# Renal, bone and cardiovascular co-morbidities

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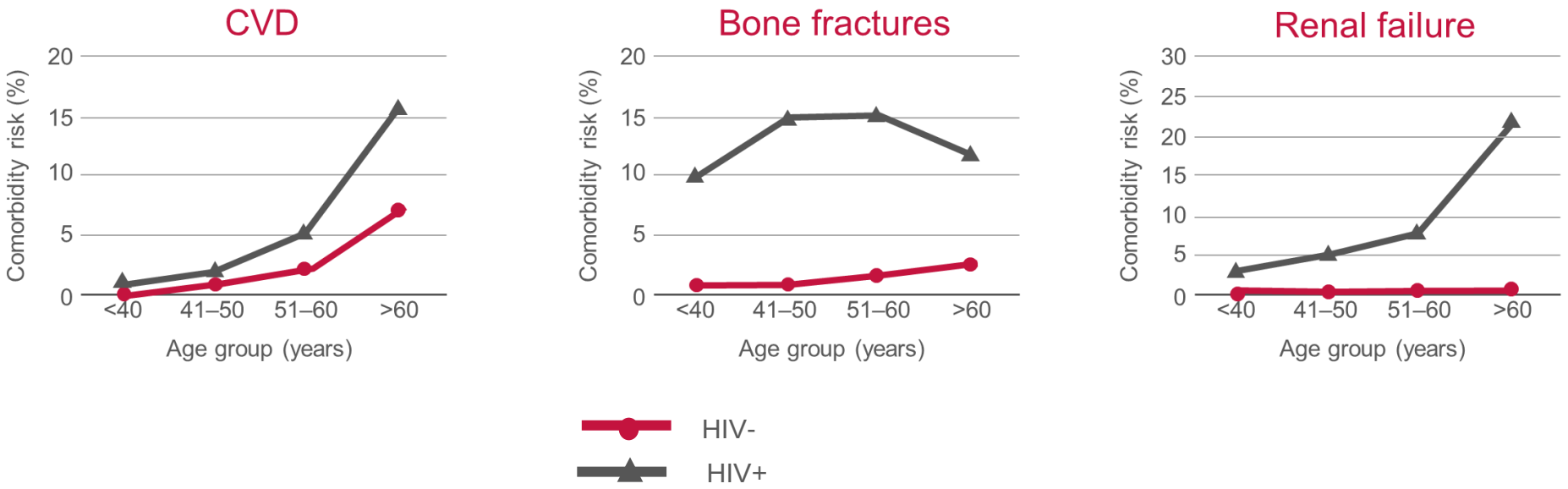
# Management of non-HIV related comorbidities is now a significant area of focus

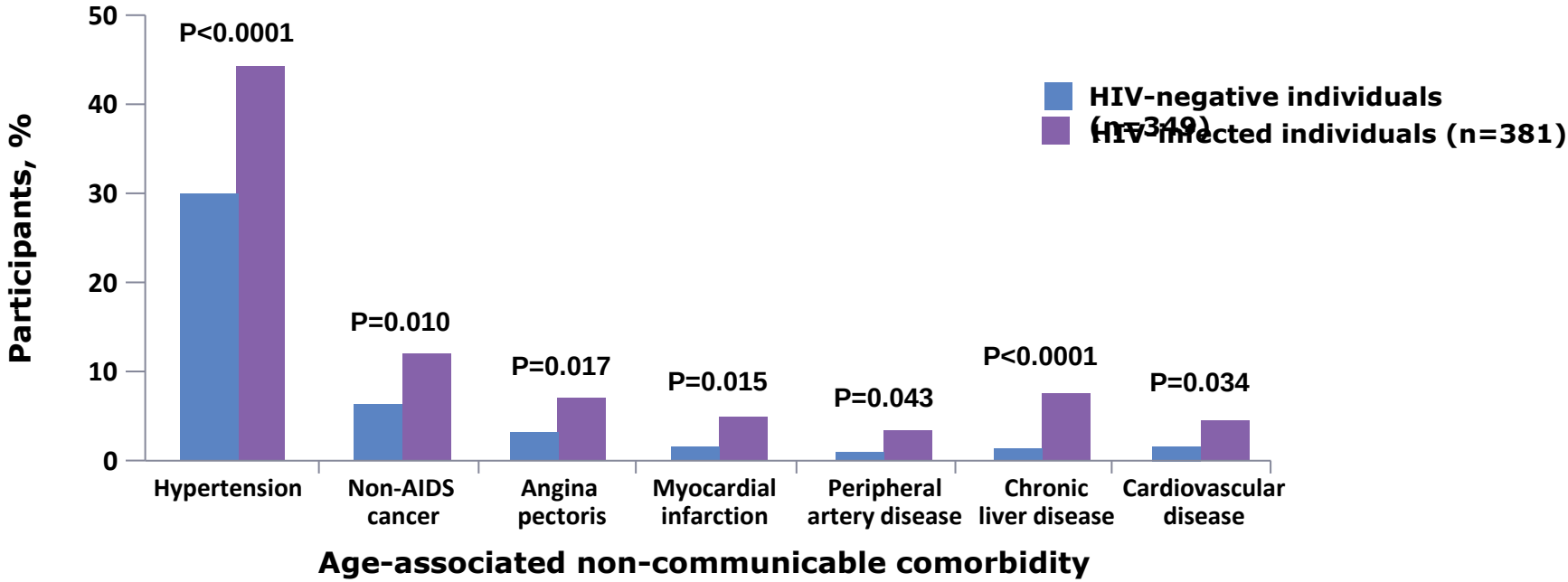



- HIV-infected individuals are more susceptible to developing cardiovascular disease, bone fractures and renal failure than HIV-negative patients[1]
  - In the 41–50-year-old cohort, HIV-infected patients are 24 times more likely to develop renal failure; this increases to 63 times for the >60-year-old cohort [2]
  - Bone fracture risk ranged between 12–16 times more likely for HIV-infected vs HIV-negative in the <40–60-year-old range[2]
- These comorbidities often develop earlier in HIV-infected individuals[1]

1. Adapted from Guaraldi G et al. Clinicoecon Outcomes Res 2013;5:481–488;
2. Guaraldi G et al. Clin Infect Dis 2011;53:1120–1126

# Comorbidities are more prevalent in HIV-infected individuals

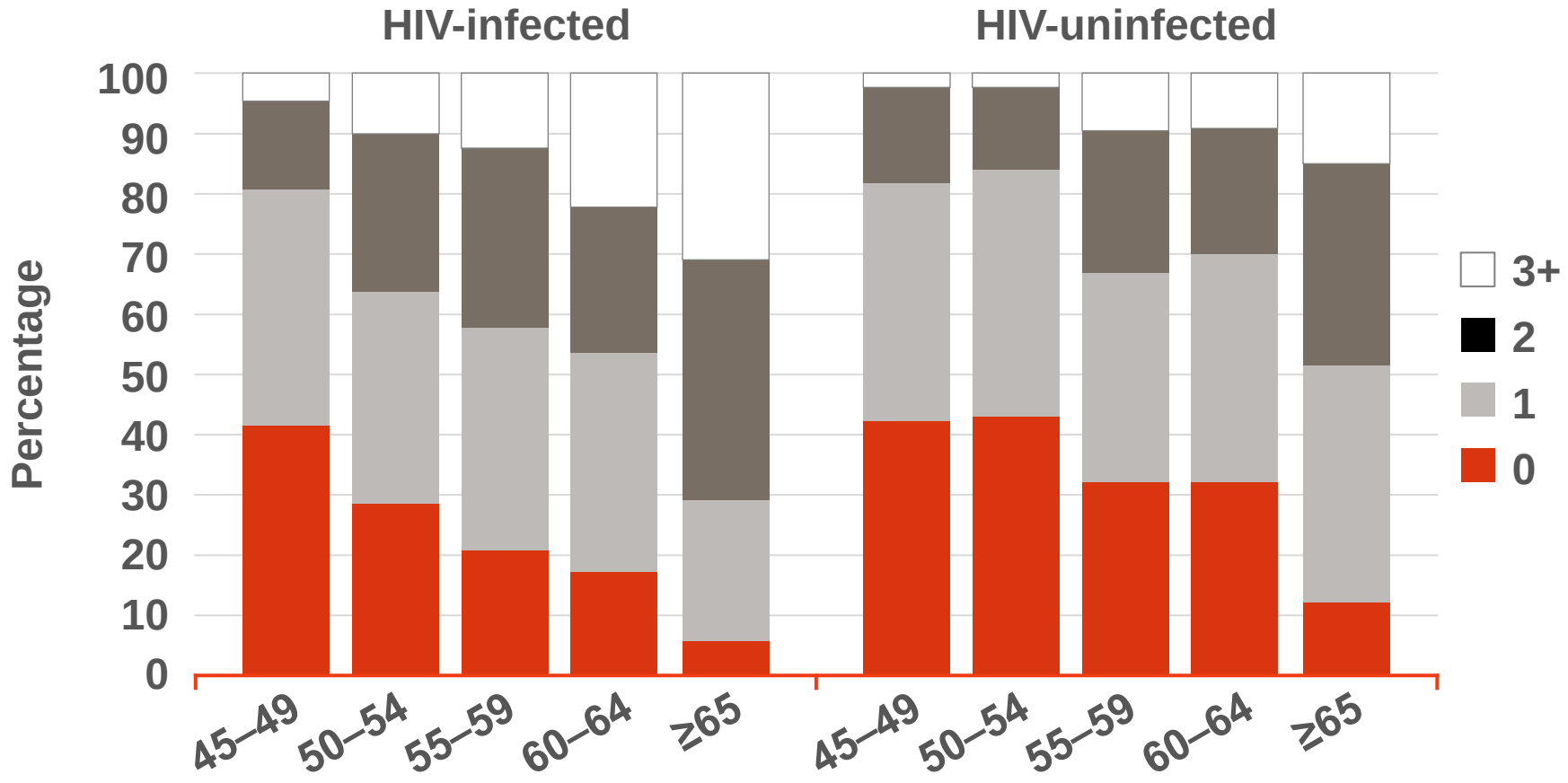
***Subjects ≥45 years with age-associated non-communicable comorbidities, by HIV serostatus (AGEhIV Study, 2010–2012)[2]***




- Similarities between the ageing process and the natural courses of HIV and AIDS suggest that HIV infection may accelerate the onset of comorbidities and frailty[1]
- Duration of ART use (odds ratio 1.24 per 5 additional years of ART use) and lower nadir CD4 count (odds ratio 1.12 per 100 less cells) were associated with an increased risk of a higher number of comorbidities[2]

