

HIV AND AGING

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Financial Disclosure

I, Dr. Dyson, declare no conflicts of interest, real or apparent, and no financial interests in any company, product, employment, gifts, stock holdings, or honoraria.

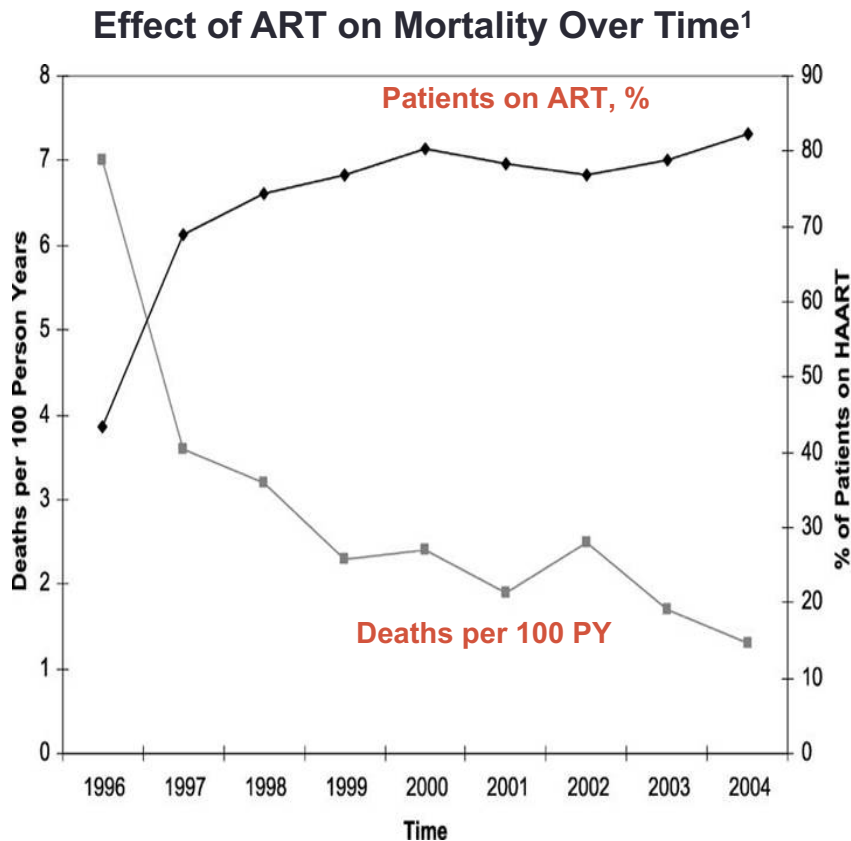
Learning Objectives

- Identify issues associated with treating older individuals with HIV infection
- Discuss epidemiology and risk factors of co-morbidities in HIV-positive patients
- Recommend management strategies for HIV antiviral treatment in highly complex patients with co-morbid illnesses

As estimated by the CDC: The percentage of HIV infected Americans older than 50 years, in the year 2013 was:

1. A. 22%
2. B. 16%
3. C. 38%
4. D. 42%
5. E. 57%

HIV-Positive Patients Are Living Longer



- Estimated percentage of persons living with HIV/AIDS aged older than 50 years has increased.²⁻⁴
- 2001 (17%) < 2010 (35%) < 2015 (50%)²⁻⁴
- A 20-year-old HIV-positive patient can now expect to live into his/her early 70s.⁵

Aging in HIV Infection

- HIV-positive patients have an increased risk for developing comorbidities.
- Potential contributors to higher rates of comorbidities in HIV-positive patients:
 - Risk factors that are more common in HIV-positive patients
 - Irreversible damage caused by HIV viremia
 - Chronic inflammation
 - Coinfections
 - Adverse effects of medications

HIV/AIDS and Aging: NIH Statement (9/9/10)

- “HIV clearly poses a risk to individuals 50 years and older and presents complex treatment challenges”
 - “In those with long-term HIV infection, the persistent activation of immune cells by the virus likely increases the susceptibility of these individuals to inflammation-induced diseases and diminishes their capacity to fight certain diseases.”
 - “Coupled with the aging process, the extended exposure of these adults to both HIV and antiretroviral drugs appears to increase their risk of illness and death from cardiovascular, bone, kidney, liver and lung disease, as well as many cancers not associated with HIV infection...”
 - “Moreover, the higher rate of pre-existing conditions in people of advanced age often complicates their treatment for HIV infection.”

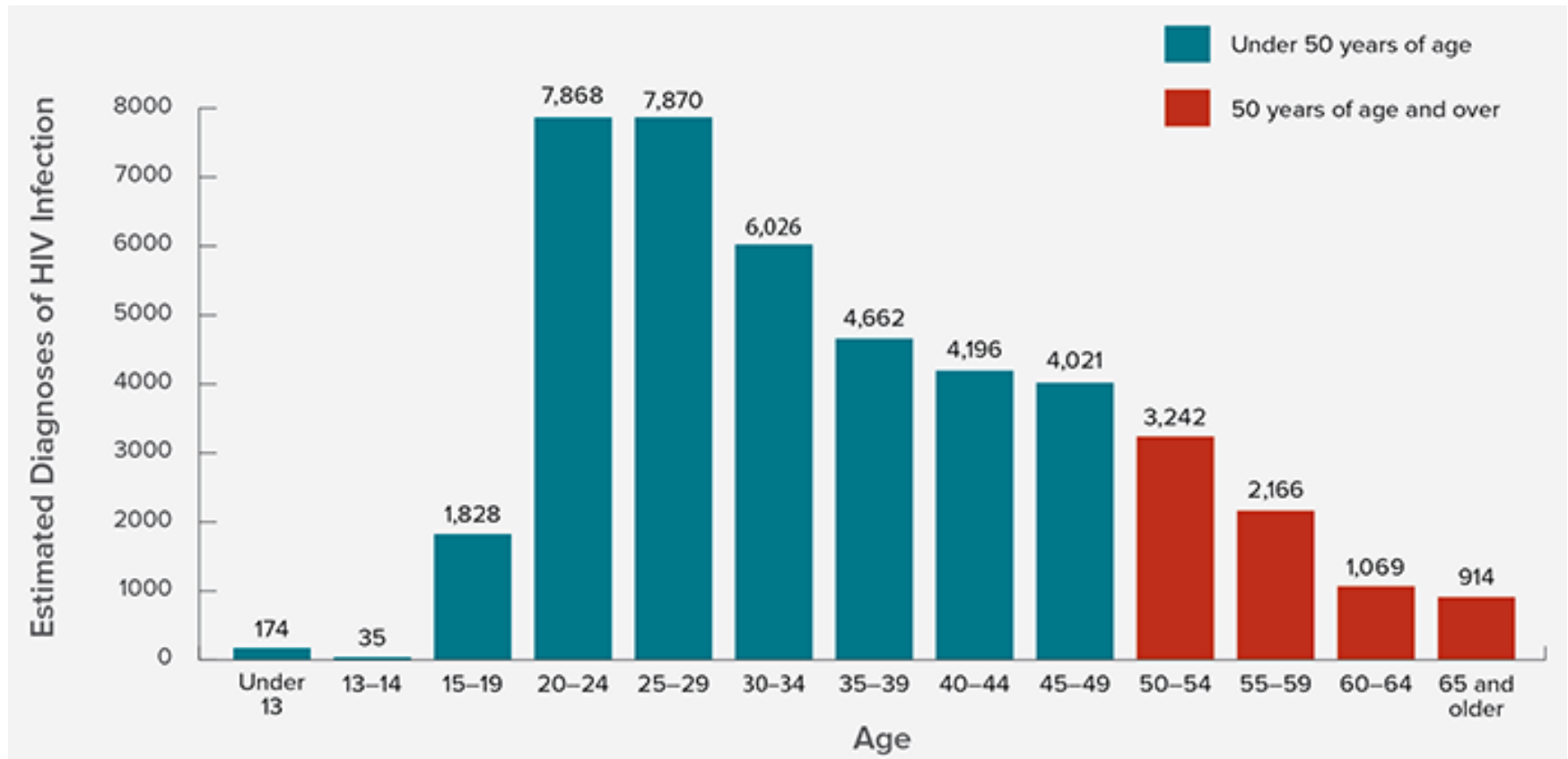
True or False: Seniors don't have sex and therefore are not at risk for HIV.

