





#### Care of The Older Adult with HIV Infection

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#### **Continuing Medical Education Disclosure**

- Program Faculty: Howard Libman, MD
- <u>Current Position</u>: Professor of Medicine, Harvard Medical School, Director, HIV Program, Healthcare Associates, Beth Israel Deaconess Medical Center, Boston, MA
- <u>Disclosure</u>: Financial Relationships: IAS-USA Lecture on HIV infection (honorarium), UpToDate (Royalty). Presentation does not include discussion of off-label products.

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## Learning Objectives

- 1. Identify epidemiologic and clinical characteristics of the older HIV-infected patient
- Describe HIV comorbidities with a focus on coronary artery disease predisposing conditions and premature bone loss
- List immunizations and screening tests for coinfections and cancers relevant to care of the older HIV-infected patient
- 4. Explain changing mortality patterns in the modern era of antiretroviral therapy





## Impact of HIV Infection on Aging

- HIV infection, even when controlled, is associated with chronic immune activation superimposed upon immunologic senescence in the older adult
- Because of IL-2 and thymic dysfunction, these patients may have delayed immune reconstitution
- Recent studies have shown that chronic immune activation results in accelerated aging of T cells
- It is not clear that these changes are reversed by antiretroviral therapy





#### Polling Question Which of the following statements about HIV-infected patients over 50 years of age is false?

- a) They present at an earlier stage of disease.
- b) They constitute 30% of HIV-infected patients.
- c) They are at increased risk of cognitive impairment compared to general population.
- d) They are at increased risk of some common malignancies compared to general population.
- e) They are more adherent to medical therapy.





## **HIV Epidemiology in Older Adult**

- Since the 1980s, an increasing percentage of HIVinfected patients are over the age of 50
- Approximately 30% of HIV-infected persons are ≥50 years of age
- In 2012, 17.1% of newly diagnosed cases of HIV infection and 25.6% of newly diagnosed AIDS cases were in adults 50 years of age or older
- MSM is the most common mode of transmission in older men, and heterosexual contact is the most common mode in older women



Centers for Disease Control and Prevention. http://www.cdc.gov/hiv/statistics/basics

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## Clinical Characteristics (1)

- Older persons may be diagnosed later and have more advanced HIV infection at presentation
- Increased risk of opportunistic infections and transmission to others
- Less robust immunologic response to antiretroviral therapy in this population
- Medication adherence is generally good, but there may be increased risk of drug toxicity because of changing pharmacokinetics





## Immunologic Response to ART

- Among 12,196 treatment-naive patients in NA-ACCORD who initiated ART (observational cohort), immunologic response after 24 months of therapy decreased with increasing age starting at 40, but there was no effect on viral suppression
- A prospective study that evaluated treatment outcomes in 3,015 patients (401 of whom were over age 50) found that, despite better virologic control, clinical progression to an AIDS-defining diagnosis was higher (HR 1.52; 95% CI 1.2-2.0)



Althoff KN, Justice AC, Gange SJ et al. *AIDS* 2010;24:2469. Grabar S, Kousignian I, Sobel A et al. *AIDS* 2004;18:2029



### **Medication Adherence**

- Literature has reported up to 95% adherence in older HIV-infected patients
- In a recent meta-analysis, older age reduced the risk for non-adherence by 27% (RR 0.72; CI 0.64-0.82)
- Those studies assessing short-term and long-term adherence showed a significant reduction in both groups (RR 0.75; CI 0.64-0.87 and RR 0.65; CI 0.50-0.85, respectively)



Ghidei L, Simone MJ, Salow MJ et al. Drugs Aging 2013;30:809



## **Drug Toxicity**

- A higher rate of adverse events (64% vs. 35%) on protease inhibitors was reported in patients older than 60 compared to those under 40
- Another study of 508 treatment-naïve patients found that regimen changes due to toxicity were associated with increasing age
- May be from age-related decrease in renal and hepatic function, decrease in serum albumin level, and changes in cytochrome p450 enzyme system



Knobel H, Guelar A, Valldecillo G et al. *AIDS* 2001;15:1591. Lodwick RK, Smith CJ, Youle M et al. *AIDS* 2008;22:1039



