

HIV AND COMORBIDITIES

Mary Anne Hoskins, RN, MPH, MSN

Objectives

- Identify the two main causes of mortality for PLWHIV
- Recognize the modifiable risk factors that compound comorbidities for PLWHIV
- Understand the role of chronic inflammation in morbidity and mortality associated with HIV

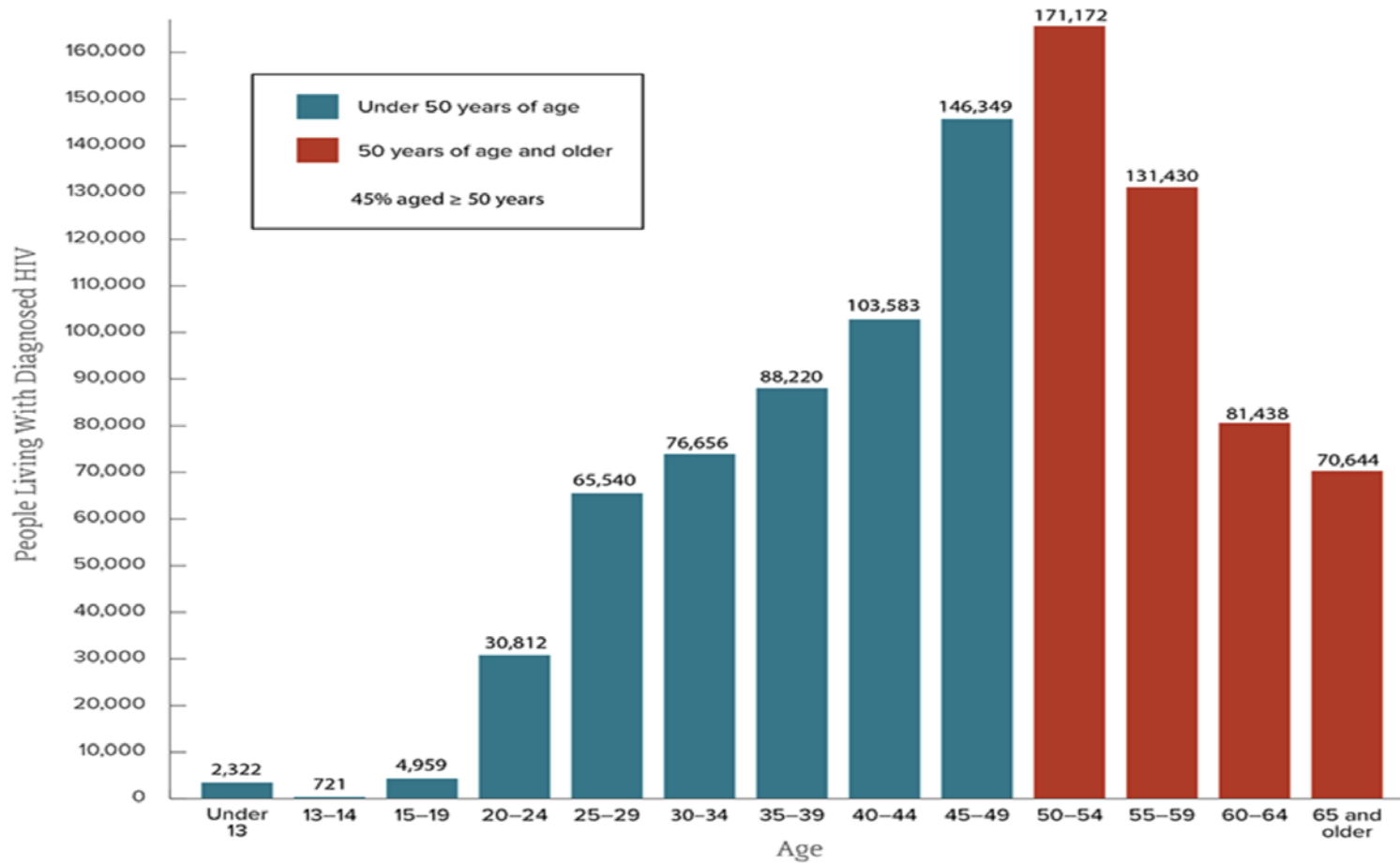
Table 22a. Persons living with diagnosed HIV infection, by year and selected characteristics, 2012–2016—United States