1. A. True

2. B. False

- ✓ Sexual desire does not wane after age 50
- ✓ More than 50% of persons over 50 years of age have sex twice a month
- ✓ 1999 AARP Survey
 - ✓ Age 64-74
 - ✓ 1/3 of men
 - ✓ 1/4 of women
 - ✓ Have sex at least once a week

Estimated Percentage of New Cases of HIV/AIDS by Age, 2014



Centers for Disease Control and Prevention. HIV Surveillance Report, 2014 CDC.gov website. Available at: <http://www.cdc.gov/hiv/pdf/library/reports/surveillance/cdc-hiv-surveillance-report-us.pdf> Published November 2015. Accessed September 2016.

Issues Specific to Older Persons with HIV Infection

- Unprotected sex
 - Pregnancy not a concern
 - “Too old to catch STIs”
 - Lower estrogen → Vaginal Dryness
- Delay in testing
- Limited incomes
- Immune restoration
- Comorbid illnesses
- Polypharmacy
- Insufficient data on drug interactions in older population

CDC: Estimated Prevalence of Undiagnosed HIV Infection in the United States

- Estimated persons living with undiagnosed HIV infection in the United States at the end of 2006 (n=232,700)
 - Overall: 21%
 - Age
 - 13-24: 47.8%
 - 25-34: 28.4%
 - 35-44: 19.4%
 - 45-54: 16.1%
 - ≥55: 19.1%
- Undiagnosed prevalence rates(per 100,000 population)
 - Overall: 94.2%
 - Age (years)
 - 13-24: 45.4
 - 25-34: 122.9
 - 35-44: 174.3
 - 45-54: 126.6
 - ≥55: 42.5

Issues with HIV Diagnosis in Older Adult

- Poor awareness of risk of HIV infection
 - Safe sex practices
 - Lack of education for older adults
- Less common routine screening
- Limited incomes
- Confusion of HIV-associated symptoms
- Physicians less likely to discuss HIV related risk factors or consider HIV infection

HCSUS and VACS 3: Symptom Expression in Older HIV Patients

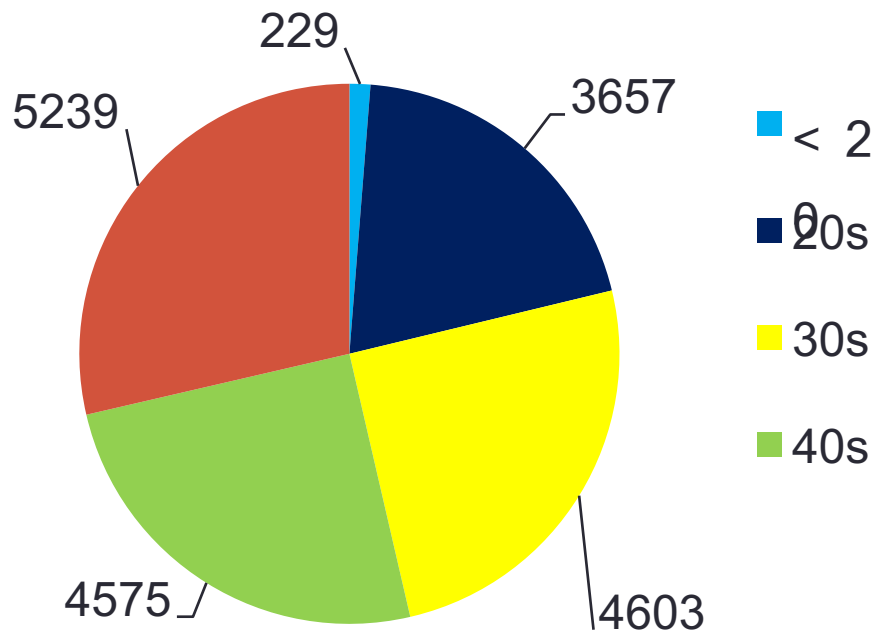
- Cross-sectional studies
 - HIV Cost and Service Utilization Study (HCSUS) (n=2864)
 - Veterans Aging Cohort 3 Site Study (VACS 3) (n=867)
- Patients < 50 years of age reported a greater number of HIV symptoms versus patients ≥ 50 years of age.
 - HCSUS
 - 4.6 vs. 3.8 ($P < .05$)
 - VACS 3
 - 10.3 vs. 9.5 ($P < .05$)

HIV/AIDS Symptoms vs. Older Age

- Mistaken HIV symptoms may be the cause for fewer reports.
 - AIDS related dementia vs. Alzheimer
 - Fatigue and weight loss vs. Aging
 - Confusion, fatigue, memory loss vs. Alcohol use
- Reports of fewer symptoms may hinder identification of HIV.

Impact of Delayed HIV Diagnosis in Older Adults

CDC: Persons with Diagnosed HIV whose Infection was Classified as Stage 3 (AIDS): 2015



