HIV & Aging Co-Morbidities: An update on bone and cardiovascular disease

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USCA SEPT 5-8, 2019 - MARRIOTT MARQUIS WDC

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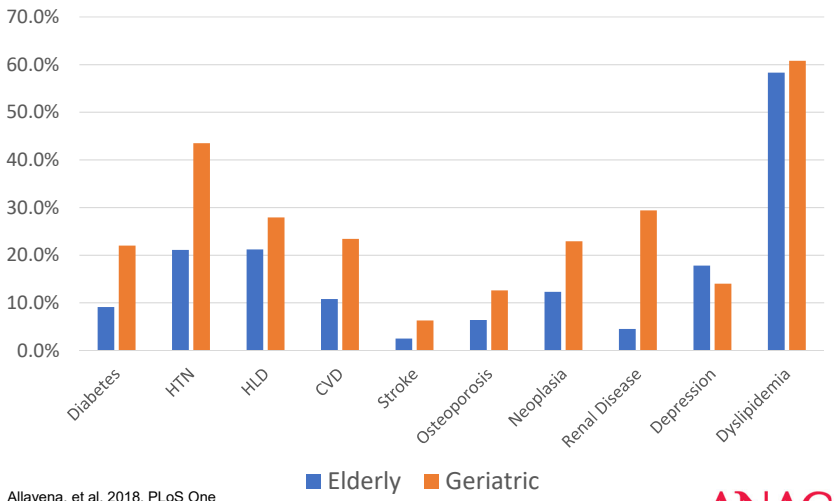
Co-Morbidities:

Elderly vs Geriatric (n=16,436; n=572)



Allavena, et al. 2018, PLoS One

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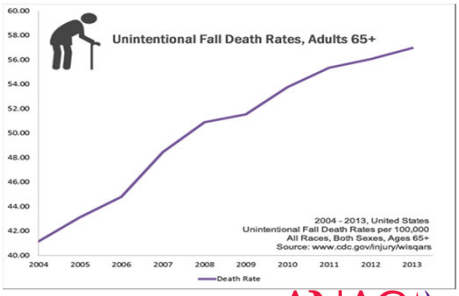
Fast Facts: Falls

- Falls result in more than **2.8 million** injuries annually,
  - 800,000 hospitalizations
  - 27,000 deaths



Source: CDC, 2019

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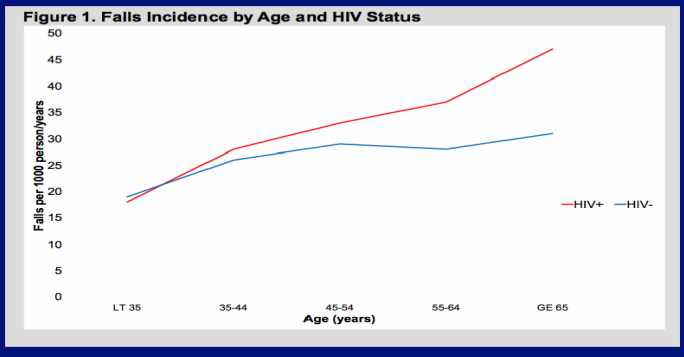
HIV infection associated with higher incidence of falls with aging: VA Study



