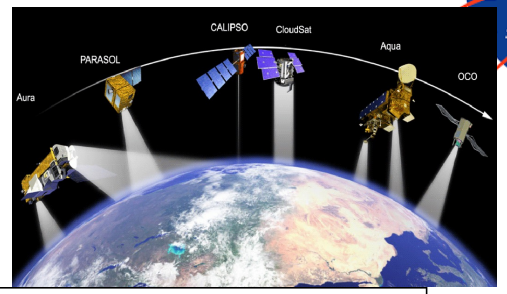


Figure 1. Regional map of UGANDAC and HopeNet participants' home locations (blue dots), the Mbarara Ambient Air Sampler (black triangle), and the four additional ambient air sampling sites (red triangles) to be established with Burke Fellowship funds.



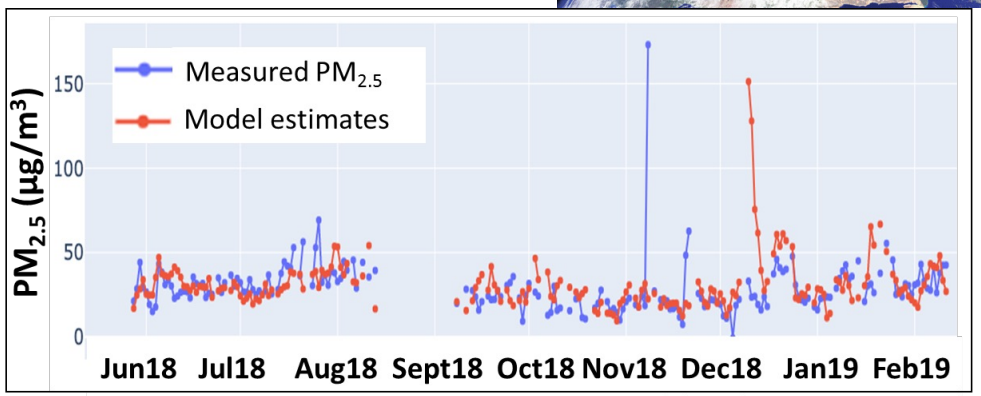
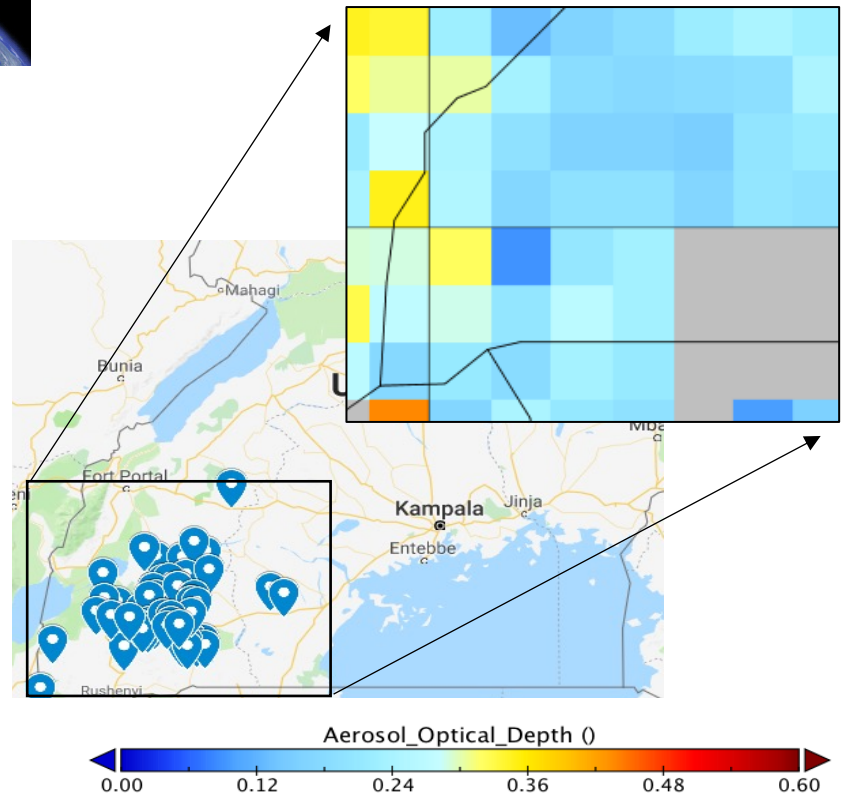