	2012		2013		2014		2015		2016	
	No.	Rate ^a	No.	Rate ^a	No.	Rate ^a	No.	Rate ^a	No.	Rate ^a
Age at end of year (yr)										
<13	2,713	5.1	2,594	4.9	2,476	4.7	2,340	4.4	2,225	4.2
13–14	893	10.8	780	9.3	739	8.8	720	8.7	675	8.2
15–19	6,313	29.5	5,712	27.0	5,301	25.2	4,975	23.6	4,629	21.9
20–24	31,850	141.0	32,013	140.3	31,733	138.7	30,858	136.0	29,800	133.1
25–29	53,748	251.2	57,226	265.1	61,377	279.4	65,419	291.7	68,563	299.0
30–34	71,309	340.9	72,584	341.0	74,426	345.8	76,386	352.8	79,729	365.0
35–39	83,532	428.2	83,778	426.8	85,031	427.2	87,741	431.3	90,455	434.5
40–44	122,431	581.9	115,986	555.7	109,812	533.9	102,760	509.2	98,768	500.5
45–49	162,349	748.0	157,037	739.6	150,024	719.2	144,966	696.5	138,717	661.6
50–54	150,072	664.4	158,700	703.1	165,923	736.0	169,315	759.4	169,919	777.6
55–59	103,570	498.4	112,263	529.7	120,732	561.9	130,020	597.2	138,543	630.1
60–64	58,415	327.8	65,295	360.3	73,108	394.1	80,600	423.2	89,322	458.3
≥65	45,040	104.4	52,299	117.1	60,255	130.4	69,816	146.3	80,102	162.6

^aRates are per 100,000 population

Age	2012		2016	
	No.	Rate	No.	Rate
50-54	150,072	664.4	169,919	777.6
55-59	103,570	498.4	138,543	630.1
60-64	58,415	327.8	89,322	458.3
>65	45,040	104.4	80,102	162.6
Total	357,097	*	477,886	*
Total, all age groups	892,235		991,447	
Percentage	40%		48%	

People Living With Diagnosed HIV by Age, 2015, United States



Source: CDC. [Diagnoses of HIV infection in the United States and dependent areas, 2016](#) . HIV Surveillance Report 2016;28.

Population Diversity

Elderly patients diagnosed when cART became available

- Long-term effects of the inflammatory process
 - Elite controllers*
- Long-term effects of cART
- Drug holidays

*Krishnan, Wilson et al. (2014)

