Metabolic Complications & Common Opportunistic Infections in HIV Primary Care

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Disclosures

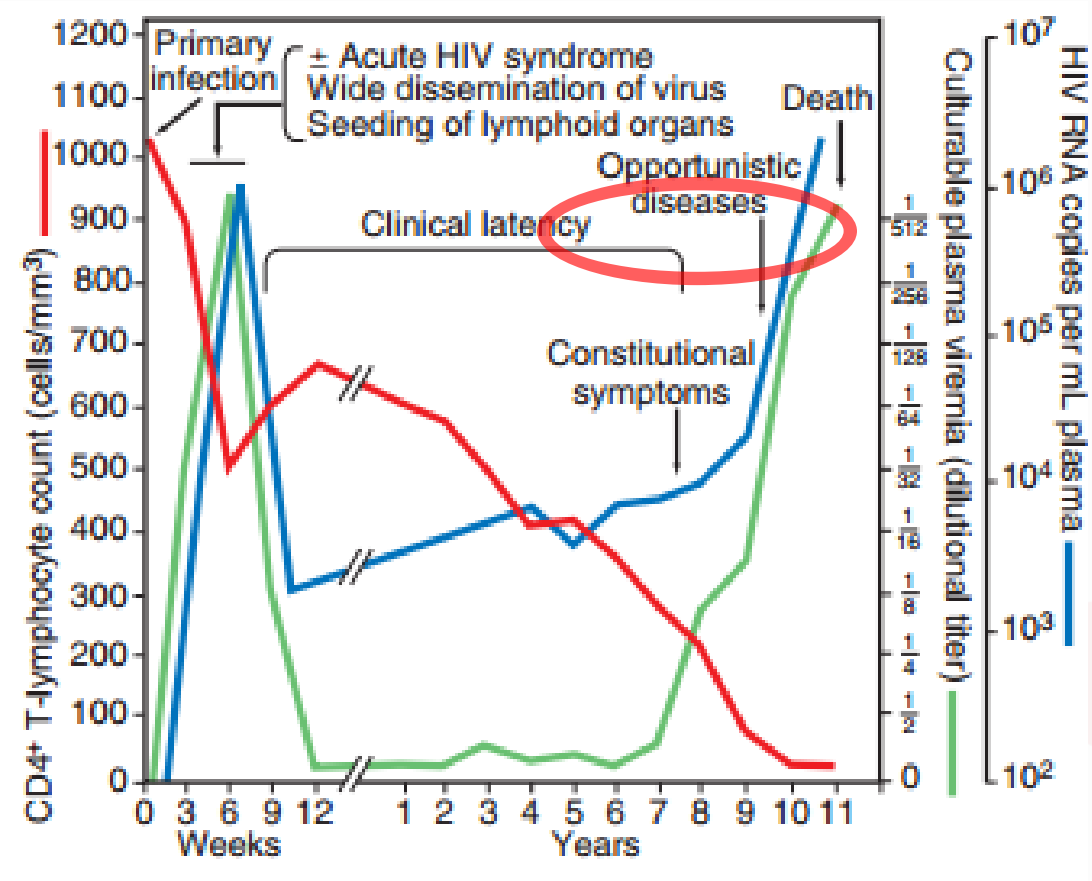
- None declared

Objectives

- Describe Common OIs
  - Risk Factors
  - Presentation
  - Treatment
  - Prophylaxis
- Describe Metabolic Complications of HIV
    - Risk Factors
    - Presentation
    - Management/Guideline Recommendations
  - Lipodystrophy
  - Bone Disease
  - Renal Disease
  - Hypogonadism
  - Insulin Resistance
  - Cardiovascular Disease

Opportunistic Infections

Natural History of Untreated HIV Infection



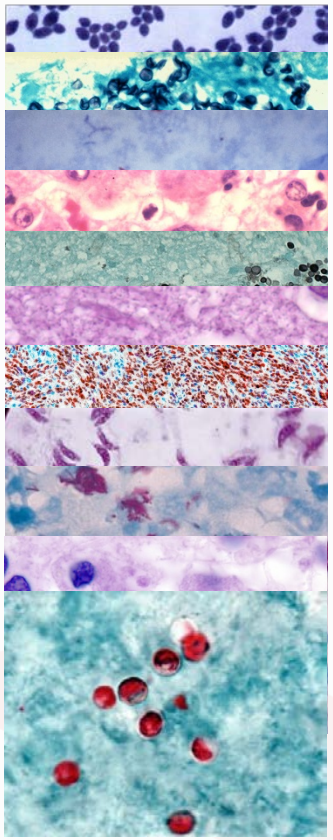
Fauci AS, Pantaleo G, Stanley S, et al. Immunopathogenic mechanisms of HIV infection. Ann Intern Med. 1996;124:654-663.

Development of an OI

- Degree of immunosuppression
  - CD4 count is the most clinically useful predictor
- Exposure to opportunistic pathogens
  - Some are ubiquitous in the environment, others require specific exposure
- The virulence of the pathogen
- Use of prophylactic medications

Incidence of OIs

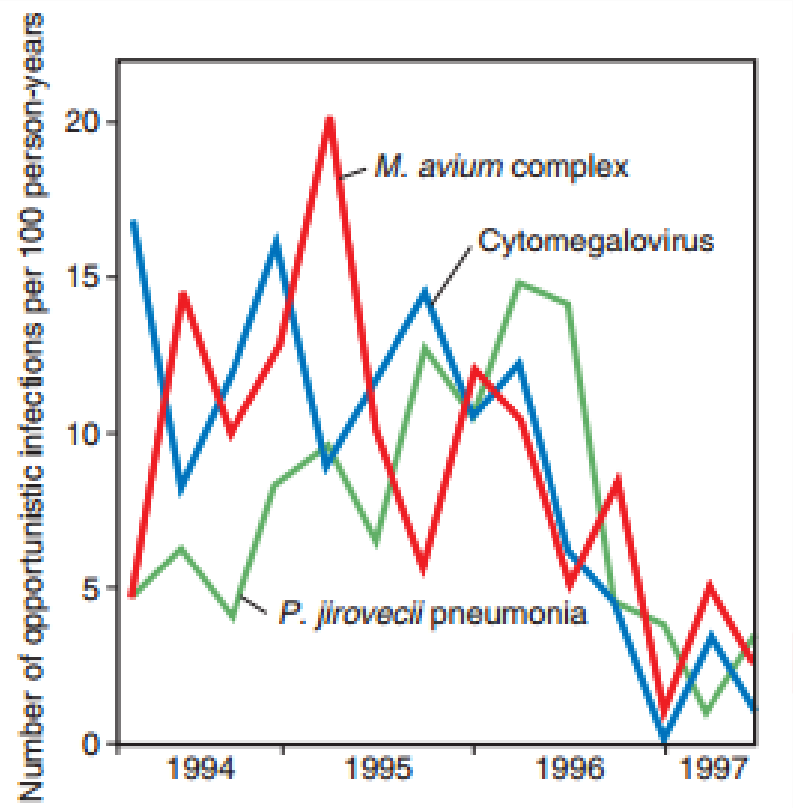
- Most common*
  - Oral candidiasis/*Candida* esophagitis
  - *Pneumocystis* pneumonia
  - *Mycobacterium avium* complex infection
  - Cytomegalovirus disease
- Moderately common*
  - Cryptococcal meningitis
  - Herpes Zoster
  - Kaposi sarcoma (HHV8)
  - Toxoplasmosis
- Least common*
  - Tuberculosis
  - PML (JC virus)
  - Cryptosporidiosis



*In resource-rich countries, prior to the advent of ART

Forrest DM, Seminari E, Hogg RS, et al. The incidence and spectrum of AIDS-defining illness in persons treated with antiretroviral drugs. Clin Infect Dis. 1998;27:1379-1385

Effective ART has reduced OI incidence



Palella FJ, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. N Engl J Med. 1998:338:853-860.