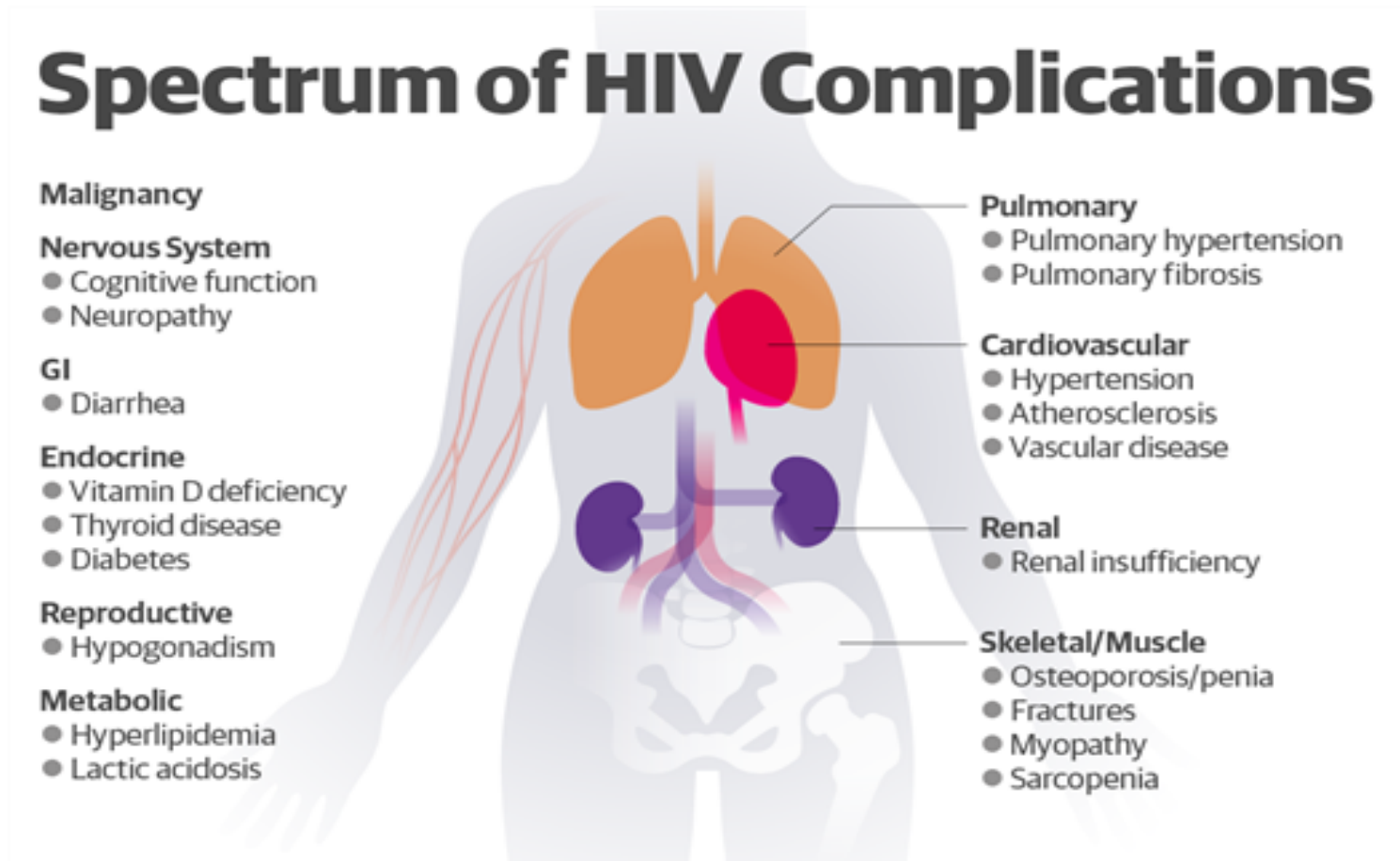
Older people in the United States are **more likely** than younger people to be diagnosed with HIV infection **late in the course of infection** which results in starting treatment late and possibly suffering more immune-system damage.

Aging and Comorbidities

- Common illnesses in older adults
 - Cardiovascular disease
 - Hypertension
 - Metabolic disorders, obesity
 - Neurocognitive decline
 - Hepatic and/or renal impairment
 - Bone fractures, osteopenia/osteoporosis
 - Malignancies

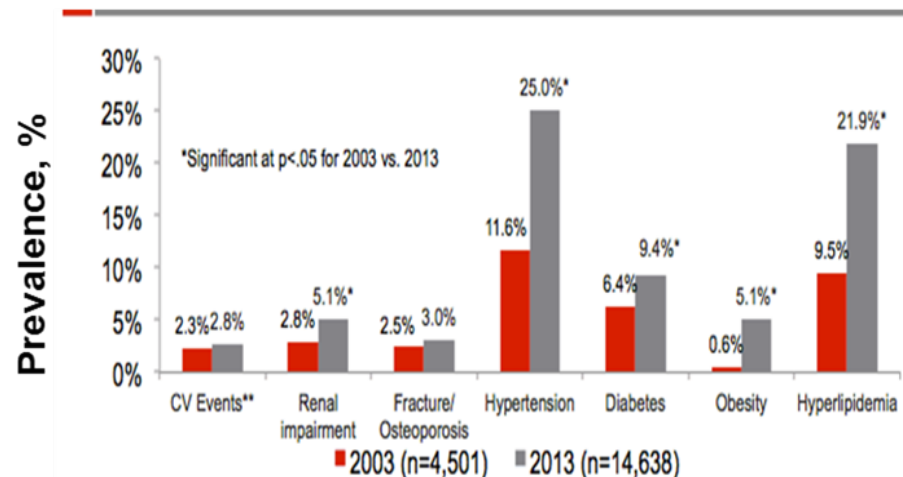
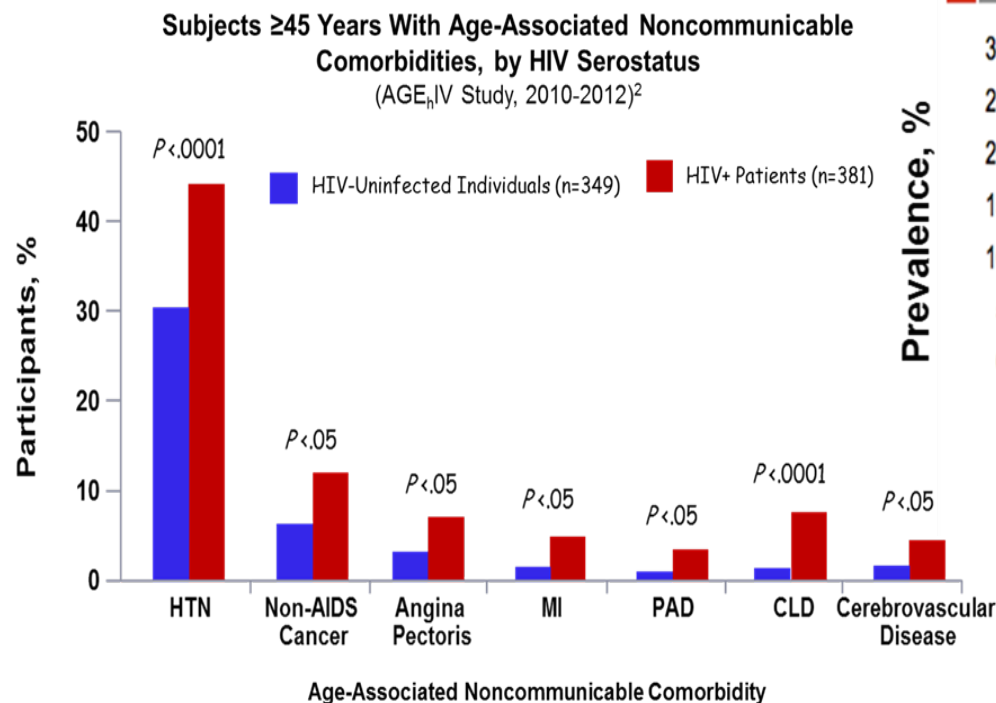
HIV and ART-related Comorbidities

