Will HIV-Infected Patients Make Old Bones?:

Osteoporotic Fractures in the Aging HIV population

Roger Bedimo, MD

ACT HIV

05-12-2012
Objectives

• Identify HIV and Hepatitis C Co-infection as risk factors for osteoporosis and osteoporotic fractures in HIV-infected patients.

• Apply recommended best practices to evaluate and manage a HIV-infected patient with increased risk of osteoporotic fracture.
Faculty and Planning Committee
Disclosures

Please consult your program book.

Off-Label Disclosure

There will be no off-label/investigational uses discussed in this presentation.
Questions

- Does HIV infection decrease bone health? Does HCV? Other risk factors to consider?
- Are antiretroviral drugs associated with increased fracture risk? Which ones?
  - Should the choice of antiretroviral therapy be made in function of patients’ fracture risk?
- Can the fracture risk of HIV-infected patients can be evaluated and improved?
Case 1: An HIV-Infected Patient Initiating Care

- 54 y/o WM, establishing care. No new complaints.
- PMH:
  - HIV disease diagnosed in 1998 (developed PCP); CD4 count: 688; Viral Load undetectable.
  - HCV: untreated
  - HTN, Hyperlipidemia
  - CAD s/p MI
- Social history:
  - EtOH, Tobacco, IVDU
- Meds:
  - Tenofovir/Emtricitabine, Lopinavir/Ritonavir
  - ASA, Lisinopril, Metoprolol, Rosuvastatin, Fenofibrate,
- Physical exam
  - Thin (BMI: 19); lipoatrophy, otherwise unremarkable
Case 1: An HIV-Infected Patient Initiating Care

- Is this patient at increased risk of fracture?
- All the following have been associated with increased risk of osteoporotic fractures in this patient, except:
  - HIV Infection
  - Hepatitis C co-infection
  - White race
  - Low BMI
  - Tenofovir exposure
  - Smoking
  - Testosterone use
  - Age
  - Lipoatrophy
# Age Distribution of HIV Infected Veterans In Care

<table>
<thead>
<tr>
<th>Year</th>
<th>Number in Care</th>
<th>Age &lt;30</th>
<th>Age 30-39</th>
<th>Age 40-49</th>
<th>Age 50-59</th>
<th>Age 60-69</th>
<th>Age 70-79</th>
<th>Age &gt;79</th>
<th>Mean Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>19,688</td>
<td>2.1%</td>
<td>18.1%</td>
<td>43.3%</td>
<td>28.1%</td>
<td>6.3%</td>
<td>2.1%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2002</td>
<td>19,346</td>
<td>1.4%</td>
<td>14.4%</td>
<td>40.7%</td>
<td>33.9%</td>
<td>7.1%</td>
<td>2.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2005</td>
<td>23,541</td>
<td>1.5%</td>
<td>10.1%</td>
<td>34.3%</td>
<td>39.8%</td>
<td>11.4%</td>
<td>2.6%</td>
<td>0.3%</td>
<td>50.5</td>
</tr>
<tr>
<td>2006</td>
<td>23,329</td>
<td>1.4%</td>
<td>9.0%</td>
<td>32.1%</td>
<td>41.1%</td>
<td>13.2%</td>
<td>2.9%</td>
<td>0.3%</td>
<td>51.2</td>
</tr>
<tr>
<td>2007</td>
<td>22,956</td>
<td>1.3%</td>
<td>8.0%</td>
<td>29.8%</td>
<td>41.3%</td>
<td>16.1%</td>
<td>3.2%</td>
<td>0.4%</td>
<td>52.0</td>
</tr>
<tr>
<td>2008</td>
<td>23,463</td>
<td>1.4%</td>
<td>7.3%</td>
<td>27.6%</td>
<td>40.8%</td>
<td>19.1%</td>
<td>3.3%</td>
<td>0.4%</td>
<td>52.6</td>
</tr>
</tbody>
</table>

Aging and Non-HIV-associated Co-morbidity in HIV+ Persons: The SHCS

Hasse et al., CROI 2011. Abstract 792

Fracture, inadequate trauma
Fracture, adequate trauma
Osteoporosis

Incidence per 1000 pyrs (95% CI)