1. Effros RB et al. Clin Infect Dis 2008;47:542–553; 2. Schouten et al. IAC 2012. Washington, DC. THAB0205

# Increase of comorbidities among ageing HIV-infected individuals

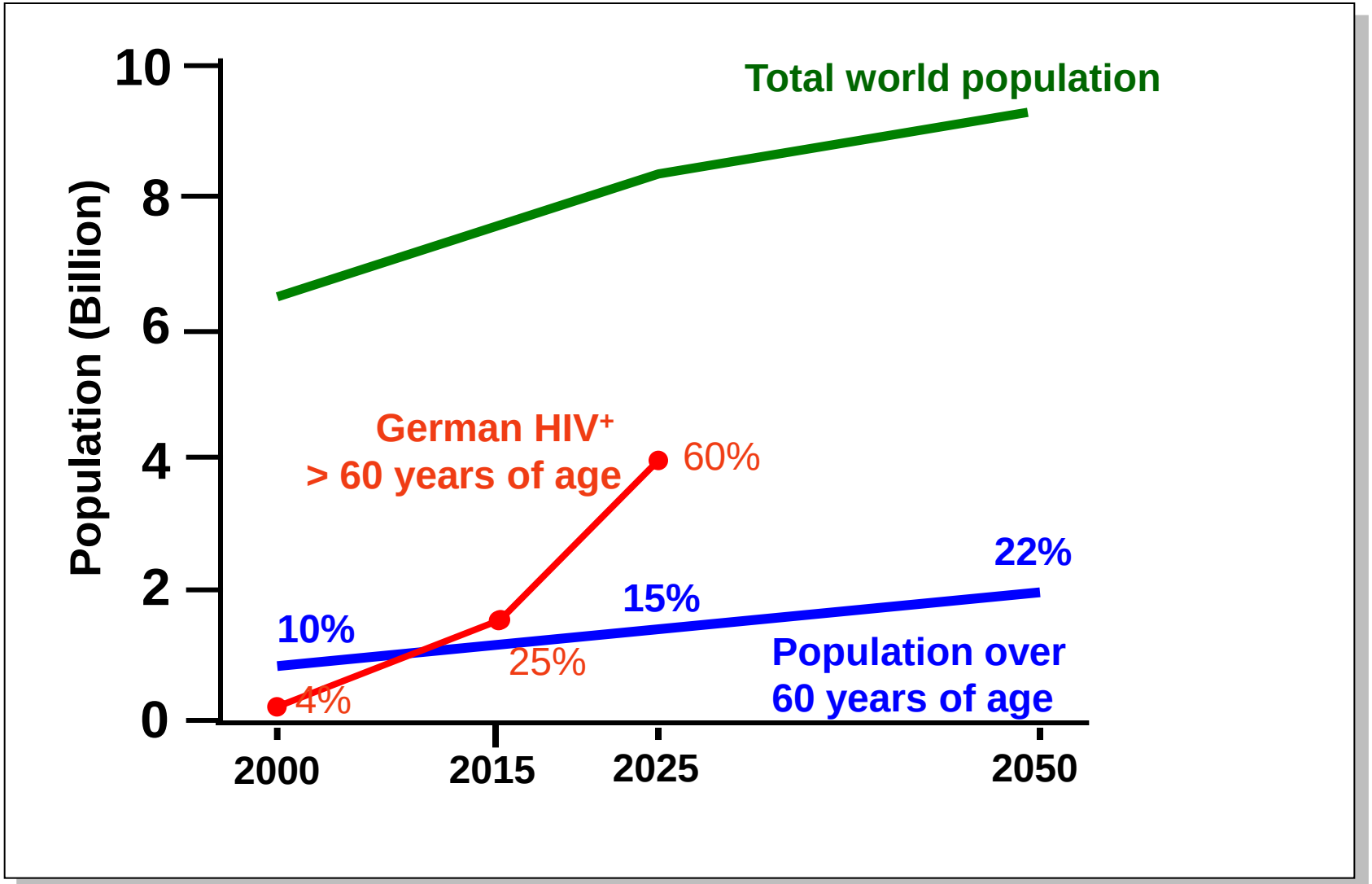



| | 45–49 | 50–54 | 55–59 | 60–64 | ≥65 | 45–49 | 50–54 | 55–59 | 60–64 | ≥65 |
|---|---|---|---|---|---|---|---|---|---|---|
| Mean number of AANCC | 0.83 | 1.18 | 1.34 | 1.52 | 1.96 | 0.79 | 0.75 | 1.11 | 1.08 | 1.51 |
| Number of participants | 184 | 126 | 97 | 58 | 55 | 193 | 130 | 84 | 66 | 41 |

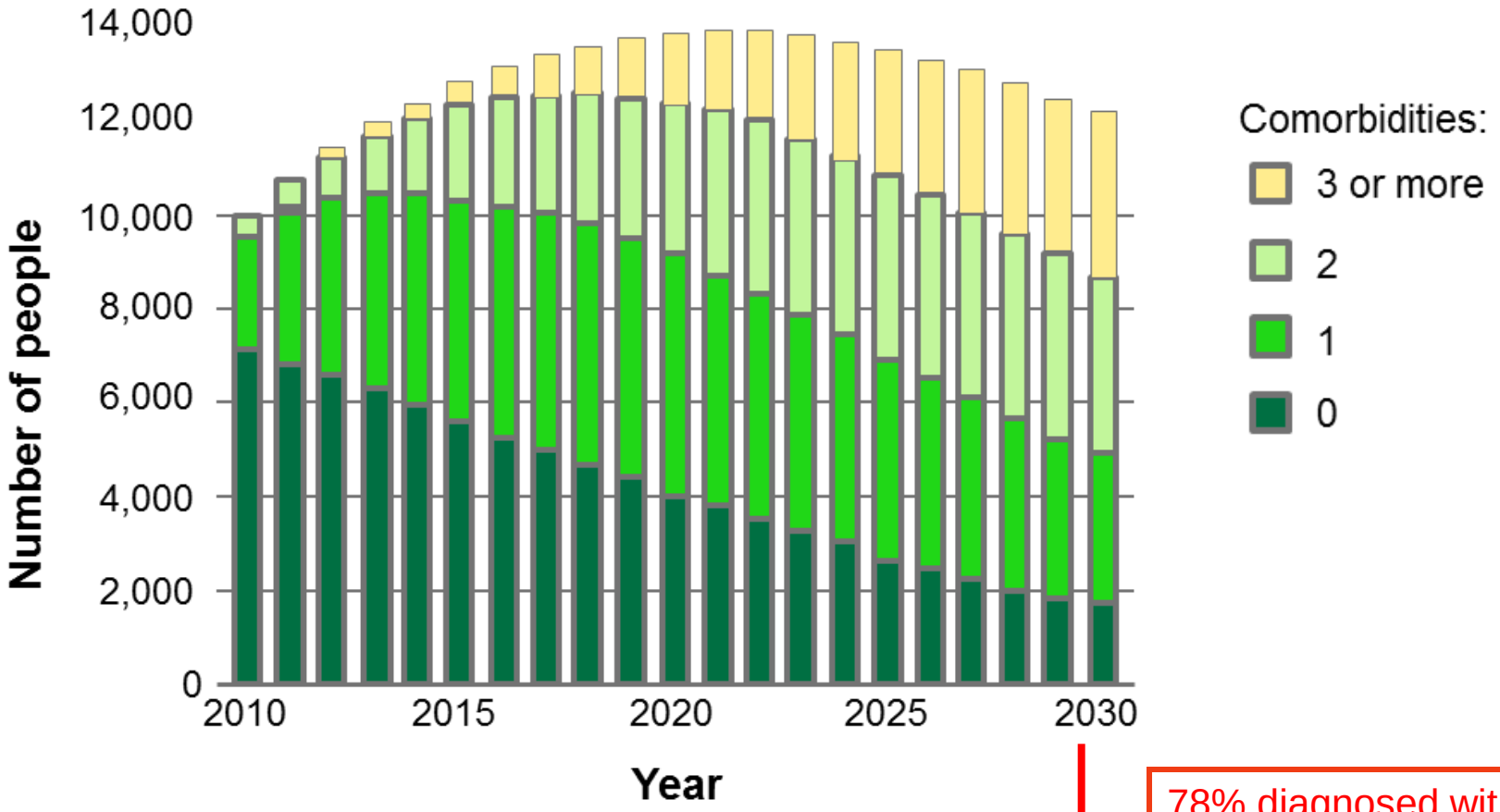
AANCC age-associated non-communicable comorbidity

Schouten J et al. Clin Infect Dis 2014:59:1787–1797

# HIV, ART and Aging: A Rough Estimate



# Predicted burden of NCDs in HIV-infected individuals between 2010 and 2030 as simulated by the model




78% diagnosed with CVD
17% with diabetes
17% with malignancies

NCD, non-communicable disease

Smit M et al. Lancet Infect Dis 2015;15:810–818

# NRTI options are limited and not always guideline recommended

| Treatment considerations | TDF/FTC | ABC/3TC |
|---|---|---|
| *High viral load[1,2] | Acceptable | Caution / Acceptable** |
| High CVD risk[1,2] | Acceptable | Caution |
| Renal impairment[2] | Caution | Acceptable |
| Decrease in BMD[2,3] | Caution | Acceptable |
| HLAB*5701 positive[1,2] | Acceptable | Avoid |

*>100,000 copies/mL; BMD: bone mineral density; CVD: cardiovascular disease
** No viral load restriction for DTG/ABC/3TC use, according to May 2014 DHHS guidelines[2]

1. EACS Guidelines 2013; Available at: http://www.eacsociety.org/Portals/0/Guidelines_Online_131014.pdf (accessed Mar 2014). 2. DHHS Guidelines 2014; Available at: www.aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf (accessed May 2014); 3. Thompson MA, et al. JAMA 2012;308:387–402.