## Clinical Characteristics (2)

- HIV-infected patients accumulate "age-related" diseases at a younger chronological age
- Neurocognitive dysfunction, some non-AIDS-defining cancers, and a wide range of pulmonary diseases are also more prevalent
- Hypothesis that increased immune activation and long-term chronic inflammation contribute to premature aging in this population





#### Chronic Complications by Age and HIV Status



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#### Chronic Complications by Age and HIV Status

- Retrospective analysis of HIV-infected outpatients compared to seronegative persons (case-control study) from 2002 through 2009
- Examined cardiovascular disease, hypertension, diabetes mellitus, bone fractures, and renal failure
- Independent predictors of polypathology (p < 0.001) included older age (OR 1.11), male gender (OR 1.77), CD4 nadir below 200 (OR 4.46), and duration of antiretroviral therapy (OR 1.01)



Guaraldi G, Orlando G, Zona G et al. Clin Infect Dis 2011;53:1120



## **Cognitive Dysfunction**

- Epidemiologic findings suggest that increasing age is risk factor for HIV-associated dementia, although the studies are small
- Longitudinal study comparing 106 HIV-infected patients over 50 years of age to 96 patients between 20-39 years of age showed a three-fold higher risk of dementia on multivariate analysis
- Study adjusted for race, education, depression, substance abuse, ART, CD4 count, and viral load



Valcour V, Shikuma C, Shiramizu B et al. Neurology 2004;63:822





- Observational studies suggest that lung, hepatic, and anal cancers occur at younger age in HIV-infected adults compared to seronegative persons
- Using 15 HIV and cancer registry databases in the US, including 212,055 persons with AIDS, the age of diagnosis of non–AIDS-defining cancers was examined
- Only lung and anal cancers were seen in AIDS patients at younger age (median 50 years old vs. 54; p < 0.001) than expected



Shiels MS, Pfeiffer RM, Engels EA. Ann Intern Med 2010;153:452



## **Pulmonary Diseases**

- Veterans Aging Cohort Study consisting of 33,420 HIVinfected patients and 66,840 seronegative controls
- Subjects were matched by age, sex, race, and ethnicity
- Incidence of chronic obstructive pulmonary disease, lung cancer, pulmonary hypertension, and pulmonary fibrosis was significantly higher in the HIV-infected group



Crothers K, Huang L, Goulet JL et al. Am J Respir Crit Care Med 2011;183:388



## Major Comorbidities

- Coronary artery disease (CAD)
- CAD predisposing conditions
- Premature bone loss including osteoporosis and pathologic fractures





## LDS Clinical Manifestations

- Lipid metabolism
  - Increased triglycerides
  - Increased cholesterol, LDL, cholesterol/HDL ratio
  - Decreased HDL
- Glucose metabolism
  - Insulin resistance
  - Glucose intolerance
  - Diabetes mellitus

- Fat accumulation
  - Increased visceral fat
  - Buffalo hump
  - Lipomatosis
  - Gynecomastia
- Fat atrophy
  - Face, extremities, buttocks

















#### Management of Lipodystrophy Syndrome

Hyperlipidemia, insulin resistance



Diet and exercise Switch therapy Older PI → atazanavir or NNRTI Statins/fibrates Insulin-sensitizing drugs Visceral fat accumulation



Diet and exercise Switch therapy Older PI → NNRTI Growth hormone or growth hormone releasing factor Cosmetic surgery Subcutaneous fat wasting



Switch therapy Older PI → NNRTI Insulin-sensitizing drugs Local injection (polylactic acid, calcium hydroxylapatite)





#### Traditional Risk Factors for Coronary Artery Disease

- Age (men  $\geq$  45 years, women  $\geq$  55 years)
- High LDL cholesterol (> 160 mg/dL)\*
- Low HDL cholesterol (< 40 mg/dL)</li>
- Hypertension
- Family history of premature coronary artery disease (CAD)
- Diabetes mellitus (DM)
- Cigarette smoking

\* With CAD, DM, or multiple risk factors, the desirable level for LDL cholesterol decreases; <100 mg/dL is ideal.