HIV infection and ART can have long-term effects on health



Prevalence of Comorbidities in HIV-Positive Patients

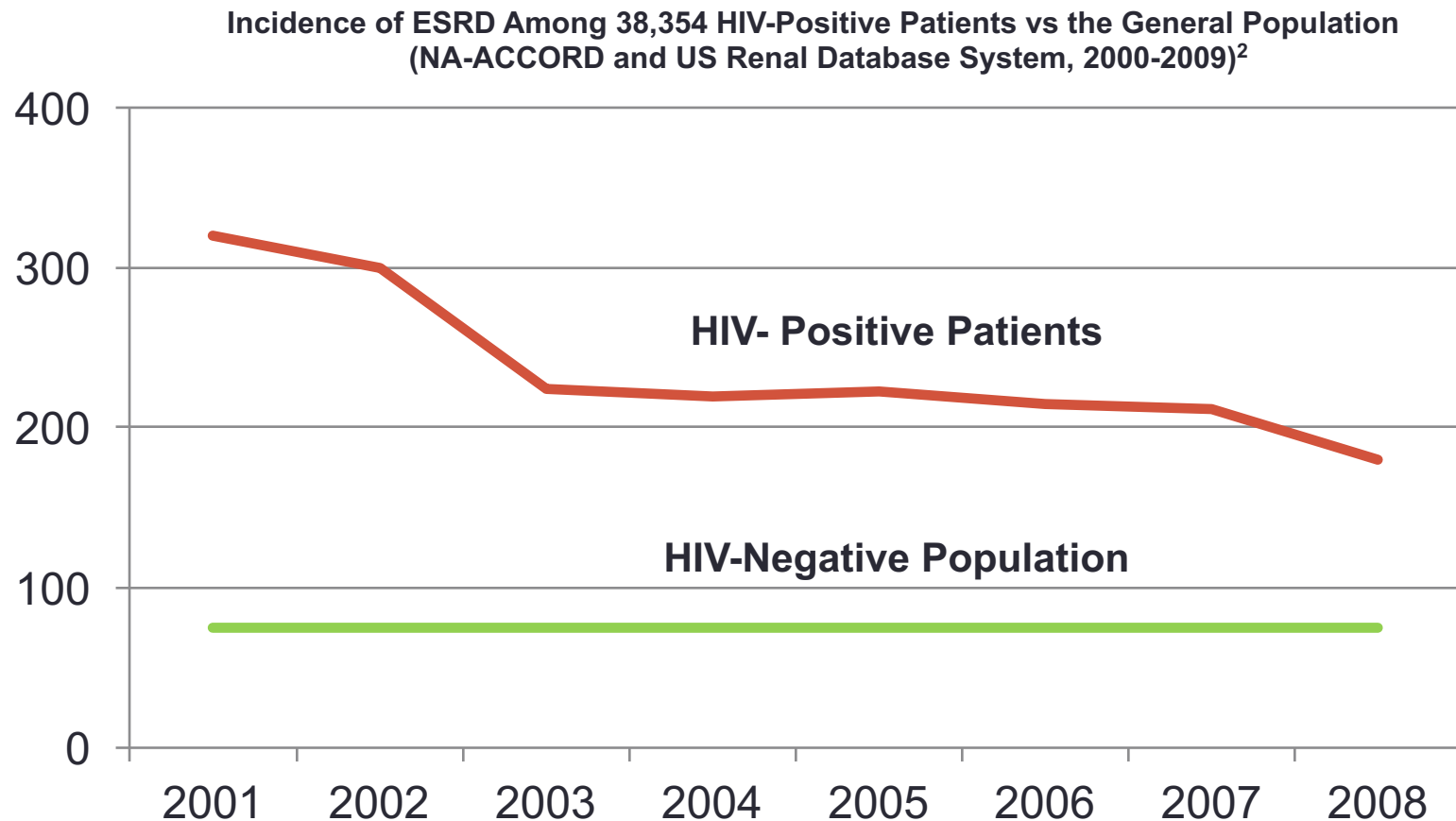
Comorbidities of Newly Diagnosed HIV Patients in the US: A Longitudinal Analysis of Prevalent HIV Patients



- HIV infection may compress certain aging processes, thereby accelerating comorbidities and frailty.¹
- Duration of ART use and lower nadir CD4 cell count were associated with increased risk of comorbidities.²
- Long-term effects of antiretroviral drug exposure may also be contributing to increased comorbidities.³
- Drug-drug interactions between antiretroviral agents and medications for other conditions can lead to comorbidities.³

ESRD in HIV-infected Patients

CKD has been reported more prevalent in HIV-positive patients when defined as reduced GFR or proteinuria¹



Factors Increasing Patient Risk for Renal Impairment

Patient-Specific Risk Factors¹

- Older Age
- Health Conditions
 - Acute Kidney Injury
 - Cardiovascular Disease
 - Diabetes Mellitus
 - Hepatic Failure with Ascites
 - Hypoalbuminemia

Nephrotoxic Drugs^{1,2}

- Antihypertensives
- Antimicrobials
- Antifungals
- Antiretrovirals
- Chemotherapeutics
- Diuretics
- Illicit Drugs
- NSAIDs
- Statins
- Herbals

Patient Case

J.W.

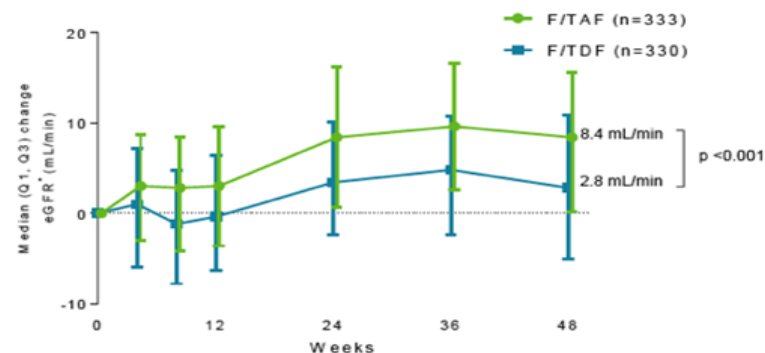


- 46 y/o WM presents to clinic for HIV management. He has heard about a “new version of his medication that is safer” and is interested in switching.
- Current regimen: TDF/FTC/ELV/cobi
- HIV RNA 25 c/ml
- CD4 count 675 cells/ul
- HIV resistance assay reveals wild type virus
- PMH: h/o HTN
- SH: Smoker 1ppd x 10 years; works as a truck driver; hasn't disclosed status; past drug use x 5 years (crystal meth); single MSM with multiple partners
- FH: unknown
- SCr: 0.8 mg/dl (eCrCl= 96 cc/min)
- HBsAb+ HBcAB- HBsAg-
- HCV +

Renal Safety of E/C/F/TAF

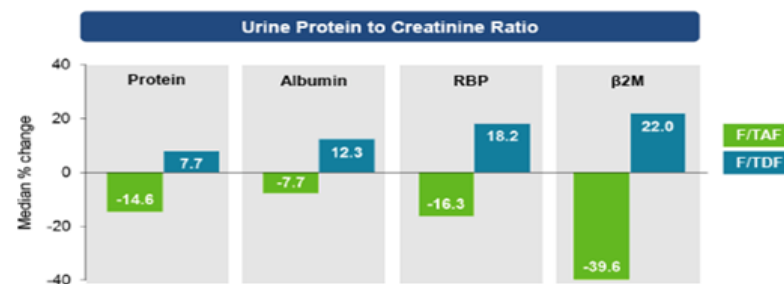
- eGFR improved significantly more with TAF than with TDF through week 48.¹
- Four renal biomarkers improved with TAF and worsened with TDF.¹
- FTC/TAF can be used in CrCl > 30 mL/min.²