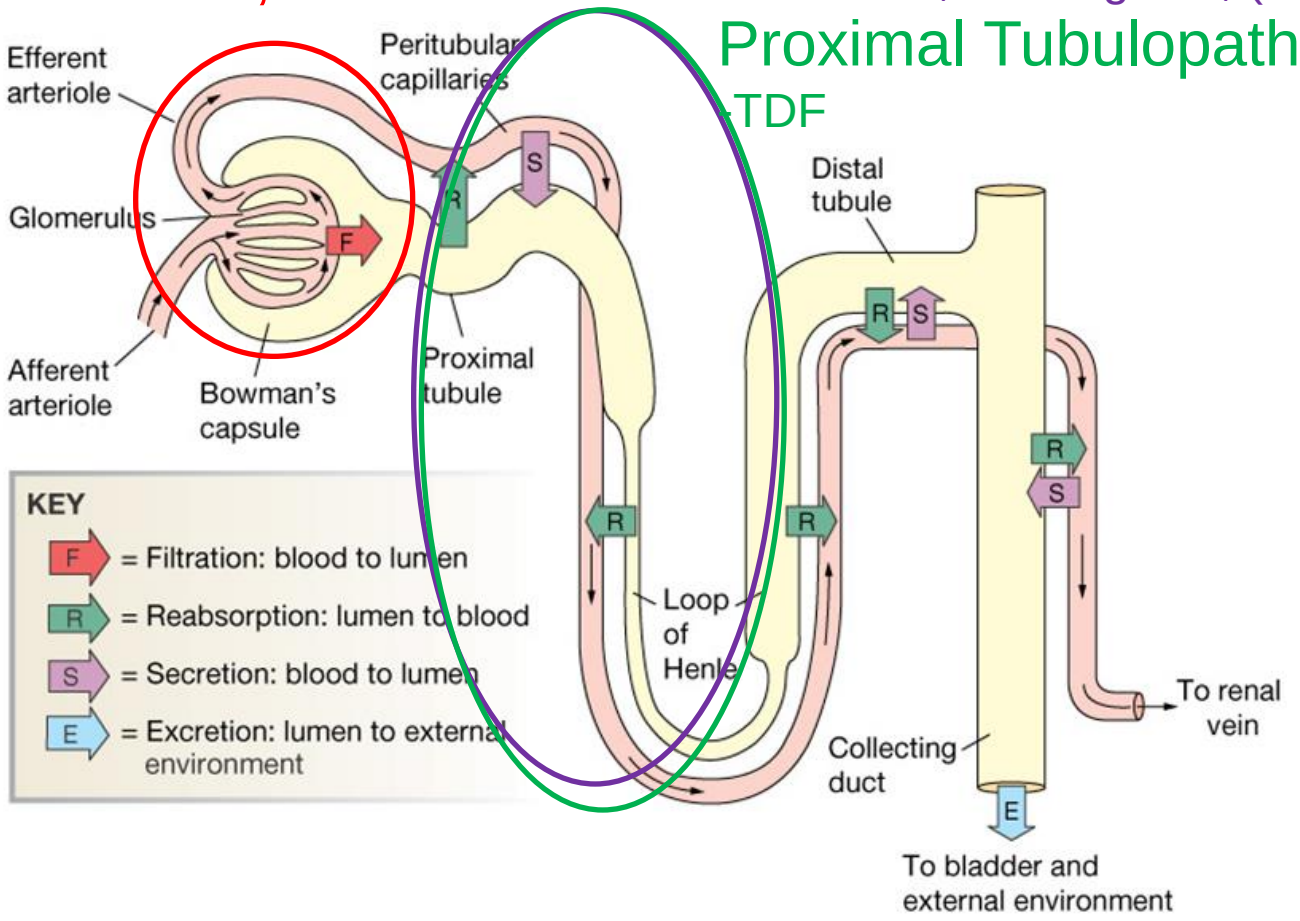
GFR, eGFR

Creatinine Secretion

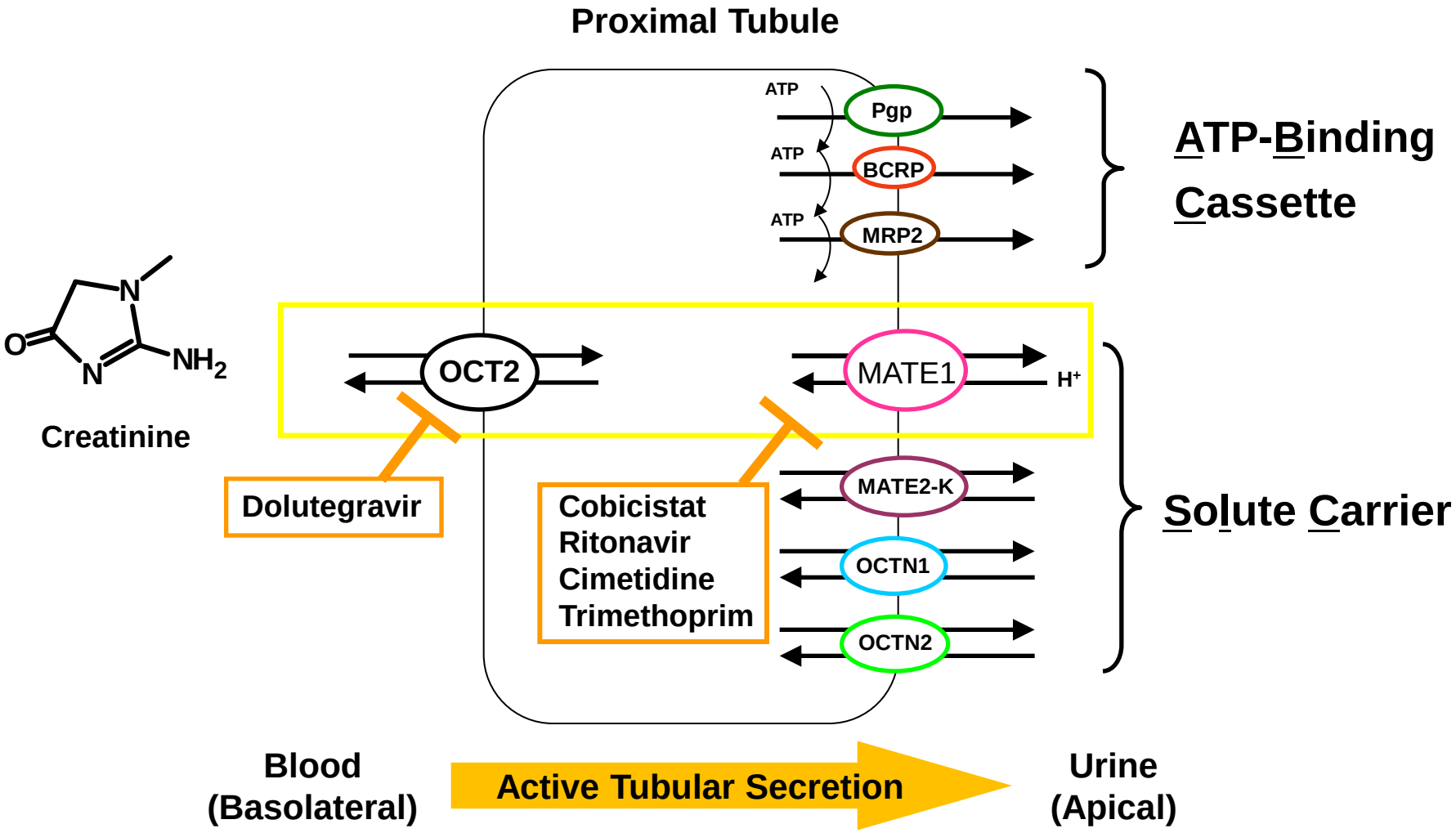
-Cobicistat, Dolutegravir, (TDF)

Proximal Tubulopathy

-TDF



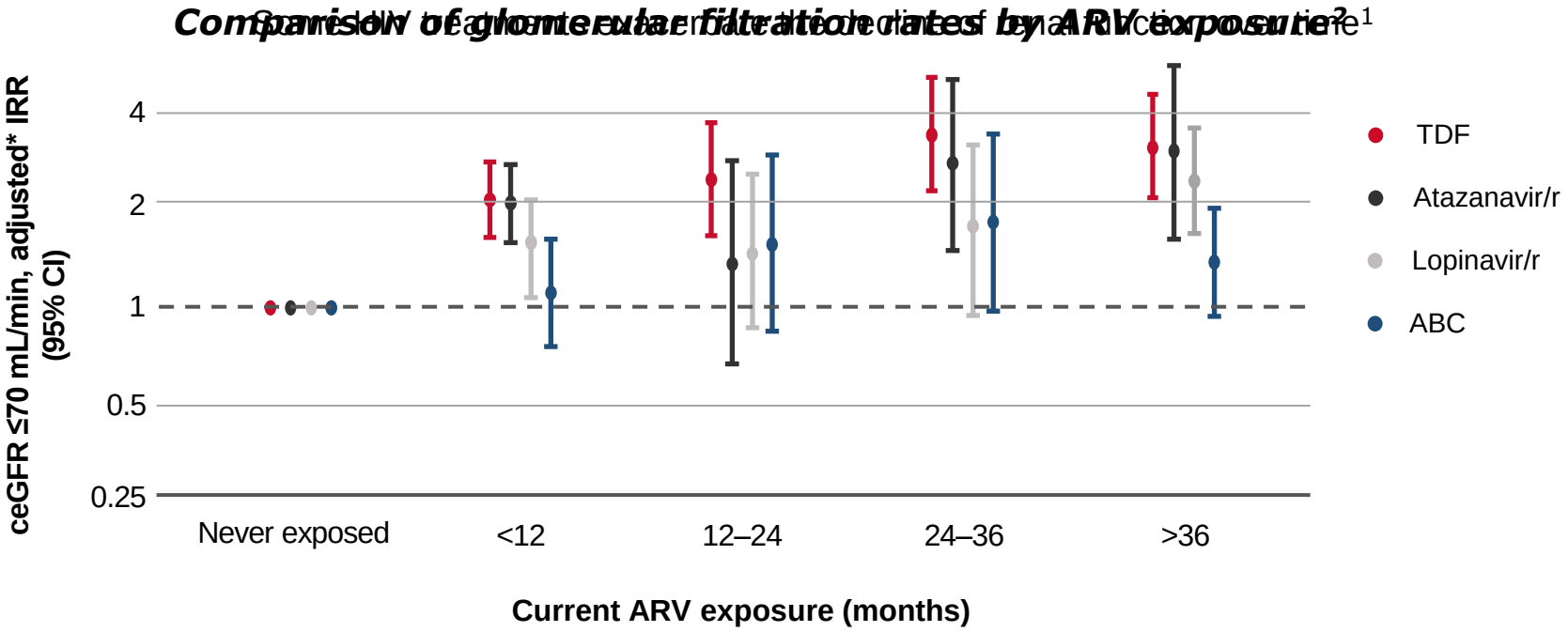
# Inhibition of active creatinine excretion by cation transporters




MATE1, multidrug and toxin extrusion 1; OCT2, organic cation transporter 2.

Lepist E-I, et al. ICAAC 2011; Chicago. #A1-1724.

# The risk of renal complications can be increased by some ARV

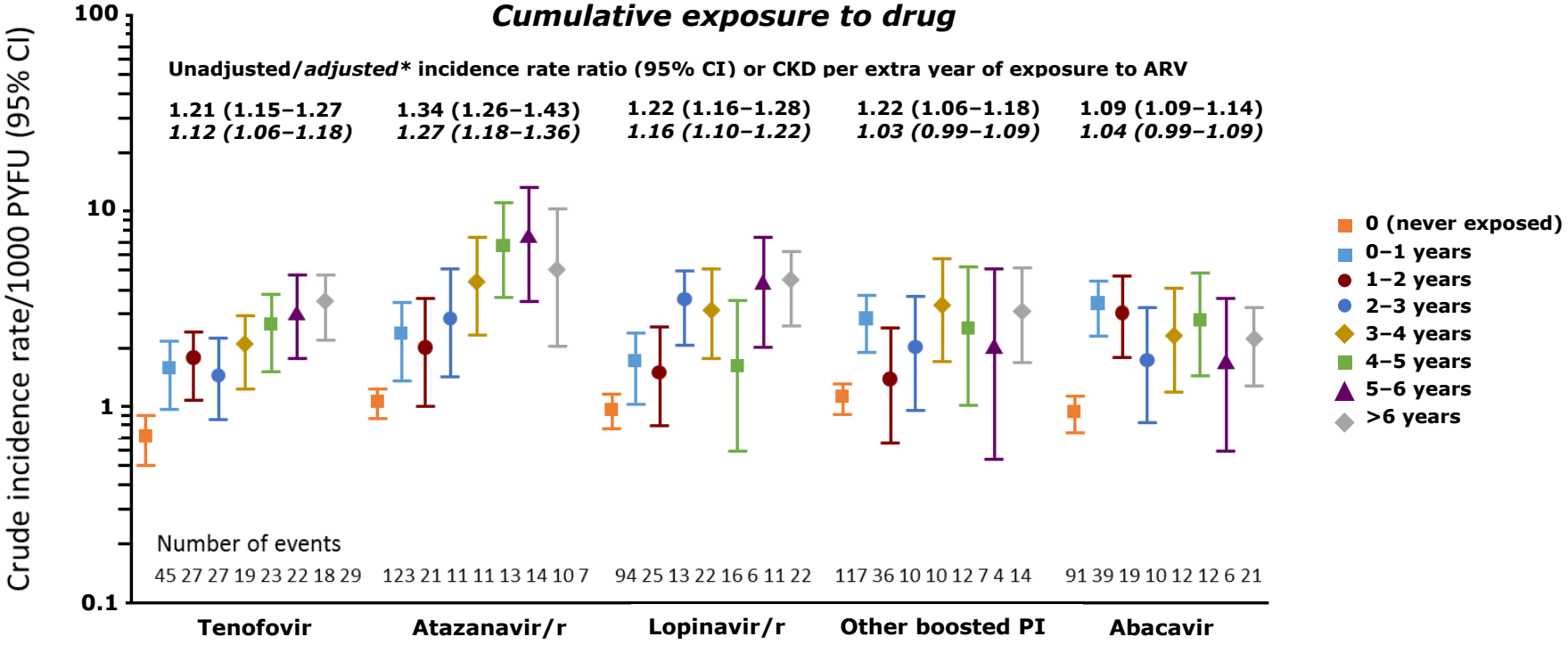



**Adjusted for baseline eGFR, age, gender, race, HIV risk group, enrolment cohort, CD4 nadir, and baseline date. AIDS, HBV/HCV status, smoking status, hypertension, diabetes, CV event, CD4, VL, and cumulative exposure to indinavir, unboosted atazanavir, and other boosted PIs (darunavir, tipranavir, (fos)amprenavir) (included as time-updated variables)**

**1. Nishijima T. et al. 2014 ;28(13):1903-1910; 2. Ryom L, et al. CROI 2012; Seattle, WA, #865**

# Incidence rates of CKD and cumulative exposure to ARVs

*D:A:D study participants were followed from baseline until earliest of CKD, last eGFR, 01 January 2013 or last visit plus 6 months*

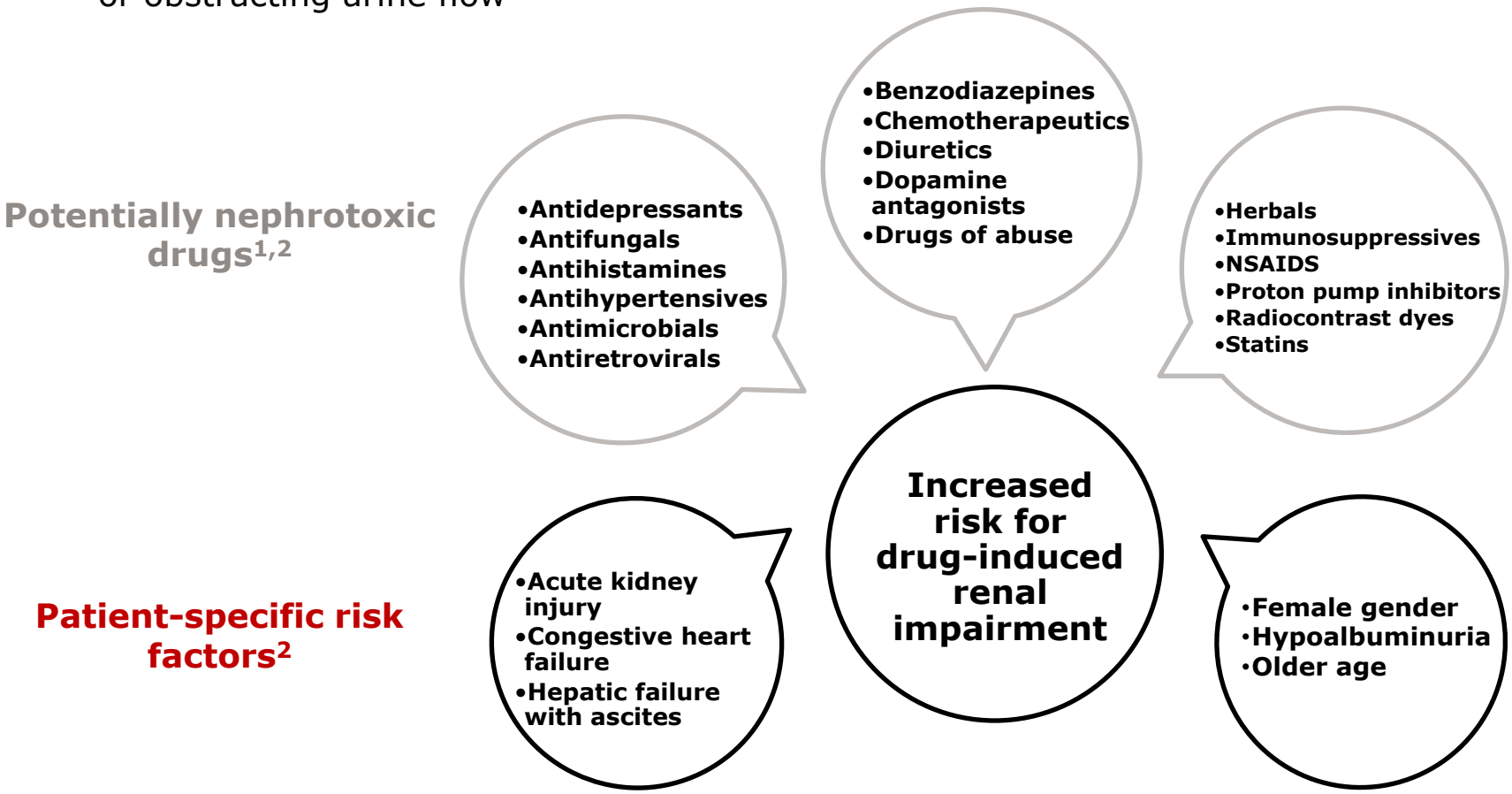



- **After 6 years' exposure, the relative risk of CKD was increased by 97%, 320% and 140% for TDF, ATV/r and LPV/r respectively**
- **A clear decrease in the incidence of CKD after stopping ARVs was only observed for TDF**