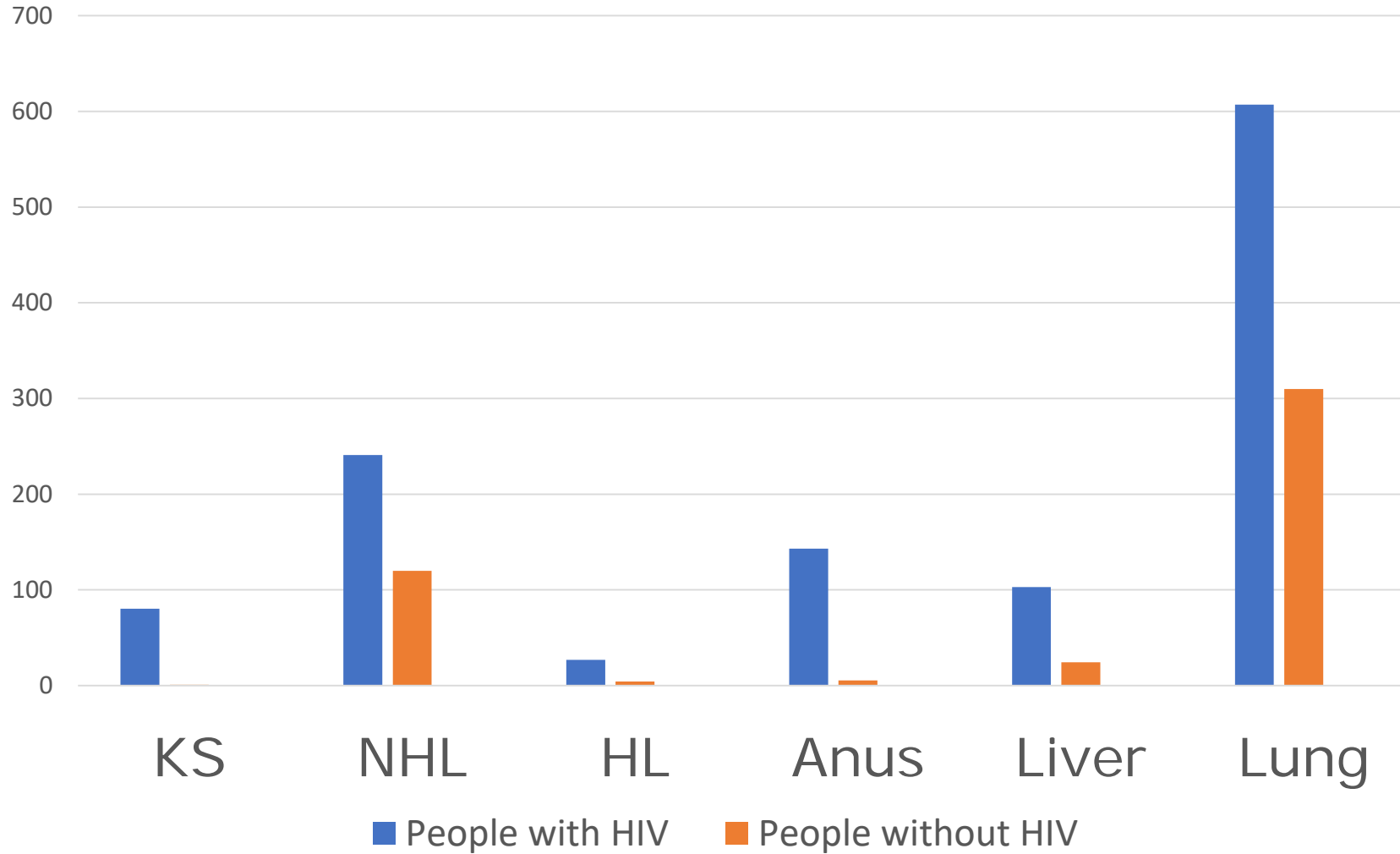
Population Diversity

- Elderly patients newly diagnosed
 - Delays in diagnosis
 - Poor CD4 recovery

What they have in common

- Interplay of multiple disease processes
- Immunosenescence
 - “Accelerated” vs “accentuated” aging
- Frailty

Cancer Incidence in Patients > 65 years old



KS=Kaposi's Sarcoma; NHL=Non-Hodgkins Lymphoma; HL=Hodgkins Lymphoma. Yanik, Katki and Engels. (2016)

Prevalence of Modifiable Risk Factors

Modifiable risk factor	% of cohort living with HIV	% of cohort without HIV
Alcohol intake*	35	5-15
Obesity	17	34
Smoking	54	23
Chronic HCV	26	0.9
HPV*	46 (c); 16 (o); 68(a)	29 (c); 4 (o); 0 (a)
HBV	5	0.3

C=cervical; o=oral; a=anal. Park et al. (2016)

Lung Cancer

Higher rate of smoking—42.4% vs 20.6% ¹

Prior lung damage by HIV ²
(PCP and other pneumonia)

HIV-related inflammation ^{2, 3}

¹Mdodo, Frasier, Dube, et al (2015). ²Shebl, Engels, et al. (2010); ³Hessol, Martínez-Maza, et al (2015)

Screening for Lung Cancer

- Annual screening with low-dose computed tomography (LDCT) in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 15 years.

US Preventive Services Task Force (2015)