Changes in eGFR



*eGFR calculated with Cockcroft-Gault equation

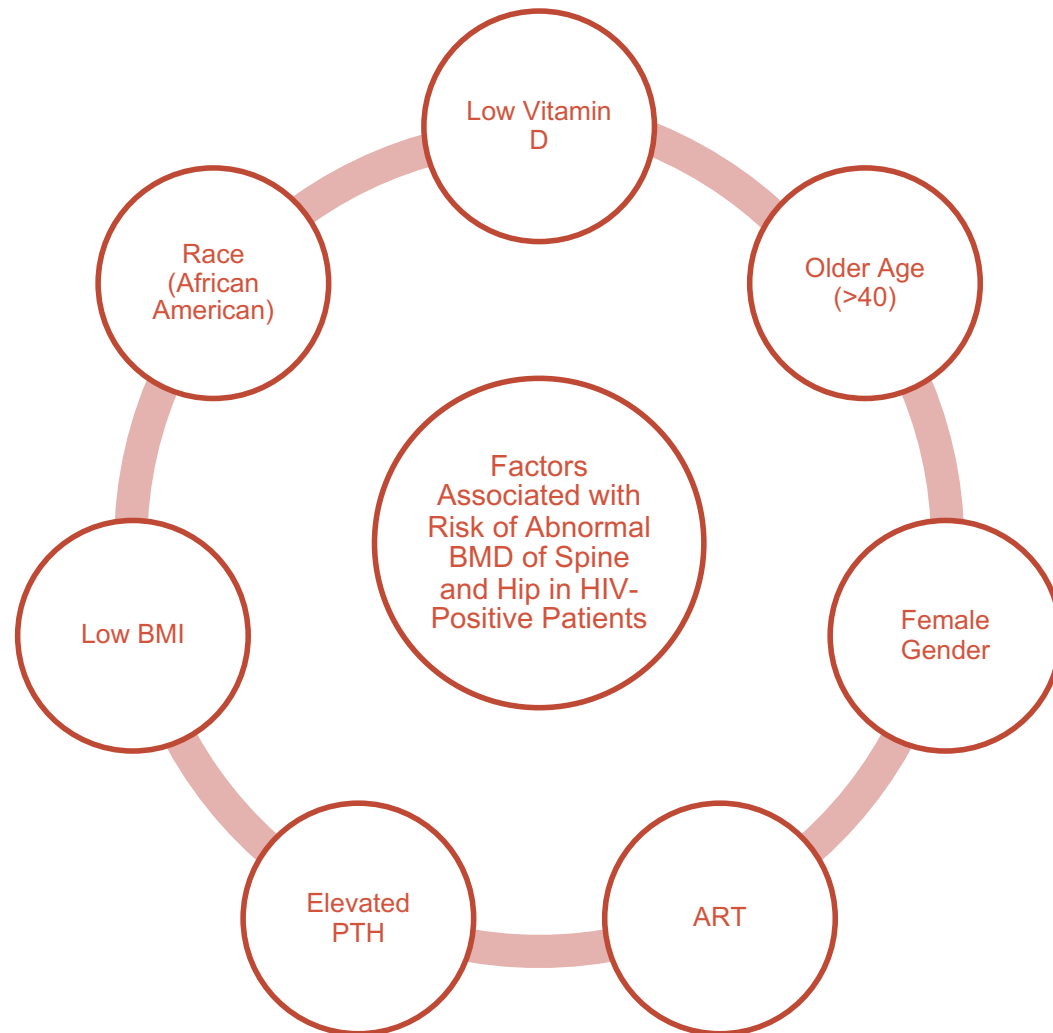
Change in Renal Biomarkers at Week 48



All differences between treatments statistically significant (p < 0.001)

RBP, retinol-binding protein; β2M, β2-microglobulin.

HIV-Infected Patients Are at Increased Risk of Bone Loss and Fractures

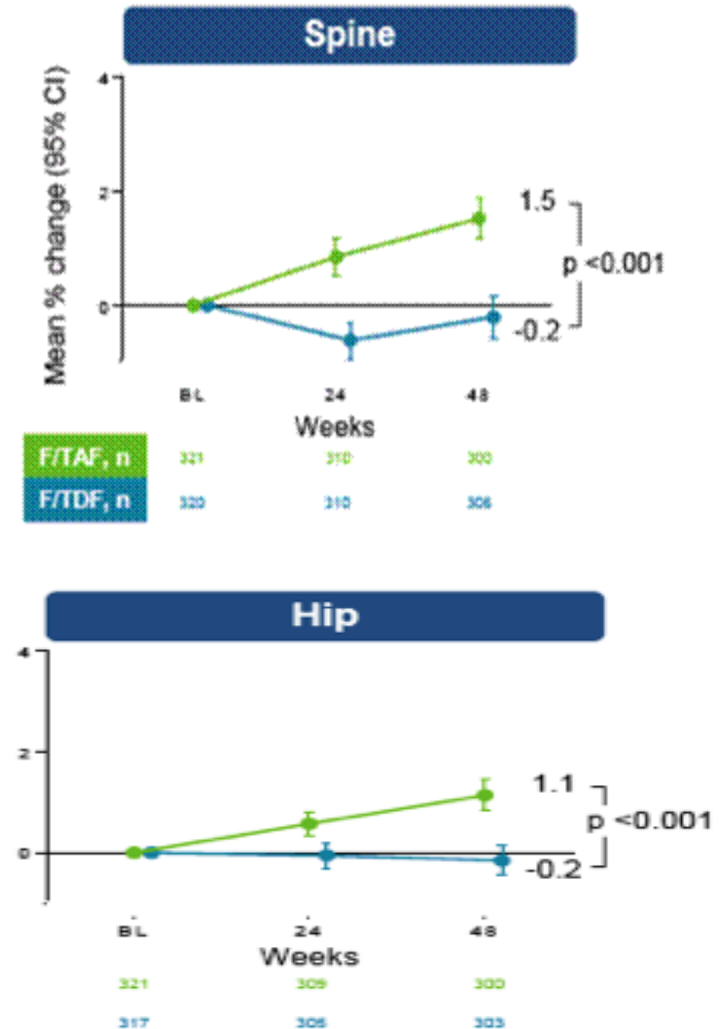


ART and Low BMD in HIV Infection

- All classes of ART may affect the skeleton
- Most BMD decline occurs early in ART initiation
 - Typically within the first 48 weeks
 - Mechanisms of bone loss possibly related to HIV disease “reversal” with ART
- Approximately 2% to 6% loss in BMD regardless of initial choice of ART
 - Tenofovir DF vs. Abacavir
 - Greater decreases in spine and hip BMD
 - Tenofovir DF
 - Insufficient evidence to recommend against TDF if patients have low BMD at start
 - If known fragility fractures or osteoporosis, consider alternative to TDF

TDF vs TAF and BMD in HIV Infection

- Spine and hip bone mineral density (BMD) improved with TAF; remained flat with TDF
- At 48 weeks:
 - TAF had at least a 3% BMD increase.