Multivariate models adjusted for race, HIV exposure risk, D:A:D cohort, study, gender, nadir CD4, baseline date and eGFR, and hepatitis B*, hepatitis C*, smoking status*, BMI*, family history of CVD*, viral load*, CD4*, a new AIDS diagnosis within the past 12 months* (time updated variables*). Models were additionally adjusted for cumulative exposure to indinavir

# Many factors increase patient risk for drug-induced renal impairment

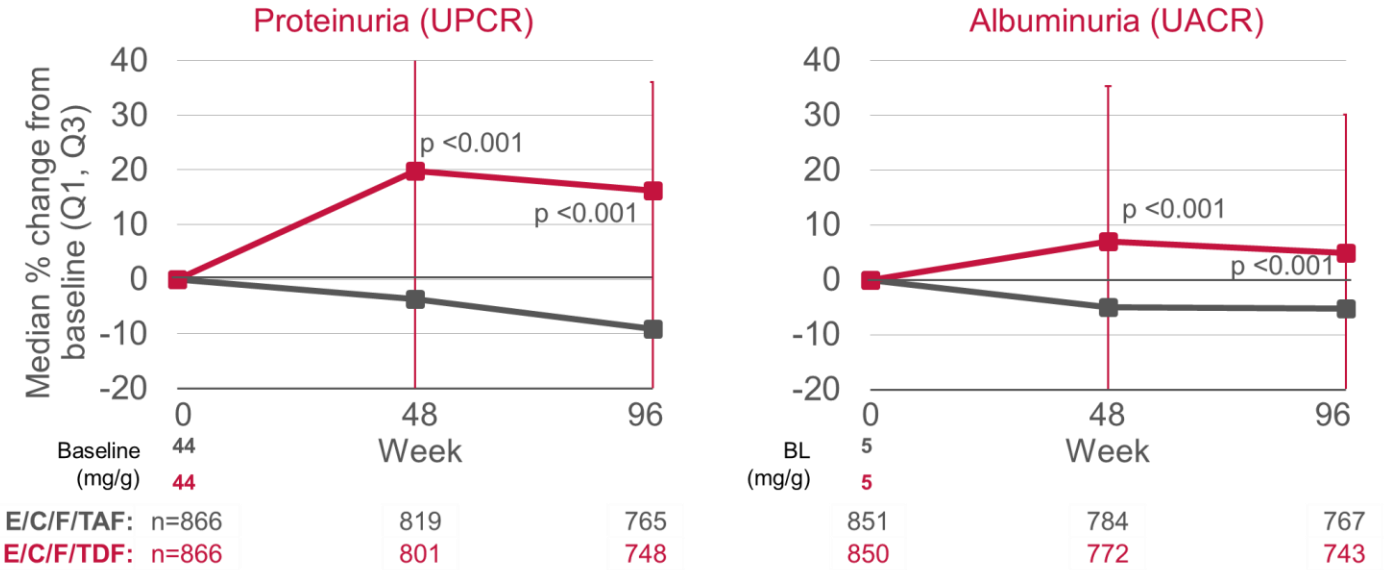
- Several classes of drugs can impair renal function at any of its composite steps, including changing renal arterial blood flow, reducing glomerular filtration, altering tubule function, or obstructing urine flow[1]




1. Pazhayattil GS and Shirali AC. Int J Nephrol Renovasc Dis 2014;7:457–468;
2. National Kidney Foundation. Frequently Asked Questions About GFR Estimates. 2014;

# Potential solutions: Less impact on renal safety by avoiding TDF with e.g. E/C/F/TAF

- More favourable changes (%) in quantitative proteinuria (UPCR and UACR) in the E/C/F/TAF group than in the E/C/F/TDF in Studies 104 and 111 (ART-naive adults, Week 96 combined analysis)

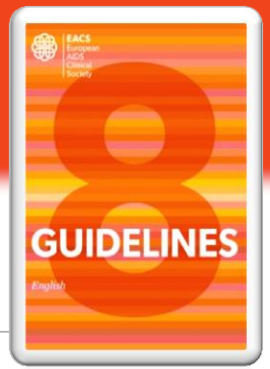


# Maintenance of HIV therapy

**Reactive**

**Proactive**

# Kideny disease in HIV




## Kidney Disease: Definition, Diagnosis and Management

**Diagnosis of kidney disease**

| | | eGFR[i] | | |
|---|---|---|---|---|
| | | ≥ 60 mL/min | 30-59 mL/min | < 30 mL/min |
| Proteinuria[ii] | UP/C[iii] < 50 | Regular follow-up | | • Check risk factors for CKD and nephrotoxic medicines including ART[iv]<br>• Discontinue or adjust drug dosages where appropriate[v]<br>• Perform renal ultrasound<br>• Urgent referral to nephrologist |
| | UP/C[iii] 50-100 | • Check risk factors for CKD[x] and nephrotoxic medicines including ART[iv, x]<br>• Discontinue or adjust drug dosages where appropriate[v]<br>• Perform renal ultrasound<br>• If haematuria present with any level of proteinuria refer to nephrologist<br>• Refer to nephrologist if new CKD or progressive decline in eGFR | | |
| | UP/C[iii] > 100 | | | |

**Management of HIV-associated kidney disease[vi]**

| Prevention of progressive renal disease | Comment |
|---|---|
| **1. ART** | Start ART immediately where HIV-associated nephropathy (HIVAN) [vii] or HIV immune complex disease strongly suspected. Immunosuppressive therapy may have a role in immune complex diseases. Renal biopsy to confirm histological diagnosis recommended |
| **2. Start ACE inhibitors or angiotensin-II receptor antagonists if:** | **Monitor eGFR and $K^+$ level closely on starting treatment or increasing dose** |

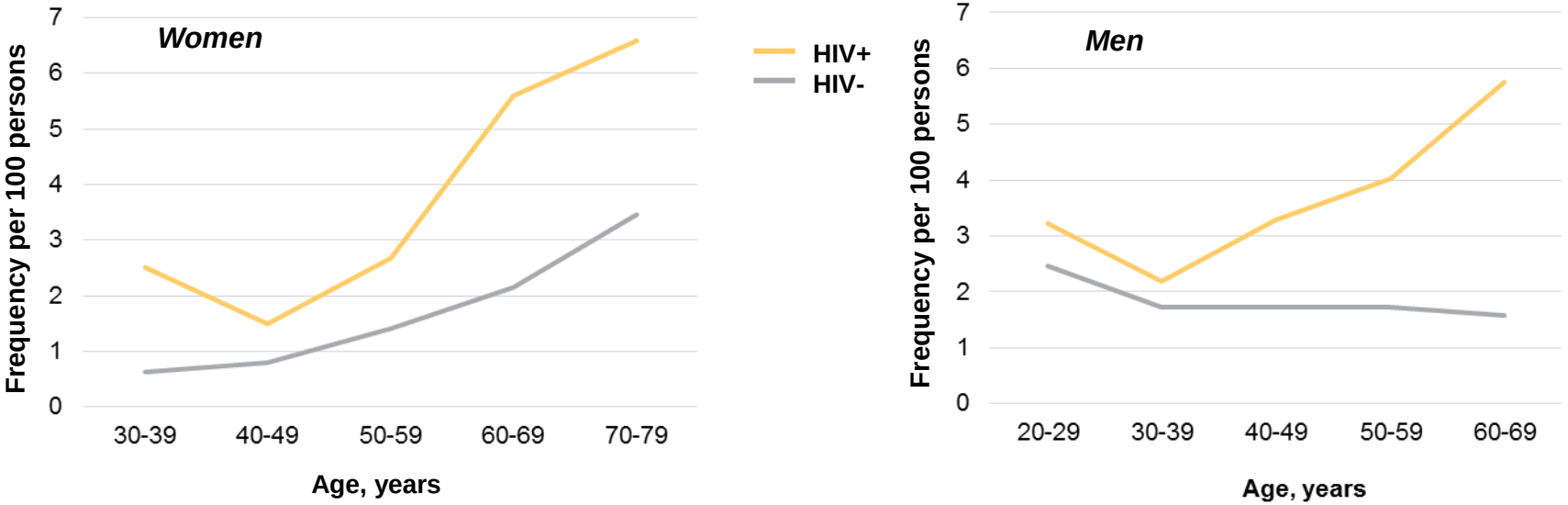
i For eGFR: Use CKD-EPI formula based on serum creatinine, gender, age and ethnicity because eGFR quantification is validated >60 mL/min. The abbreviated modification of diet in renal disease (aMDRD) or the Cockcroft-Gault (CG) equation may be used as an alternative; see http://www.hivpv.org/.
Definition CKD: eGFR < 60 ml/min for > 3 months (see http://kdigo.org/home/guidelines/ckd-evaluation-management). If not previously known to have CKD, confirm pathological eGFR within 2 weeks. Use of DTG, COBI and RTV boosted PIs is associated with an increase in serum creatinine/reduction of eGFR due to inhibition of proxi-mal tubular creatinine transporters without impairing actual glomerular filtration: consider new set point after 1-2 months

ii Urinalysis: use urine dipstick to screen for haematuria. To screen for proteinuria, use urine dipstick and if ≥ 1+ check urine protein/creatinine (UP/C), or screen with UP/C. Proteinuria defined as persistent if con-

# Bones

# HIV-infected individuals are at increased risk of bone loss and fractures

***Incidence of bone fractures among 8,525 HIV-positive patients and 2,208,792 HIV-negative individuals, by gender, 1996–2008[2]***




- Compared to HIV-negative individuals, HIV-infected individuals have a 6.4-fold increased risk of low BMD (bone mineral density) and a 3.7-fold increased risk of osteoporosis[1]
- Prevalence of fractures of the spine, hip, and wrist, sites commonly associated with osteoporosis can be 60% higher in HIV-infected individuals compared with the uninfected[2]
- For HIV-infected individuals, there is a nearly 5 times increased risk in hip fracture incidence commonly associated with osteoporosis, independent of sex, age, smoking[3]
- Younger patients still developing initial bone growth will be adversely impacted with BMD-lowering HIV treatments[5]

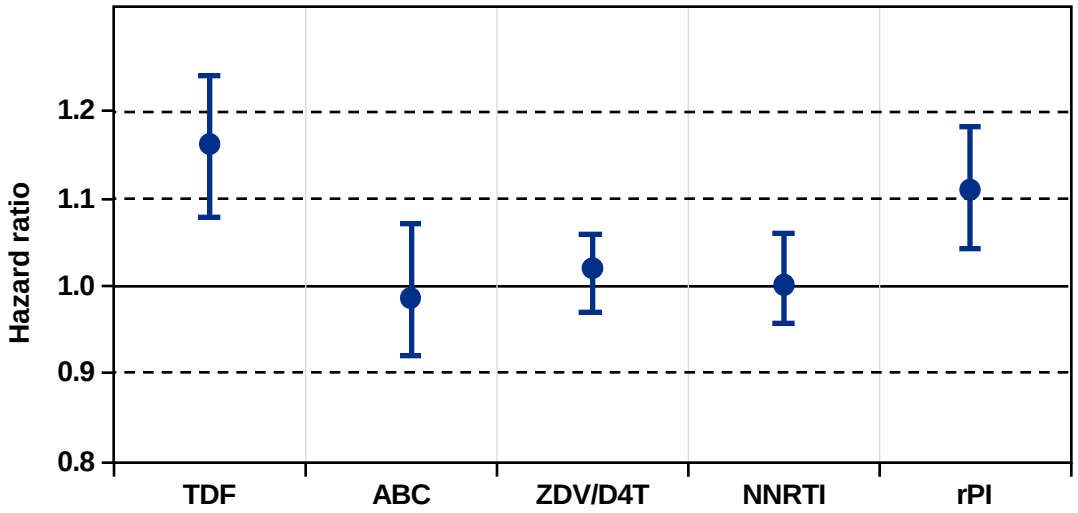
1. Brown TT et al. AIDS 2006;20:2165–2174; 2. Triant VA et al. J Clin Endocrinol Metab 2008;93(9):3499–3504
3. Guerri-Fernandez R et al. J Bone Miner Res 2013;28(6):1259–1263;
4. Taras J et al. Patient Prefer Adherence 2014;8:1311–1316; 5. Mora S et al. AIDS 2001;15(14):1823–1829