Cervical and Anal Cancers

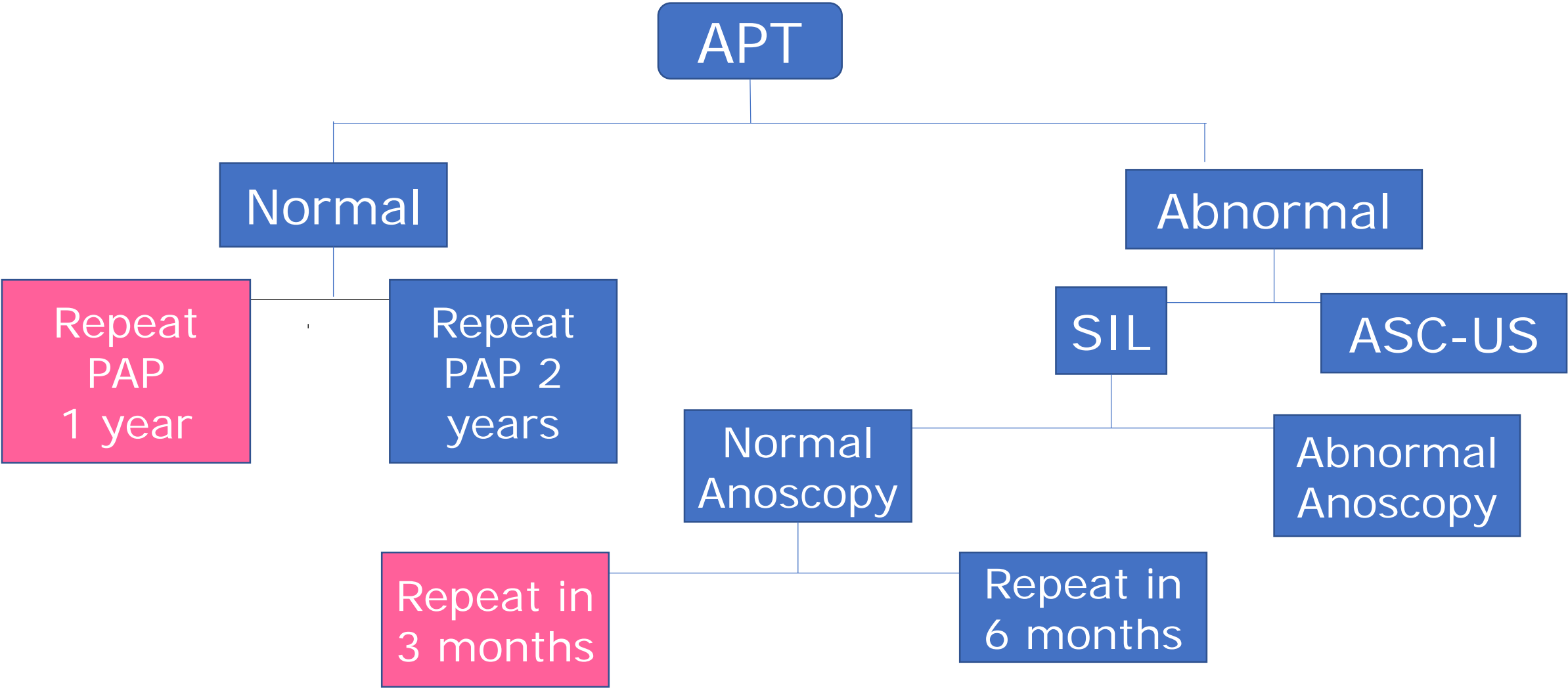
ACS 2019 estimates:

- Anal cancer
 - ≈8,300 new cases (5,530 in women; 2,770 in men)
 - ≈1,280 deaths (760 in women; 520 in men)
- Cervical cancer
 - ≈13,1700 new cases
 - ≈4,250 deaths

- HPV 16, 18
- Gardasil
 - FDA approved up to age 45
- Screening
 - ANCHOR
 - SPANC

Anal Cancer Screening

Morency, E. G., Harbert, T., Fatima, N., Samolczyk, J., Maniar, K. P., & Nayar, R. (2019).



Abbreviations: APT=anal Papanicolaou test; ASC-US=atypical squamous cells of undetermined significance; SIL=squamous intraepithelial lesion.

Cervical Cancer Screening

- Use of both cytology and HPV testing every five years is preferred for healthy women 30 to 65 years of age. (ACS, USPSTF, ACOG)
- Women with human immunodeficiency virus infection should be screened with cytology twice in the year after diagnosis, even if younger than 21 years, and annually thereafter.

Liver Cancer/Other Liver Diseases

- Hepatocellular carcinoma

Liver disease

- Hepatitis C
 - 2.3 million estimated worldwide
 - In the US, 25% of PLWHA
- Nearly 75% of people with HIV who inject drugs also are infected with HCV.
- More than triples the risk for liver disease, liver failure, and liver-related death.

Hepatitis C

- Cirrhosis
- Immune function
- Reinfection

Hepatitis B

- A person in the acute phase could be asymptomatic or could experience
 - Fatigue
 - Jaundice
 - Dark urine
- The virus may resolve on its own or it may progress to chronic hepatitis, cirrhosis or hepatocellular carcinoma
- Reactivation

Hepatitis B—Prevention

- Postvaccination serologic testing 1–2 months after the final dose†
- Immune memory?