Cancer Risk Among HIV-Infected Individuals

- Cancer risk is higher among HIV-infected individuals¹
 - 50% higher in HIV-infected
- HIV-positive patients are diagnosed at an earlier age than HIV-uninfected Individuals²
 - Prevalence of some traditional risk factors is higher (smoking, heavy ETOH use)
 - Viral coinfection⁴
 - Weakened immune system⁴
- Significant changes in incidence over the past 10 years^{3,5,6}
 - AIDS-related malignancies
 - DECREASE in Kaposi sarcoma and CNS lymphoma
 - INCREASE in Non-Hodgkin's lymphoma
 - Non-AIDS-defining malignancies
 - Incidence increased by > 3-fold
 - Greatest increases in liver, larynx, anal, and lung cancers
 - No increase in prostate and breast cancers

Viral Coinfection as a Risk Factor for Cancer

- Human Herpes Virus 8
 - Kaposi sarcoma
- Human Papillomavirus
 - Cervical, anal, penile, vaginal, vulvar and head and neck
- Epstein-Barr Virus
 - Subtypes of non-Hodgkin and Hodgkin lymphoma
- Hepatitis Virus
 - Hepatocellular carcinoma

ART Use in HIV Patients with Cancer

- MD Anderson Cancer Center
- Retrospective analysis of HIV-positive patients with cancer or hematopoietic stem cell transplantation (2001-2012)
- Endpoints
 - Primary- safety and tolerability
 - Secondary- ART efficacy
- INSTIs
 - More commonly used in patients concomitantly receiving high-dose steroids, topoisomerase inhibitors, alkylating agents, or antimetabolites
 - INSTI or NNRTI-based ART resulted in increased efficacy and safety without significant adverse effects
 - INSTI preferred when drug-drug interactions a concern.

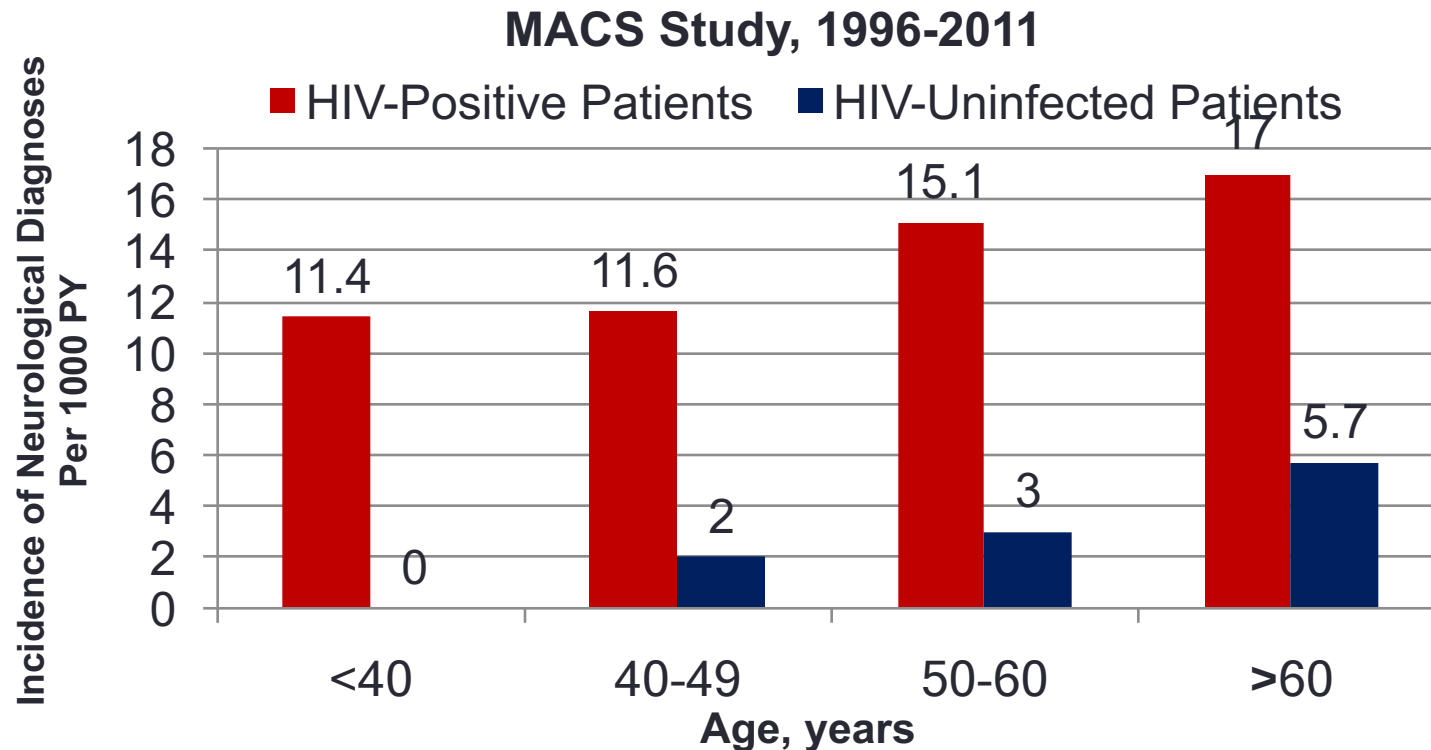
Cognitive Aging in HIV-Positive Patients

- HIV and ART have been found to have a significant impact on the brain
 - AIDS-related dementia (less common)
 - HIV-Associated Neurocognitive Disorder (HAND)
 - Neuropsychiatric Diagnoses (eg. Depression, Anxiety Disorder)
- Neurocognitive impairment occurs soon after initial HIV infection and continues throughout infection
- More than half of HIV-positive patients will have an HIV-Associated Neurocognitive Disorder (HAND)

HIV-Associated Neurocognitive Disorder

- HAND occurs due to neural damage caused by HIV replication and immune activation¹
- Evidence of HAND can be observed early in diagnosis and even in patients with low viral loads and high CD4 cell counts²
- Early initiation of therapy can slow down and even reverse severe HAND
- HAND accelerates in aging
- Milder forms of cognitive impairment are harder to identify and treat