# Osteoporotic fracture risk in HIV-infected individuals on ART

*Veterans Health Administration (VHA)'s Clinical Case Registry (CCR), from 1988–2009*

The rate of osteoporotic fractures was significantly higher in the HAART era (4.09 events/1000 patient-years) compared to the pre-HAART era (1.61 events/1000 patient-years)[1]

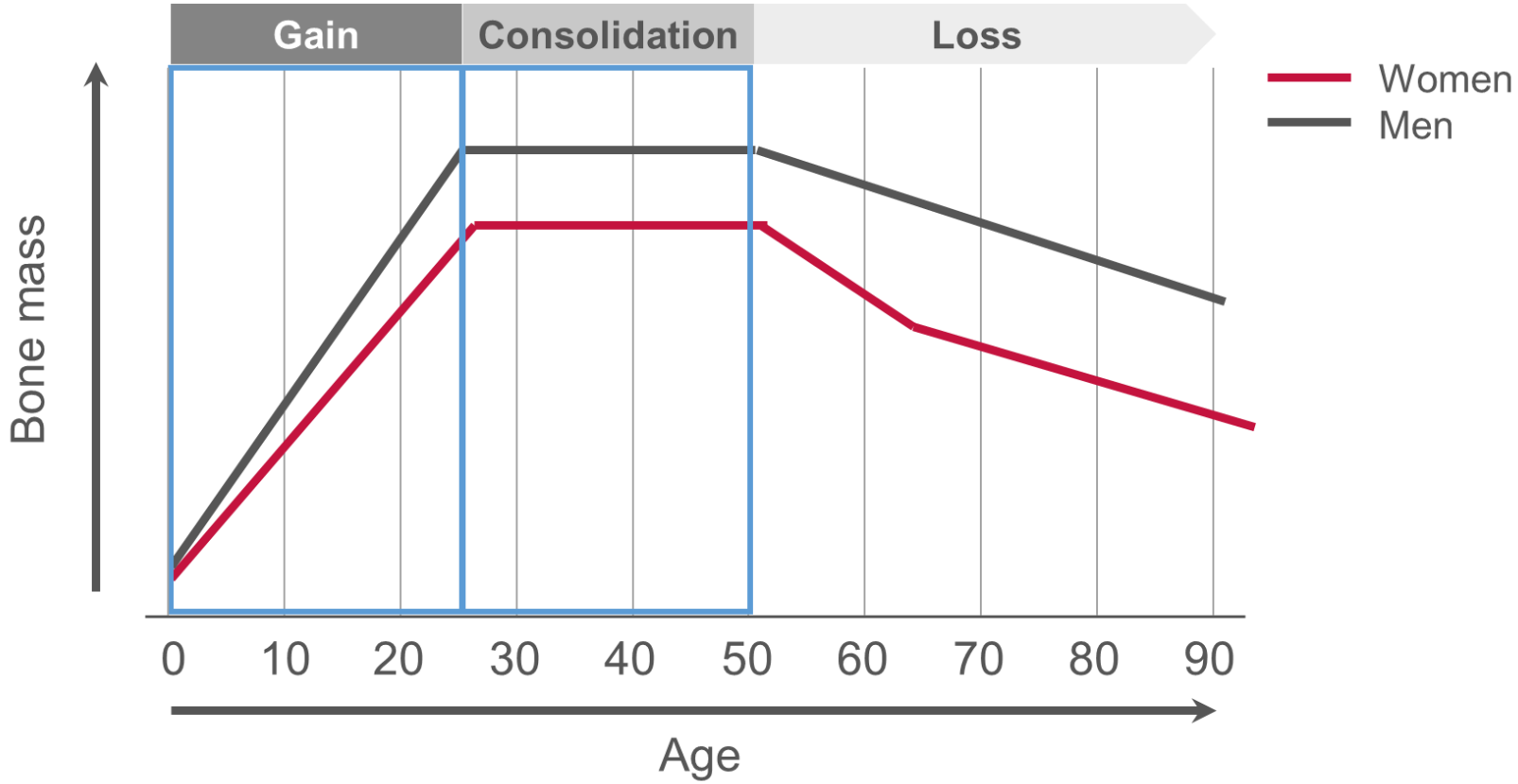
***Antiretroviral exposure and risk of osteoporotic fractures: 1988–2009[1]***




- **TDF and boosted PI are associated with increased risk of osteoporotic fracture**

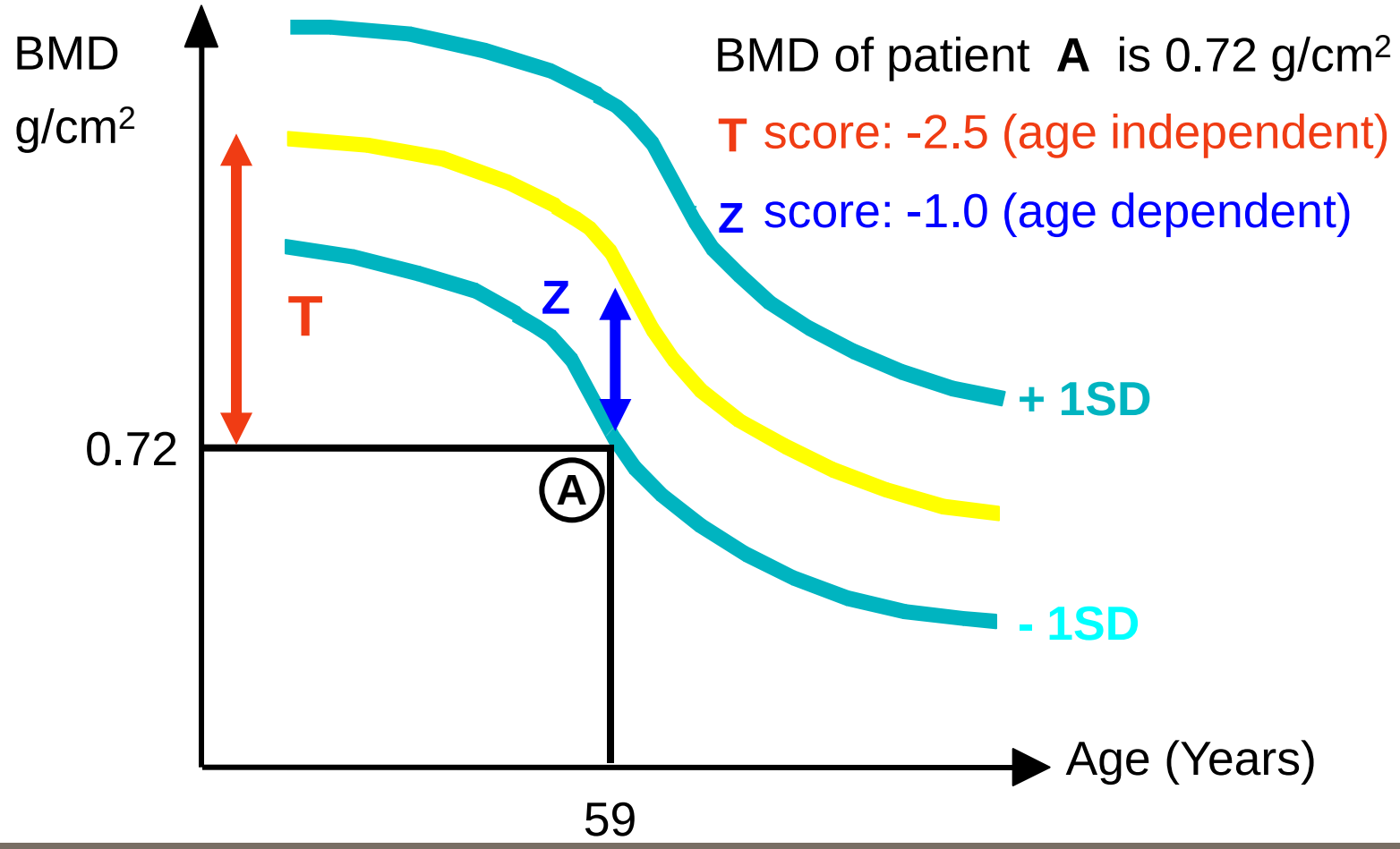
# Bone mass and osteoporosis

## Lifetime changes in bone mass[1]




1. Compston J. Clin Endocrinol (Oxf) 1990;33(5):653–82,

# Interpretation of DEXA data (scores)



# Prevalence of osteopenia in HIV patients

| Publication | Number of patients | | % ↓ BMD | |
|---|---|---|---|---|
| | HIV+ | HIV– | HIV+ | HIV– |
| Amiel *et al* 2004 | 148 | 81 | **82.5** | 35.8 |
| Brown *et al* 2004 | 51 | 22 | **63** | 32 |
| Bruera *et al* 2003 | 111 | 31 | **64.8** | 13 |
| Dolan *et al* 2004 | 84 | 63 | **63** | 35 |
| Huang *et al* 2002 | 15 | 9 | **66.6** | 11 |
| Knobel *et al* 2001 | 80 | 100 | **87.5** | 30 |
| Loiseau-Peres *et al* 2002 | 47 | 47 | **68** | 34 |
| Madeddu *et al* 2004 | 172 | 64 | **59.3** | 7.8 |
| Tebas *et al* 2000 | 95 | 17 | **40** | 29 |
| Teichman *et al* 2003 | 50 | 50 | **76** | 4 |
| Yin *et al* 2005 | 31 | 186 | **77.4** | 56 |

Overall:

67% reduced BMD

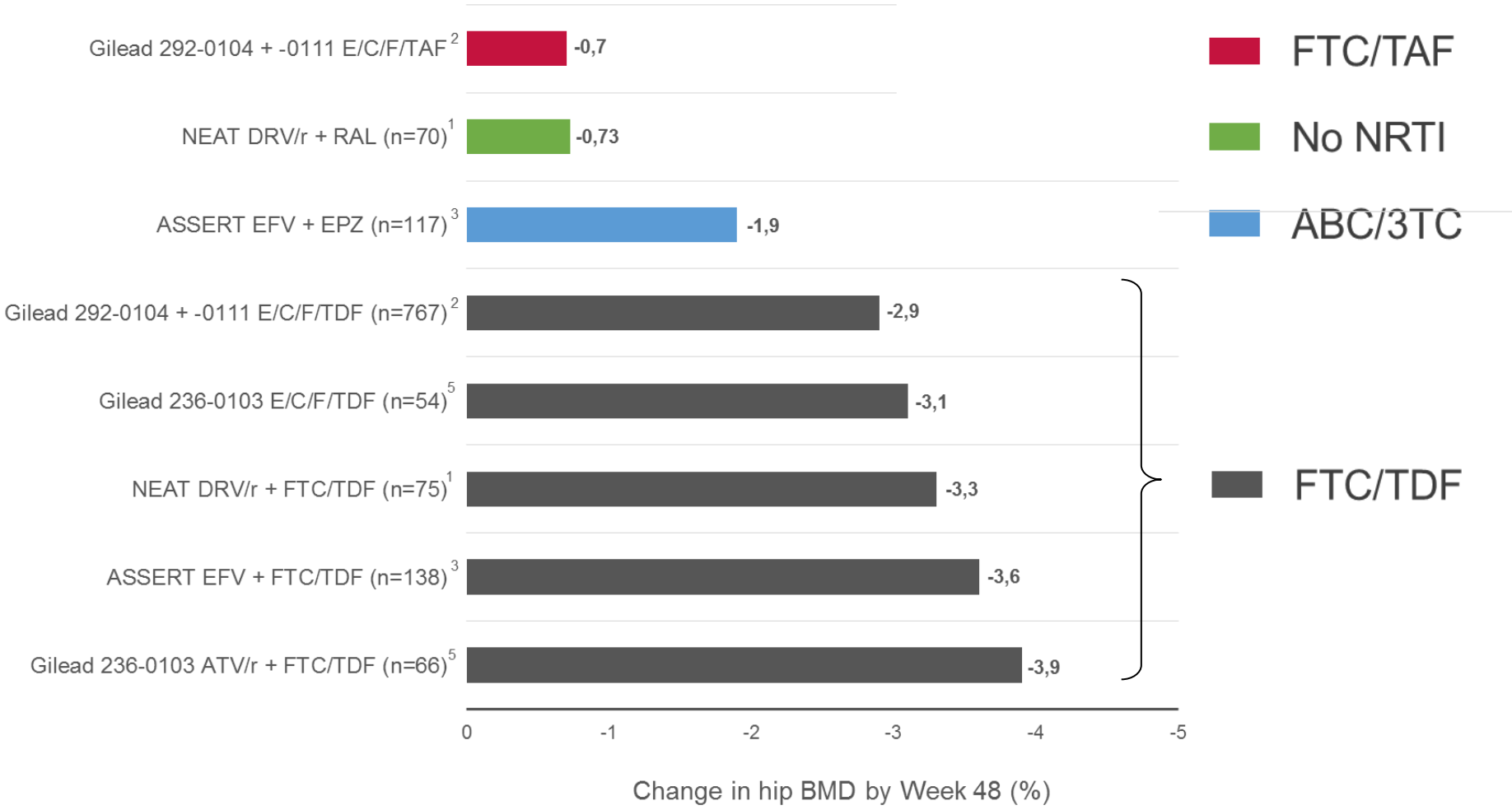
15% osteoporosis

6.4 ↑ risk low BMD

3.7 ↑ risk osteoporosis

Brown TT & Qaqish RB. *AIDS* 2006; **20:**2165-2174

# Treatment-naïve studies with BMD assessments

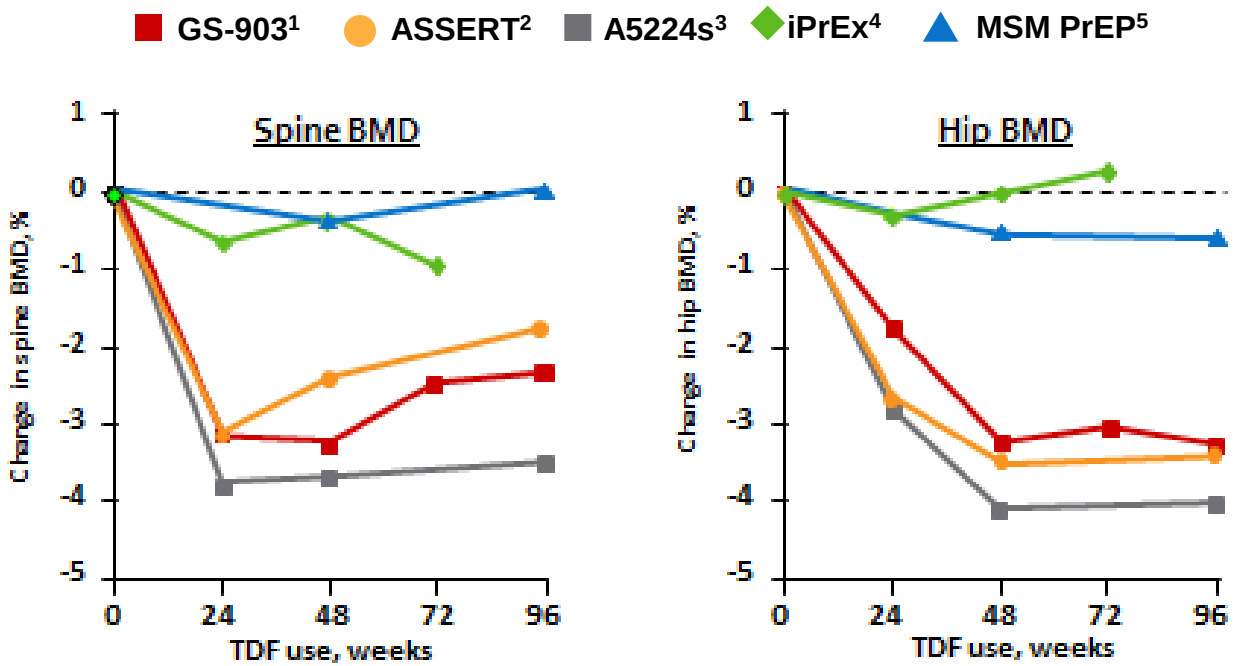



1. Bernardino JI, et al. Lancet HIV 2015; 2:e464-e473; 2. Wohl D, et al. J Acquir Immune Defic Syndr. 2016 Jan 29. [Epub ahead of print]; 3. Stellbrink HJ, et al. Clin Infect Dis 2010;51:963-972; 4. Qaqish R, et al. IAS 2011, Rome, Italy: TULBPE021; 5. DeJesus E, et al. Lancet 2012; 379: 2429-2438.

# Mean changes in bone mineral density during TDF-containing trials (HIV-infected and HIV-negative)

*Trials of HIV-infected subjects: GS-903, ASSERT, A5224s*
*Trials of HIV-negative subjects (HIV PrEP): iPrEx & MSM PrEP*

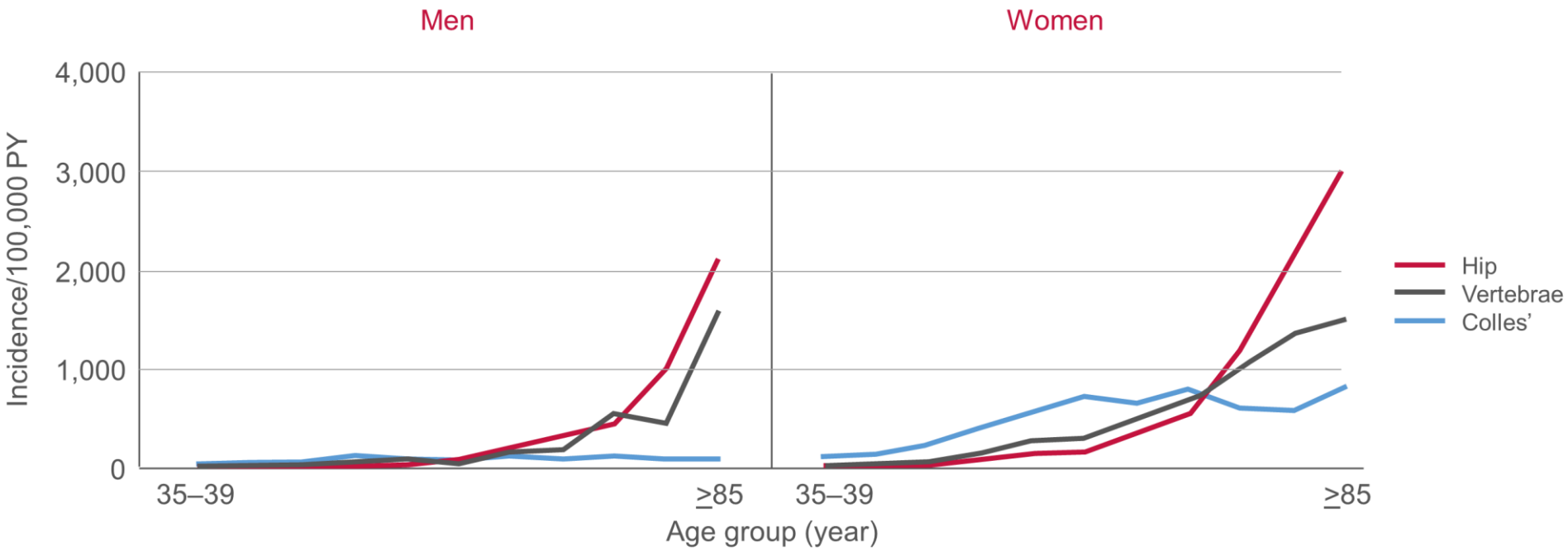
*Data from multiple studies published from 2004–2011*




***PreP not currently approved in Europe**


1. Gallant JE et al. JAMA 2004;292:191–201; 2. Moyle G et al. LIPO 2010. London, UK. #23;
3. McComsey G et al. J Infect Dis 2011;203:1791–1801; 4. Mulligan K et al. Clin Infect Dis 2015. (epub ahead of print);
5. Liu A et al. CROI 2011. Boston, MA. #93

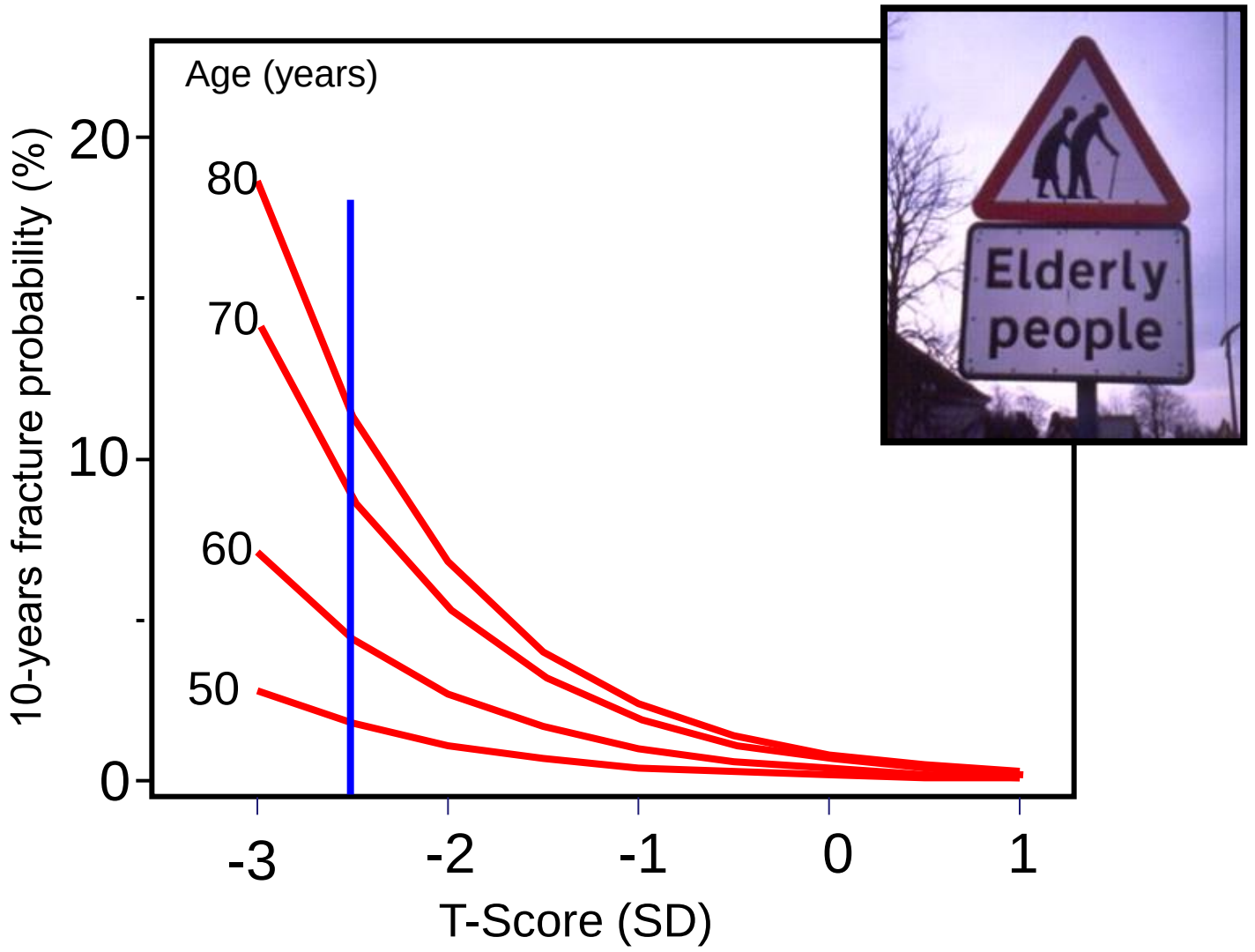
# Age-related increase in osteoporotic fractures




PY, person-years

Cooper and Melton. Trends Endocrinol Metab 1992 Aug;3(6):224–9

# Age is an important factor in osteoporotic fractures



# Pathogenesis of osteoporotic fractures

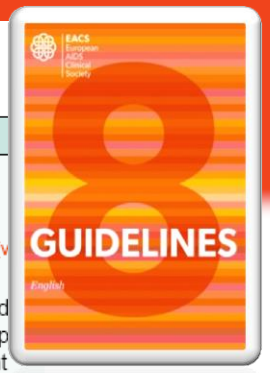
- Diet
- Smoking
- Steroids
- Menopause
- Morbidity
- Genetics