Womack, CROI, 2017

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Bone Mass Over Time

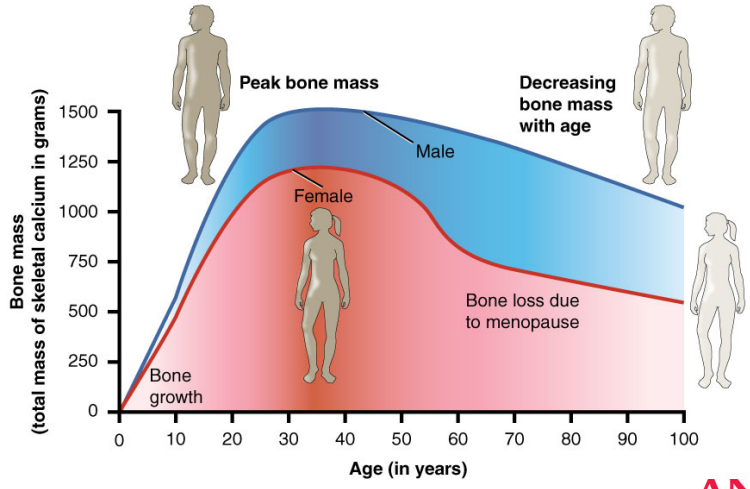

Image Source: https://opentextbc.ca

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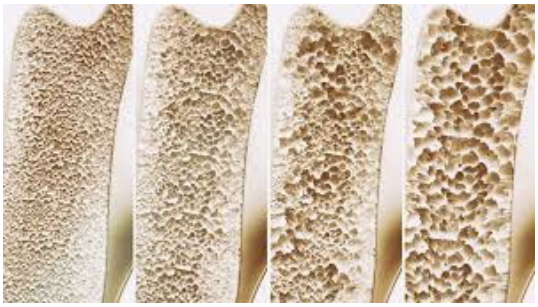
Bone Loss

- Osteo**penia** vs Osteo**porosis**



HEALTHY/ NORMAL **OSTEOPENIA** **OSTEOPOROSIS**

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Bone Health: Epidemiology

- Age-adjusted fracture rates were **1.98 to 3.69 times higher** in PLWH vs general population
- 48 - 67% osteopenia
- 5 - 34% osteoporosis

Source: Young et al. CID, 2011;
Brown et al AIDS 2006:

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Risk Factors for Bone Loss

- Female gender
- Advanced age
- Lower BMI
- Physical inactivity
- Corticosteroids
- Menopause
- Smoking
- Weight loss
- Malnutrition
- Hypogonadism
- Vitamin D deficiency
- HIV ART
- Medications
- HCV infection

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ART and Bone Loss

- Studies indicate increased rate of bone loss with ART.
- Further studies needed to clarify clinical significance of these BMD declines
- Protease Inhibitors > NNRTI

Moran et al. Curr Treat Options Infect Dis. 2017 Mar; 9(1): 52–67.

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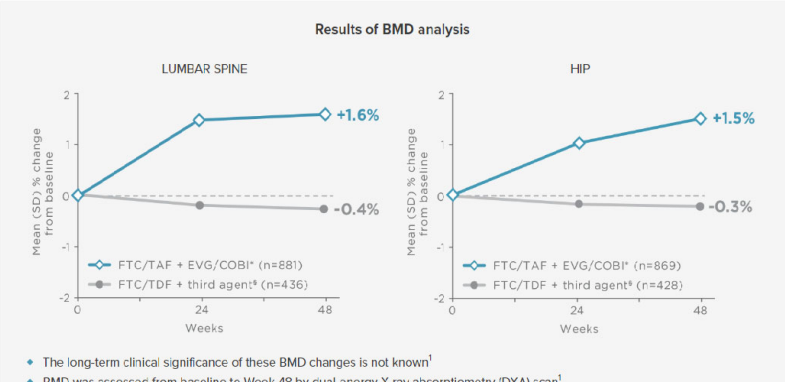
ART and Bone Loss

- Tenofovir DF > Tenofovir AF

Study 109: Change in lumbar spine and hip BMD at Weeks 24 and 48[1,2]



- The long-term clinical significance of these BMD changes is not known[1]

Source: Descovy Prescribing Information, 2019

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DXA Scan

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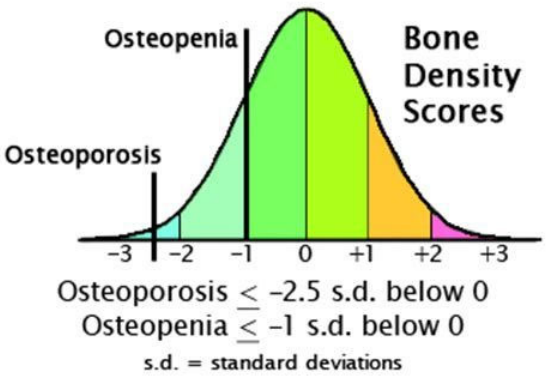
T and Z Scores