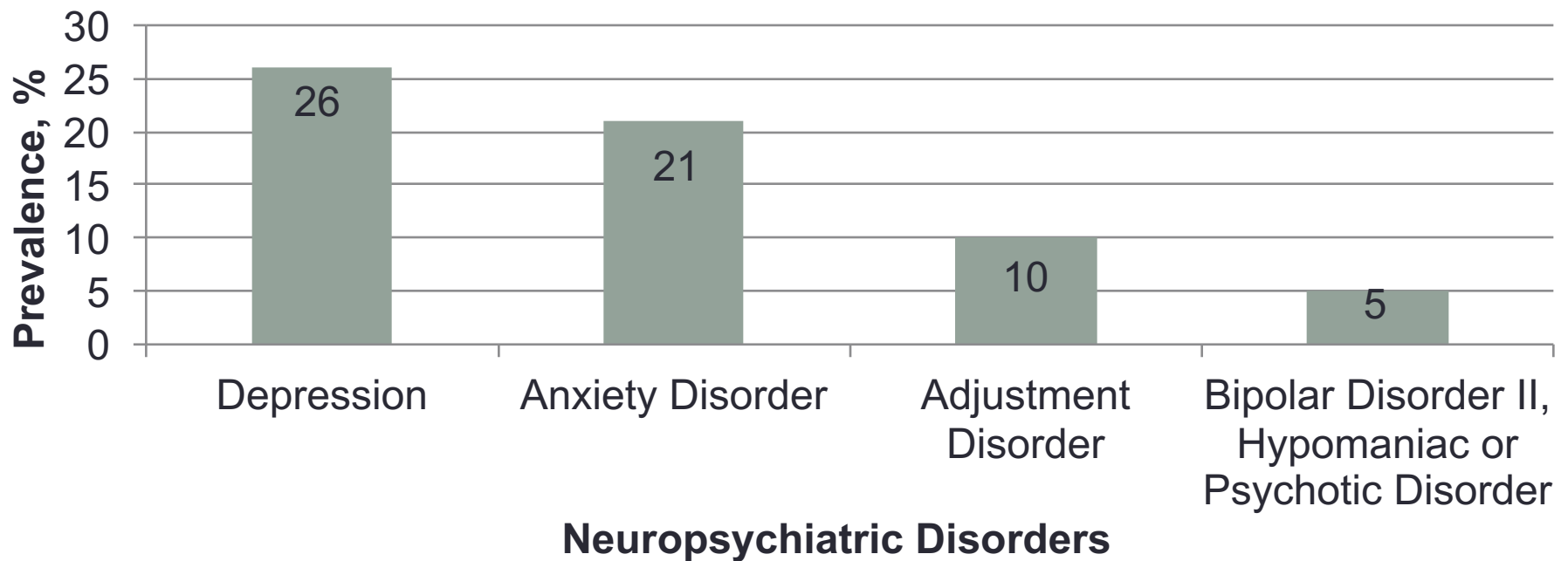
Incidence of Neurological Diagnoses in HIV-Positive Patients



- 1776 HIV-Positive Males; 2083 HIV-Uninfected Males
- CDC-defined neurological diagnoses start earlier and are more prevalent in HIV-positive patients

Prevalence of Neuropsychiatric Conditions in HIV-Positive Patients

Prevalence of Neuropsychiatric Diagnoses Among 196 HIV-Positive Patients (ATHENA Study, 2006-2009)



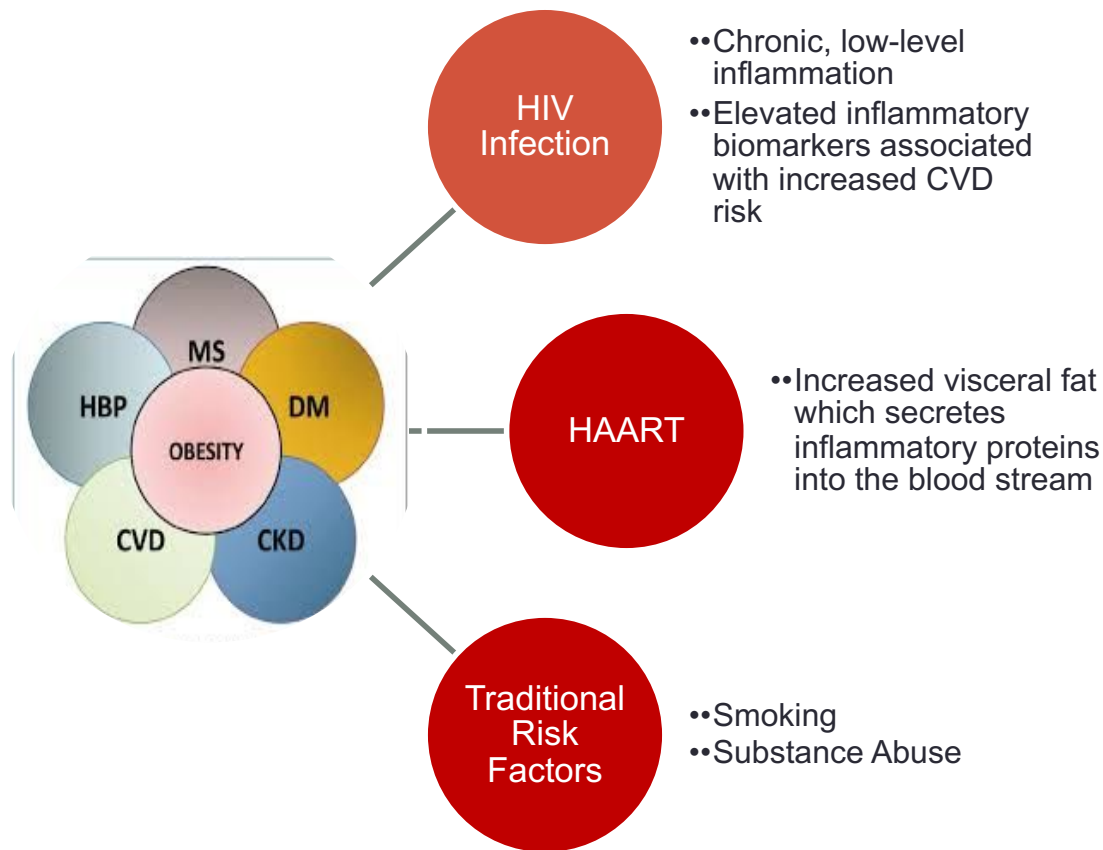
All of the following are true about neuropsychiatric conditions in HIV-positive patients except:

1. A. Psychiatric symptoms are common among HIV-positive patients.
2. B. Depression may lead to use of alcohol or other substances.
3. C. HIV-positive patients suffering from depressive symptoms are less likely to engage in risky sexual behavior.
4. D. Effective treatment for mental health conditions may lead to better adherence to ART, sustained virologic suppression and better health outcomes.

Risk of Hepatic Dysfunction and Related Death

- HIV-positive patients have a higher risk of hepatic dysfunction and death related to hepatic dysfunction.
 - Incidence studied in a cohort of 20,775 HIV-positive patients; 215,1558 HIV-uninfected persons
 - Hepatic Dysfunction
 - HIV+: 491 cases per 100,000 PY
 - HIV-: 67 cases per 100,000 PY
 - Death related to hepatic dysfunction
 - HIV+: 188 cases per 100,000 PY
 - HIV-: 17 cases per 100,000 PY
- Common risk factors for liver disease are more prevalent in HIV-positive patients:
 - Chronic hepatitis infection
 - Alcohol abuse

Chronic Inflammation combined with HAART and Traditional Risk Factors are associated with Comorbidities and Clinical Disease



Anti-inflammatory drugs are currently under study as adjuncts to ART in younger HIV-infected individuals: aspirin; omega-3 fatty acids, vitamin D, low-dose methotrexate, and statins

HAART and CVD Risk

Association Found

- DAD study (Updated 2016)
- SMART
- STEAL
- Quebec's Public Health Insurance database
- VA Clinical Case Registry (1997-2007)
- NA-ACCORD
- Swiss HIV Cohort Study
- Kaiser Permanente California

No Association

- GSK analysis
- FDA meta-analysis
- ACTG A5001
- HOPS
- US Healthcare System Cohort
- VA Clinical Case Registry (1996-2004)

- Reducing CVD risk factors and using ARTs less likely to cause metabolic disturbances may be an option when choices are available.
- Risk vs. benefit should be considered when choosing ART.