- Bacterial pneumonia
- Cerebral infarction
- Coronary angioplasty
- Myocardial infarction
- Procedures on other arteries
- Pulmonary embolism

- Age 65+ years
- Age 50-64 years
- Age <50 years

Non AIDS defining malignancies
AIDS defining event
Death
Age-adjusted Rates of Osteoporotic Fractures (Entire Cohort)

VA Cohort: n=56,660; Person-years: 305,237
951 osteoporotic fractures

Fracture Rate (per 1,000 patient-years)

Vertebral
Hip
Wrist
Total

General population

1Data from Triant V, et al., JCEM 2008;93: 3499–3504

### Fracture Incidence in HIV+ and HIV- Veterans Aging Cohort Study Virtual Cohort (VACS-VC) – 119,318 men, 33% HIV+

<table>
<thead>
<tr>
<th>Factor</th>
<th>Model with HIV only**</th>
<th>Model with everything but BMI**</th>
<th>Full Model**</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td>1.32 (1.20, 1.47)</td>
<td>1.24 (1.11, 1.39)</td>
<td>1.10 (0.97, 1.25)</td>
</tr>
<tr>
<td>Age (10 year increments)</td>
<td>--</td>
<td>1.33 (1.26, 1.41)</td>
<td>1.32 (1.25, 1.40)</td>
</tr>
<tr>
<td>White race</td>
<td>--</td>
<td>1.74 (1.56, 1.94)</td>
<td>1.80 (1.60, 2.03)</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>--</td>
<td>1.81 (1.53, 2.15)</td>
<td>1.80 (1.50, 2.17)</td>
</tr>
<tr>
<td>Liver disease†</td>
<td>--</td>
<td>1.33 (1.08, 1.63)</td>
<td>1.38 (1.10, 1.73)</td>
</tr>
<tr>
<td>Current corticosteroid use</td>
<td>--</td>
<td>1.57 (1.28, 1.92)</td>
<td>1.45 (1.21, 1.74)</td>
</tr>
<tr>
<td>Smoker</td>
<td>--</td>
<td>1.44 (1.25, 1.66)</td>
<td>1.21 (1.04, 1.42)</td>
</tr>
<tr>
<td>Any proton pump inhibitor use</td>
<td>--</td>
<td>1.64 (1.47, 1.84)</td>
<td>1.70 (1.51, 1.92)</td>
</tr>
<tr>
<td>BMI</td>
<td>--</td>
<td>--</td>
<td>0.82 (0.79, 0.85)</td>
</tr>
<tr>
<td>BMI²</td>
<td>--</td>
<td>--</td>
<td>1.002 (1.002, 1.003)</td>
</tr>
</tbody>
</table>

# Risk of Fractures in HIV and HIV/HCV Patients – Danish Cohort

5306 HIV+ and 26,530 controls; median age: 36.7.  F/u period: 1995-2009

<table>
<thead>
<tr>
<th>Fracture type</th>
<th>HIV-monoinfected.</th>
<th>HIV/HCV-coinfected</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>IRR (95% CI)</td>
</tr>
<tr>
<td>All</td>
<td>562</td>
<td>1.3 (1.2–1.4)</td>
</tr>
<tr>
<td>Low-Energy</td>
<td>256</td>
<td>1.6 (1.4–1.8)</td>
</tr>
<tr>
<td>Before HAART</td>
<td>57</td>
<td>1.8 (1.5–2.1)</td>
</tr>
<tr>
<td>After HAART</td>
<td>199</td>
<td>1.8 (1.5–2.1)</td>
</tr>
</tbody>
</table>

By type of fracture:

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<th>HIV/HCV-coinfected</th>
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<tr>
<td></td>
<td>No</td>
<td>IRR (95% CI)</td>
</tr>
<tr>
<td>Wrist</td>
<td>60 (23)</td>
<td>1.3 (1.0–1.7)</td>
</tr>
<tr>
<td>Humerus</td>
<td>42 (16)</td>
<td>3.3 (2.3–4.7)</td>
</tr>
<tr>
<td>Hip</td>
<td>27 (11)</td>
<td>2.5 (1.6–3.8)</td>
</tr>
<tr>
<td>Vertebra</td>
<td>17 (7)</td>
<td>1.4 (1.1–1.7)</td>
</tr>
<tr>
<td>Other</td>
<td>110 (43)</td>
<td>1.4 (1.1–1.7)</td>
</tr>
<tr>
<td>High-energy</td>
<td>320</td>
<td>1.1 (0.97–1.2)</td>
</tr>
<tr>
<td>Before HAART</td>
<td>95</td>
<td>1.0 (0.8–1.2)</td>
</tr>
<tr>
<td>After HAART</td>
<td>225</td>
<td>1.2 (1.0–1.3)</td>
</tr>
</tbody>
</table>

Risk of Fractures in HIV and HIV/HCV Patients – Danish Cohort

Fig. 1. Cumulative incidence of low-energy fractures (left) and high-energy fractures (right) in HIV-monoinfected patients, HIV/HCV-coinfected patients and population controls.

Risk of Fractures in HIV and HIV/HCV Patients – Danish Cohort

Fig. 2. Cumulative incidence of low-energy fractures before and after HAART initiation in HIV-monoinfected patients and matched population controls. The left figure shows timing of fracture from entry into the study until initiation of HAART or censoring which ever comes first. The right figure shows timing of fracture from initiation of HAART until censoring.

Factors Predicting Osteoporotic Fracture in HIV Patients

<table>
<thead>
<tr>
<th>Factors</th>
<th>Hazard Ratio (95% Confidence Interval; p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariate Analysis</td>
</tr>
<tr>
<td>Cumulative ART Use (per year)</td>
<td>1.05 (1.01 - 1.10; p=0.02)</td>
</tr>
<tr>
<td>CKD (eGFR &lt;60)</td>
<td>1.48 (1.04 - 2.09; p=0.03)</td>
</tr>
<tr>
<td>White Race</td>
<td>1.76 (1.46 - 2.13; p &lt; 0.0001)</td>
</tr>
<tr>
<td>Age (per 10 year increase)</td>
<td>1.51 (1.39 - 1.63; p &lt;0.0001)</td>
</tr>
<tr>
<td>Tobacco Use</td>
<td>1.25 (1.06 - 1.47; p=0.01)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.27 (1.05 - 1.53; p=0.01)</td>
</tr>
<tr>
<td>BMI &lt; 20</td>
<td>1.61 (1.29 - 2.00; p&lt;0.0001)</td>
</tr>
<tr>
<td>HCV Co-infection</td>
<td>1.43 (1.21 - 1.69; p&lt;0.0001)</td>
</tr>
</tbody>
</table>

### Osteopenia in Pre-menopausal HIV+ Women prior to HAART

<table>
<thead>
<tr>
<th></th>
<th>HIV (N=50)</th>
<th>Controls (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>37.4 +/- 7.1</td>
<td>35.1 +/- 3.6</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>25.2 +/- 3.9</td>
<td>26.9 +/- 2.4</td>
</tr>
<tr>
<td><strong>Serum Ca+</strong></td>
<td>2.23 +/- 0.10</td>
<td>2.48 +/- 0.17</td>
</tr>
<tr>
<td><strong>1,25OH D</strong></td>
<td>19.4 +/- 7.2</td>
<td>47.3 +/- 9.1</td>
</tr>
<tr>
<td><strong>25 OH D</strong></td>
<td>37.3 +/- 7.9</td>
<td>61.5 +/- 8.4</td>
</tr>
<tr>
<td><strong>PTH</strong></td>
<td>21.4 +/- 7.2</td>
<td>38.1 +/- 6.2</td>
</tr>
<tr>
<td><strong>Osteocalcin</strong></td>
<td>2.11 +/- 0.57</td>
<td>3.9 +/- 0.47</td>
</tr>
<tr>
<td><strong>Crosslinks</strong></td>
<td>63.5 +/- 10.5</td>
<td>18.3 +/- 9.6</td>
</tr>
<tr>
<td><strong>Urinary Ca+</strong></td>
<td>3.01 +/- 0.30</td>
<td>1.62 +/- 0.30</td>
</tr>
<tr>
<td><strong>% osteopenia LS</strong></td>
<td>76%</td>
<td>4%</td>
</tr>
<tr>
<td><strong>% osteopenia TH</strong></td>
<td>22%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Odds of osteoporosis in HIV-infected patients

Comparing HIV-infected to HIV-uninfected

Among HIV-infected, comparing patients receiving ART with ART-naïve patients

What Happened in the HAART Era?