Grundy SM, Cleeman JI, Bairey Merz CN et al. JAMA 2001;285:2486



#### HIV Infection and Coronary Artery Disease (1)

- Incidence of CAD is higher than that in HIV-negative patients matched for age and gender
- Studies have demonstrated an increase in subclinical atherosclerosis (eg, carotid intima media thickness) and clinical endpoints (eg, acute myocardial infarction)
- HIV infection is associated with increased soluble and cellular markers of inflammation, endothelial dysfunction, and altered coagulation, all of which have been shown to contribute to cardiovascular disease





#### HIV Infection and Coronary Artery Disease (2)

- Degree to which HIV infection itself, antiretroviral therapy, and other risks contribute to increased risk in this population is unknown
- High prevalence of traditional risk factors in this population
- Protease inhibitor class appears to be associated with higher risk of CAD; some data suggesting abacavir and efavirenz may also increase risk
- Discontinuation of ART is associated with higher risk of CAD





#### Polling Question HIV infection has been associated with the following increased percentage risk of acute myocardial infarction beyond that explained by recognized risk factors:

- a) 90 percent
- b) 30 percent
- c) 70 percent
- d) 10 percent
- e) 50 percent





#### The Risk of Coronary Artery Disease in HIV-infected Patients

#### Table 2. Rates of AMI by HIV Status and Age Group<sup>a</sup>

	Age Group, y								
Status	<30	30-39	40-49	50-59	60-69	70-79	80-89	>89	
			Unir	fected					
No. of participants	1175	6783	21866	19805	4209	1120	148	3	
No. of AMI events	0	10	164	218	66	36	14	0	
AMI rates per 1000		0.3	1.5	2.2	3.3	6.7	21.5		
person-years (95% CI)		(0.2-0.6)	(1.3-1.7)	(1.9-2.5)	(2.6-4.2)	(4.8-9.2)	(12.7-36.4)		
			HIV I	nfected					
No. of participants	725	3848	10575	9342	2065	557	56	0	
No. of AMI events	0	13	105	171	46	25	3	0	
AMI rates per 1000		0.7	2.0	3.9	5.0	10.0	13.5		
person-years (95% CI)		(0.4 - 1.2)	(1.6-2.4)	(3.3 - 4.5)	(3.8 - 6.7)	(6.7 - 14.7)	(4.3 - 42.0)		
Incidence rate ratio (95% CI)		<b>2.19</b>	<u>1.34</u>	`1.80 ´	1.53 (1.03-2.26)	<b>1.50</b>	0.63		
()		(0.89-5.58)	(1.04-1.72)	(1.47-1.21)	,	(0.86-2.57)	(0.12-2.25)		

Abbreviations: AMI, acute myocardial infarction; HIV, human immunodeficiency virus.

<sup>a</sup> An ellipsis indicates that a rate was not calculated because there were 0 events.



Freiberg MS, Chang CC, Kuller LH et al. JAMA Intern Med 2013;173:614



## Hypertension

- Similar approach to that in patients without HIV infection
- Defined as ≥140/90 in three separate visits over a week or more
- In the absence of history or physical exam pointing to secondary hypertension, baseline evaluation should include renal function, potassium, urinalysis, and electrocardiogram
- Nonpharmacologic management consists of modest salt restriction, increased physical activity, and weight reduction
- Initial drug therapy should consist of thiazide diuretic, ACE inhibitor or receptor blocker, or calcium channel blocker in most patients
- For those who are more than 20/10 mmHg above goal, ACE inhibitor or receptor blocker plus calcium channel blocker is recommended
- No important ART interactions for commonly used drugs





### **Diabetes Mellitus**

- Similar approach to that in patients without HIV infection
- Diagnosis is often based upon HgbA1c  $\geq$  6.5%
- Treatment goals include prevention of symptomatic hyperglycemia and vascular complications; HgbA1c target < 7.0%</li>
- Nonpharmacologic management consists of weight reduction through dietary modification and increased physical activity
- Initial drug therapy generally consists of metformin with sulfonylurea (eg, glipizide) added as the second agent
- Metformin may cause lactic acidemia as do older NRTI drugs
- No other important ART interactions for commonly used drugs
- DM and HIV have particularly detrimental effect on renal function (Medapalli RK et al. J Acquir Immune Defic Syndr 2012;60:393)