†Schillie S, Vellozzi C, Reingold A, et al.

HBV Treatment

- Peg IFN
- Entecavir
- TDF/TAF

Cardiovascular Disease

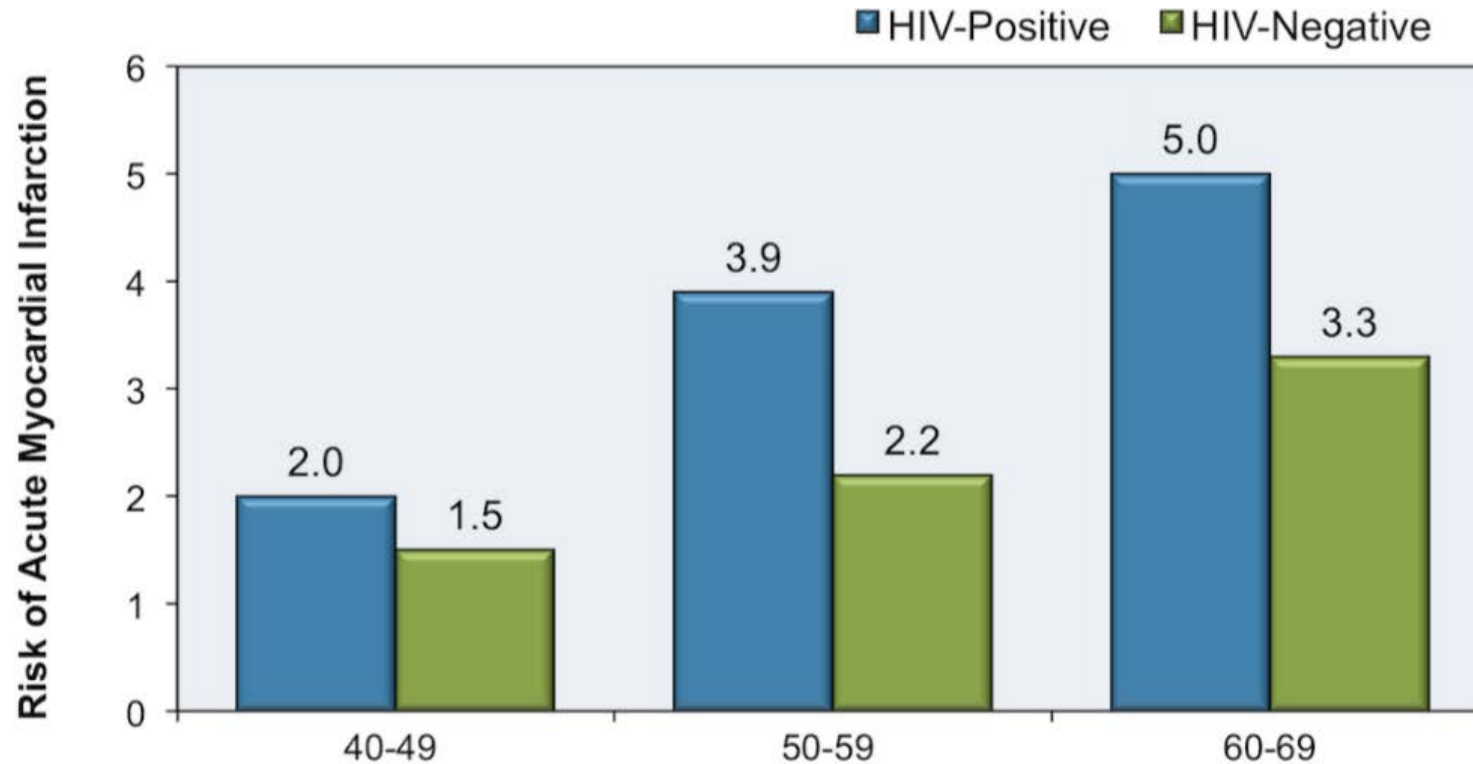


Figure 10 - Risk of Acute Myocardial Infarction Based on HIV Status and Age

This graph is based on data from 82,459 participants in the Veterans Aging Cohort Study (Virtual Cohort) from April 1, 2003 through December 31, 2009. Persons with HIV clearly had a higher risk of developing acute myocardial infarction and this risk was seen across multiple decades of age.