Osteoporosis ≤ −2.5 s.d. below 0
Osteopenia ≤ −1 s.d. below 0
s.d. = standard deviations

T-score shows bone density vs a healthy 30-year old adult.

Z-score shows bone density vs age-matched adult.

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FRAX®

- Fracture risk prediction tool developed by WHO
- Combines BMD + clinical risk factors to predict fracture risk better than either alone
- Predicts the 10-year probability of major osteoporotic fracture

https://www.sheffield.ac.uk/FRAX/

WHO FRAX® Tool. http://www.shef.ac.uk/FRAX/. Accessed September 13, 2013.

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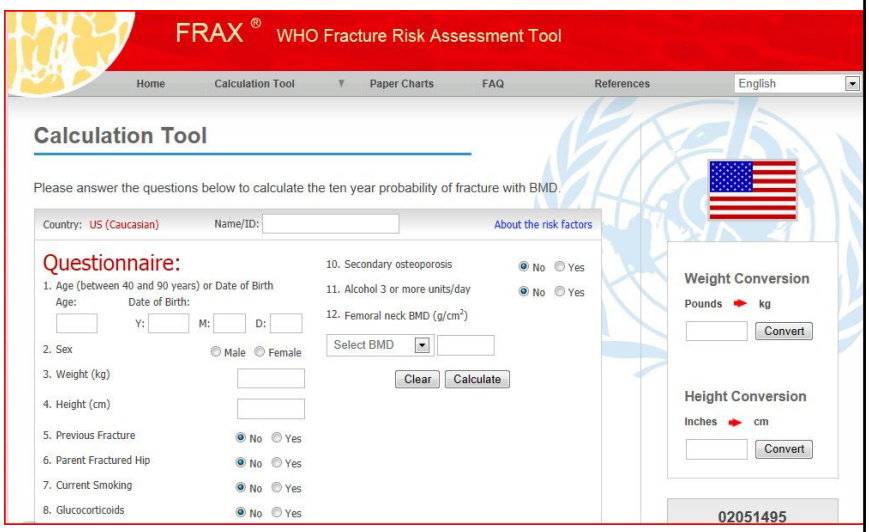

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Benefits of FRAX®

- Treatment decisions in osteopenic patients clearer
  - –Decision is based on the risk of fracture, not T-score alone
- Identifies patients at high-risk for fractures to ensure that they are offered treatment to lower their risk
- Helps avoid giving medication to those who are at low risk and have little to gain from treatment

"Specific treatment decisions must be individualized"

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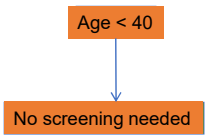
Bone Health: Screening Recommendations for PLWH



Brown TT, et.al. Recommendations for evaluation and management of bone disease in HIV Clin Infect Dis, January 21, 2015
Aberg et al. Clin Infect Dis. 2014;58(1):1.

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Bone Health: Follow Up Screening

- **FRAX**: recalculate every 2-3 years
- **DXA**
  - If T score was -1 to -1.99, repeat in 5 years
  - If T score was -2 to -2.49, repeat in 1-2 years
- **If started on bisphosphonates**:
  - repeat DXA in 2 years
  - reassess need for bisphosphonates in 3-5 years

- Brown TT, et.al. Recommendations for evaluation and management of bone disease in HIV Clin Infect Dis, January 21, 2015

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Calcium Intake Recommendations From the IOM

Life Stage Group	Estimated Requirement (mg/day)	Recommended Dietary Allowance (mg/day)	Upper Level Intake (mg/day)
31–50 y.o.	800	1,000	2,500
51–70 y.o. male	800	1,000	2,000
51–70 y.o. female	1,000	1,200	2,000
>70 years old	1,000	1,200	2,000

Institute of Medicine. Dietary Reference Intakes for Calcium and Vitamin D: Report Brief. Washington, DC: IOM ; 2010. Available at: http://www.iom.edu/Reports/2010/Dietary-Reference-Intakes-for-Calcium-and-Vitamin-D.aspx. Accessed September 13, 2013.