Candidiasis

- Increased incidence when CD4 count <200-300 cells/µL
- Thrush (soft palate, buccal mucosa, tonsils, hard palate)
  - Traditionally as smooth, removable white plaques, also can be atrophic (erythematous lesions)
- Candida esophagitis
  - Odynophagia, often with concurrent thrush
  - Diagnosis: endoscopy
- Angular chelitis

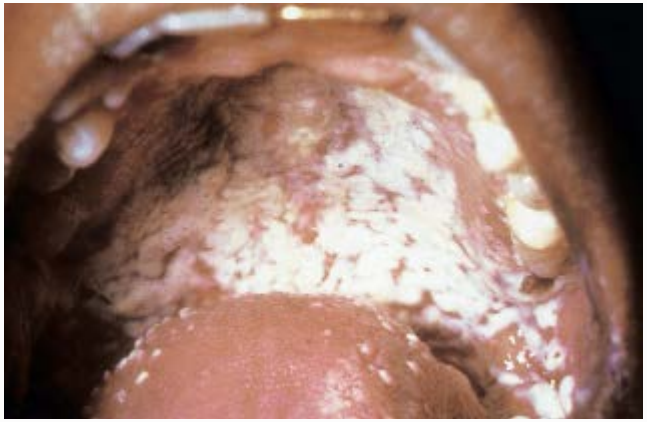


Photo credit: Dr. Raffanti

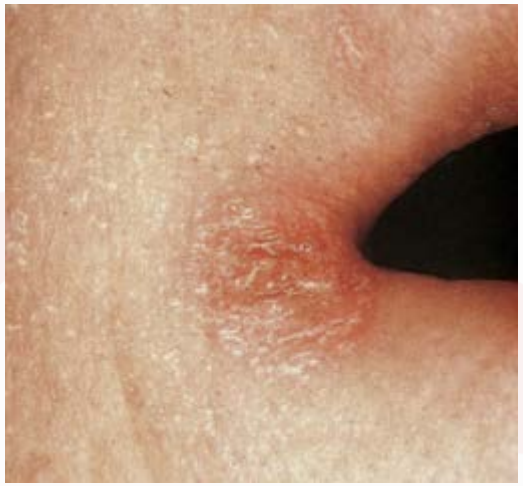


Photo credit: Dr. Raffanti

Lifson AR, Hilton JF, Westenhouse JL, et al. Time from HIV seroconversion to oral candidiasis or hairy leukoplakia among homosexual and bisexual men enrolled in three prospective cohorts. AIDS. 1994;8:73-79

Candidiasis

- Treatment
  - Oral candiasis: oral fluconazole 200mg – 400mg daily for 7 - 14 days
  - Esophageal candidiasis: oral (or IV) fluconazole 200mg – 400mg daily for 14 – 21 days

https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/321/pcp

Where is Pneumocystis naturally found?

A: Soil

B: Bird droppings

C: Mammal lung tissue

D: Feline droppings

E: Nonsterile water

Pneumocystis pneumonia

- Clinical features:
  1. Progressive dyspnea
  2. Fever
  3. Non-productive cough
- Compared to other immunosuppressed populations, infection is HIV is generally more subtle and indolent
- Chest x-ray
  - Diffuse interstitial infiltrates
  - Atypical: focal infiltrates, cystic lesions, nodular infiltrates
- Diagnosis: Induced sputum or bronchoscopy
  - Silver stain
  - Immunofluorescence
  - Polymerase chain reaction (PCR)

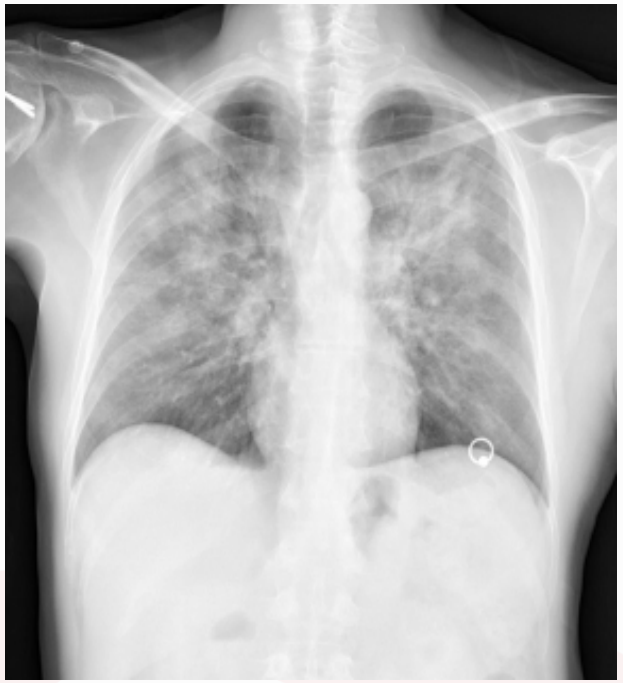
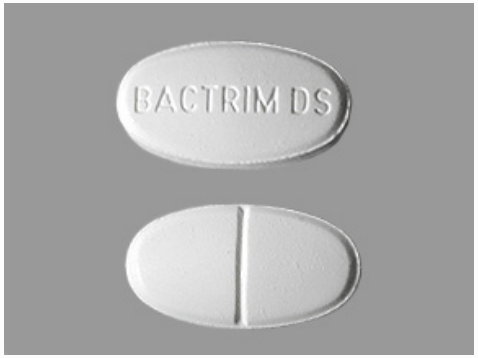


Photo credit: R. Miller

https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/321/pcp

Pneumocystis chemoprophylaxis

- Primary prevention:
  - CD4 count <200 cells/µL *AND/OR* CD4% <14%
  - Patients with AIDS-defining condition
- Secondary prevention
  - History of *Pneumocystis* pneumonia
- Regimens:
  - TMP/SMX (Bactrim DS): 1 tab MWF OR daily
  - Atovaquone
  - Dapsone
  - Inhaled pentamidine
    - Least effective
- Duration
  - Can stop when CD4+ count >200 cells/µL and CD4% ≥14% for 3 months
  - If developed *Pneumocystis* pneumonia when CD4 >200 cells/µL, must remain on prophylaxis for life



https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/321/pcp

Where does *Toxoplasma gondii* reproduce?

A: Contaminated soil

B: Feline intestines

C: Mammalian skeletal muscle

D: Nonsterile water

E: Bloodsucking insects

Toxoplasmosis

- *Toxoplasma gondii* is a long-lived parasite acquired from feline excrement, soil, undercooked meat
- Prevent exposure
  - Check Toxoplasma IgM/IgG
  - Advise to wash hands thoroughly after contact with soil
  - Advise against changing cat litterboxes
  - Advise against eating undercooked meat
- Chemoprophylaxis
  - TMP/SMX (Bactrim DS): 1 tab MWF OR daily
  - Initiation: CD4+ count <100 cells/µL
  - Discontinue: CD4+ count >200 cells/µL for 3 months

https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/322/toxo

From what source is *Mycobacterium avium* Complex infection acquired?

A: Another infected person

B: Bird Droppings

C: Contaminated meat

D: Nonsterile water

E: Bat droppings

Mycobacterium avium Complex

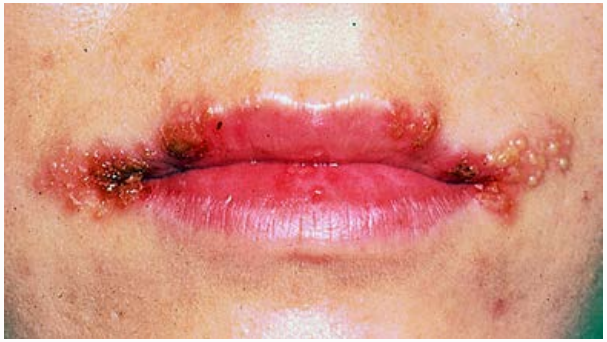
- Variable presentation
- Disseminated disease
  - Constitutional symptoms: fever, night sweats, weight loss
  - Bone marrow suppression: anemia
  - Lymphadenopathy, hepatosplenomegaly, diarrhea, abdominal pain
- Diagnosis: Culture of organism (usually blood, lymphoid tissue)

Mycobacterium avium Complex

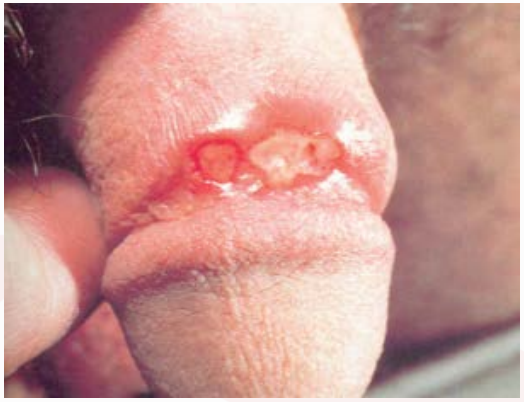
- Prophylaxis
  - CD4 count <50 cells/µL (these patients have a 20% risk/year of disseminated disease!)
  - Azithromycin 1200mg weekly
  - Rifabutin if cannot tolerate a macrolide
  - Can stop when CD4 >100 cell/µL for ≥3 months

Herpes simplex virus

- In HIV infection:
  - Very high prevalence of HSV-2 seropositivity (>70%)
  - HSV reactivations can be more frequent severe
  - More atypical presentations
  - Asymptomatic shedding is more frequent (up to 6-fold when CD4 <200 cells/µL).



