Current HIV Treatment Issues in the US: Managing Long-Term Non-AIDS Co-Morbidities

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Texas-Oklahoma AIDS Education and Training Center

El Paso, Texas, USA
Outline

• Non-AIDS comorbidities and premature aging
• Comorbidities:
  – Cardiovascular disease
  – Liver disease
  – Renal disease
  – Osteoporosis
• Prevention / treatment of premature aging
Increased Rates of Non-AIDS Comorbidities

Being seen in **TREATED** HIV+ patients

- Cardiovascular disease
- Cancer (non-AIDS)
- Osteoporosis
- Liver disease
- Renal disease
- Neurocognitive disorders
- Metabolic disorders: diabetes, dyslipidemias

**The same as in** **OLDER** HIV+ patients
↑ Comorbidities & Premature Aging
Even After Adjusting for Age, HAART Exposure & Traditional Risk Factors

Adapted from Deeks, RWCA Clinical Update 2009
Rising Number of Adults Aged ≥50 Living With HIV in the US

• In 2005, persons aged ≥50 accounted for
  – 15% of new HIV/AIDS diagnoses
  – 24% of persons living with HIV/AIDS
    • Increased from 17% in 2001
  – 29% of persons living with AIDS
  – 35% of all deaths of persons with AIDS

• Projections indicate that by 2015, older adults will constitute 50% of persons living with HIV/AIDS

• This increase has resulted in part from:
  – The availability of effective ART and
  – From newly diagnosed infections in older adults

Elevated Inflammatory Markers in Treated HIV-Infected Patients

Even after adjusting for demographics and CV risk factors

Participants 45-76 years of age

hsCRP, IL-6, D-dimer, Cystatin-C

# Immune Dysfunction: Lower CD4 Count and Non-AIDS Complications

<table>
<thead>
<tr>
<th>Study</th>
<th>Non-AIDS malignancies</th>
<th>Renal disease/death</th>
<th>CVD events/death</th>
<th>Liver disease/death</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIRST</td>
<td>Yes</td>
<td>Yes</td>
<td>Trend, NS</td>
<td>No</td>
</tr>
<tr>
<td>D:A:D</td>
<td>Yes</td>
<td>Yes</td>
<td>Trend, NS</td>
<td>Yes</td>
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<tr>
<td>CASCADE</td>
<td>Yes</td>
<td>NA</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>SMART</td>
<td>Trend, NS</td>
<td>Trend, NS</td>
<td>Trend, NS</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Low CD4 On-Therapy Predicts Risk of AIDS & Non-AIDS Events (D:A:D)

Relative Risk

CD4+ Cells/mm³

Outline

- Non-AIDS comorbidities and premature aging
- Comorbidities:
  - Cardiovascular disease
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  - Osteoporosis
- Prevention / treatment of premature aging
Increased Risk of Cardiac Events With Increasing Years of PI Exposure

D:A:D Study Group: ↑ Risk independent of other risk factors

<table>
<thead>
<tr>
<th>Exposure (yr)</th>
<th>Protease Inhibitors</th>
<th>Total</th>
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<tbody>
<tr>
<td></td>
<td>No. of events</td>
<td>No. of person-yr</td>
</tr>
<tr>
<td>0</td>
<td>33</td>
<td>21,623</td>
</tr>
<tr>
<td>&lt;1</td>
<td>21</td>
<td>8410</td>
</tr>
<tr>
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<td>33</td>
<td>10,947</td>
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<td>2-3</td>
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<td>3-4</td>
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<td>13,742</td>
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<td>4-5</td>
<td>57</td>
<td>10,734</td>
</tr>
<tr>
<td>5-6</td>
<td>33</td>
<td>7576</td>
</tr>
<tr>
<td>&gt;6</td>
<td>47</td>
<td>7821</td>
</tr>
<tr>
<td></td>
<td>345</td>
<td>94,469</td>
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</table>