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Vitamin D Intake Recommendations From the IOM

Life Stage Group	Estimated Avg Requirement (IU/day)	Recommended Dietary Allowance (IU/day)	Upper Level Intake (IU/day)
31–50 years old	400	600	4,000
51–70-year-old male	400	600	4,000
51–70-year-old female	400	600	4,000
>70 years old	400	600	4,000

Institute of Medicine. Dietary Reference Intakes for Calcium and Vitamin D: Report Brief. Washington, DC: IOM; 2010. Available at: http://www.iom.edu/Reports/2010/Dietary-Reference-Intakes-for-Calcium-and-Vitamin-D.aspx. Accessed September 13, 2013.

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Exercise for Osteoporosis

- Weight bearing Exercise:
  - **30 min**
  - **most days**
- Muscle-strengthening:
  - **20 min**
  - **2-3 days/week**
- Flexibility/Balance/Posture:
  - **Daily**
  - **Rotate**

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Pharmacologic Treatment for Osteoporosis/Osteopenia in PLWH

- Data with alendronate (Fosomax)
- Limited data with:
  - Zoledronic acid (Reclast)
  - Teriparatide (Forteo)
  - Denosumab (Prolia)
  - Calcitonin (Fortical)
  - Raloxefine (Evista)

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Bisphosphonates

- **Alendronate (Fosomax)**: 10 mg daily (tablet) or 70 mg weekly (tablet or liquid) for treatment, 5 mg daily or 35 mg weekly for prevention
- **Risedronate (Actonel)**: 5 mg daily or 35 mg weekly (tablet); 150 mg monthly (tablet)
- **Ibandronate (Boniva)**: 150 mg monthly by tablet; 3 mg intravenously over 15 to 30 seconds every 3 months
- **Zoledronic acid (Reclast)**: 5 mg by intravenous infusion over a minimum of 15 minutes once every year for treatment—and every other year for prevention

National Osteoporosis Foundation. *Clinician's Guide to Prevention and Treatment of Osteoporosis.* Washington, DC: National Osteoporosis Foundation; 2014. Available at: http://www.nof.org/hcp/clinicians-guide.

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Bisphosphonates

Contraindications/Warnings/Precautions

- Creatinine clearance <30 cc/min (<35 cc/min for zoledronic acid)
- For oral dosing: Esophageal stricture or impaired esophageal motility (alendronate); inability to stand or sit for at least 30 minutes (alendronate/risedronate) or 60 minutes (ibandronate)

Oral dosing requirements

- Tablets (with exception of delayed release risedronate) taken on an empty stomach after overnight fast with 6 to 8 oz of plain water while in an upright position
- Patients should not eat or lie down for at least 30 minutes (alendronate and risedronate) or 60 minutes (ibandronate)

National Osteoporosis Foundation. *Med Lett.* 2011;53(1360):24.

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"Osteonecrosis" of the Jaw (ONJ)

- 95% of cases have been reported with high-dose, chronic IV bisphosphonate treatment of myeloma and cancer metastatic to bone[1]
- Can occur with denosumab[2]
- Known risk factors: invasive dental procedures, oral trauma, periodontitis, poor oral hygiene, radiotherapy to the jaw, chemotherapy, corticosteroids, infection
- Pathogenesis is not known[3]

1. Woo SB, et al. *Ann Intern Med.* 2006;144:753-761. 2. Sutton EE, Riche DM. *Ann Pharmacother.* 2012;46:1000-1009.
3. Khosla S, et al. *J Bone Miner Res.* 2007;22:1479-1491.