Neville B, et al: Color Atlas of Clinical Oral Pathology. Philadelphia: Lea & Febiger, 1991



Corey L. Herpes simplex virus infections. In: Mandell GL, series ed; Rein MF, ed. Atlas of Infectious Diseases. vol. V. Sexually Transmitted Diseases. Philadelphia: Churchill Livingstone; 1996. Courtesy H. H. Handsfield, MD

Schacker T, et al. J Infect Dis. 1998;178(6):1616.
Mostad SB, at al. Am J Obstet Gynecol. 2000;183(4):948.

Herpes simplex virus

- Atypical presentations:
  - Chronic, severe mucosal ulceration
  - Deep genital and perianal ulcerations/fissures
  - Hypertrophic lesions
    - Mimic HPV, tumors
  - Esophagitis
  - Tracheitis
  - Disseminated disease

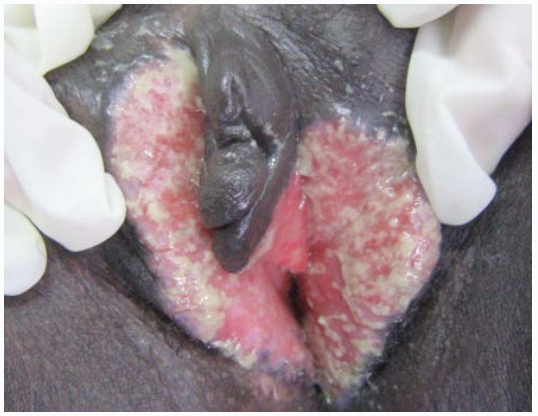


Photo credit: Christine Johnston, MD, MPH and Anna Wald, MD, MPH

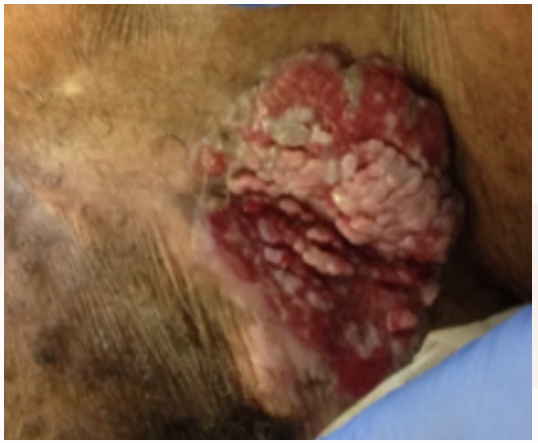


Photo cred: Sade Arinze, MD

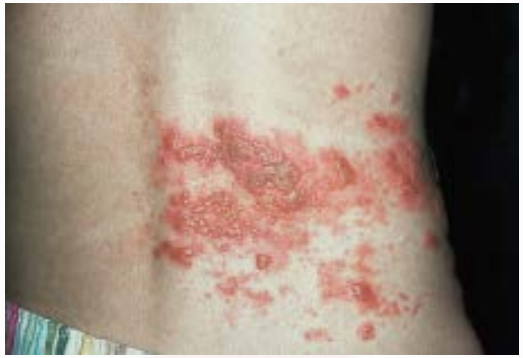
Herpes simplex virus

- Diagnosis :
  - Send for HSV 1/2 PCR if active lesion present
  - Serologic testing for HSV-1 and HSV-2
    - USPSTF recommends against this in the asymptomatic, HIV-uninfected general population
    - HIV treatment guidelines recommend considering this in certain circumstances (atypical lesions, CD4 <250 cells/µL, infected partner)
- Treatment:
  - Mild/Moderate episodic outbreaks: acyclovir or valacyclovir for 5-10 days
  - Severe disease: IV acyclovir
- Prophylaxis:
  - Chronic, indefinite therapy with daily acyclovir or valacyclovir can be considered in those with frequent or severe recurrences
  - Consider especially if history of HSV outbreak and CD4 <250 cells/µL

USPSTF. Serologic Screening for Genital Herpes Infection: US Preventive Services Task Force Recommendation Statement. JAMA. 2016 12 20; 316(23):2525-2530
https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/339/hsv

Varicella zoster virus

- If HIV+/VZV-
  - Varicella zoster vaccine acceptable if CD4 ≥200 cells/µL, over age 8
- Herpes zoster (shingles)
  - Incidence 15-fold higher in HIV infection (occurring in 8-11% of HIV-infected patients)
  - Can occur at any CD4 count
  - Dermatomal herpes zoster:
    - valacyclovir 1g PO TID x 7-10 days (similar to in HIV-uninfected patients)
    - Extend course if slow to resolve



https://aidsinfo.nih.gov/guidelines/html/4/adult-and-adolescent-oi-prevention-and-treatment-guidelines/341/vzv
Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, Updated Edition, Eighth Edition. 2015

Metabolic Complications of HIV

Metabolic Complications of HIV

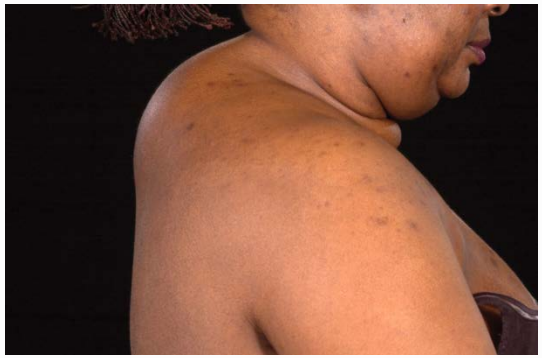
- Lipodystrophy
- Bone Mineral Density Loss
- Renal Disease
- Hypogonadism
- Insulin Resistance/Diabetes Mellitus
- Heart Disease
  - Dyslipidemia
  - Atherosclerotic cardiovascular disease

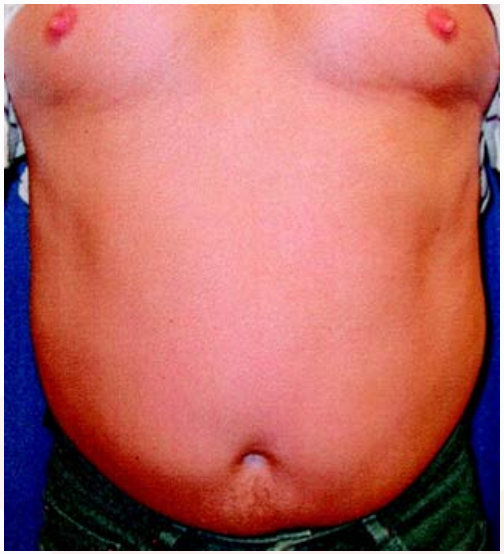
HIV and Lipodystrophy

- Lipohypertrophy: CENTRAL fat accumulation
  - Dorsocervical fat pad (buffalo hump)
  - Abdominal/visceral fat (including liver)
  - Breast enlargement/gynecomastia
- Lipoatrophy: PERIPHERAL fat wasting
  - Face, arms, legs, buttocks
- These are distinct, but often concurrent
- Often associated with dyslipidemia and insulin resistance

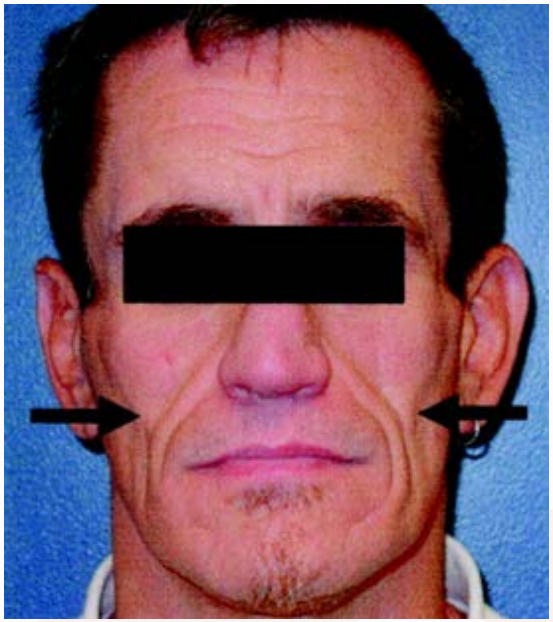
HIV and Lipodystrophy

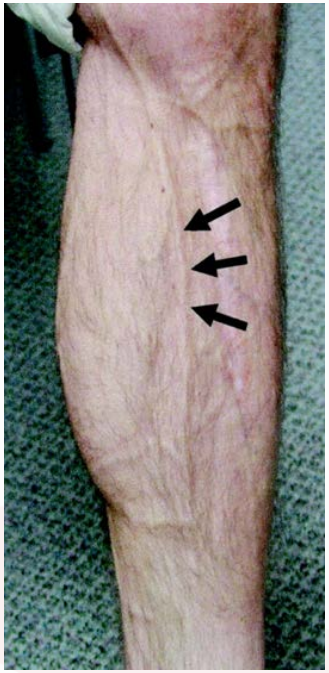
Lipohypertrophy





Lipoatrophy





Aesthet Surg J. 2012;32(6):685-691.
Priscilla Y. Hsue, and David D. Waters
Circulation. 2005;112:3947-3957