Source: Freiberg MS, Chang CC, Kuller LH, et al. HIV infection and the risk of acute myocardial infarction. *JAMA Intern Med.* 2013;173:614-22.

Risk Factors

- Increased duration of ART
- HIV immune activation/inflammation
 - Intestinal bacterial translocation
 - Concurrent viral infections (CMV, HBV, HCV, HSV)
 - Residual HIV viremia or HIV proliferation

Risk Factors

- Hypertension
- Diabetes
- Dyslipidemia
- Smoking
- Metabolic Syndrome
- Hypogonadism

Focus on risk factors the patient can control

Renal Disease

Predictors of chronic kidney disease in adults with HIV

- Older age
- Use of TDF
- Female sex
- Diabetes
- Hypertension
- Hepatitis C infection
- Injection drug use
- History of acute kidney injury
- Lower CD4 cell count
- Higher HIV RNA levels

Diabetes

- Protease Inhibitors (LPV/r, FPV/r)
- Lifestyle/Family history/Age

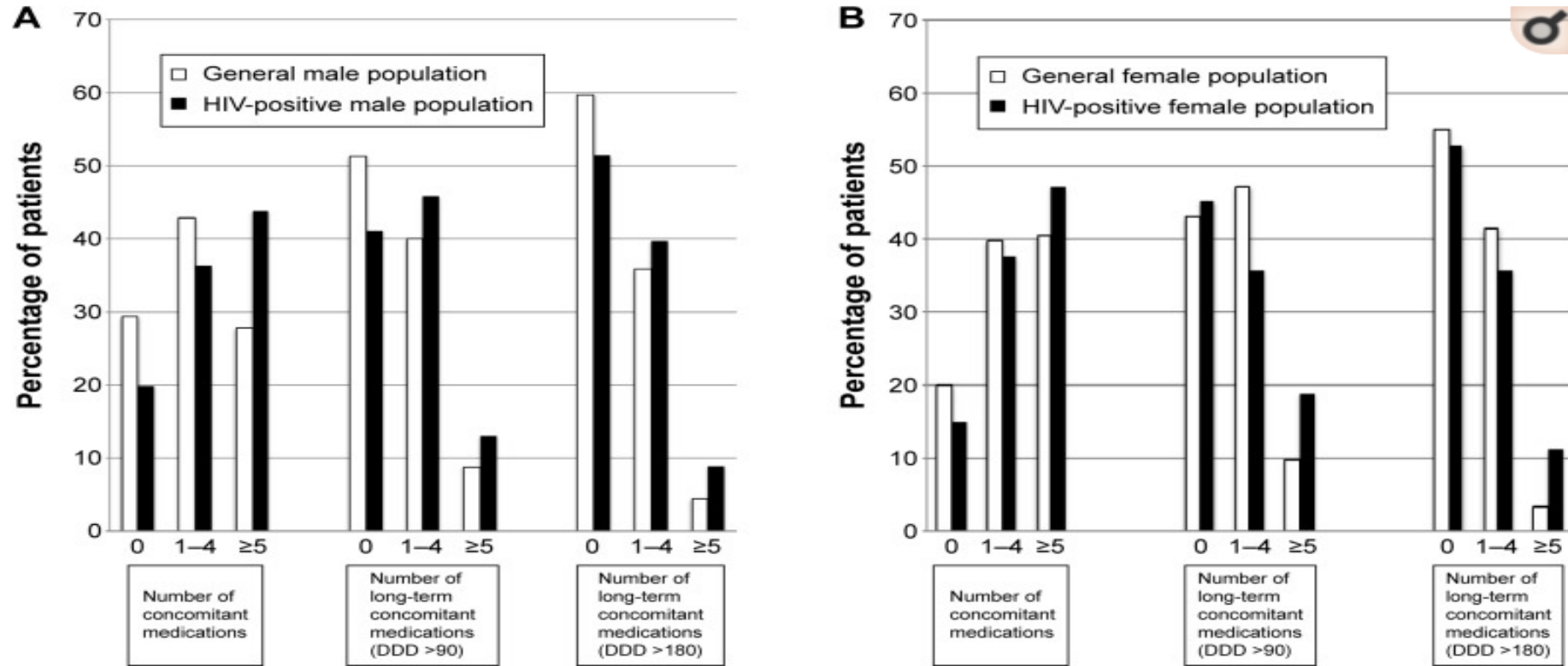
Bone density issues

- lower body weight, smoking, and vitamin D deficiency
- use of tenofovir DF

Tuberculosis

- The risk of developing TB is estimated to be between 16-27 times greater in people living with HIV

Polypharmacy



Concomitant medication use in HIV-positive patients and general population, aged 50–64 years.

