MANAGING COMORBID DISEASE IN HIV-INFECTED PATIENTS IN AFRICA IN 2014. Diabetes, Hypertension, Cholesterol.

Dr Dave Spencer Head Infectious Diseases
Helen Joseph Hospital Johannesburg South Africa
The diagnosis of type 2 diabetes:

- a glycated hemoglobin value of 6.5% or more
- a fasting plasma glucose level of 126 mg/dL (7.0 mmol/L) or more
  or a
- 2-hour plasma glucose level of 200 mg/dL (11.1 mmol/L) or more
during an oral glucose tolerance test.

American Diabetes Association
Approximately 3 (14%) million Africans over the age of 50 years are living with HIV infection

Negin J, Cumming RG. HIV infection in older adults in sub-Saharan Africa: extrapolating prevalence from existing data. *Bull World Health Organ* 2010; 88: 1847-53

CONSERVATIVE PROJECTIONS FOR THE SUB-SAHARAN REGION IN 2030 PREDICT THAT 18.65 MILLION PEOPLE WILL HAVE DIABETES. THE MAJORITY WILL HAVE TYPE II DM AND WILL BE OVERWEIGHT/OBESE

The projected growth of type II DM in sub-Saharan Africa between the years 2010 and 2030 is 98%.

Impaired glucose tolerance in the region is expected to rise by 75.8% from 26.9 million in 2010 to 47.3 million in 2030.

Figure. Prevalence of diabetes mellitus and impaired glucose tolerance in community surveys in Africa. *1998 WHO criteria
### Reported prevalence of Type II DM in Africa:

<table>
<thead>
<tr>
<th>COUNTRY</th>
<th>PREVALENCE</th>
<th>SOUTH AFRICA URBAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benin</td>
<td>3%</td>
<td>Investigator</td>
</tr>
<tr>
<td>Mauritania</td>
<td>6%</td>
<td>DM</td>
</tr>
<tr>
<td>Cameroon</td>
<td>6.1%</td>
<td>GTT impaired</td>
</tr>
<tr>
<td>Congo</td>
<td>7.1%</td>
<td>Omar (1993)</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>10.2%</td>
<td>5.3%</td>
</tr>
<tr>
<td>DRC</td>
<td>14.5%</td>
<td>Levitt (1993)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mollentze (1995)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mollentze: peri-urban (1995)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.8%</td>
</tr>
</tbody>
</table>

Figure. Trends in age-standardised mean fasting plasma glucose (FPG) by region between 1980 and 2008 for (A) men and (B) women.

Figure. Trends in Age-standardised diabetes prevalence by region between 1980 and 2008 for (A) men and (B) women.

Figure. Percentage growth in age-standardised diabetes prevalence, 1980–2008, by region. Data from reference 2; percentage change calculated by fitting linear model to all 29 annual age-standardised (WHO World Population) prevalence values from 1980 to 2008 for each region; diabetes defined by current American Diabetes Association definition.

Tobias M. Global control of diabetes: information for action. Lancet 2011; 378: 3-4
Swiss HIV Cohort Study

DESCRIPTION:

Prospective cohort-study, clinic based. Started in 1988

N=6681 patients with at least 2 follow-up visits over at least 1 year

N=123 newly diagnosed patients with diabetes while in the clinic viz. 4.42 cases per 1000 PYFU (95% CI, 3.71-5.28)

Current exposure to NRTI therapy, NRTI+PI combination therapy or NRTI+PI+NNRTI combination therapy increased the risk of developing DM in the univariable model with IRRs of 2.22 (1.11-4.45), 2.48 (1.42-4.31) and 3.25 (1.59-6.67) respectively.