## **Cigarette Smoking**

- HIV-infected patients are more likely to smoke and less likely to quit compared to general population (Ann Intern Med 2015;162:335-44)
- No evidence that specific smoking cessation approaches are more or less effective
- Management includes behavioral intervention and/or pharmacologic therapy; evidence suggests that combination approach works better than either alone
- Drug options include nicotine replacement (eg, patch, gum, lozenge), bupropion, and varenicline, which can be used alone or in combination
- No important ART interactions for commonly used drugs





#### Hyperlipidemia in General Population

- Desirable total cholesterol is less than 200 mg/dl and LDL cholesterol is less than 130 mg/dl in general population
- Epidemiologic studies show a graded relationship between total cholesterol level and CAD risk
- Patients with clinical atherosclerosis (eg, CAD, CVD, PVD) or combination of factors that result in a 10-year risk of new event of > 20% benefit substantially from statin therapy
- Patients without clinical atherosclerosis achieve a lesser absolute benefit from statin treatment
- Relative risk reduction in all populations is 20%-30%





## Framingham Risk Calculator

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	Public	Health Professionals	Researchers	Clinical Trials	News & Resources	About NHLBI				
	Home » Clinical Practice Guidelines » Cholesterol » CVD Risk Calculator									
	Thursday, October 15, 201	5								
	Information for Health Professionals	Risk Assessme	nt Tool for Es	timating Your	10-year Risk of	Having a				
	Clinical Practice Guideline	₅Heart Attack								
	Heart & Vascular Information Lung Information Blood Information Sleep Information Interactive Tools and Resources Education Campaigns National Education Programs Continuing Education Opportunities Health Observances	The risk assessment tool bel in the next 10 years. This to enter your information in th Age: Gender: Total Cholesterol: HDL Cholesterol: Smoker: Systolic Blood Pressure: Are you currently on any me	ow uses information from ol is designed for adults aç e calculator below. edication to treat high bloo	the Framingham Heart Stu jed 20 and older who do no d pressure.	dy to predict a person's chance t have heart disease or diabete years Female Male mg/dL No Yes mm/Hg No Yes	of having a heart attack s. To find your risk score,				
		Total cholester the greater your Less than 200 m greater increases	ol - Total cholesterol is the risk for heart disease. Her ng/dL 'Desirable' level that s your risk.	alculate Your 10-Year a sum of all the cholesterol e are the total values that i puts you at lower risk for h	RISK in your blood. The higher your matter to you: eart disease. A cholesterol level	total cholesterol, l of 200 mg/dL or				

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Uses data from an urban northeastern United States population.

Many consider it the preferred risk calculator.

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#### **ACC/AHA CV Risk Calculator**

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The American Heart Association and the American College of Cardiology are excited to provide a series of new cardiovascular prevention guidelines for the assessment of cardiovascular risk, lifestyle modifications that reduce risk, management of elevated blood cholesterol, and management of increased body weight in adults. To support the implementation of these guidelines, the new Pooled Cohort Equations CV Risk Calculator and additional Prevention Guideline Tools are available below. Others may be developed and available in the near future.





2013 Prevention Guidelines Tools

**CV RISK CALCULATOR** 

Estimates of 10-year risk for ASCVD are based on data from multiple community-based populations and are applicable to African-American and non-Hispanic white men and women 40 through 79 years of age. For other ethnic groups, we recommend use of the equations for non-Hispanic whites, though these estimates may underestimate the risk for persons from some race/tehnic groups, especially American Indians, some Asian Americans (e.g., of south Asian ancestry), and some Hispanics (e.g., Puerto Ricans), and may overestimate the risk for others, including some Asian Americans (e.g., of east Asian ancestry) and some Hispanics (e.g., Mexican Americans) (e.g., of east Asian ancestry) and some Hispanics (e.g., Mexican Americans).