HIV and Lipodystrophy

- Lipohypertrophy
  - Risk factors
    - Protease inhibitor use
    - Duration of antiretroviral therapy
    - Markers of disease severity (low CD4, high viral load)
- Lipoatrophy
  - Risk factors
    - Older age
    - Markers of disease severity (low CD4, high viral load)
    - White race
    - Use of NRTI stavudine, zidovudine

Lichtenstein KA. JAIDS 2005;39:395-400

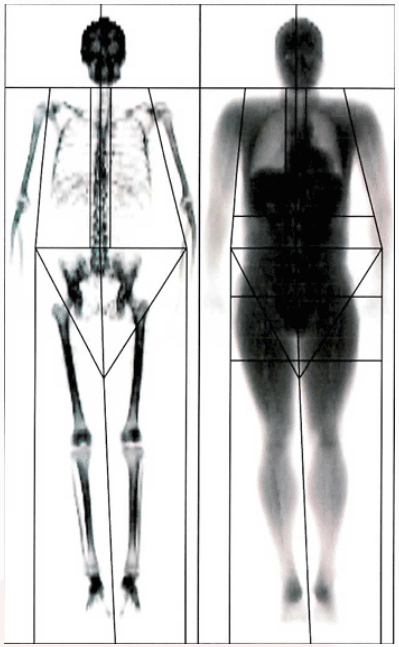
HIV and Lipodystrophy

- Management
  - Lifestyle modification
    - Can help in lipohypertrophy by reducing overall body fat
  - Limited benefit from changing ART regimen
    - NRTI-sparing regimens may help with lipoatrophy
    - PI-sparing regimen not effective in reversing lipohypertrophy
  - Cosmetic procedures
    - Liposuction
    - Filler injections
  - Diabetic medications
    - Glitazones may increase limb adiposity
    - Metformin may reduce central/visceral adiposity
      - Can also treat associated metabolic complications

Jones SP et al. AIDS 2001 Oct 19;15(15):2049-51
Lichtenstein KA. JAIDS 2005;39:395-400
Valantin MA et al. AIDS 2003, 17:2471–2477
Sutinen J, et al. Antivir Ther 2007; 12: pp. 97-105

HIV and Bone Disease

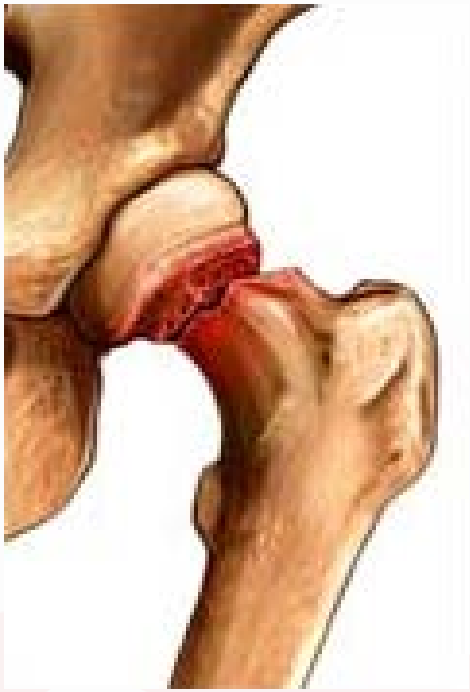
- High prevalence of osteopenia and osteoporosis among HIV-infected patients relative to the general population
  - Up to two thirds affected at the time of HIV diagnosis
- Bone mineral density (BMD) loss may be up to 6.4 times than among the general population.
- Fracture prevalence is 3.5 times higher than among general population
- Mechanism: multifactorial
  - Comorbid smoking, alcohol and recreational drug use
  - Endocrine abnormalities: androgen and parathyroid dysfunction, vitamin D deficiency
  - Chronic immune activation/inflammation
    - Enhanced osteoclast activation
  - Antiretroviral therapy
    - NRTI (tenofovir)
    - PI



Brown TT, Qaqish RB. AIDS. 2006 Nov 14; 20(17):2165-74.
Bolland MJ, Grey A. IBMS BoneKEy. 2011;8(1):7–15.
Vikulina T, et al. Proc Natl Acad Sci U S A. 2010 Aug 3; 107(31):13848-53.
Castillo AB, et al. J Orthop Res. 2002 Nov; 20(6):1185-9.
Bonjoch A, et al. AIDS. 2010 Nov 27; 24(18):2827-33.

HIV and Bone Loss

- Risks of osteopenia/osteoporosis in HIV
  - NRTI (especially tenofovir) and PI use
  - Lower weight
  - Female gender
  - Older age
  - Smoking status
  - Post-menopausal state
- Evaluation
  - DXA scan
    - In HIV, consider at >50 years of age
    - Workup for secondary cause
      - Thyroid/parathyroid dysfunction
      - Hypogonadism
      - Vitamin D deficiency



Katlama C, et al. AIDS. 2013; 27 (15); 2425-30
Carr A, et al. AIDS . 2001; 15 (6); 703-9
Guaraldi G, et al. HIV Clin Trials. 2004; 5 (5); 269-77
Mallon PW, et al. Curr Opin HIV AIDS. 2014 Jul;9(4):428-35

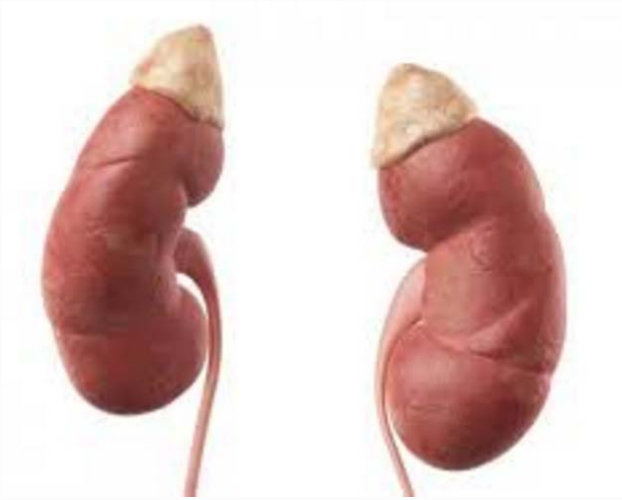
HIV and Bone Loss

- Management
  - Vitamin D, Ca^{2+} supplementation
  - Alendronate can improve BMD
  - Consider avoiding tenofovir

Guaraldi G, et al. HIV Clin Trials. 2004; 5 (5); 269-77
Mallon PW, et al. Curr Opin HIV AIDS. 2014 Jul;9(4):428-35

HIV and Renal Disease

- Secondary to HIV itself
  - HIV-Associated Nephropathy
    - Usually when CD4 <200 cells/uL
    - Usually progresses quickly
  - IgA nephropathy
- Secondary to other infections
  - HCV co-infection
- Secondary to medications
  - Tenofovir
    - Fanconi syndrome
  - TMP/SMX, pentamadine, sulfadiazine



Rao TK, et al. N Engl J Med. 1984;310:669-673. 294.
Rao TK. Semin Nephrol. 1998;18: 378-395. 295.
Kimmel PL, et al. Ann Intern Med. 2003;139:214-226.

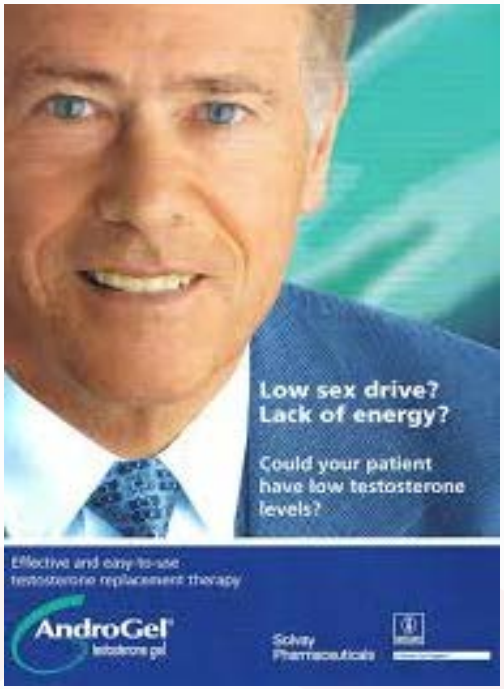
HIV and Male Hypogonadism

- Testosterone deficiency in 15-25% of young/middle-aged HIV-infected men
- Prevalence has declined with effective ART
- More likely due to hypothalamic-pituitary axis dysfunction than testicular dysfunction
- Can lead to BMD loss, lipodystrophy
- Clinical Presentation:
  - Depression
  - Low energy
  - Low libido, erectile dysfunction
  - Decreased muscle mass
  - Gynecomastia

Rochira V, Guaraldi G. Endocrinol Metab Clin North Am. 2014 Sep;43(3):709-30.
Rochira V, et al. PLoS One. 2011;6(12):e28512.
Klein RS, et al. Clin Infect Dis. 2005;41(12):1794.