<table>
<thead>
<tr>
<th>Exposure (yr)</th>
<th>Nonnucleoside Reverse-Transcriptase Inhibitors</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>No. of events</td>
<td>No. of person-yr</td>
</tr>
<tr>
<td>0</td>
<td>136</td>
<td>42,013</td>
</tr>
<tr>
<td>&lt;1</td>
<td>59</td>
<td>15,866</td>
</tr>
<tr>
<td>1-2</td>
<td>42</td>
<td>13,476</td>
</tr>
<tr>
<td>2-3</td>
<td>47</td>
<td>10,204</td>
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<tr>
<td>3-4</td>
<td>37</td>
<td>6739</td>
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<tr>
<td>4-5</td>
<td>24</td>
<td>6172</td>
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<tr>
<td></td>
<td>345</td>
<td>94,469</td>
</tr>
</tbody>
</table>

Friis-Moller N et al. NEJM 2007;326:1723-1735
Inconsistent Results: From major studies on CVD risk in HIV-infected and HAART-treated patients

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Event</th>
<th>ARV</th>
<th>Effect</th>
<th>Traditional risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA</td>
<td>36,766</td>
<td>R</td>
<td>1,207 CHD</td>
<td>HAART or PI</td>
<td>No</td>
</tr>
<tr>
<td>HOPS</td>
<td>1807</td>
<td>P</td>
<td>84 CV events</td>
<td>Specific ARVs</td>
<td>No</td>
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<tr>
<td>SMART</td>
<td>5472</td>
<td>P</td>
<td>63 CHD</td>
<td>Intermittent HAART</td>
<td>No – stopping therapy led to complication</td>
</tr>
<tr>
<td>Kaiser</td>
<td>4408</td>
<td>R</td>
<td>86 MI</td>
<td>PIs</td>
<td>Risk of HIV+ vs. HIV- No risk on PI</td>
</tr>
<tr>
<td>Medi-Cal</td>
<td>28,513</td>
<td>R</td>
<td>NA</td>
<td>ART</td>
<td>Risk with ART in 18–33 year olds</td>
</tr>
<tr>
<td>DAD</td>
<td>23,490</td>
<td>P</td>
<td>345 MI</td>
<td>cART and PI</td>
<td>Yes</td>
</tr>
<tr>
<td>French</td>
<td>34,976</td>
<td>R</td>
<td>49 MI</td>
<td>PI</td>
<td>Yes</td>
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<tr>
<td>Johns Hopkins</td>
<td>2671</td>
<td>Case control</td>
<td>43 CHD</td>
<td>HIV+ vs. HIV-</td>
<td>Yes</td>
</tr>
<tr>
<td>Frankfurt</td>
<td>4993</td>
<td>R</td>
<td>29 MI</td>
<td>HAART</td>
<td>Yes</td>
</tr>
</tbody>
</table>

2. Friis-Møller N, 13th CROI, Denver 2006, #144
6. Moore RD, 10th CROI, Boston 2003, #132
8. Lichtenstein K, 13th CROI, Denver 2006, #735
Factors Affecting Risk for CVD in Patients With HIV

- Genetic Influences
- Dyslipidemia
- Diabetes
- Body Fat Redistribution
- Antiretroviral Therapy
- HIV Infection

Possible Non-Cholesterol Causes of CVD Risk With Protease Inhibitor Therapy in HIV

- Endothelial dysfunction
- Increased endothelial permeability
- Insulin resistance
- Accelerated lipid accumulation in vessel wall
- Inflammation
- Impaired response to vascular injury
- Increased oxidative stress
- Lipoatrophy / reduced adiponectin

M/ Dube, AAHIVM-AHA CVD Conference Chicago June 2007
FRAM 2 cIMT Study: HIV Infection is an Independent Risk for Atherosclerosis

- Cross-sectional study
- Evidence of pre-clinical atherosclerosis
  Internal cIMT (mm)

<table>
<thead>
<tr>
<th>HIV+ (n=433)</th>
<th>Controls (n=5479)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.17</td>
<td>1.06</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>

- After adjusting for demographics and CVD risk factors, HIV infection has more atherosclerosis than controls
  - Difference 0.15 mm (P = .0001)
- HIV infection similar to traditional CV risk factors

### Multivariable Analysis of Associated Factors

<table>
<thead>
<tr>
<th>Estimated Effect of</th>
<th>Difference in Internal cIMT (mm)a</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV infection</td>
<td>0.15</td>
</tr>
<tr>
<td>Current smoker</td>
<td>0.17</td>
</tr>
<tr>
<td>Past smoker</td>
<td>0.09</td>
</tr>
<tr>
<td>Age (per 10 yr)</td>
<td>0.16</td>
</tr>
<tr>
<td>Maleb</td>
<td>0.13</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.12</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>0.05</td>
</tr>
</tbody>
</table>

aP <.001 for all values.
bSignificant gender interaction (women > men).