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FDA Safety Warning

- Be aware of the possibility of atypical fractures in patients taking bisphosphonates
- Evaluate any patient who presents with new groin or thigh pain to rule out fracture of the femoral shaft
- Discontinue potent antiresorptive medication in patients with atypical fractures
- Periodic reevaluation of need to continue bisphosphonate therapy, particularly in patients treated > 5 years

Source: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-safety-update-osteoporosis-drugs-bisphosphonates-and-atypical

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Bisphosphonate Holidays

- In patients at high risk for fractures, continued treatment seems reasonable. Consider a drug holiday of 1 to 2 years after 10 years of treatment
- For lower risk patients, consider a “drug holiday” after 4 to 5 years of stability
- Follow BMD and bone turnover markers during a drug holiday period, and reinitiate therapy if bone density declines or markers increase

Watts NB et al; AACE Osteoporosis Task Force. *Endocr Pract.* 2010;16(Suppl 3):1-37.
Whitaker M, et al. *N Engl J Med.* 2012;366(22):2048-2051.

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Switching ART

- There is no evidence that switching ART will reduce fracture risk in those with established osteoporosis
- Consider avoiding TDF and boosted-protease inhibitors in patients at high risk for fragility fracture
- Switch TDF ->TAF

McComsey et al. Clin Infect Dis. 2010;51(8):937.

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Fall Prevention Strategies

- Wear Sensible Shoes
- Check Vision
- Avoid Sedating Meds
- Declutter Environment
- Watch Pet
- Lighten up your Space
- Use Assistive Devices
- Exercise

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Summary of Optimal Osteoporosis Management

- Utilize tools to identify high-risk patients
- Target any patient with a fracture for evaluation
- Ensure adequate calcium and vitamin D
- Promote physical activity
- Discuss pharmacologic options with high-risk patients

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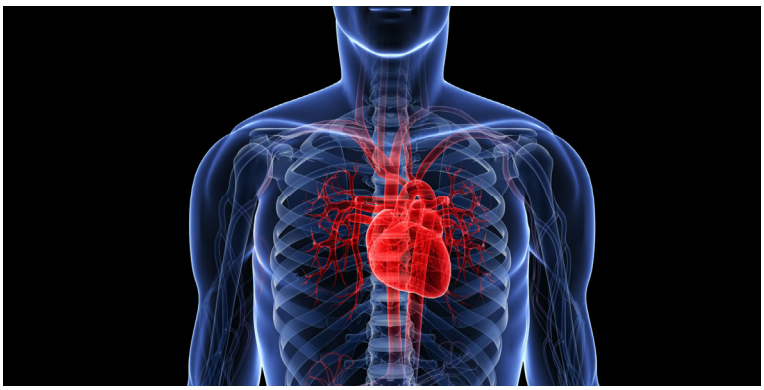

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HIV and CVD

- PLWH are at higher risk of atherosclerotic disease – including MI and Stroke, heart failure, and PAD
- Lower CD4 and HIV viremia are risk factors
- Even in setting of virologic control, MI risk is > than non-PLWH

Rate of mortality if VL > 400copies/mL:	**7.7/1000pt yr**
Rate of mortality if VL suppressed:	**3.9/1000pt yr**
General population:	**3.2/1000pt yr**

AHA Scientific Statement, 2019

Hanna et al. Clin Infect Dis. 2016;63(8):1122-1129.
Freiberg et al. JAMA Intern Med. 2013 Apr 22;173(8):614-22.