- Higher % of patients on ARVs, low viremia.
- Increased survival (and time at risk) and increased fracture rates

Fracture Rate by Year

Pre-HAART Era: 1.61 Events/1000 PY
HAART Era: 4.09 Events/1000 PY

Antiretroviral Exposure and Risk of Osteoporotic Fractures: HAART Era

MV Model 1: Controlling for CKD, age, race, tobacco use, diabetes and BMI; MV Model 2: Controlling for Model 1 variables + concomitant exposure to other ARVs.

Exposure to Specific Protease Inhibitors and OF Risk: HAART Era

MV Model 1: Controlling for CKD, age, race, tobacco use, diabetes and BMI;
MV Model 2: Controlling for Model 1 variables + concomitant exposure to other ARVs.

Case 1: An HIV-Infected Patient Initiating Care

• Is this patient at increased risk of fracture?

• All the following have been associated with increased risk of osteoporotic fractures in this patient, except:

  - HIV Infection
  - Hepatitis C co-infection
  - White race
  - Low BMI
  - Tenofovir exposure
  - Smoking
  - Testosterone use
  - Age
  - Lipoatrophy
Case 1: An HIV-Infected Patient Initiating Care

- **54 y/o WM**, establishing care. No new complaints.
- **PMH:**
  - HIV disease diagnosed in 1998 (developed PCP); CD4 count: 688; Viral Load undetectable.
  - HCV: untreated
  - HTN, Hyperlipidemia
  - CAD s/p MI
- **Social history:**
  - EtOH, Tobacco, IVDU
- **Meds:**
  - Tenofovir/Emtricitabine, Lopinavir/Ritonavir
  - ASA, Lisinopril, Metoprolol, Rosuvastatin, Fenofibrate
- **Physical exam**
  - Thin (BMI: 19); lipoatrophy, otherwise unremarkable
Factors Likely Associated with Decreased Bone Health in HIV

**OSTEOPOROSIS** and ↑ **FRACTURE RISK**

- **HIV**
- **HAART**
- **HCV**

- Hypogonadism
- Glucocorticoids
- Inflammatory Cytokines
- Vitamin D deficiency
- Chronic kidney disease
- Malnutrition, low BMI
- Tobacco, Alcohol

**Women:** Post-menopausal state/estrogen deficiency; Hormonal agents (aromatase inhibitors, Medroxyprogesterone)

**Men:** Hypogonadism
Change in BMD After HAART Initiation: Tenofovir vs. Stavudine

Figure 3. Mean Percentage Change in Hip and Lumbar Spine Bone Mineral Density From Baseline to Week 144

<table>
<thead>
<tr>
<th>No. of Participants</th>
<th>Baseline</th>
<th>24</th>
<th>48</th>
<th>72</th>
<th>96</th>
<th>120</th>
<th>144</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir DF + Lamivudine and Efavirenz</td>
<td>299</td>
<td>261</td>
<td>234</td>
<td>221</td>
<td>209</td>
<td>193</td>
<td>185</td>
</tr>
<tr>
<td>Stavudine + Lamivudine and Efavirenz</td>
<td>301</td>
<td>267</td>
<td>246</td>
<td>226</td>
<td>205</td>
<td>185</td>
<td>181</td>
</tr>
</tbody>
</table>

DF indicates disoproxil fumarate. The range of variability (SD) of percentage change in lumbar spine and hip bone mineral density was from 2.5% to 5.2%.