Figure. Incidence rate ratios (IRRS) for the development of new-onset type 2 diabetes mellitus (DM) based on 123 events among 6513 participants with 27,798 person-years of follow-up. Shown are associations with current receipt of specific drug classes and individual protease inhibitor (PI) and nucleoside or nucleotide reverse transcriptase inhibitor (NRTI) combinations.
<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>ADVERSE METABOLIC EFFECT</th>
<th>IMPACT ON CORONARY HEART DISEASE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PROTEASE INHIBITOR</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LOPINAVIR/r</td>
<td>Dyslipidemia+++; insulin resistance++</td>
<td>Cumulative exposure= an independent risk for MI</td>
</tr>
<tr>
<td>ATAZANAVIR/r</td>
<td>Dyslipidemia+; insulin resistance+</td>
<td>No data available: insufficient patients (numbers) exposed</td>
</tr>
<tr>
<td>DARUNAVIR/r</td>
<td>Dyslipidemia+; insulin resistance+</td>
<td>No data available: insufficient patients exposed</td>
</tr>
<tr>
<td>RITONAVIR</td>
<td>Dyslipidemia+++; insulin resistance+++</td>
<td>This drug is never used on its own i.e. a used as a pharmacological ‘booster’.</td>
</tr>
<tr>
<td>SAQUINAVIR</td>
<td>Dyslipidemia+; insulin resistance+</td>
<td>No associated risk for MI</td>
</tr>
<tr>
<td>INDINAVIR</td>
<td>Dyslipidemia and insulin resistance+++</td>
<td>Controversial results</td>
</tr>
<tr>
<td>AMPRENAVIR/r</td>
<td>Dyslipidemia+; insulin resistance+</td>
<td>No data available: insufficient numbers exposed</td>
</tr>
<tr>
<td>TIPRANAVIR/r</td>
<td>Dyslipidemia++; insulin resistance+</td>
<td>No data available: insufficient numbers exposed</td>
</tr>
<tr>
<td>NELFINAVIR</td>
<td>Dyslipidemia+; insulin resistance+</td>
<td>No associated risk for MI</td>
</tr>
</tbody>
</table>

**Main classes of Antiretrovirals and Their Impact on Lipid and Glucose Metabolism and Coronary Heart Disease.** + weak effect; ++ moderate effect; +++ important effect

<table>
<thead>
<tr>
<th>DRUG CLASS</th>
<th>ADVERSE METABOLIC EFFECT</th>
<th>IMPACT ON CORONARY HEART DISEASE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NUCLEOTIDE/SIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIs)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NRTIs</td>
<td>Insulin resistance+: stavudine&gt;zidovudine; dyslipidemia with didanosine and stavudine</td>
<td>Two NRTIs viz. abacavir and didanosine have been associated with an increased risk for MI but results ‘controversial’</td>
</tr>
<tr>
<td><strong>NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIs)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NNRTIs</td>
<td>Dyslipidemia variable with different members of this class: efavirenz but to a lesser degree than the PIs; nevirapine = a mild dyslipidemia but with increased HDL cholesterol</td>
<td>No association with an increased risk for MI</td>
</tr>
<tr>
<td><strong>INTEGRASE INHIBITORS (RALTEGRAVIR) and CCR5 CO-RECEPTOR INHIBITOR (MARAVIROC)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No adverse metabolic effects reported</td>
<td>No data available: insufficient numbers exposed</td>
</tr>
</tbody>
</table>

**Main classes of Antiretrovirals and Their Impact on Lipid and Glucose Metabolism and Coronary Heart Disease.**  
+ weak effect; ++ moderate effect; +++ important effect

HIV and Coronary Heart Disease.  
*JACC* 2013; 61: 511-23
LIFESTYLE MODIFICATION

Weight loss/diet:
Balanced diet rich in grains and legumes, <7% saturated fat and reduced trans fats + limited calories + foods with a high glycemic index

Exercise:
150 minutes of moderate-intensity aerobic exercise per week

Ismail-Beigi F. Glycemic Management of Type 2 Diabetes Mellitus. 
Figure. Increasing complexity of the drug management of diabetes mellitus over time.