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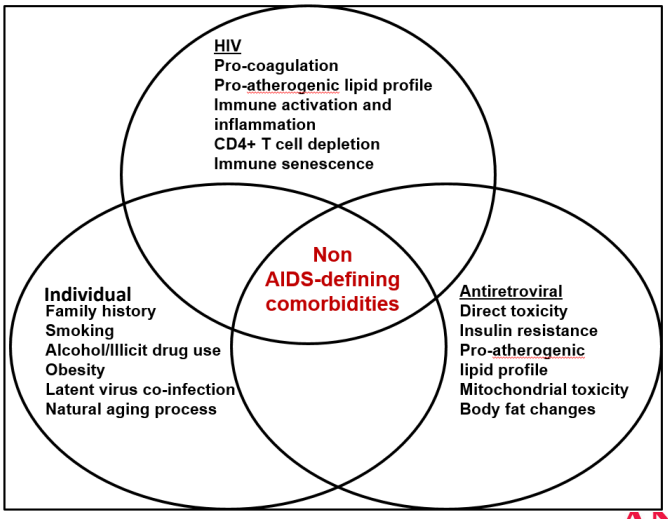
Increased CVD Risk is Multifactorial



Önen and Overton. Current Aging Science 2011. 4: 33-41.

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ASCVD Management in PLWH

- Initial step is to get all PLWH on ART and virologically suppressed.
- If on ART and virologically controlled, then consider other risk factors, including modifiable and non-modifiable risk factors.

AHA Scientific Statement, 2019

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Prevention and Treatment of HIV-associated ASCVD and HF

- Lifestyle optimization
  - Smoking cessation
  - Limiting alcohol consumption
  - Regular physical activity
  - Diet (healthy protein, whole grains, limiting sugar and red meats)
- Managing Co-Morbid Conditions
  - Diabetes
  - Hypertension

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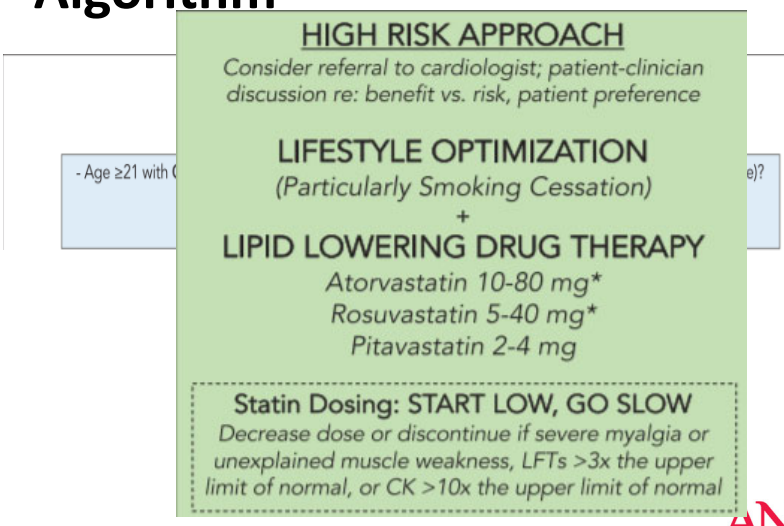
ASCVD Risk Assessment Algorithm



AHA Scientific Statement, 2019

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Add-On Therapy or Intolerant of Statin

- Ezetimibe (Zetia) 10mg once daily
- Proprotein convertase subtilisin/kexin type 9 inhibitor (PCSK9)
  - Evolocumab (Repatha) 140 mg q 2 weeks or 240mg monthly
  - Alirocumab (Praluent) 75mg q 2 weeks or 300mg q 4 weeks