ACTG 5224

Mean (95% CI) Percent Change in Spine and Hip BMD (ITT)

• Bone fractures
  - 5.6% had ≥ 1 fracture (all traumatic)
  - No statistically significant differences between NRTI components or NNRTI/PI components in fracture rate (Fisher’s exact) or time to first fracture (log-rank test)

McComsey G. JID 2011;203(12):1791-801
Case 1: An HIV-Infected Patient Initiating Care

- Which of the following account for the increased risk of osteoporosis associated with HIV and HAART:
  - Decreased Vitamin D levels
  - Increased levels of inflammation
  - Accelerated/imbalanced bone turnover
  - Hypogonadism

- Which of the following antiretrovirals are associated with decreased vitamin D
  - Efavirenz
  - Tenofovir
  - Atazanavir
High Rates of Vitamin D Deficiency in cART Naïve and Treated HIV+ Patients

- N=211 naïve pts starting cART
- Vitamin D deficiency was 3 fold higher in Spring (42-52%) than Fall (14-18%)
- Initiation of cART, overall, had minimal impact on 25 (OH) D levels
- In multivariate analysis, predictors of vitamin D deficiency were Black race, active IDU, longer duration of HIV, Spring season, and NNRTI use
- TDF use was not associated with vitamin D deficiency
- Authors suggest routine screening for vitamin D deficiency in all HIV+ patients
Vitamin D Metabolism in HIV

Vitamin D $\rightarrow$ 25-OH-D $\rightarrow$ 25-hydroxylase $\rightarrow$ Calciferol

Calciferol $\rightarrow$ Calcidiol $\rightarrow$ 24-hydroxylase $\rightarrow$ Calcitriol $\rightarrow$ 24-hydroxylase $\rightarrow$ 1,24,25-(OH)$_3$-D $\rightarrow$ Calcitroic acid

- **Tenofovir?**
  - Proximal tubular dysfunction
  - ↑ urinary calcium and phosphorus losses

- **Protease Inhibitors**
  - Efavirenz
  - Cyt P450 inhibitor

- **Cyt P450 Inducer**
  - Tenofovir?
## Change in $25_{OH}D$ with ART initiation

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Change in $25_{OH}D$ with ART</th>
<th>Mean/median interval</th>
<th>Effect of ART</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dao (US) 2010</td>
<td>87</td>
<td>-12.7 nmol/L (-20.7, 2.7) with EFV</td>
<td>6-12 months</td>
<td>EFV-based regimens associated with decrease in $25_{OH}D$, even after adjustment for baseline $25_{OH}D$, race, season</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+1.0 nmol/L (-10.2, 14.5) with PI (89%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Borden (ICONA cohort, Italy)</td>
<td>116/ 865</td>
<td>-7.6+7.3 nmol/L, p=0.11, overall</td>
<td>14 mo</td>
<td>No difference NNRTI vs PI in subjects with $25_{OH}D$ pre- and post-ART</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-10.5+6.5 nmol/L with NNRTI</td>
<td></td>
<td>In MV model in full cohort, NNRTI use associated with increased OR for Vit D deficiency</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-6.8+7.6 nmol/L with PI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mueller (Swiss HIV cohort)</td>
<td>211</td>
<td>-9.0 nmol with NNRTI ( 89% EFV)</td>
<td>12 mo</td>
<td>Significant decrease in $25_{OH}D$ from baseline with NNRTI but not PI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>+1.8 nmol with PI</td>
<td></td>
<td>In MV model, NNRTI use has negative association with $25_{OH}D$ levels</td>
</tr>
</tbody>
</table>

Vitamin D Deficiency in HIV

- Baseline data from SUN Study of HIV-infected adults at 7 specialty clinics in 4 cities
- The age-, race-, and sex-adjusted prevalence of vitamin D insufficiency/deficiency (serum 25-OH-D < 30 ng/ml) was 70% among 672 HIV-infected individuals

Risk factors:
- Non-Caucasian race,
- ↑ BMI,
- lack of exercise,
- ↓ UV exposure,
- efavirenz

No association between BMD and vitamin D insufficiency or deficiency.

Interaction of low bone mineral density and increased bone turnover in predicting fracture risk.