“Independent association of HIV infection with atherosclerosis should be taken into account when counseling HIV-infected patients with regard to their CVD risk factors.”

Grunfeld C, et al. 16th CROI; 2009; Montreal. Abstract #146.
Framingham CVD Risk Score

• To estimate 10-year Risk of Developing Myocardial Infarction or Coronary Death
• For adults ≥ aged 20 years who do not have heart disease or diabetes
• Score based on the factors listed below
  • ↑Age
  • Gender
  • ↑Total Cholesterol
  • ↓HDL Cholesterol
  • Smoker
  • ↑Systolic Blood Pressure
  • On medication to treat high BP

Framingham Risk Score: Underestimates CVD Risk in HIV+ Patients

Observed and Predicted MI Rates According to ART Exposure (D:A:D Study)

- Observed rates
- Best estimate of predicted rates

Duration of ART Exposure (Years)

Rates per 1000 Person-Years

Outline

- Non-AIDS comorbidities and premature aging
  - Comorbidities:
    - Cardiovascular disease
    - Liver disease
    - Renal disease
    - Osteoporosis
  - Prevention / treatment of premature aging
HIV/HBV Coinfection Increases the Risk of ESLD

- **Multicenter AIDS Cohort Study**
  - 4967 HBsAg-negative MSM
    - HIV: 47% (n=2346)
  - 326 HBsAg-positive
    - HIV: 65% (n=213)

- **HIV/HBV coinfection**
  - 19-fold-higher risk of liver death than HBV monoinfection
  - Risk of liver-related mortality increased with
    - Alcohol consumption
    - Low nadir CD4+ cell counts
    - Antiretroviral therapy

Liver Mortality by HIV and HBV Status

- No HIV or HBV: 0.0
- HBV Only: 0.8
- HIV Only: 1.7
- HIV/HBV: 14.2

*P value is for HIV/HBV vs HBV only and HIV only.

### DHHS Recommendations For Treatment of HBV/HIV Coinfected Patients

<table>
<thead>
<tr>
<th>Infection(s)</th>
<th>Treatment Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV and not HBV</td>
<td>TDF/FTC or TDF + 3TC considered first choice NRTI backbones</td>
</tr>
<tr>
<td></td>
<td><em>Caveat: Use of 3TC, FTC, or TDF as the only active anti-HBV agent should be avoided because of the risk of HBV resistance</em></td>
</tr>
<tr>
<td>HIV and HBV</td>
<td>TDF/FTC or TDF + 3TC considered first-choice NRTI backbones (activity against both viruses) OR</td>
</tr>
<tr>
<td></td>
<td>ETC (entecavir) with 1 NRTI above</td>
</tr>
<tr>
<td></td>
<td><em>Caveat: Use of 3TC, FTC, or TDF as the only active anti-HBV agent should be avoided because of the risk of HBV resistance</em></td>
</tr>
<tr>
<td>HBV and not HIV</td>
<td>Peg-IFN-α (does not lead to development of drug-resistant HIV or HBV mutants) or ADV (with risk of HIV mutants)</td>
</tr>
<tr>
<td></td>
<td>Avoid FTC, 3TC, TDF and ETC w/o full HAART regimen to prevent rapid development of drug-resistant HIV mutations</td>
</tr>
</tbody>
</table>

Hepatitis C Infection in HIV+ Increased Morbidity & Mortality

- HIV worsens HCV disease:
  - Persistent HCV viremia without viral clearance
  - ↑ End-stage-liver-disease (fibrosis & cirrhosis)
  - ↑ Hepatocellular carcinoma
  - Accelerated fibrosis: ~20 vs 30 yrs
  - Higher inflammatory grade (vs HCV alone)
  - More extra-hepatic manifestations