HIV and Male Hypogonadism

- Risk Factors:
  - Older age (but as young as 35!)
  - Low CD4
  - Detectable HIV RNA
  - IVDU
  - Hepatitis C
  - High BMI



Klein RS, et al. Clin Infect Dis. 2005;41(12):1794.

HIV and Male Hypogonadism

- Evaluation:
  - Free and total serum testosterone
    - Early morning, confirm result with second test
  - If testosterone deficiency, evaluate for secondary cause with FSH/LH (and consider other anterior pituitary hormone testing, TSH, prolactin)
  - Evaluate for presence of prostate cancer, depression prior to treatment
- Testosterone replacement
  - Use with caution in older age, presence of CVD risk factors
  - Post-treatment testosterone level monitoring (within 3-6 months)
  - Discontinue if no subjective improvement after several months

Klein RS, et al. Clin Infect Dis. 2005;41(12):1794.

HIV and Insulin Resistance/DM

- Association with use of protease inhibitors, some NRTIs
  - Frequency of insulin resistance: 6% to 33%
  - Frequency of DM: 0.6–4.7 per 100 person-years
  - Onset weeks to months after starting therapy
- Mechanism
  - Inhibition of GLUT4 glucose transport function
  - Stimulation of hyperglycemia by other mechanisms

Carper MJ et al. Am J Physiol Endocrinol Metab. 2008

HIV and Insulin Resistance/DM

- Screening recommendations
  - DHHS: Screen with FPG every 6-12 months
  - Consider screening 1-3 months after ART initiation
- Treatment recommendations
  - Lifestyle modification
    - Registered dietician
  - Medical therapy
  - Comprehensive CVD risk reduction

American Diabetic Association Standards of medical care in diabetes—2014, *Diabetes Care*, 2014, vol. 37 suppl. 1 (pg. S14-80)

HIV and cardiovascular disease

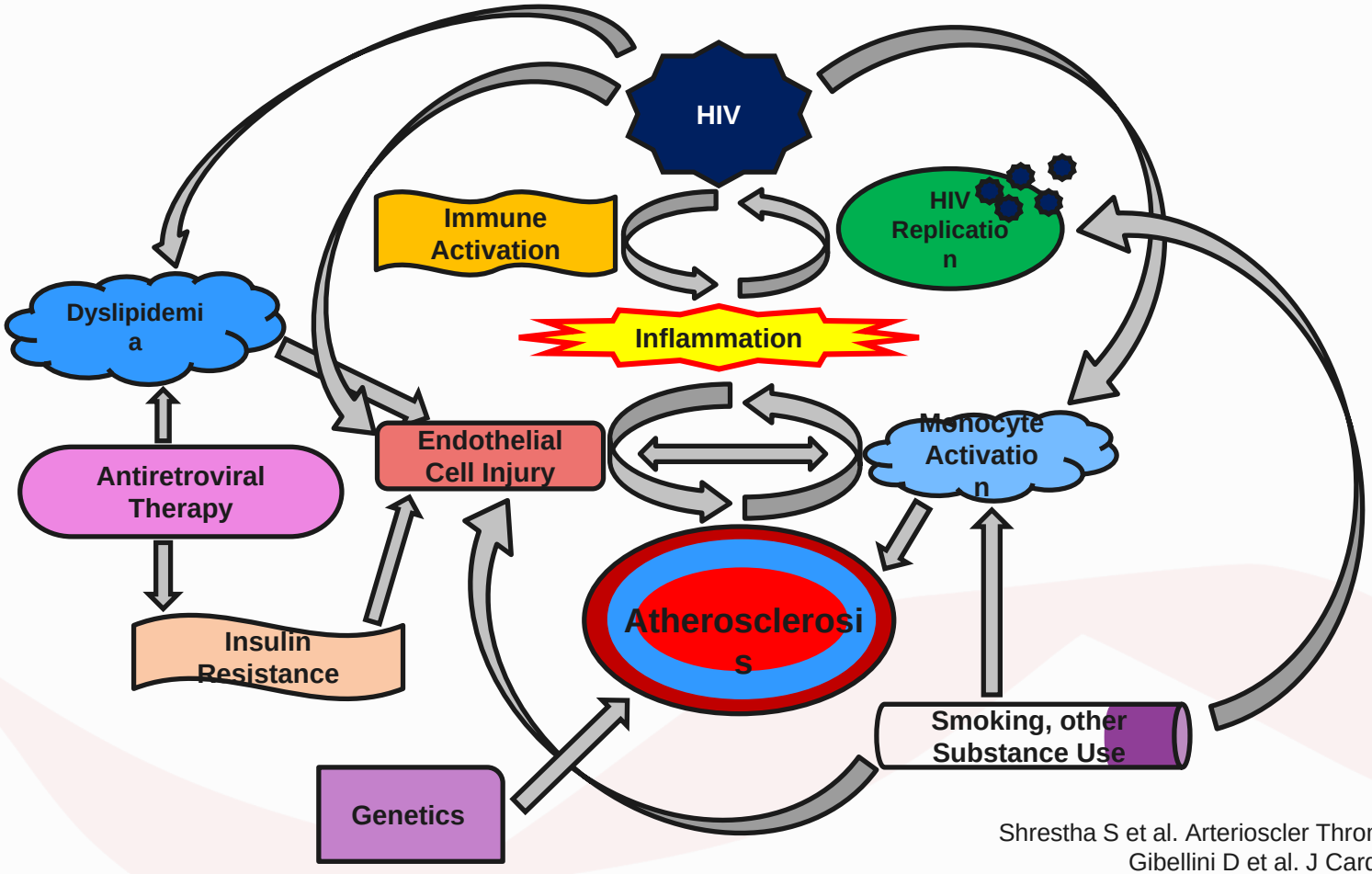
HIV+ persons have 1.5-2x higher MI risk than general population, even among chronically suppressed patients.

Why?

- Chronic immune activation/inflammation
- Increased prevalence of traditional CVD risk factors
- Increasing age → 50% HIV+ persons are >50 years old
- More high-risk coronary artery plaque
- Higher prevalence of smoking and substance use
- Specific ART drug exposure
- Clinical practice

Freiberg MS, et al. HIV Infection and the Risk of Acute Myocardial Infarction. *JAMA Intern Med.* 2013;173(8):614-622.

HIV and cardiovascular disease

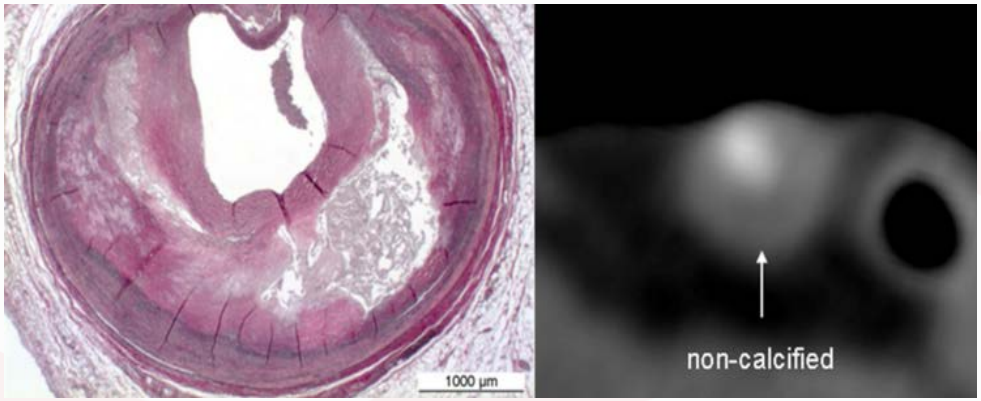


Shrestha S et al. Arterioscler Thromb Vasc Biol. 2014
Gibellini D et al. J Cardiovasc Med . 2013
Piconi S et al. AIDS. 2013

HIV and cardiovascular disease

Non-calcified Plaque

- Non-calcified plaque is
  - Considered high-risk plaque morphology
  - Of all plaque types, carries highest risk of mortality
  - Lipid-rich, pro-inflammatory, higher concentration of activated foamy macrophages, more prone to rupture/thrombosis
- HIV+ patient have higher prevalence of non-calcified plaque



Leschka S et al. ECR. 2010

Post WS et al. Ann Intern Med. 2014

HIV and cardiovascular disease

Chronic immune activation/inflammation

- Multiple markers of inflammation are associated with risk of CVD in HIV-infected patients
  - IL-6, hsCRP, D-Dimer
  - Duration of UNTREATED infection may substantially contribute to CVD risk
    - Lower CD4 nadir associated with high CVD-related mortality

Duprez DA, et al. Strategies for Management of Antiretroviral Therapy (SMART). *PLoS One*. 2012;7:e44454.