- Muscle strenght
- Balance
- Eye-sight
- Enviroment
- Sedativs
- Age

**„Skeletal“-Components**

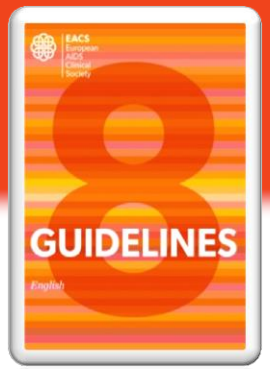
**„Fall“-Components**

# Bone Disease: Screening and Diagnosis



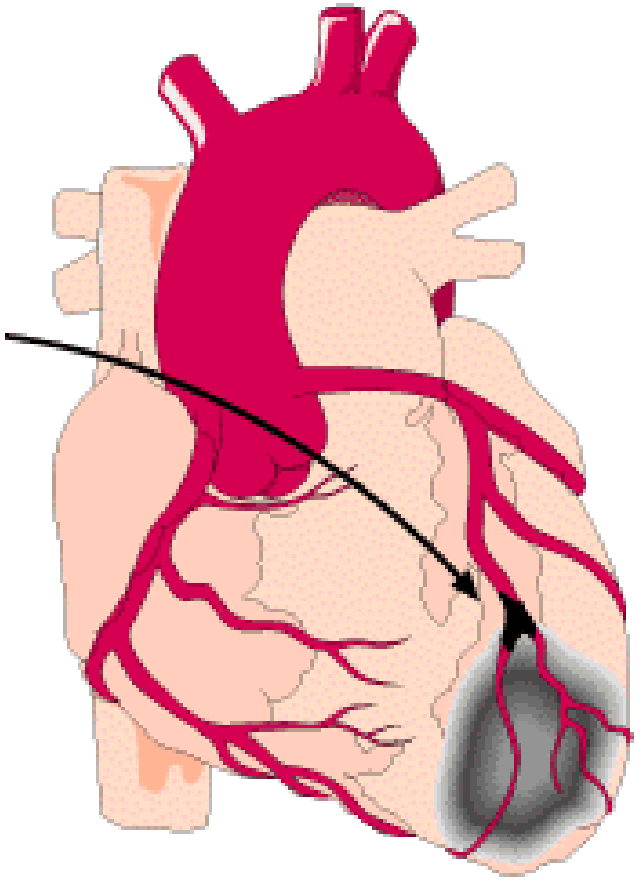

| CONDITION | CHARACTERISTICS | RISK FACTORS | DIAGNOSTIC TESTS |
|---|---|---|---|
| **Osteopenia**<br>• Postmenopausal women and men aged ≥ 50 years with T-score -1 to -2.5<br><br>**Osteoporosis**<br>• Postmenopausal women and men aged ≥ 50 years with T-score ≤ -2.5<br>• Premenopausal women and men aged < 50 years with Z-score ≤ -2 and fragility fracture | • Reduced bone mass<br>• Increased prevalence of fractures in people with HIV<br>• Asymptomatic until fractures occur<br><br>Common in HIV<br>• Up to 60% prevalence of osteopenia<br>• Up to 10-15% prevalence of osteoporosis<br>• Aetiology multifactorial<br>• Loss of BMD observed with antiretroviral initiation<br>• Greater loss of BMD with initiation of certain ARVs(i) | Consider classic risk factors(ii)<br><br>Consider DXA in any person with ≥ 1 of:(iii)<br>1. Postmenopausal women<br>2. Men ≥ 50 years<br>3. History of low impact fracture<br>4. High risk for falls(iv)<br>5. Clinical hypogonadism (symptomatic, see Sexual Dysfunction)<br>6. Oral glucocorticoid use (minimum 5 mg/d prednisone equivalent for > 3 months)<br>Preferably perform DXA in those with above risk factors prior to ART initiation. Assess effect of risk factors on fracture risk by including DXA results in the FRAX® score (www.shef.ac.uk/FRAX)<br>• Only use if > 40 years<br>• May underestimate risk in HIV-positive persons<br>• Consider using HIV as a cause of secondary osteoporosis(v) | **DXA scan**<br><br>**Rule out causes of secondary osteoporosis if BMD abnormal**(v)<br><br>**Lateral spine X-rays** (lumbar and thoracic) if low spine BMD, osteoporosis on DXA, or significant height loss or kyphosis develops. (DXA-based vertebral fracture assessment [VFA] can be used as an alternative to lateral spine X-ray). |
| **Osteomalacia** | • Defective bone mineralisation<br>• Increased risk of fractures and bone pain<br>• Vitamin D deficiency may cause proximal muscle weakness<br>• High prevalence (> 80%) of vitamin D insufficiency in some HIV cohorts | • Dark skin<br>• Dietary deficiency<br>• Avoidance of sun exposure<br>• Malabsorption<br>• Obesity<br>• Renal phosphate wasting(vii) | Measure 25(OH) vitamin D in all persons at presentation<br><br>\| \| ng/ml \| nmol/L \|<br>\| Deficiency \| < 10 \| < 25 \|<br>\| Insufficiency \| < 20 \| < 50 \|<br><br>If deficient or insufficient, check PTH levels<br>Consider vitamin D replacement if clinically indicated, see page 38 |
| **Osteonecrosis** | • Infarct of epiphyseal plate of long bones resulting in acute bone pain<br>• Rare but increased prevalence in HIV | **Risk factors:**<br>• Low CD4 cell counts<br>• Glucocorticoid exposure<br>• IVDU | **MRI** |

# Approach to Fracture Reduction




| | |
|---|---|
| **Reducing risk of fractures** | • Aim to decrease falls by addressing fall risks[(i)]<br>• Ensure sufficient dietary calcium (1-1.2 g daily) and vitamin D (800-2,000 IU daily) intake[(ii)]<br>• Where appropriate, screen for osteoporosis[(iii)] and refer to national/regional guidelines on treatment of osteoporosis<br>– If no guidelines available, consider bisphosphonate[(iv)] treatment in all osteoporotic postmenopausal women and men > 50 years old (BMD T-score ≤ -2.5) and those with a history of fragility fracture. Consider treatment based on BMD alongside consideration of other risk factors for fracture, especially age.<br>– Use bisphosphonate and ensure adequate calcium and vitamin D intake<br>– No significant interactions between bisphosphonates and antiretrovirals<br>– If antiretroviral naive, consider options for ART that preserve BMD[(v)]<br>– If diagnosed with osteoporosis and requiring therapy, consider optimising ART to preserve or improve BMD[(vi)] |

**Cardio-vascular**



# Epidemiological Data: CVD Events in HIV-Patients[1]

- Retrospective cohort studies
- Prospective HIV cohort studies
- Administrative/clinical databases
- Randomized clinical trails of ART

| | No. of patients/ No. of events | Event rate per 1,000 HIV+ | Event rate per 1,000 HIV- |
|---|---|---|---|
| DAD I[2] | 23,468/126 | 3.5 | NA |
| DAD I[3] | 23,437/345 | 3.6 | NA |
| VA[4] | 36,766/1,207 | 8.1 | NA |
| Kaiser 2002[5] | 4,159/47 | 4.3 | 2.9 |
| Kaiser 2007 | 5,000/162 | 3.7 | 2.2 |
| MGH[6] | 3,851/189 | 11.13 | 6.98 |
| MediCal[7] | 28,512/294 | 4.12 | 3.32 |

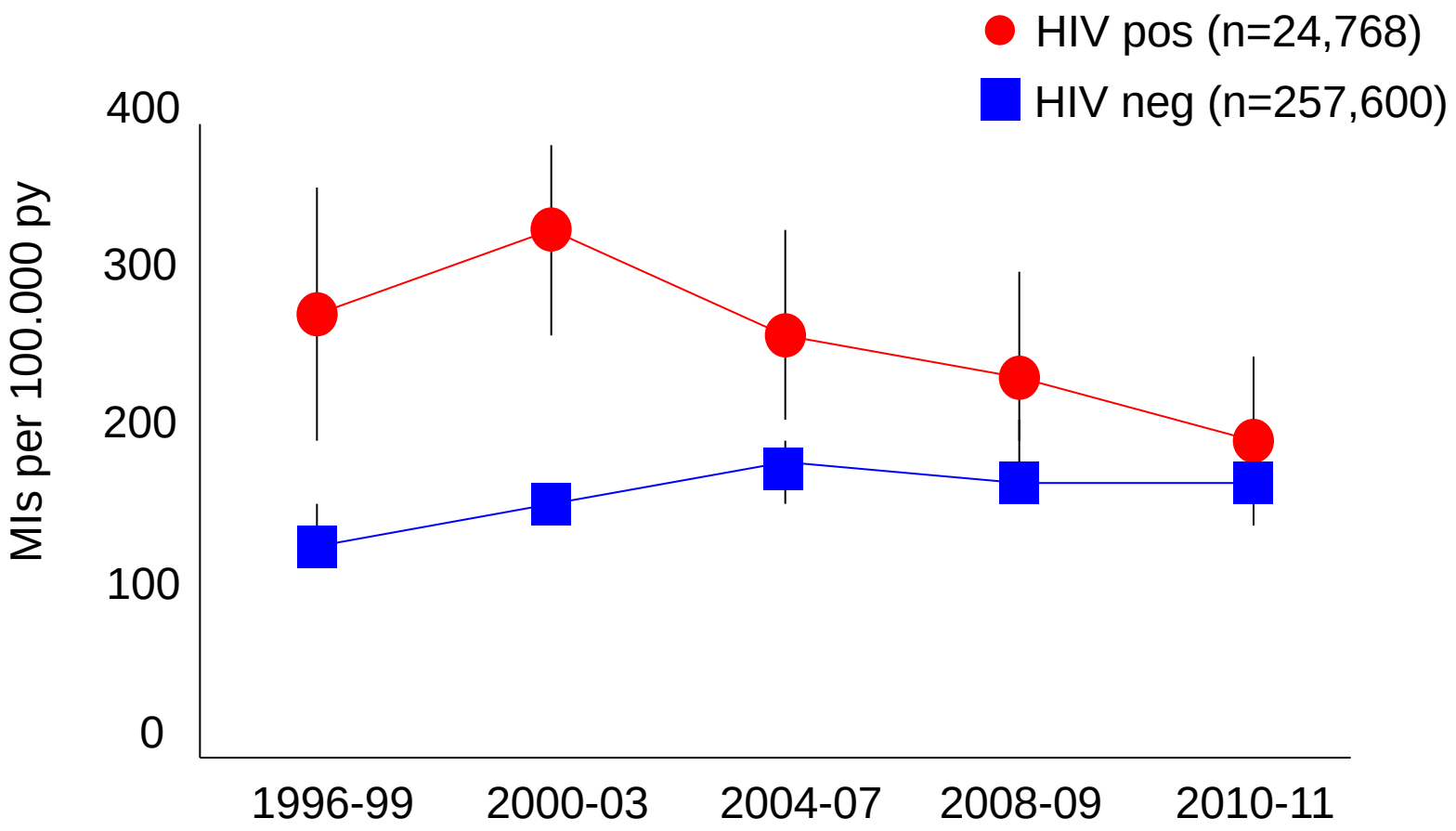
[1]Currier Circulation 2008; [2]Friis-Moller N Engl J Med 2003; [3] Friis-Moller N Engl J Med 2007; [4]Bozette N Engl J Med 2003; [5]Klein J AIDS 2002; [6]Triant J Clin Endocrinol Metab 2007; [7]Currier J AIDS 2003