- HCV worsens HIV disease:
  - ↑ Liver toxicity from HIV ARV medications
  - Accelerates HIV disease progression
Hepatitis C Morbidity & Mortality
Hospitalizations & Death in HAART Era

• New England Medical Center in Boston, Mass.
• HIV-related deaths:

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ESLD:</td>
<td>13.9%</td>
<td>11.5%</td>
<td>50 %</td>
</tr>
<tr>
<td>HCV+:</td>
<td>58 %</td>
<td>93.8%</td>
<td></td>
</tr>
</tbody>
</table>

DHHS Recommendations For Treatment of HCV/HIV Coinfected Patients

- Evaluate all coinfected patients for HCV therapy
- Treat of HCV according to standard guidelines
  - At CD4 < 200 consider deferring HCV treatment until some immune reconstitution achieved with HAART (to improve HCV response)
  - At higher CD4 consider deferring HAART until after HCV treatment due to pill burden, drug toxicities and drug interactions
  - Try to treat HCV medication side effects rather than dose reduce in order to maximize HCV response rates
- Use concurrent ARV therapy with caution
  - Monitor ARVs for potential hepatotoxicity
  - Avoid AZT with ribavirin due to increased anemia

HCV Associated with Blunted CD4 Gains During HAART

Non-AIDS comorbidities and premature aging

Comorbidities:
- Cardiovascular disease
- Liver disease
- Renal disease
- Osteoporosis

Prevention / treatment of premature aging
Epidemiology of CKD in US
≥20 Years of Age

16.8% of Americans have CKD
• White, non-hispanic 16.1%
• Black, non-hispanic 19.9%
• Mexican-American 18.7%

*GFR measurement in mL/min/1.73 m²; MMWR, 2007;56:161-165.; NHANES 1999-2004
## Risk Factors Contributing to Development of Kidney Disease

<table>
<thead>
<tr>
<th>Modifiable risk factors</th>
<th>Non-modifiable risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Diabetes mellitus</td>
<td>• Age</td>
</tr>
<tr>
<td>• High blood pressure</td>
<td>• Trauma or accident</td>
</tr>
<tr>
<td>• Overuse of painkillers</td>
<td>• Family history of kidney disease</td>
</tr>
<tr>
<td>• Allergic reactions to medications (eg, antibiotics)</td>
<td>• Presence of other diseases</td>
</tr>
<tr>
<td>• Drug abuse</td>
<td>– HIV/AIDS, hepatitis C, lupus, sickle cell anemia, cancer, and congestive heart failure</td>
</tr>
<tr>
<td>• Kidney stones</td>
<td></td>
</tr>
<tr>
<td>• Inflammation (eg, glomerulonephritis)</td>
<td></td>
</tr>
</tbody>
</table>
Johns Hopkins HIV Clinical Cohort: CKD in HIV-Infected Patients by Race (1990-2004)

Lucas G et al. 15th CROI; 2008; Boston. Abstract 972.

Number at risk

<table>
<thead>
<tr>
<th></th>
<th>White</th>
<th>African American</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 months</td>
<td>924</td>
<td>3261</td>
</tr>
<tr>
<td>24 months</td>
<td>819</td>
<td>2949</td>
</tr>
<tr>
<td>36 months</td>
<td>696</td>
<td>2464</td>
</tr>
<tr>
<td>48 months</td>
<td>565</td>
<td>2031</td>
</tr>
<tr>
<td></td>
<td>464</td>
<td>1629</td>
</tr>
</tbody>
</table>

HR 1.9, 95% CI (1.2-2.8)  
\( P = .002 \), log rank test
Swiss HIV Cohort: TDF Associated With Increased Risk for Proximal Renal Tubulopathy (PRT)

- Cross-sectional analysis of Swiss HIV Cohort Study (N = 1202)
- PRT = pathological status of ≥ 3 of the following 4 measures: fractional excretion (FE) of phosphate or uric acid, protein/creatinine ratio in urine, euglycemic glucosuria
- Incidence of PRT highest in patients receiving TDF plus a PI (vs no TDF, no PI): OR: 7.1 (95% CI: 2.5-19.8; P < .001)