Estimates of lifetime risk for ASCVD are provided for adults 20 through 59 years of age and are shown as the lifetime risk for ASCVD for a 50-year old without ASCVD who has the risk rc.ahajournals.org/lookup/.../01.cir.0000437741.48606.98 If lifetime risk are most directly of these values for other

Figure 1. Implementation of Risk Assessment Work Group Recommendations See 2011 AHA/ACC Seconda Prevention Guideline and 2013 dult Prevention Guidelines Does the patient have existing clinical ASCVD? **Blood Cholesterol** Obesity Lifestyle Management See 2012 NHLBI Pediatric CV Risk Reduction Guidelines and 2013 Adult Prevention s the patient <20 y or >79 y of age Guidelines Blood Cholestero Obesity Communicate risk data and refer to 2013 Adult Prevention ssess traditional risk factors every Elevated 4-6 y in patients 20-79 y of age; estimate 10-y risk in those 40-79 y o age using Pooled Cohort Equations Blood Cholesterol Obesity Low 10-y risk (<7.5%)

> Assess 30-y or lifetime risk in those 20-59 y of age; Communicate risk

Uses data primarily from non-Hispanic whites and African Americans in the United States.

Concerns about accuracy of results have been made (statin recommendations, DM yes vs. no categorization, FMH of premature CAD not included).





### **ACC/AHA Cholesterol Guidelines**

- Categories of patients to be considered for treatment:
  - Group 1: known cardiovascular disease
  - Group 2: LDL cholesterol ≥ 190 mg/dL
  - Group 3: diabetes mellitus aged 40 to 75 years and LDL cholesterol ≥ 70 mg/dL
  - Group 4: age 40 to 75 years with LDL cholesterol ≥ 70 mg/dL and an estimated 10-year risk of a cardiovascular event of ≥ 7.5%
- Groups 1 and 2: high-intensity statin (rosuvastatin 20 to 40 mg or atorvastatin 40 to 80 mg), although patients with known cardiovascular disease > 75 years of age can receive moderate-intensity statin
- Group 3: high-intensity statin if 10-year risk is ≥ 7.5%; otherwise they can receive a moderate-intensity statin
- Group 4: moderate- to high-intensity statin

Stone NJ, Robinson JG, Lichtenstein AH et al. Circulation 2014;129:S1





#### Polling Question Which of the following statements regarding hyperlipidemia in HIV infection is true?

- a) It is defined differently than in the general population.
- b) It is usually related to antiretroviral drug therapy.
- c) It should always be treated with medication.
- d) Simvastatin cannot be administered with cobicistat.
- e) High dose atorvastatin is recommended as initial treatment in patients with concurrent CAD.





## Hyperlipidemia in HIV Infection

- Dyslipidemia is common in HIV-infected patients on ART; it may be isolated or seen in combination with other features of LDS
- HIV-infected patients should be evaluated and treated for dyslipidemia in a similar fashion to seronegative persons
- Cardiac risk factor assessment should be considered when designing an initial ART regimen; avoid protease inhibitors (except possibly atazanavir) and abacavir if there are other risks
- Protease inhibitors, particularly ritonavir, increase most statin levels
- Simvastatin and lovastatin are contraindicated with protease inhibitors and cobicistat; atorvastatin and rosuvastatin can be used as alternatives
- Prudent to start with low dose and to monitor LFTs and CPK on treatment





## Premature Bone Loss (1)

- Osteopenia, osteoporosis, and pathological fractures have been described
- Osteopenia is asymptomatic condition
- Osteoporosis may present with fractures of vertebrae, forearms, or hips
- HIV infection itself, tenofovir, protease inhibitors, alterations in vitamin D metabolism, and lactic acidemia related to older NRTI drugs may be contributing factors to premature bone loss





## Premature Bone Loss (2)

- Immobility, cigarette smoking, excessive alcohol use, chronic renal disease, hypogonadism, hyperparathyroidism, hyperthyroidism, and steroid use accentuate bone loss
- Optimal use of bone densitometry as screening test in this population is uncertain
- Calcium and vitamin D should be given in high-risk patients; regular exercise and smoking cessation should be advised





#### Antiretroviral Exposure and Risk of Osteoporotic Fractures



Bedino R, Maalouf NM, Zhang S et al. AIDS 2012;26:825

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#### Polling Question Which of the following statements reflects current IDSA/HIVMA recommendations about bone densitometry screening in HIV-infected persons?