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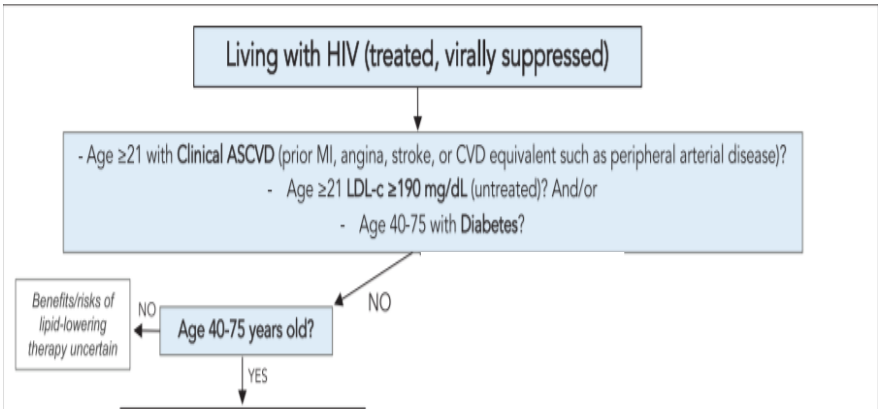
ASCVD Risk Assessment Algorithm



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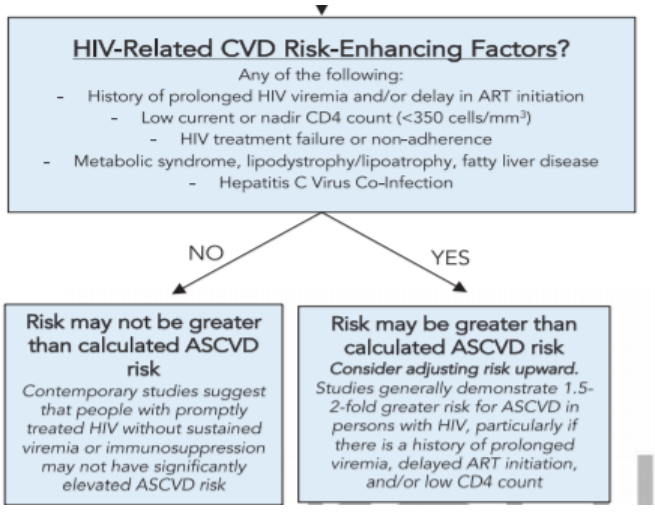
ASCVD Risk Assessment Algorithm



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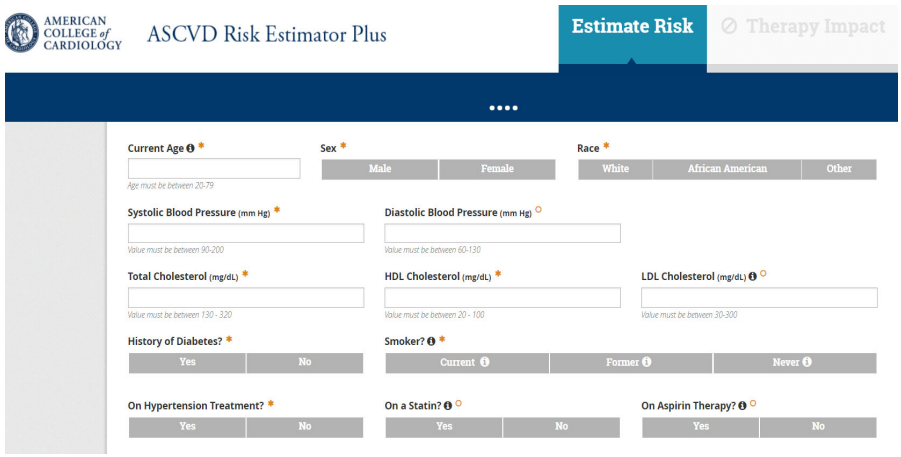

http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/

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If YES?