Johns Hopkins HIV Clinical Cohort: TDF Renal Safety

Kaplan-Meier Plot of GFR Decline >25% and >50% From Baseline Value

Multivariate Associations With 25% GFR Decline

<table>
<thead>
<tr>
<th></th>
<th>Hazard Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>TDF vs NRTI use</td>
<td>1.04</td>
<td>0.68, 1.59</td>
</tr>
<tr>
<td>Black race</td>
<td>1.52</td>
<td>0.85, 2.72</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.56</td>
<td>1.00, 2.45</td>
</tr>
<tr>
<td>PI (ritonavir-boosted)</td>
<td>2.14</td>
<td>1.37, 3.34</td>
</tr>
<tr>
<td>Age &gt;45 years</td>
<td>2.31</td>
<td>1.44, 3.69</td>
</tr>
<tr>
<td>CD4 &lt;200 (baseline)</td>
<td>2.66</td>
<td>1.65, 4.29</td>
</tr>
</tbody>
</table>

Outline

• Non-AIDS comorbidities and premature aging
• Comorbidities:
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  – Liver disease
  – Renal disease
  – Osteoporosis
• Prevention / treatment of premature aging
BMD Decreases With Age

Relative influence on peak bone mass (men):
• 40% to 83% genetic
• 27% to 60% environmental

0.5% to 1.0% reduction in bone volume/year

Many Potential Contributors to Decreased BMD in HIV-infected Patients

- HIV infection
- Liver disease
- Premature menopause
- Hypogonadism
- Smoking

- Decreased bone acquisition
- Fat deposition in marrow
- Decreased Physical Activity
- Decreased muscle mass
- Decreased fat mass
- Malnutrition

- Nucleoside analogs/mitochondrial dysfunction
- Protease inhibitors
- Other medications (e.g. corticosteroids, anticonvulsants)
- Alcohol use

- Family history
- Female sex
- Increasing age

Glesby M et al. CID supplement September 2003.
Meta-Analysis of BMD Changes in HIV+ Patients

### HIV+ Patients

- **Reduced BMD:**
  - Prevalence: 67%
  - Risk: 6.4x

- **Osteoporosis:**
  - Prevalence: 15%
  - Risk: 6.4x

<table>
<thead>
<tr>
<th>Publication</th>
<th>% reduced BMD</th>
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<tbody>
<tr>
<td><strong>HIV+</strong></td>
<td></td>
</tr>
<tr>
<td>Amiel et al 2004</td>
<td>82.5</td>
</tr>
<tr>
<td>Brown et al 2004</td>
<td>63</td>
</tr>
<tr>
<td>Bruera et al 2003</td>
<td>64.8</td>
</tr>
<tr>
<td>Dolan et al 2004</td>
<td>63</td>
</tr>
<tr>
<td>Huang et al 2002</td>
<td>66.6</td>
</tr>
<tr>
<td>Knobel et al 2001</td>
<td>87.5</td>
</tr>
<tr>
<td>Loiseau-Peres et al 2002</td>
<td>68</td>
</tr>
<tr>
<td>Madeddu et al 2004</td>
<td>59.3</td>
</tr>
<tr>
<td>Tebas et al 2000</td>
<td>40</td>
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<tr>
<td>Teichman et al 2003</td>
<td>76</td>
</tr>
<tr>
<td>Yin et al 2005</td>
<td>77.4</td>
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<table>
<thead>
<tr>
<th><strong>HIV–</strong></th>
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<tbody>
<tr>
<td></td>
<td>35.8</td>
</tr>
<tr>
<td>Brown et al 2004</td>
<td>32</td>
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<tr>
<td>Bruera et al 2003</td>
<td>13</td>
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<td>Dolan et al 2004</td>
<td>35</td>
</tr>
<tr>
<td>Huang et al 2002</td>
<td>11</td>
</tr>
<tr>
<td>Knobel et al 2001</td>
<td>30</td>
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<tr>
<td>Loiseau-Peres et al 2002</td>
<td>34</td>
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<tr>
<td>Madeddu et al 2004</td>
<td>7.8</td>
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<tr>
<td>Tebas et al 2000</td>
<td>29</td>
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<tr>
<td>Teichman et al 2003</td>
<td>4</td>
</tr>
<tr>
<td>Yin et al 2005</td>
<td>56</td>
</tr>
</tbody>
</table>