- a) It should be performed in post-menopausal women and in men who are 50 years of age.
- b) It should performed in women who are 65 years of age.
- c) It should be performed in women and men who are 65 years of age.
- d) It should not be routinely performed in this population.





#### Screening for Long-Term Complications

- Glucose Intolerance/Diabetes Mellitus
  - Fasting glucose and/or HgbA1c every 6-12 months
- Lipid Abnormalities
  - Fasting lipid profile every 6-12 months
- Body Fat Maldistribution
  - Patient self-report, weight at each visit, and anthropometric measurements (skin fold, waist, and hip) periodically
- Lactic Acidemia/Acidosis
  - Venous lactic acid level only in symptomatic patients
- Premature Bone Loss
  - Baseline bone densitometry in post-menopausal women and in men at age 50
- Avascular Necrosis of Hips
  - X-rays and MRI only in symptomatic patients

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#### Immunization Principles in HIV Infection

- Avoid live vaccine preparations, especially in patients with a low CD4+ cell count, unless the benefits clearly outweigh risks
- Vaccines are generally more immunogenic in patients with higher CD4+ cell counts and lower viral loads and should be delayed pending immune reconstitution when appropriate
- Immunologic response to vaccine preparations should be assessed when possible in HIV-infected patients





#### Polling Question In an HIV-infected patient who has not been immunized against pneumococcal infection:

- a) Give pneumococcal polysaccharide vaccine 23 (PPSV23) once.
- b) Give pneumococcal conjugate vaccine (PCV13) first followed by PPSV23 at least 8 weeks later and second PPSV23 dose 5 years later.
- c) Give PPSV23 first followed by PCV13 at least 8 weeks later and second PPSV23 dose 5 years later.
- d) Give PPSV23 with second dose 5 years later.





## Pneumococcal Vaccine (1)

- Rationale: HIV-infected patients are at increased risk for serious pneumococcal infections, including pneumonia and bacteremia
- May result from altered antibody production leading to decreased opsonization
- There are 2 types: 1) 23-valent polysaccharide vaccine;
  2) 13-valent conjugate vaccine
- Recent revision of the recommendations for immunocompromised persons





## Pneumococcal Vaccine (2)

- Pneumococcal vaccine-naive persons:
- PCV13 first followed by PPSV23 at least 8 weeks later and second PPSV23 dose 5 years later
- Previous vaccination with PPSV23:
- PCV13 at least one year after the last PPSV23 dose; for those who require additional doses of PPSV23, the first should be given no sooner than 8 weeks after PCV13 and at least 5 years after most recent PPSV23 dose



Centers for Disease Control and Prevention. MMWR 2012;61:816



## Influenza Vaccine

- Rationale: HIV-infected patients appear to be at increased risk for complications of influenza
- However, there is limited literature on subject
- Recommendation: Administer inactivated seasonal flu vaccine to all patients; especially important for those at risk for influenza exposure or complications from other underlying conditions
- Do not use live (intranasal) vaccine preparation





#### Polling Question Which of the following statements is consistent with CDC recommendations regarding zoster vaccine in HIV-infected persons?

- a) It should never be given to such patients since it is a live attenuated vaccine preparation.
- b) It should routinely be given in adults who are 60 years of age or older.
- c) It may be considered in some adults who are 60 years of age or older.
- d) It should be given to all HIV-infected patients who have never had shingles.





#### Zoster Vaccine in HIV-infected Adults

- 395 adults on stable ART with CD4 count > 200 were randomized 3:1 to receive two doses of zoster vaccine or placebo
- After 24 weeks, the only significant difference in safety was higher incidence of local reactions in those receiving active vaccine
- Antibody titers increased in vaccine recipients
- No significant difference in number of zoster cases in the two groups



Benson C. CROI 2012. Abstract 96



## **Infectious Diseases Screening**

- Sexually Transmitted Diseases: Annual chlamydia, gonorrhea, and syphilis testing in adults at ongoing risk for STDs
- Tuberculosis: Annual PPD or interferon-gamma testing in adults at ongoing risk for tuberculosis infection