BMD: Bone Mineral Density
CTX: urinary C-terminal collagen crosslink excretion
D-Pyr: free deoxypyridinoline excretion

Bone Metabolism: Remodeling

- Purposes:
  - 1. Repairs microdamage within skeleton to maintain skeletal strength (formation by osteoblasts)
  - 2. Supplies calcium from skeleton to maintain serum calcium. (Resorption by osteoclasts)

- Regulated by estrogens, androgens, vitamin D, PTH, insulin growth factors, etc.

- Markers of bone metabolism:
  - formation: bone sp alk phos, osteocalcin, propeptide of type I procollagen
  - resorption: urine or serum N-telopeptide & C-telopeptide, urine hydroxyproline
Low BMD and High Turnover in HIV

• HIV+ vs. HIV- Women:
  - Serum TNF, N-telopeptide, and C-telopeptide were significantly higher in HIV+ than HIV- women, particularly those receiving ART.
  - Formation markers, BAP, and OC were slightly but not significantly higher in HIV+ women.
  - Resorption markers, NTx and CTx, were significantly higher in HIV+ women.

• HIV+ Women with our without ART
  - Serum BAP, OC, and CTx were significantly higher in HIV+ ART+ than HIV+ ART- women.
Changes in Bone Turnover Occur Early after ART Initiation

Figure 2. Change in markers of bone resorption. Estimated means±SEM (adjusted for baseline differences, ITT).
# p<0.05 within arm 0-24 months

Figure 3. Change in markers of bone formation. Estimated means±SEM (adjusted for baseline differences, ITT).
# p<0.05 within arm 0-24 months

van Vonderen et al, CROI 2011; Abstract 833
Increased Bone Turnover in HIV Patients on HAART

- 113 HIV-positive patients (86 on ART)
- Markers measured 3 to 5 months after ART initiation

**FIGURE 1.** ART versus no ART. ART, antiretroviral treatment; BSAP, bone-specific alkaline phosphatase; PYD, pyridinoline; DPD, deoxypyridinoline.

Piso et al., *J Acquir Immune Defic Syndr.* 2011 Apr;56(4):320-4
Increased Bone Turnover in HIV Patients on HAART

- No difference in levels of bone turnover markers after exposure to tenofovir (TDF) vs. other nucleoside reverse transcriptase inhibitors (no TDF)

**FIGURE 2.** TDF versus no TDF. TDF, tenofovir; BSAP, bone-specific alkaline phosphatase; PYD, pyridinoline; DPD, deoxypyridinoline.

Piso et al., J Acquir Immune Defic Syndr. 2011 Apr;56(4):320-4
Increased Bone Turnover in HIV Patients on HAART

- No difference in levels of bone turnover markers after exposure to protease inhibitors (PI) vs. non-nucleoside reverse transcriptase inhibitors (NNRTI)

Piso et al., J Acquir Immune Defic Syndr. 2011 Apr;56(4):320-4
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- Physical exam
  - Thin (BMI: 19); lipoatrophy, otherwise unremarkable
Case 1: An HIV-Infected Patient Initiating Care

- Should this patient be screened with DEXA scan?
Approach to Bone Disease in HIV

**Initial approach**

HIV infected individual

- **Assess risk factors**
  - Age
  - Sex
  - Weight/Height
  - Hx. of Fractures
  - Secondary causes

- **Lifestyle advice**
  - Smoking cessation
  - Vitamin D and Calcium intake
  - Weight bearing exercise
  - Sun exposure

**Indications for DXA**

- < 50 years ♂
  - PREmenopausal ♀
  - AND NO hx. of fracture?
  - WAIT

- ≥ 50 years ♂
  - POSTmenopausal ♀
  - AND/OR hx. of fracture?
  - Measure BMD by DXA

IDSA Guidelines. McComsey et al., CID 2010; 51(8):937–946
Case 1: An HIV-Infected Patient Initiating Care

• Should this patient be screened with DEXA scan? Yes

• DEXA Scan Findings:
  - Lumbar Spine (L1-L4): BMD: 0.942 g/cm²; T-score: -1.5
  - L femoral neck: BMD: 0.632 g/cm²; T-score: -1.9

• How would you manage this patient?
  - No treatment
  - Calcium + Vitamin D
  - Calcium + Vitamin D + Alendronate
Example for T-Score = -2.0, 60 year-old and Z-Score = -0.5