<table>
<thead>
<tr>
<th>Oral drugs approved for treatment of hyperglycemia in type 2 diabetes.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Second-generation sulfonylureas:</strong> Gilbenclamide; Gliclazide; Glimeriride; Glipizide</td>
</tr>
<tr>
<td><strong>Biguanide:</strong> Metformin</td>
</tr>
<tr>
<td><strong>Peroxisome proliferator-activated receptor γ agonists:</strong> Thiazolidinediones: Pioglitazone; Rosiglitazone</td>
</tr>
<tr>
<td><strong>α-Glucosidase inhibitors:</strong> Acarbose; Miglitol; Voglibose</td>
</tr>
<tr>
<td><strong>DPP4 inhibitors:</strong> Alogliptin; Linagliptin; Saxagliptin; Sitagliptin; Vildagliptin</td>
</tr>
<tr>
<td><strong>SGLT2 inhibitors:</strong> Canagliflozin; Dapagliflozin</td>
</tr>
<tr>
<td><strong>Glinides:</strong> Nateglinide; Repaglinide</td>
</tr>
<tr>
<td><strong>Bile-acid-binding resins:</strong> Colesevelam</td>
</tr>
<tr>
<td><strong>Dopamine-receptor agonists:</strong> Bromocriptine</td>
</tr>
</tbody>
</table>
Key areas to be addressed if diabetes is to be tackled in sub-Saharan Africa as identified by the International Insulin Foundation.

- Organisation of the health system
  - Prevention
  - Data collection
  - Diagnostic tools and infrastructure
  - Drug procurement and supply
- Accessibility and affordability of medicines and care
  - Training and availability of health-care workers
  - Adherence issues
  - Patient education and empowerment
- Community involvement and diabetes associations
  - Positive policy environment

Beran D, Yudkin JS. Diabetes care in sub-Saharan Africa. *Lancet* 2006; 368: 1689-95
Table. Present level of preparedness of human resources to ensure quality primary care for HIV, hypertension and diabetes at 24 health facilities in northwestern Tanzania, among 335 health-care workers by health facility level.

<table>
<thead>
<tr>
<th></th>
<th>Hospitals (n=176)</th>
<th>Health centres (n=92)</th>
<th>Dispensaries (n= 67)</th>
<th>P value</th>
<th>Total</th>
<th>P value vs HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>At least fair knowledge</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td>134 (76%)</td>
<td>74 (08%)</td>
<td>53 (79%)</td>
<td>0.67</td>
<td>261 (78%)</td>
<td>“</td>
</tr>
<tr>
<td>HTN</td>
<td>108 (61%)</td>
<td>57 (62%)</td>
<td>33 (49%)</td>
<td>0.52</td>
<td>198 (59%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>DM</td>
<td>109 (62%)</td>
<td>42 (46%)</td>
<td>36 (54%)</td>
<td>0.24</td>
<td>187 (56%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>Experienced</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td>140 (80%)</td>
<td>67 (73%)</td>
<td>30 (45%)</td>
<td>0.01</td>
<td>237 (71%)</td>
<td>“</td>
</tr>
<tr>
<td>HTN</td>
<td>101 (57%)</td>
<td>19 (21%)</td>
<td>14 (21%)</td>
<td>0.001</td>
<td>134 (40%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>DM</td>
<td>96 (55%)</td>
<td>6 (7%)</td>
<td>7 (10%)</td>
<td>&lt;.0001</td>
<td>109 (33%)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>Comfortable</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td>26 (15%)</td>
<td>13 (14%)</td>
<td>13 (19%)</td>
<td>0.78</td>
<td>52 (16%)</td>
<td>“</td>
</tr>
<tr>
<td>HTN</td>
<td>17 (10%)</td>
<td>8 (9%)</td>
<td>9 (13%)</td>
<td>0.84</td>
<td>34 (10%)</td>
<td>0.01</td>
</tr>
<tr>
<td>DM</td>
<td>14 (8%)</td>
<td>10 (11%)</td>
<td>8 (12%)</td>
<td>0.78</td>
<td>32 (10%)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