HIV and cardiovascular disease

Dyslipidemia

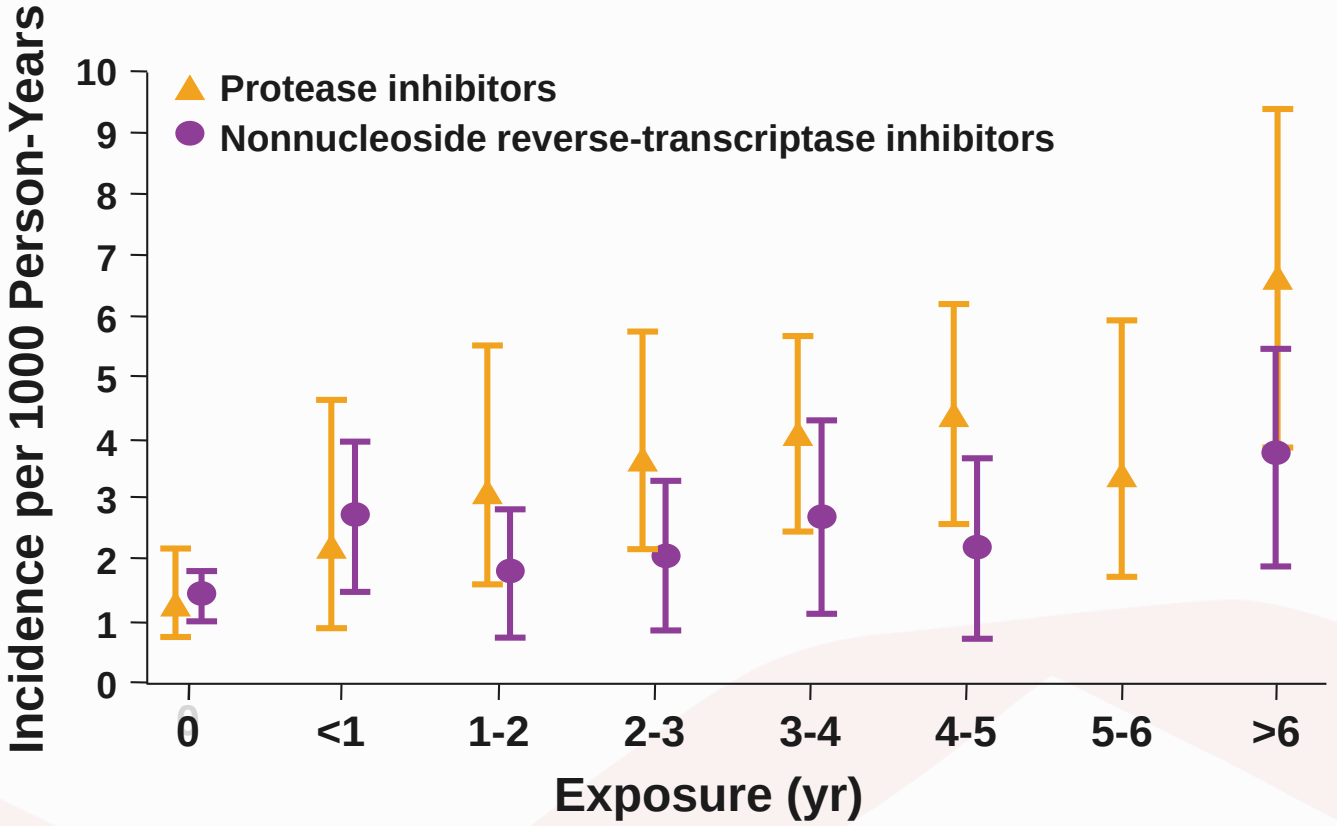
- Before ART
  - Total cholesterol ↓, LDL ↓, HDL ↓
    - LDL appears more prone to oxidation in HIV infection
  - Triglycerides increase ↑
- After ART
  - Total cholesterol, LDL ↑ (to pre-infection levels)
  - HDL remains low, may modestly ↑
    - HDL level inversely associated with CVD risk
  - Triglycerides remain ↑, PI use can further ↑

LDL more easily damaged and pro-inflammatory, protection from HDL diminished

Kotler DP. J Acquir Immune Defic Syndr. 2008
Duong M et al. HIV Clin Trials. 2006
Duprez DA et al. Atherosclerosis. 2009

HIV and cardiovascular disease

Protease Inhibitor Use



PIs: adjusted RR = 1.16 (1.10-1.23, p<0.001)

NNRTIs: adjusted RR = 1.05 (0.98-1.13, p=0.17)

DAD Study Group. N Engl J Med. 2007.

HIV and cardiovascular disease

Protease Inhibitor Use

- This increased risk with PI use was thought to be restricted to first-generation PIs, but…

- Boosted darunavir was recently found to be associated with a 59% increase in CVD per 5 years of exposure

Ryom L, et al. Association between cardiovascular disease and contemporarily used protease inhibitors. CROI 2017; Abstract 128LB. Seattle WA, February 13 – February 16, 2017.

HIV and cardiovascular disease

Substance Use

- HIV+ patients more likely smoke tobacco, to abuse alcohol, use recreational substances (marijuana, cocaine, methamphetamines) than general population
- HIV+ smokers carry 2x risk of MI than HIV+ non-smokers
- Smoking is associated with non-calcified plaque in general population
- Cocaine use is associated with atherosclerosis progressions among HIV+ men
- Interaction of HIV and other substances on atherosclerosis poorly characterized

Yi et al. Int J Cardiovasc Imaging. 2015

HIV and cardiovascular disease

Substance Use

- Smoking is associated with many plaque measures (coronary artery calcium, total plaque, calcified plaque, and coronary artery stenosis >50%) among HIV+ men, compared to HIV- men

- No conclusive significant associations with recreational substance use and subclinical atherosclerosis

Kelly SG et al. Plos One. 2016

HIV and cardiovascular disease

Primary and Secondary Prevention

- 2013 ACC/AHA Practice Guidelines
  - Statin therapy recommended for

    1) Clinical ASCVD – MI, CVA, angina, PAD (Secondary Prevention)

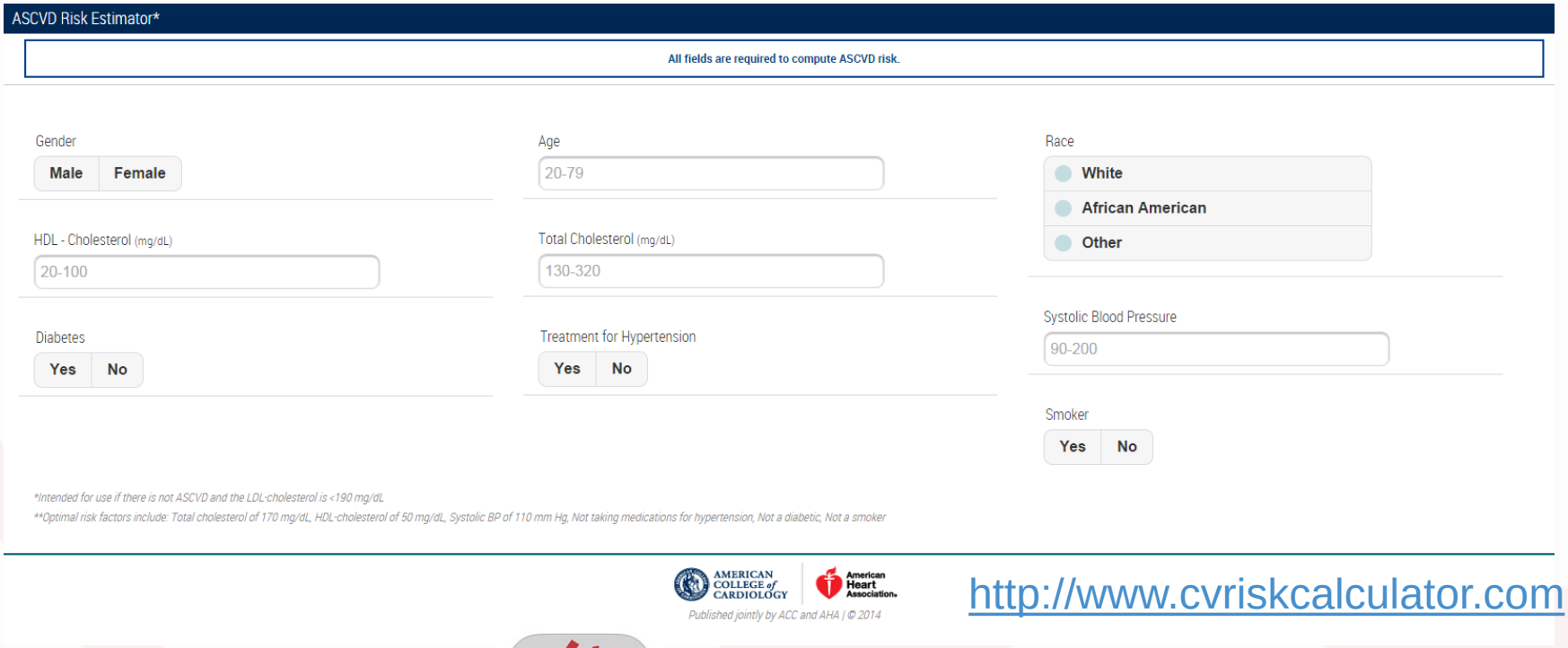
    2) LDL >190 mg/dL (Primary Prevention)