1. Behrens GM. et al. Curr Opin Infect Dis. 2010;23:9-14; 2. Ding X. et al. JAIDS. 2012;61:441-447; 3. Brothers CH. et al. JAIDS. 2009;51:20-28; 4. Triant VA. et al. JAIDS 2010;15:615-619; 5. Ribbaudo HJ. et al. Clin Infect Dis. 2011;52:929-940; 6. Durand M. et al. JAIDS. 2011;57:245-253; 7. Lichtenstein KA. et al. Clin Infect Dis. 2010;51:435-447; 8. Bedimo RJ, et al. Clin Infect Dis. 2011;53:84-91; 9. Choi AL. et al. AIDS, 2011;25:1289-1298; 10. Palella FJ. et al. 22nd CROI. Seattle, 2015. Abstract 749LB; 11. Fris-Moller N. et al. Eur J Prev Cardiol. 2016;23:214-223; 12. Young J. et al. JAIDS. 2015;69:413-421; 13. Marcus J. et al. JAIDS. 2016;71:413-419

HAART and CVD Risk

DAD Study (2008)

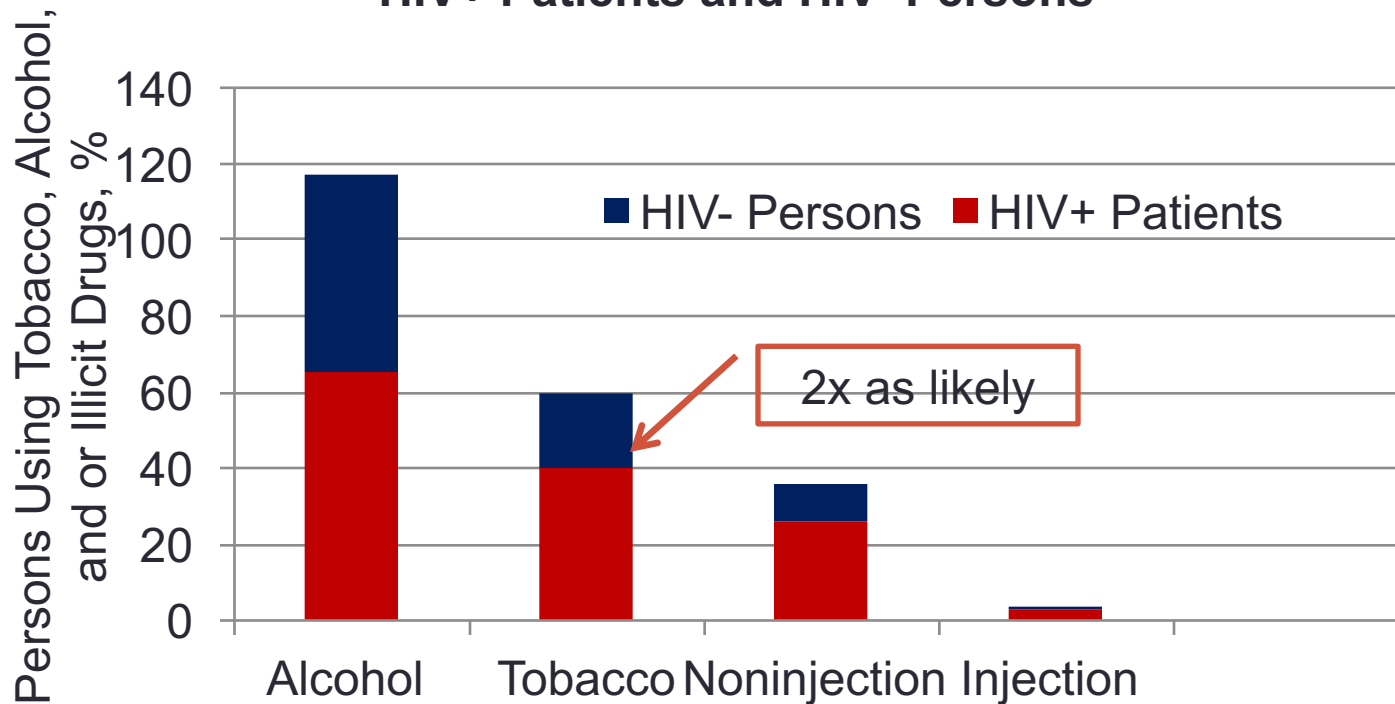
- 23,468 patients receiving ART
- Incidence of MI increased with greater exposure to ART per year of exposure
- CV risk was also associated with established risk factors such as older age

DAD Study (2016)

- > 49,000 HIV-positive patients
- Current ABC use was associated with a 98% increase in MI rate
 - No change from 2008
- No consensus on either the association between ABC use and MI risk or the mechanism
- Proposed mechanisms:
 - Increased inflammation, leukocyte activation, platelet activation

Traditional Risk Factors: Use of Tobacco, Alcohol, and/or Illicit Drugs in HIV-Positive Patients

Prevalence of Tobacco, Alcohol, and/or Illicit Drug Use Among HIV+ Patients and HIV- Persons



- Some HIV-positive patients have higher-risk behaviors
- HIV-positive persons are twice as likely to smoke than the general population⁴
- Reducing traditional CVD risk factors can decrease risk of CVD in Older HIV-positive patients⁵

CVD Risk Prediction Equations Developed for the General Population:

1. A. Better estimate CVD risk for HIV-positive patients
2. B. Underestimate CVD risk for HIV-positive patients
3. C. Estimate CVD risk equally for HIV-positive patients and the general population
4. D. Are no longer needed to calculate CVD risk for the general population

CVD Risk Prediction Equations Developed for the General Population Underestimate CVD Risk in HIV-Positive Patients

- Two cohort studies
 - Partners Healthcare System HIV Longitudinal Cohort of 2270 HIV-Positive Patients
 - HIV Outpatient Study (HOPS) Cohort of 2392 HIV-Positive Patients
- HOPS utilized four risk equations:
 - Framingham Point Score (FPS)
 - Pooled Cohort Equation (PCE)
 - Systematic Coronary Risk Evaluation (SCORE)
 - Delta Collection on Adverse Events in Anti-HIV Drugs
- Partners Healthcare System utilized two risk equations:
 - ACC/AHA Risk Prediction Algorithm
 - Framingham Point Score (FPS)

CVD Risk Prediction Equations Developed for the General Population Underestimate CVD Risk in HIV-Positive Patients

- Both studies found and concluded:
 - HIV infection is associated with increased risk of CVD
 - Current CVD risk prediction equations underestimate CVD risk in HIV-positive patients
 - Incorporating HIV or HIV-specific factors may increase the accuracy of CVD risk prediction

Conclusions

- The life span of HIV-positive patients on effective ART is nearing that of the general population.
- Some risk factors are more prevalent in HIV-positive patients thus increasing the possibility of higher risk for comorbidities.
- Some tools available for measuring risk in uninfected persons may underestimate the risk for HIV-positive patients.
- The overall health of HIV-positive patients can be improved by adhering to ART regimens and improving risk factors for comorbidities.
- ART should be initiated in patients > 50 years of age, regardless of CD4 cell count.

Conclusions

- Close monitoring of organ systems is important in HIV-positive patients as ART-associated adverse events may occur more frequently.
- Older HIV-patients are often on multiple medications thus there is an increased risk of drug-drug interactions between ART and other medications.
- Coordinated care between HIV experts and all members of the healthcare team can ensure HIV-positive patients with comorbidities receive the best care.
- Increasing awareness about HIV/AIDS and counseling on prevention of secondary transmission of HIV is an important aspect of care.