Aberg JA, Gallant JE, Ghanem KG et al. Clin Infect Dis 2013;doi:10.1093/cid/cit665



## **Cancer Screening**

- Breast Cancer: Biannual mammography in women aged 50 to 74 years; individualize for younger ages
- Cervical Cancer: Annual Pap test in women after 2 normal Pap tests documented; role of HPV testing in HIV-infected patients is unclear
- Colon Cancer: Colonoscopy every 10 years starting at age 50; earlier and more often screening if history of polyps or inflammatory bowel disease
- Prostate Cancer: Consider annual digital exam in males aged 50 to 74 years; prostate-specific antigen (PSA) testing is no longer recommended in most patients



Adapted from US Preventive Services Task Force Guidelines, 2013



#### Heart and Vascular Disease Screening

- Hypertension: Regular blood pressure checks
- Abdominal Aortic Aneurysm: One-time ultrasound in men ages 65-75 who ever smoked
- Coronary Artery Disease: ASA for men ages 45-79 when risk of atherosclerosis outweighs risk of GI bleeding
- Cerebrovascular Disease: ASA for women ages 55-79 when risk of atherosclerosis outweighs risk of GI bleeding



Adapted from US Preventive Services Task Force Guidelines, 2013



#### Polling Question Which of the following statements regarding mortality in the modern era of ART is false?

- a) The overall mortality rate in HIV-infected adults has declined over the past three decades.
- b) A higher percentage of causes of death are related to non– AIDS-defining conditions.
- c) The age group with the highest percentage of HIV-infected adults who die is 55 or older.
- d) Life expectancy of a 20-year-old person recently diagnosed with HIV infection is similar to that of the general population.





#### Trends in Annual Rates of Death due to HIV Infection by Age Group, United States, 1987–2010



Note: For comparison with data for 1999 and later years, data for 1987–1998 were modified to account for ICD-10 rules instead of ICD-9 rules.



#### Trends in the Percentage Distribution of Deaths due to HIV Infection by Age Group, United States, 1987–2010



Note: For comparison with data for 1999 and later years, data for 1987–1998 were modified to account for *ICD-10* rules instead of *ICD-9* rules.



## **Mortality Trends**

- In the D:A:D study, 3,909 deaths occurred among 49,731 subjects followed from 1999 through 2011
- Crude mortality rate of 12.7 per 1000 person-years
- AIDS-related causes were responsible for 29% of deaths, non-AIDS-related cancers for 15%, liver disease for 13%, and cardiovascular disease for 11%
- Deaths attributable to AIDS-related events decreased from 34% to 22%

Smith CJ, Ryom L, Weber R et al. Lancet 2014;384:241

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 Proportion attributable to non-AIDS-defining malignancies increased from 9% to 23%



#### Mid-point Life Expectancy Estimates at Age 20 Years in Three Calendar

Periods, Overall and by Sociodemographic Characteristics, 2000–2007



Samji H, Cescon A, Hogg RS et al. 2013; PLoS ONE 8(12): e81355.

doi:10.1371/journal.pone.0081355

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# Summary (1)

- Aging is characterized by progressive physiologic changes associated with increased susceptibility to many diseases
- HIV infection, even when controlled, is associated with chronic immune activation that is superimposed upon immunologic senescence in the older adult
- Older persons may be diagnosed later and have more advanced HIV infection at presentation
- There is a less robust immunologic response to antiretroviral therapy in this population
- HIV-infected patients accumulate "age-related" diseases at a younger chronological age
- Hypothesis that increased immune activation and long-term chronic inflammation contribute to premature aging in this population





## Summary (2)

- Lung, hepatic, and anal cancers occur at younger age in HIV-infected adults compared to seronegative persons
- Incidence of CAD is higher than that in HIV-negative patients matched for age and gender
- CAD risk calculator results need to be interpreted in context of increased risk in the HIV-infected population
- HIV infection and its treatment have been associated with premature bone loss
- Age-related immunizations and screening tests for cancers and other conditions should be addressed
- Mortality in HIV-infected persons has fallen substantially over past two decades with non-AIDS-related conditions accounting for the majority of deaths