HYPERTENSION. HIV. AFRICA

Study population:
N = 4162 confirmed with cardiovascular disease

N = 1593 (38%) newly diagnosed
N = 2569 (62%) previously diagnosed and on treatment
N = 74 (5%) HIV-positive

Cohort drawn from consecutive referrals to the cardiac unit at the CHBH in Soweto from Jan.1-Dec 31, 2006

N = 45 400 in-patients in the Department of Medicine of the CHBH in 2006

1593 new cases of cardiac disease

897 HTN (56%)
310 lone HTN

310 cases
19% [95%CI 17-21]

844 CCF (53%)
296 dilated CMO (35%)
281 HTN heart failure (33%)
225 R heart failure (27%)
77 ischemic CMO (9%)
67 valvular heart failure (8%)

704 cases
44% [95% CI 42-47]

360 valvular heart dis/dysfunctn (23%)
208 rheumatic (58%)
103 functional (29%)
78 degenerative (22%)

268 cases
17% [95% CI 15-19]

165 coronary artery disease (10%)
28 CAD without risk factors (17%)

165 cases
10% [95% CI 8-12]

146 other diagnoses (9%)
67 pericardial effusn. (46%)
25 cardiac arrhythmia (17%)
22 congenital HD (15%)
16 stroke (11%)

146 cases
9% [95% CI 8-11]
Almost half of those patients diagnosed with hypertension in the absence of clinical heart disease were obese.

That black African women were most likely to be obese both in this hospital cohort and in the general Sowetan community, is noteworthy in view of the male dominance and older age of similar cohorts in developed countries.

### THE HEART OF SOWETO STUDY (2006)

<table>
<thead>
<tr>
<th>Profile</th>
<th>All (n=1593)</th>
<th>HTN (n=310)</th>
<th>CCF (n=704)</th>
<th>Valve dis (n=268)</th>
<th>CAD (n=165)</th>
<th>Other (n=146)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yr)</strong></td>
<td>52.8 (17.1)</td>
<td>58.3 (15.3)</td>
<td>55.1 (16.2)</td>
<td>45.7 (18.2)</td>
<td>56.7 (12.4)</td>
<td>38.0 (16.6)</td>
</tr>
<tr>
<td><strong>Black African</strong></td>
<td>1359 (85%)</td>
<td>265 (86%)</td>
<td>640 (91%)</td>
<td>243 (91%)</td>
<td>77 (47%)</td>
<td>134 (92%)</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td>939 (59%)</td>
<td>199 (64%)</td>
<td>409 (58%)</td>
<td>179 (67%)</td>
<td>68 (41%)</td>
<td>84 (58%)</td>
</tr>
<tr>
<td><strong>High cholesterol</strong></td>
<td>159 (22%)</td>
<td>54 (38%)</td>
<td>45 (17%)</td>
<td>16 (21%)</td>
<td>37 (35%)</td>
<td>7 (20%)</td>
</tr>
<tr>
<td><strong>Smoker</strong></td>
<td>661 (41%)</td>
<td>112 (36%)</td>
<td>327 (46%)</td>
<td>84 (31%)</td>
<td>84 (51%)</td>
<td>54 (37%)</td>
</tr>
<tr>
<td><strong>Renal dysf.</strong></td>
<td>115 (10%)</td>
<td>23 (10%)</td>
<td>51 (10%)</td>
<td>20 (8%)</td>
<td>16 (11%)</td>
<td>5 (5%)</td>
</tr>
<tr>
<td><strong>Anemia</strong></td>
<td>156 (13%)</td>
<td>30 (12%)</td>
<td>64 (11%)</td>
<td>22 (12%)</td>
<td>7 (6%)</td>
<td>33 (28%)</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>165 (10%)</td>
<td>41 (13%)</td>
<td>66 (9%)</td>
<td>13 (5%)</td>
<td>35 (21%)</td>
<td>10 (7%)</td>
</tr>
<tr>
<td><strong>HIV+ve</strong></td>
<td>74 (5%)</td>
<td>4 (1%)</td>
<td>35 (5%)</td>
<td>10 (4%)</td>
<td>2 (1%)</td>
<td>23 (16%)</td>
</tr>
<tr>
<td><strong>NYHA Class III/IV</strong></td>
<td>486 (31%)</td>
<td>84 (27%)</td>
<td>255 (36%)</td>
<td>63 (24%)</td>
<td>32 (19%)</td>
<td>52 (36%)</td>
</tr>
</tbody>
</table>