    3) DM, age 40-75 (Primary Prevention)
      - High-intensity statin if 10y ASCVD risk ≥7.5%

    4) No ASCVD or DM, but 10yr ASCVD risk ≥7.5% (Primary Prevention)

HIV?

2013 ACC/AHA Practice Guidelines



http://www.cvriskcalculator.com

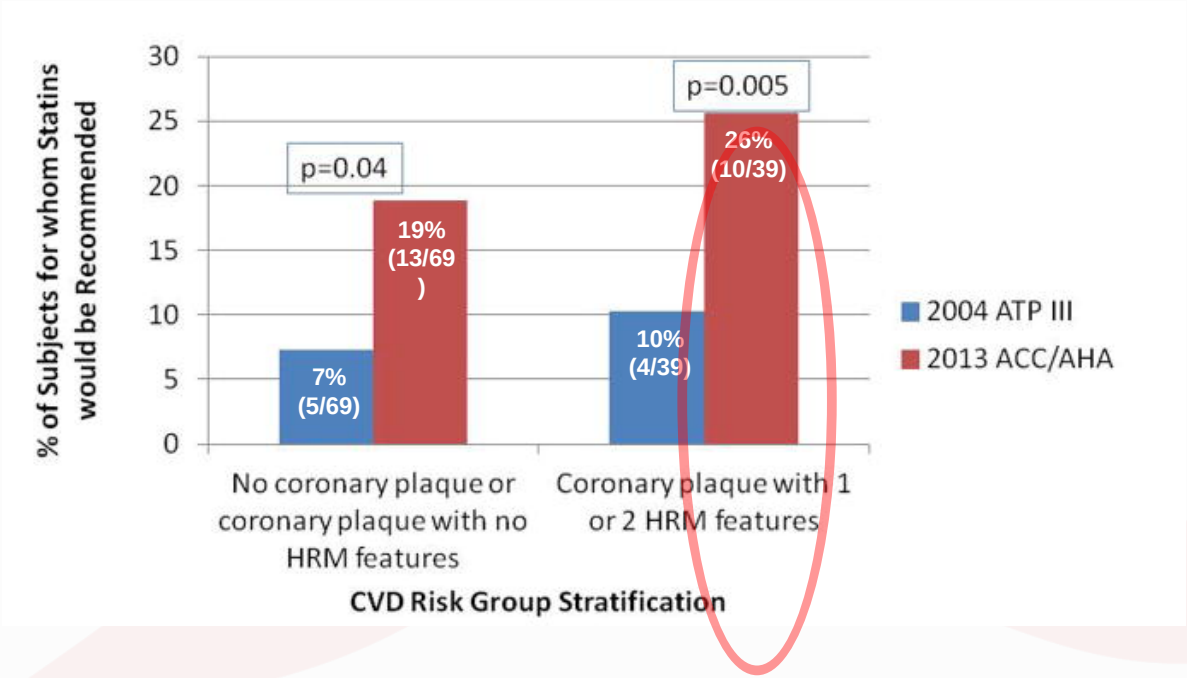
And there's an app!

HIV and cardiovascular disease

Primary and Secondary Prevention

- 2013 ACC/AHA Practice Guidelines miss the majority of HIV-infected persons with subclinical, high-risk plaque

~75% with high risk atherosclerotic plaque would NOT meet recommendation.



Zanni MV et al. AIDS. 2014

HIV and cardiovascular disease

Primary and Secondary Prevention

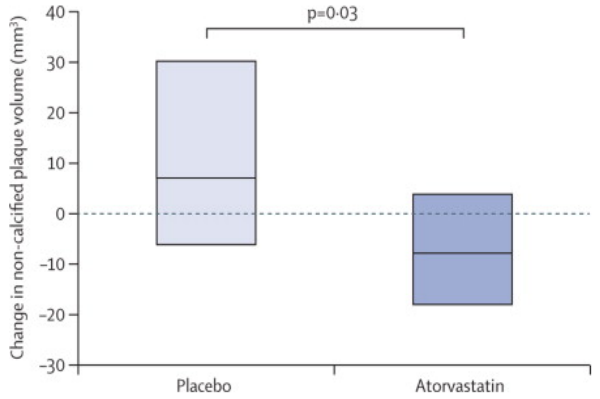
- HIV+ subjects with subclinical atherosclerosis are unique:
  - Young (15% <40 years)
  - Low LDL/TC, possibly due to HIV itself (46.4% had LDL cholesterol <100 mg/dl)

Zanni MV et al. AIDS. 2014

HIV and cardiovascular disease

Primary and Secondary Prevention

- Statins can reduce non-calcified plaque volume and high-risk features in HIV+ individuals
  - After 1 year of therapy
    - 19.4% reduction with atorvastatin
    - 20.4% increase with placebo



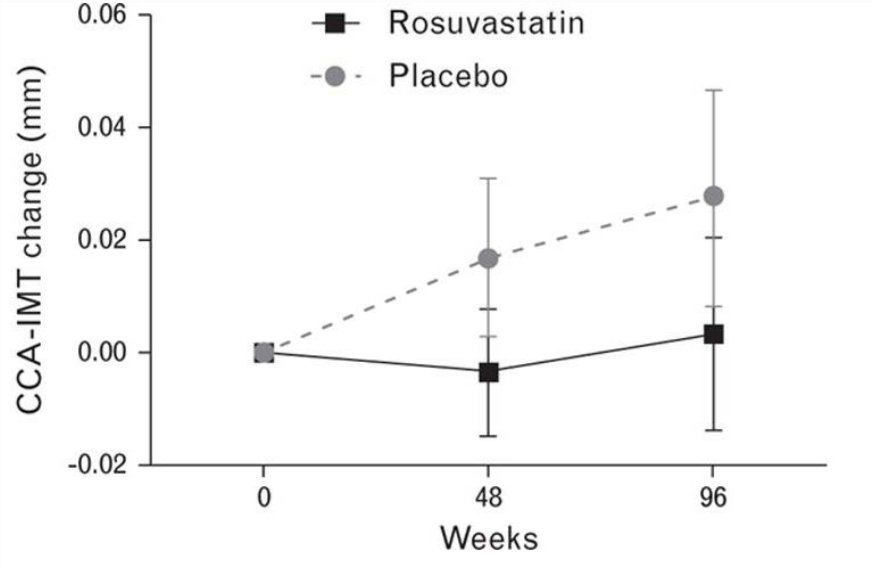
Comparison of the 1 year change in non-calcified plaque volume in study participants
Median and IQR.

Lo L et al. Lancet HIV. 2015

HIV and cardiovascular disease

Primary and Secondary Prevention

- Statins can reduce progression of atherosclerosis
  - Rosuvastatin 10mg daily
  - 0.019 mm (95% CI 0.002–0.037 mm) lower coronary artery intimal medial thickness change over the 96-week study period compared with placebo



Longenecker CT et al. AIDS. 2016 Sep 10;30(14):2195-203

So… How are we doing?

Among people living with HIV in North America who are eligible for statin therapy, approximately what percent is taking a statin?

A: 90%

B: 75%

C: 50%

D: 25%

E: 10%

HIV and cardiovascular disease

How are we doing?

THE STATIN GAP!

About half of all HIV+ patients in North America who should receive a statin actually do*

- Patients who are younger (<40 years), black, have CD4 <200 and are on PI-based ART are more likely to fall into the gap

*In 2013

Mascolini M. Big Gap Between Statin Eligibility and Prescriptions in 15 HIV Cohorts. CROI, February 13-16, 2017, Seattle WA

HIV and cardiovascular disease

How are we doing?