HIGH RISK APPROACH

Consider referral to cardiologist; patient-clinician discussion re: benefit vs. risk, patient preference

LIFESTYLE OPTIMIZATION

(Particularly Smoking Cessation)

+

LIPID LOWERING DRUG THERAPY

*Atorvastatin 10-80 mg**
*Rosuvastatin 5-40 mg**
Pitavastatin 2-4 mg

Statin Dosing: START LOW, GO SLOW

Decrease dose or discontinue if severe myalgia or unexplained muscle weakness, LFTs >3x the upper limit of normal, or CK >10x the upper limit of normal

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Suggested Statins in the Setting of ART

Ritonavir or Cobicistat Containing Regimens		
High Intensity Statin	**Moderate Intensity Statin**	**Low Intensity Statin**
Atorvastatin 20mg	Atorvastatin 10mg	Pravastatin 10-20mg
Rosuvastatin 10-20mg	Rosuvastatin 5mg	Fluvastatin 10-20mg
	Pravastatin 40-80mg*	Pitavastatin 1mg
	Pitavastatin 1mg	

Simvastatin and lovastatin are contraindicated for patients receiving a PI or cobicistat.
*With darunavir, reduce pravastatin to 20-40mg.

NNRTI, Raltegravir, or Dolutegravir Containing Regimens		
High Intensity Statin	**Moderate Intensity Statin**	**Low Intensity Statin**
Atorvastatin 40-80mg	Atorvastatin 10-20mg	Pravastatin 10-20mg
Rosuvastatin 20mg	Rosuvastatin 10mg	Fluvastatin 20-40mg
	Pravastatin 40-80mg	Pitavastatin 1mg
	Pitavastatin 2-4mg	Lovastatin 20mg
	Lovastatin 40mg	Simvastatin 10mg
	Simvastatin 20-40mg	

Dubé MP. *Lipid Management*, DOI 10.1007/978-3-319-11161-2_14

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Aspirin For Primary Prevention

US Preventive Services Task Force

Population	Recommendation
Age <50 yrs	Insufficient Evidence to Recommend
Age 50-59 with 10% CVD risk	Low Dose ASA for primary CVD prevention
Age 60-69 with 10% CVD risk	Low Dose ASA for primary CVD prevention (Unless bleeding risks prohibit)
Age ≥70 yrs	Insufficient Evidence to Recommend

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What about other forms of screening?

- "Insufficient data to recommend routine measurement of subclinical atherosclerosis on imaging or inflammatory biomarkers because the additive value in risk stratification in HIV is unclear."

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Disparities in CVD and HIV

- PLWH **less likely** to receive **ASA** therapy (5.1% vs 13.8%), **or** use **statins** (23.6% vs 35.8%).
- **Women** LWH **less likely** to receive lipid-lowering, anti-HTN, ACE/ARB, an invasive cardiovascular procedures post-MI
- Persons with **SUD less** statin use (23% vs 40%)
- Disparities in the South 4x higher vs other regions

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How to address this?

- More research
- Healthcare reimbursement
- Care coordination and IPCP

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Lifestyle Modification: Diet

- Cutting 500 calories per day will decrease your weight by 1-2 lbs week
- Watch portion sizes
- Watch liquid calories (soda, juice, fruit drinks
- Go natural
  - Avoid foods in boxes and cans (less salt and preservatives)
  - Maximize fresh fruits and vegetables

Hermsdorff HH. Endocrine. 2009 Dec;36(3):445-51

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Lifestyle Modification: Exercise

- **150 minutes**/week of exercise (minimum)
  - Do something you like (combination of cardio/strength)
- Set a fitness goal
- Find a fitness buddy
- Be active during day: If job is sedentary, take breaks to walk
- Take stairs rather than elevator; park further away to walk to work

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HIV and CVD Summary

- CVD is a **growing concern** as population ages.
- **ART** remains an **important** aspect of managing risk.
- **Lifestyle modification** can reduce risk.
- Important to **assess** patients for **CVD risk** and educate on ways to decrease risk.
- **Primary** and **secondary risk reduction** is an important aspect of caring for PLWH as they age.

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References & Resources

- HIV-Age.org

www.hiv-age.org

- HIV and Aging: HIV –NYS Guidelines

http://www.hivguidelines.org/clinical-guidelines/hiv-and-aging

- Adults 50 and Over

http://www.cdc.gov/hiv/group/age/olderamericans/index.html

- American Heart Association

www.heart.org

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