* HIV test = only “if clinically indicated and consent given”

Methods:

Prospective study of HTN over 24 months on ART

ART-naïve adults April 2004-2011 n=17 378 patients

Patients with HTN at ART-initiation excluded:
  n = 5002 (28.8%) of 17 378 clinic patients

HTN defn.: systolic BP> 140 and/or diastolic BP>90mmHg
  and characterized as mild (140-159.9/90-99.9)
  or moderate/severe (≥160/≥100)

### PREDICTORS OF HYPERTENSION IN HIV-POSITIVE ADULTS OVER 24 MONTHS ON ART IN SOUTH AFRICA

<table>
<thead>
<tr>
<th>Age</th>
<th>HR for HTN at 24m [95%CI]</th>
<th>HR for mild HTN at 24m [95%CI]</th>
<th>HR for mod/severe HTN at 24m [95%CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49.9y</td>
<td>1.6 [1.4-1.7]</td>
<td>1.5 [1.4-1.7]</td>
<td>1.7 [1.2-2.3]</td>
</tr>
<tr>
<td>≥50y</td>
<td>2.5 [2.2-2.9]</td>
<td>2.3 [2.0-2.6]</td>
<td>4.3 [3.1-6.0]</td>
</tr>
<tr>
<td>BMI at ART start</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25-29.9</td>
<td>1.5 [1.3-1.7]</td>
<td>1.5 [1.3-1.7]</td>
<td>1.6 [1.2-2.3]</td>
</tr>
<tr>
<td>30-34.9</td>
<td>1.8 [1.5-2.2]</td>
<td>1.8 [1.5-2.2]</td>
<td>1.9 [1.1-3.3]</td>
</tr>
</tbody>
</table>

No correlation with other variables viz. initiating ART, sex, CD4 count, HB and WHO Stage at initiation of ART,

PREDICTORS OF HYPERTENSION IN HIV-POSITIVE ADULTS OVER 24 MONTHS ON ART IN SOUTH AFRICA

OUTCOME:

20% of patients in this cohort (n = 12,376 patients) developed HTN over 24 months while taking ART.

Obese patients and those older than 40 years should be targeted for frequent BP monitoring and for identification of additional cardiac risk factors.

CLINICAL OUTCOME in patients with OBESITY or HYPERTENSION IN A SOUTH AFRICAN HIV-POSITIVE COHORT

Methods:

Prospective cohort study
ART naïve adults starting ART April 2004-2009
Cox regression re. mortality and loss to follow-up among patients with obesity and HTN

Total patients  n = 9693
Female n = 6095 (62.9%)
Age median (IQR) = 36yr (31.2-42.5)
Baseline CD4 at ART initiation:
CD4 >350  n = 86 (0.9%)
CD4 200-350  n = 816 (8.4%)
CD4 101-200  n = 3427 (35.4%)
CD4 51-100  n = 2078 (21.4%)
CD4 ≤50  n = 3286 (33.9)
RESULTS:

DEATH

BMI > 30 HR 1.8
[1.3-2.6 95% CI]
at 12m
HR 1.3 [1.0-1.8 95% CI]
at 48m

Mod/severe HTN at ART initiation:
HR 1.4 [1.0-2.1 95% CI]
at 48m

LOSS TO FOLLOW-UP

BMI > 30 HR 0.6
[0.4-0.9 95% CI]
at 12m
HR 0.7 [0.6-0.9 95% CI]
at 48m

CD4 RESPONSE

Increase of CD4 cells at 12 and 48m in those with BMI ≥ 30 level*

- 8.6 cells at 12m [-7.3-24.5 95% CI]
- 40.7 cells at 48m [-12.4- 93.8]

*92% initiated on d4T+3TC+EFV

Brennan AT, Fox MP, Maskew M, Sanne I, et al. Obesity or Hypertension at ART Initiation and Outcomes Among HIV Patients in South Africa. CROI Boston, February 2014, Poster #803
BY 48M, 1001 (10%) OF PATIENTS HAD DIED and 2069 (21%) were lost to follow-up

Patients with a BMI>30 = increased mortality over 48m on ART but lower LTFU and an improved CD4 cell recovery

Patients with a moderate or severe hypertension had a slight increase in mortality (40%) but no relationship with LTFU, CD4 response or having a detectable viral load

Brennan AT, Fox MP, Maskew M, Sanne I, et al. Obesity or Hypertension at ART Initiation and Outcomes Among HIV Patients in South Africa. CROI Boston, February 2014, Poster #803
Figure. Estimated decrease in blood pressure mediated by non-pharmacological anti-hypertensive interventions.

Messerli FH, Williams B, Ritz E. Essential hypertension. 
*Lancet* 2007; 370: 591-603
DYSLIDIPEMIA. HIV. AFRICA.
A CROSS-SECTIONAL MULTICENTER STUDY of 173 HIV-infected between ages 14-24 yr all of whom acquired infection sexually.

4 CATEGORIES:

- ART NAÏVE N = 85
- ON NNRTI-BASED ART N = 33
- ON PI-BASED ART N = 36
- ON NON-NNRTI or PI-BASED ART N = 19

GOAL OF THE STUDY:
Determine the nature and prevalence of biochemical changes in lipid and glucose metabolism and body composition in young HIV infected women on and off antiretroviral medication


- TG >130mg/dL
- Total Chol. >200mg/dL
- HDL-C <35mg/dL
- LDL-C >130mg/dL
- Non-HDL-C >160mg/dL
- hsCRP >3mg/L

HIV-negative matched controls, Antiretroviral Therapy Naive, NNRTI-based ART, PI-based ART, Non-NNRTI and Non-PI-based ART

N = 61
N = 85
N = 33
N = 36
N = 19
NEW ACA/AHA GUIDELINES: CHOLESTEROL LEVELS and CARDIOVASCULAR RISK

For primary prevention for those who are currently free of cardiovascular disease, **statin therapy** is recommended for persons with

**total cholesterol levels above 190mg/dL (4.90mmol/l)**

and for those with **diabetes whose LDL cholesterol is 70mg/dL (1.8mmol/l) or higher.**

<table>
<thead>
<tr>
<th>HMG-Co-A Reductase Inhibitor</th>
<th>Antiretroviral Agent:</th>
<th>Dosing Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ATOVASTATIN</strong></td>
<td>All PIs</td>
<td>Use lowest possible starting dose and monitor carefully: rhabdomyolysis</td>
</tr>
</tbody>
</table>

**NNRTIs reduce the atorvastatin, simvastatin and lovastatin blood levels by 40-80%**

- **Efavirenz**: Adjust atorvastatin dose according to lipid response. Don’t exceed max dose.
- **Etravirine**: Adjust dose according to lipid response. Don’t exceed max dose.
- **Nevirapine**: No data but decreased atorvastatin conc. expected. Adjust accord. 2 lipid response.
- **Rilpivirine**: No interaction expected. No dose adjustment necessary.