Figure 3. $PM_{2.5}$ concentrations as estimated by the NASA GEOS model (red) compare well to corresponding observations at the Mbarara Ambient Air Sampler (blue) from May 2018 through Feb 2019. (Figure courtesy of C. Keller, NASA)



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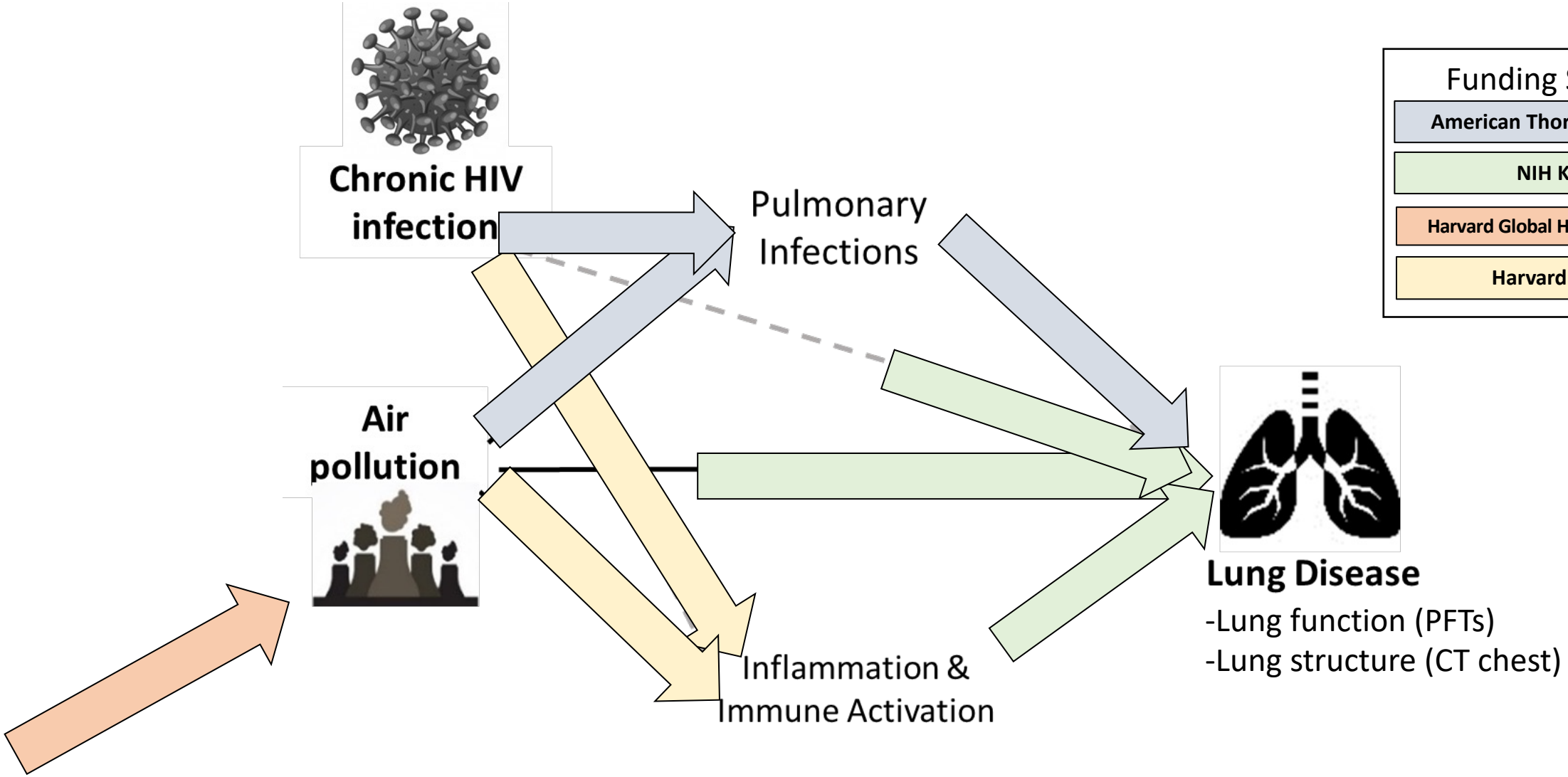
Ongoing Work and Next Steps



Funding Sources

- American Thoracic Society
- NIH K23
- Harvard Global Health Institute
- Harvard CFAR

Questions?

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