Fracture Prevalence is Associated with HIV Infection: Boston Data Base

1996-2008: N = 8,525 HIV-positive / 2,208,792 HIV-negative

Women

Men

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\[ P=0.0002 \] (overall comparison)

\[ P=0.0001 \] (overall comparison)

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\(^a\) Clinical care data registry from the Partners HealthCare System: Brigham Women’s Hospital and Massachusetts General Hospital. Triant, VA et al. *JCEM*. 2008;93:3499-504.
Vitamin D Deficiency Associated With Race, Low CD4+ Nadir, and EFV Use

- Cross-sectional study conducted in London cohort in 2008
  - Levels of vitamin D, 25(OH)D, measured in consecutive adult pts
  - **35% had severe vitamin D deficiency; only 9% had optimal levels**

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>All Pts (N = 1077)</th>
<th>Pts on HAART (n = 845)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Black race</td>
<td>3.4 (2.5-4.7)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Winter season</td>
<td>2.2 (1.6-2.9)</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>CD4+ cell count nadir &lt; 200 cells/mm³</td>
<td>1.40 (1.03-1.80)</td>
<td>.03</td>
</tr>
<tr>
<td>Current HAART</td>
<td>1.7 (1.2-2.3)</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>EFV</td>
<td></td>
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<tr>
<td>PIs</td>
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</tr>
</tbody>
</table>

Vitamin D Levels and the Effects of Supplementation in HIV+ Patients

Bisphosphonates Improve BMD in HIV Patients with Osteopenia/Osteoporosis

- Percent change in lumbar BMD, N=31 HIV+ patients on HAART
- Treatment: alendronate 70mg weekly + Calcium + Vitamin D

Outline

• Non-AIDS comorbidities and premature aging
• Comorbidities:
  – Cardiovascular disease
  – Liver disease
  – Renal disease
  – Osteoporosis
• Prevention / treatment of premature aging
Prevention / Treatment of Accelerated “Aging”

• Earlier HIV diagnosis and HAART treatment
• Treat co-infections (↓ additional inflammation)
  – Hepatitis C, STDs, etc.
• Consider PI-based HAART regimens
• Consider addition of anti-inflammatory therapy
  – Aspirin & statins
• Consider immune-based therapies
  – CCR5 inhibitors
  – HAART intensification
  – Interleukins, growth hormone
Failure to Achieve Normal CD4 Levels Based on Low CD4 Nadir

~40% failure of CD4 normalization in patients with CD4 nadir <200

Low CD4 Nadir at Treatment Initiation: Reduced Life Expectancy

<table>
<thead>
<tr>
<th>CD4 Nadir at Start of HAART</th>
<th>&lt;100</th>
<th>100-200</th>
<th>&gt;200</th>
</tr>
</thead>
<tbody>
<tr>
<td>Life Expectancy, years (from age 20)</td>
<td>32</td>
<td>42</td>
<td>50</td>
</tr>
</tbody>
</table>

10-30 years less life expectancy in modern HAART era

Need for Earlier Diagnosis: Pervasive Low CD4 at Start of HAART

2003-2005, 42 countries, 176 sites, n=33,008.

Overall Conclusions

- Virologic suppression and immune restoration remain the most important goals of HIV disease management.

- With increasing longevity of HIV-infected patients, focus is shifting toward whole health patient care:
  - Management of age-related comorbidities is critical in order to optimize long-term outcomes.

- Comprehensive initial laboratory assessment and patient workup ensure that the patient receives the best care.
New Paradigm of HIV Treatment

Untreated HIV:
↑ Inflammatory bio-markers = associated with disease progression, worse with low CD4 nadirs at start of HAART

HIV Treatment:
- CVD
- CKD
- Osteoporosis
- Diabetes
- Dyslipidemia
- Lipodystrophy

Chronic Inflammation
Antiretroviral Sequelae