NB. When using statins with NNRTIs, work up to maximal recommended doses of the statin but do not exceed these doses.

Clinically Relevant Interactions With Concomitant use of HMG Co-A Reductase Inhibitors and Antiretrovirals

## Clinically Relevant Interactions With Concomitant use of HMG Co-A Reductase Inhibitors and Antiretrovirals

<table>
<thead>
<tr>
<th>HMG-Co-A Reductase Inhibitor</th>
<th>Antiretroviral Agent:</th>
<th>Dosing Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simvastatin</td>
<td>PIs</td>
<td>CONTRAINDIATED</td>
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<tr>
<td></td>
<td>NNRTI</td>
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</tr>
<tr>
<td></td>
<td>Efavirenz</td>
<td>Adjust dose of simvastatin according 2 lipid response</td>
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<tr>
<td></td>
<td>Etravirine</td>
<td>Do not exceed maximum recommended dose</td>
</tr>
<tr>
<td></td>
<td>Nevirapine</td>
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<tr>
<td></td>
<td>Rilpivirine</td>
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</tr>
</tbody>
</table>

NNRTIs reduce the atorvastatin, simvastatin and lovastatin blood levels by 40-80%

Where statin concentrations are decreased, use of potent statins such as simvastatin, atorvastatin and rosvuastatin may be more likely to achieve lipid goals.

**Clinically Relevant Interactions With Concomitant use of HMG Co-A Reductase Inhibitors and Antiretrovirals**

**EZETIMIBE**

Drug interactions with the NNRTIs and PIs are not anticipated except for atazanavir.

Ezetimibe is metabolized in the small intestine and liver via glucuronide conjugation and excreted in the bile. Half-life is 22 hours. It does not interfere with cytochrome P450 enzymes. Concomitant use of antacids and cholestyramine will reduce the absorption of ezetimibe.

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**CHOLESTYRAMINE**

No anticipated drug interactions with the NNRTIs, PIs or Integrase inhibitors.

However absorption of drugs from the GIT may be reduced:

monitor carefully.
MANAGEMENT of METABOLIC and related DISORDERS

EXERCISE
Aerobic & Resistance

QUIT SMOKING

DIET and WEIGHT CONTROL

STATINS and FIBRATES
Pravastatin, Atorvastatin, Bezafibrate

ANTIRETROVIRAL ‘SWITCH’ REGIMENS
Avoid thymidine NRTIs and ddI; NVP may be better than EFV; ATV and DRV likely to be better than LPV/r; Raltegravir ‘safe'; maraviroc

MISCELLANEOUS
Growth hormone, Testosterone; Cosmetic surgery and Liposuction

Kamin S, Grinspoon SK. Cardiovascular Disease in HIV-positive patients. AIDS 2005;19:641-52
HIV and the KIDNEY

Recent studies highlight the burden of CKD in sub-Saharan Africa where up to 25% of HIV infected individuals starting ART have decreased eGFRs and 72% have microalbuminuria.

Cross-sectional, observational study of Patients presenting to a Rural Hospital in KZN with Chronic Renal Disease

N=302 patients

Age (mean) = 47y ±SD7y

BMI overweight/obese n=86.4% women; 54.4% men (p<.001)
Dyslipidemia n=47.9% females; 29.2% males (p<.001)
eGFR<30ml/min/1.73m² in 50.6% of cohort

Risk factors associated with eGFR<30 =
HIV: OR 2.4 (1.3-3.4, p=.004)
HTN: OR 2.3 (1.3-4.2, p=.007)

HIV-positive patients in this study were approx. 10 years younger than those presenting with other causes of chronic kidney disease.

HIV age (mean) 39.5±11.9yr vs cohort (mean) 47.1±17.0yr

KWA-ZULU NATAL: Ngwelazana Hospital
Rural South Africa