Notes: (A) Males, (B) females. Use of 0, 1–4, and ≥ 5 prescribed concomitant medications (excluding antiretrovirals) was calculated according to 1) drugs with a DDD >1; 2) drugs with a DDD >90 (treatments lasting >90 days); and 3) drugs with a DDD >180 (treatments lasting >180 days).

Abbreviations: DDD, defined daily dose; HIV, human immunodeficiency virus.

Polypharmacy

- Impaired renal and hepatic function
- Cytochrome p450
 - 3A4
 - 2C8
 - 2C9

Polypharmacy

- Calcium-containing antacids may impair absorption
 - Atazanavir
 - Rilpivirine
 - Integrase inhibitors
 - Raltegravir 1200 mg QD

Polypharmacy

- TB medications
- Statins†
- Inhaled corticosteroids†
- Boosted PI†

Resources

- The American Academy of HIV Medicine
 - The HIV & Aging Consensus Project
- Liverpool HIV iChart

References

- <http://hiv-age.org/wp-content/uploads/2019/02/FINALANNOTATEDHIVAGE2018-7.pdf>
- <http://hiv-age.org/wp-content/uploads/2013/11/HIVandAgingConsensusProject051815.pdf>
- <https://www.cdc.gov/hiv/group/age/olderamericans/index.html>

References, cont.

- Aberg JA, Gallant JE, Ghanem KG, Emmanuel P, Zingman BS, Horberg MA. Primary care guidelines for the management of persons infected with HIV: 2013 update by the HIV medicine association of the Infectious Diseases Society of America. *Clin Infect Dis*. 2014;58:e1-34.
- Bischoff, J., & Rockstroh, J. K. (2018). Are there any challenges left in hepatitis C virus therapy of HIV-infected patients? *International Journal of Antimicrobial Agents*.
<https://doi.org/10.1016/j.ijantimicag.2018.08.019>
- Centers for Disease Control and Prevention. HIV Surveillance Report, 2017; vol. 29. <http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html>. Published November 2018.
- Ceres, M., et al. (2018). "Cancer Screening Considerations and Cancer Screening Uptake for Lesbian, Gay, Bisexual, and Transgender Persons." *Semin Oncol Nurs* 34(1): 37-51.
- Colon-Lopez, V., et al. (2018). "Anal Cancer Risk Among People With HIV Infection in the United States." *J Clin Oncol* 36(1): 68-75.

- De Wit S, Sabin CA, Weber R et al. Incidence and risk factors for new-onset diabetes in HIV-infected patients: the Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) study. *Diabetes Care* 2008; 31: 1224–1229.
- Demir, Ozan M., Candilio, L., Fuster, D., Muga, R., Azzalini, L. [Cardiovascular disease burden among human immunodeficiency virus-infected individuals](#) *International Journal of Cardiology*, Volume 265, 15 August 2018, Pages 195-203.
- Goulet JL, Fultz SL, Rimland D, et al. Aging and infectious diseases: do patterns of comorbidity vary by HIV status, age, and HIV severity? *Clin Infect Dis.* 2007;45:1593-601.
- Guaraldi, Giovanni, Zona, Stefano, Silva, Ana Rita, Menozzi, Marianna, Dolci, Giovanni, Milic, Jovana, Carli, Federica, Mussini, Cristina The dynamic association between Frailty, CD4 and CD4/CD8 ratio in people aging with HIV. By: , PLoS ONE, 19326203, 2/14/2019, Vol. 14, Issue 2
- Hessol, N. A., Martínez-Maza, O., Levine, A. M., Morris, A., Margolick, J. B., Cohen, M. H., ... Seaberg, E. C. (2015). Lung cancer incidence and survival among HIV-infected and uninfected women and men. *AIDS (02699370)*, 29(10), 1183–1193.
- Krishnan, S., Wilson, E. M. P., Sheikh, V., Rupert, A., Mendoza, D., Yang, J., ... Sereti, I. (2014). Evidence for Innate Immune System Activation in HIV Type 1–Infected Elite Controllers. *Journal of Infectious Diseases*, 209(6), 931–939.

- Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents Living with HIV. Department of Health and Human Services. Considerations for antiretroviral use in special patient populations: HIV and the older patient. January 28, 2016.

References, Cont.

- Mahale, P., et al. (2018). "Cancer risk in older people living with human immunodeficiency virus infection in the United States." *Clin Infect Dis*.
- Park LS, Hernandez-Ramirez RU, Silverberg MJ et al. Prevalence of non-HIV cancer risk factors in persons living with HIV/AIDS: a meta-analysis. *AIDS* 2016; 30: 273–291.
- Samad F, Harris M, Puskas CM et al. Incidence of diabetes mellitus and factors associated with its development in HIV-positive patients over the age of 50. *BMJ Open Diabetes Res Care* 2017; 5: e000457. 22.
- Sharma, A., et al. (2018). "HIV Infection Is Associated With Abnormal Bone Microarchitecture: Measurement of Trabecular Bone Score in the Women's Interagency HIV Study." *JAIDS: Journal of Acquired Immune Deficiency Syndromes* 78(4): 441.
- Shiels, M. S., et al. (2018). "Projected Cancer Incidence Rates and Burden of Incident Cancer Cases in HIV-Infected Adults in the United States Through 2030." *Ann Intern Med* 168(12): 866-873.

References, cont.

- Mast, EE, Margolis, HS, et al. (2005). A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices (ACIP) Part 1: Immunization of Infants, Children, and Adolescents. *Morbidity and Mortality Weekly Report: Recommendations and Reports*, 54(RR-16),
- Mdodo R, Frazier EL, Dube SR, et al. Cigarette smoking prevalence among adults with HIV compared with the general adult population in the United States: cross-sectional surveys. *Ann Intern Med*. 2015;162(5):335-344.
- Morency, E. G., Harbert, T., Fatima, N., Samolczyk, J., Maniar, K. P., & Nayar, R. (2019). Anal Cytology: Institutional Statistics, Correlation With Histology, and Development of Multidisciplinary Screening Program With Review of the Current Literature. *Archives of Pathology & Laboratory Medicine*, 143(1), 23–29.

References, cont.

- Reddy KP, Kong CY, Hyle EP, et al. Lung Cancer Mortality Associated With Smoking and Smoking Cessation Among People Living With HIV in the United States. *JAMA Intern Med.* 2017;177(11):1613–1621. doi: 10.1001/jamainternmed.2017.4349
- Rossi, C., Young, J., Martel-Laferrrière, V., Walmsley, S., Cooper, C., Wong, A., ... Klein, M. B. (2019). Direct-Acting Antiviral Treatment Failure Among Hepatitis C and HIV–Coinfected Patients in Clinical Care. *Open Forum Infectious Diseases*, 6(3), N.PAG. Retrieved from <https://search-ebscohost-com.southuniversity.libproxy.edmc.edu/login.aspx?direct=true&db=edb&AN=136580143&site=eds-live>
- Schillie S, Vellozzi C, Reingold A, et al. Prevention of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. *MMWR* 2018;67(1):1-31.
- Shebl FM, Engels EA, Goedert JJ, Chaturvedi AK. Pulmonary infections and risk of lung cancer among persons with AIDS. *J Acquir Immune Defic Syndr.* 2010;55:375–379.
- Sims, O. T., & Womack, B. G. (2015). Hepatitis C and HIV Coinfection for Social Workers in Public Health, Medical and Substance Use Treatment Settings. *Social Work in Public Health*, 30(4), 325.
- Yanik EL, Katki HA, Engels EA. High cancer risk among the hiv-infected elderly in the United States. Conference on retroviruses and opportunistic infections, 23–26 February, 2015, Seattle, Washington. Abstract 725.

- <https://www.cancer.org/cancer/anal-cancer/about/what-is-key-statistics.html>
- <https://www.cancer.org/cancer/cancer-causes/infectious-agents/hiv-infection-aids/hiv-aids-and-cancer.html>
- *Final Update Summary: Lung Cancer: Screening*. U.S. Preventive Services Task Force. July 2015.
[https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/lung-cancer-screening?ds=1&s=lung cancer screening](https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/lung-cancer-screening?ds=1&s=lung%20cancer%20screening)