T-score: compares result to younger “normal” value.
Z-score: compares individual results to age matched “normal” value
T-score ≤ -2.5 = osteoporosis
T-score ≤ -1.0 = osteopenia

Example: T-score: -2.0; Patient is 60 y/o: Z-score: -0.5
Approach to Bone Disease in HIV

http://www.shef.ac.uk/FRAX/tool.jsp?country=9

IDSA Guidelines. McComsey et al., CID 2010; 51(8):937–946
## FRAX Score Calculation

Please answer the questions below to calculate the ten year probability of fracture with BMD.

**Questionnaire:**

1. Age (between 40-90 years) or Date of birth
   - Age: 64
   - Date of birth: Y 1948 M 03 D 31

2. Sex
   - Male

3. Weight (kg)
   - 58.97

4. Height (cm)
   - 172.72

5. Previous fracture
   - No

6. Parent fractured hip
   - No

7. Current smoking
   - No

8. Glucocorticoids
   - No

9. Rheumatoid arthritis
   - No

10. Secondary osteoporosis
    - No

11. Alcohol 3 or more units per day
    - No

12. Femoral neck BMD (g/cm²)
    - Select DXA
    - 0.632

**Weight Conversion**

- Pounds ➔ kg
  - 130

**Height Conversion**

- Inches ➔ cm
  - 68

**BMI**

- 19.8

**The ten year probability of fracture (%)**

- Without BMD
  - Major osteoporotic: 5.9
  - Hip fracture: 1.6

**Country:** US (Caucasian)

[http://www.shef.ac.uk/FRAX/tool.jsp?country=9](http://www.shef.ac.uk/FRAX/tool.jsp?country=9)
Work-up of HIV patient with osteoporosis: Secondary causes

- Most common secondary causes in women: premenopausal estrogen deficiency and glucocorticoid exposure; accounting for 35%-40% of cases.

- Most common secondary causes in men: vitamin D deficiency, hypogonadism, alcoholism, and glucocorticoid use; together account for 40%-60% of cases.
  - Meds: Steroids, PPIs, SSRI, HAART, hormonal agents

- Labs to order: CBC, BMP, Testosterone, +/- TSH, 25-OH-D, PTH, urine and serum phosphorus if on TDF.

- Management of secondary causes if found; consider referral to endocrinology.
Biphosphonates in the Management of Osteoporosis in HIV

- 82 HIV patients (71% men, 77% white), median age: 48 years; Lumbar spine t-score <2.1

McComsey AIDS. 2007 Nov 30;21(18):2473-82.
IDSA Guidelines. McComsey et al., CID 2010; 51(8):937–946
Management of Osteoporosis

- **Calcium**: All patients with osteopenia or osteoporosis
  - RDA: 1,000 – 1,200 mg/d; Preferred: Ca Carbonate (with food)
  - 300 mg in: yogurt (6 oz), milk (8 oz), fortified OJ (8 oz), cheese (large slice), spinach (1 cup).
  - Calcium carbonate not well absorbed with PPIs (use citrate)

- **Additional vitamin D if baseline 25-OH vit D <30**
  - IOM 2010; RDA: 600 IU/d (<70 y); 800 IU/d (>70 y)
  - Endo Society (pts at risk): 1,500 – 2000 IU/d

- **Bisphosphonates**
  - Osteoporosis or history of osteoporotic fracture
  - FRAX score: 10-year risk of major fracture is >20% or risk of hip fracture is >3%
FRAX not yet validated in HIV; BMD and FRAX underestimate fracture risk in DM

Schwartz. JAMA 2011;305(21):2184-2192
Wrap-Up: HIV-infected patient establishing care

- Recognize increased risk of osteoporosis and fracture risk in aging HIV population
- Identify predictors of decreased BMD and fracture in HIV patients
- Evaluate HIV-infected patient’s fracture risk
- Use best practices to manage fracture risk in HIV-infected patient
Case Studies in HIV and Bone Disorders

ACTHIV 2012: A State-of-the-Science Conference for Frontline Health Professionals