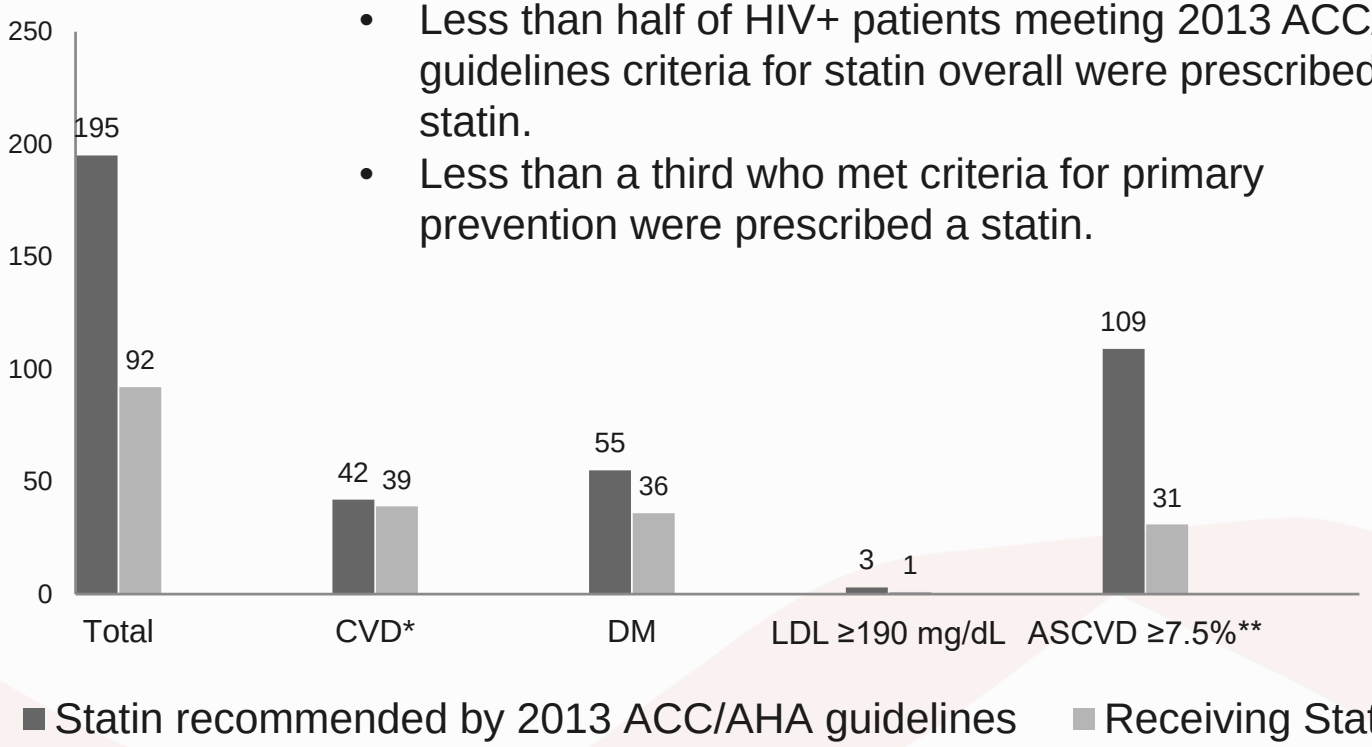
- In Chicago
  - Convenience sample of 460 HIV+ clinic patients seen 6/2015-6/2016

- Prescribing practices per 2013 ACC/AHA Guidelines of HIV providers were evaluated

HIV and cardiovascular disease

How are we doing?

- Less than half of HIV+ patients meeting 2013 ACC/AHA guidelines criteria for statin overall were prescribed a statin.
- Less than a third who met criteria for primary prevention were prescribed a statin.



*Includes peripheral arterial disease, ischemic stroke

**In absence of CVD, DM, and LDL<190 mg/dL

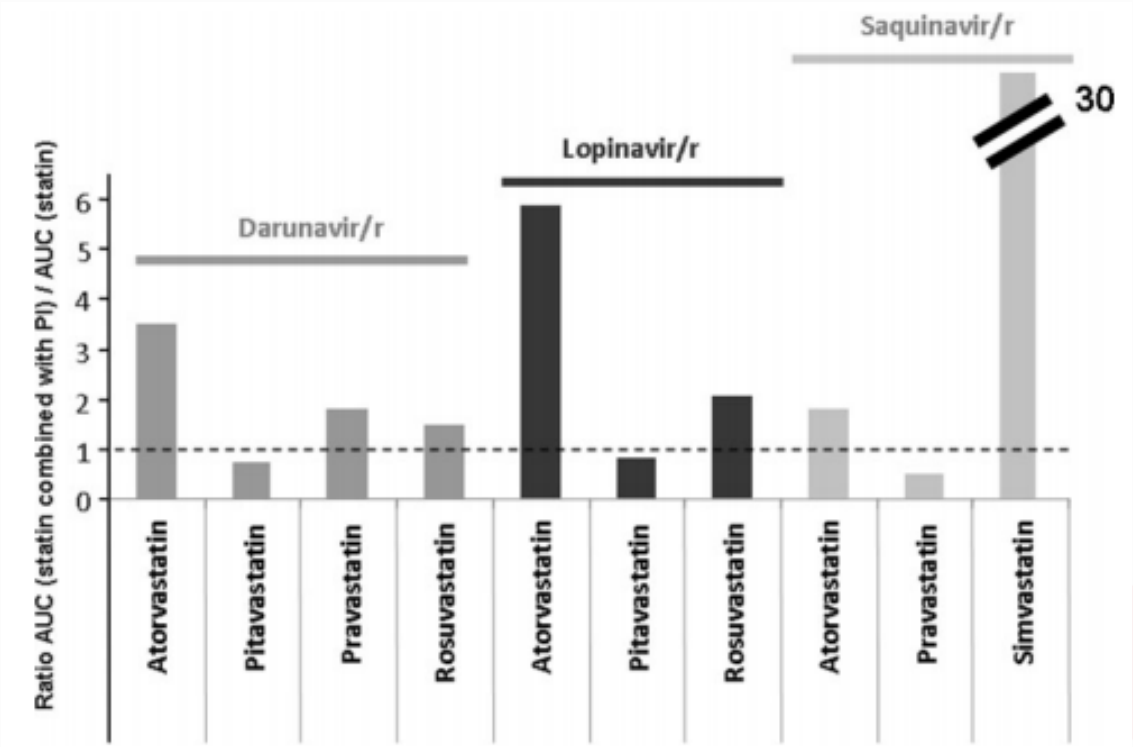
HIV and cardiovascular disease

Statin Therapy

- Challenges
  - Increased pill burden
  - Drug-drug interactions
    - Many statins metabolized by cytochrome P450 system (CYP3A4)
    - PIs can inhibit (mostly) and induce CYP3A4
    - NNRTIs can inhibit and induce CYP3A4 (to a lesser extent)

HIV and cardiovascular disease

Statin Therapy



Statin AUC decreases with successive generations of PIs

Chauvin B et al. Clinical Pharmacokinet. 2013

HIV and cardiovascular disease

Statin Therapy

- Safest statins (with highest dose tested in a trial)
  - Atorvastatin 20mg* (submaximal dose) – level IIb
  - Rosuvastatin 10mg* (submaximal dose) – level Ib
  - Pitavastatin 4mg – level Ib
  - Pravastatin 40mg – level Ib

*Increased safety monitoring required if exceeding doses

Soler A et al. Med Clin. 2006
Smith et al. Drug Class Review: HMG-CoA Reductase Inhibitors (Statins) and Fixed-dose Combination Products Containing a Statin. 2009. http://www.ncbi.nlm.nih.gov/books/NBK47273/ [Accessed October 16, 2015]
Feinstein MJ et al. Amer J Cardio. 2015
Chauvin B et al. Clinical Pharmacokinet. 2013

HIV and cardiovascular disease

- Know your patients' risk factors
- Calculate their 10-year ASCVD risk scores
- Initiate statin therapy if recommended
- Smoking cessation

Conclusions

- Recognize (and PREVENT) common OIs
- Some OIs can be treated in the outpatient primary care setting
- Lipodystrophy is difficult to reverse, and associated with metabolic complications
- Osteopenia/osteoporosis is very common in HIV
- Hypogonadism is common as well, should be thoughtfully evaluated and treated
- HIV+ patients are vulnerable to CVD, and to the worst kind of atherosclerotic plaque (non-calcified)
- HIV+ patients have **UNDIAGNOSED** high-risk atherosclerosis
- HIV+ patients have many CVD risk factors: dyslipidemia, aging, smoking and other substance use
- Current statin guidelines aren't being applied vigorously to HIV+ patients
- Statins can be safely used, when ART taken into account

Thank you!

Questions?