# Cause of Death in D:A:D

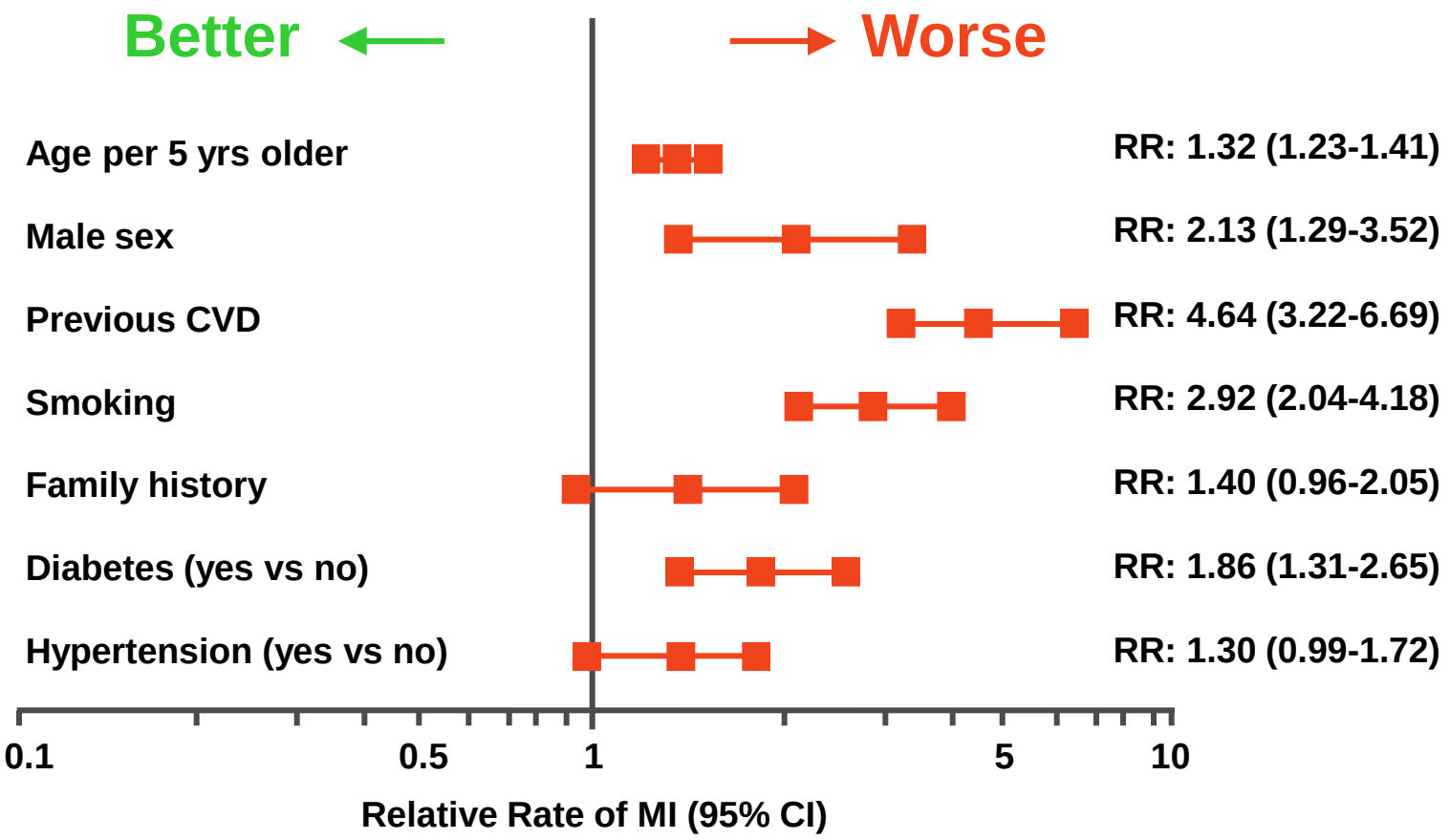
| Cause of death | Percentage[1] | |
|---|---|---|
| AIDS-related | 29 | |
| Liver-ralated | 13 | |
| Non-AIDS cancers | 15 | |
| CVD-related | 11 | 7.9 (ATCC)[2] |
| Non-natural | 10 | |
| Bacterial infections | 7 | |
| Renal | 1 | |
| Lactic acidosis/pancreatitis | <0.5 | |
| Others/Unknown | 15 | |

[1]Smith Lancet 2014; [2]ATCC, Clin Infect Dis 2010

# No Differences in Incidence of MI for HIV+ and HIV- Individuals in Recent Years



# D:A:D: Traditional Risk Factors for CHD in an HIV-infected Population




Multivariable Poisson model adjusted for age, sex, BMI, HIV risk, cohort, calendar year, race, family history of CVD, smoking, previous CVD event, TC, HDL, hypertension, diabetes.

Friis-Møller N et al. *N Engl J Med.* 2007;356:1723-1735.

# Prevalence of Cardiovascular Risk Ractors in HIV

## Traditional risk factors

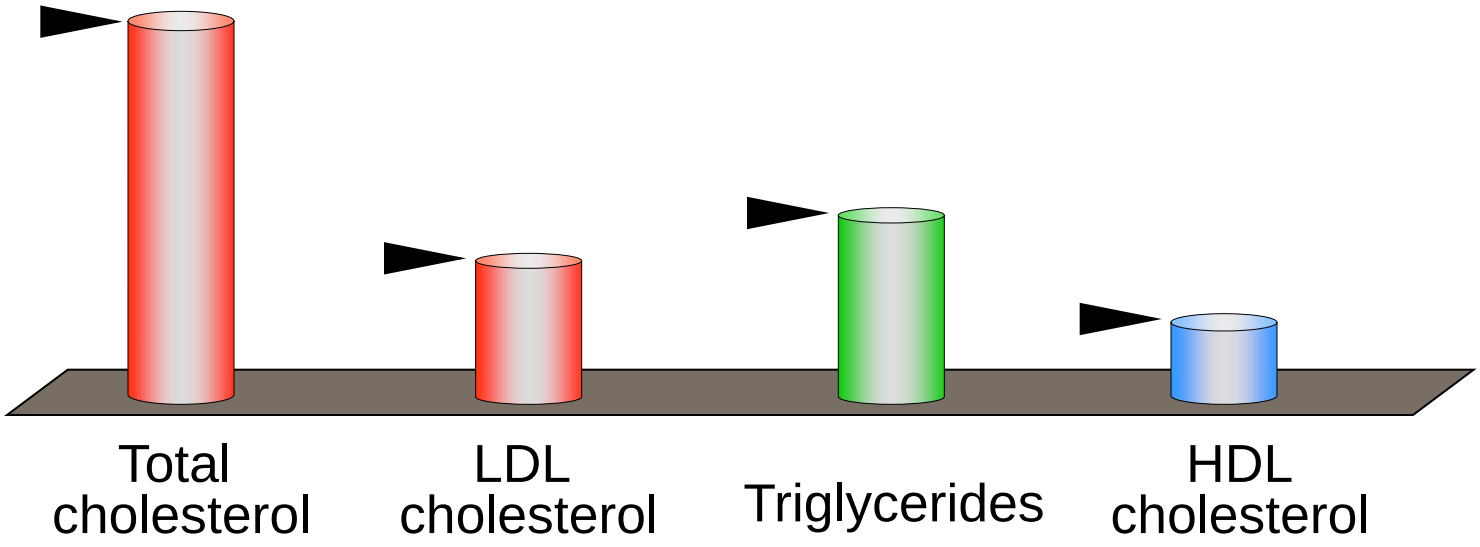
- Smoking (47-71%) [1,2]
- Obesity (40-60%) [3]
- Hypertension (31%) [4]
- Dyslipidemia (40-60%) [5]
- Glucose intolerance
- Type 2 diabetes

Traditional risk factors powerfully predict cardiovasular risk in HIV patients

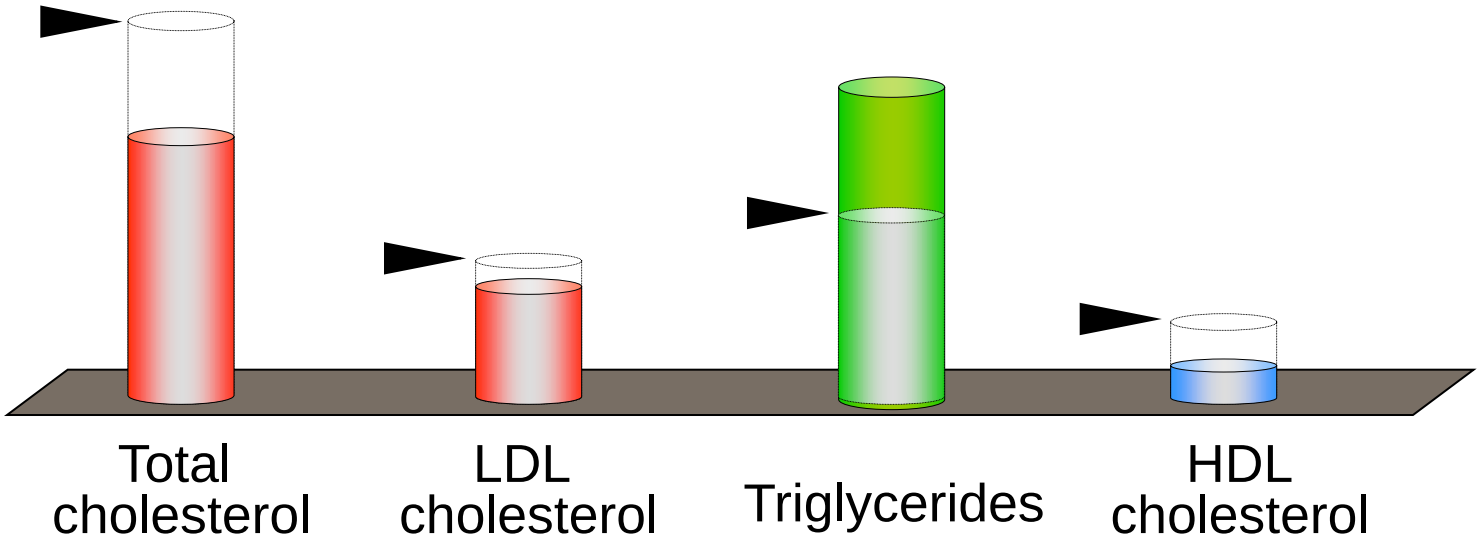
BUT: Lack of specificity

[1]Saves Clin Infect Dis 2003; [2]Gritz Nicotine Tob Res 2004; [3]Kaplan Clin Infect Dis 2007; [4]Seaberg AIDS 2005; [5]Samaras Diabetes Care 2007

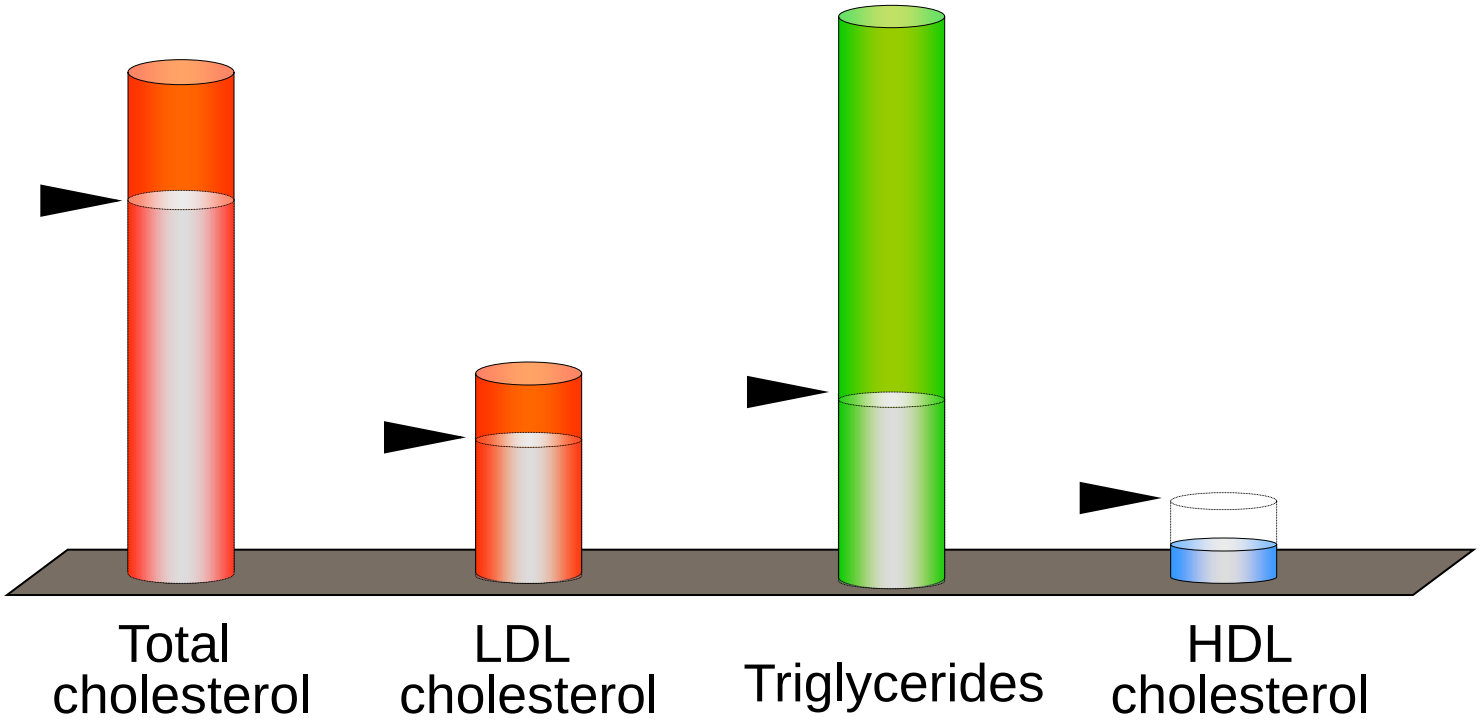
# Lipid >Profile *before* HIV Infection



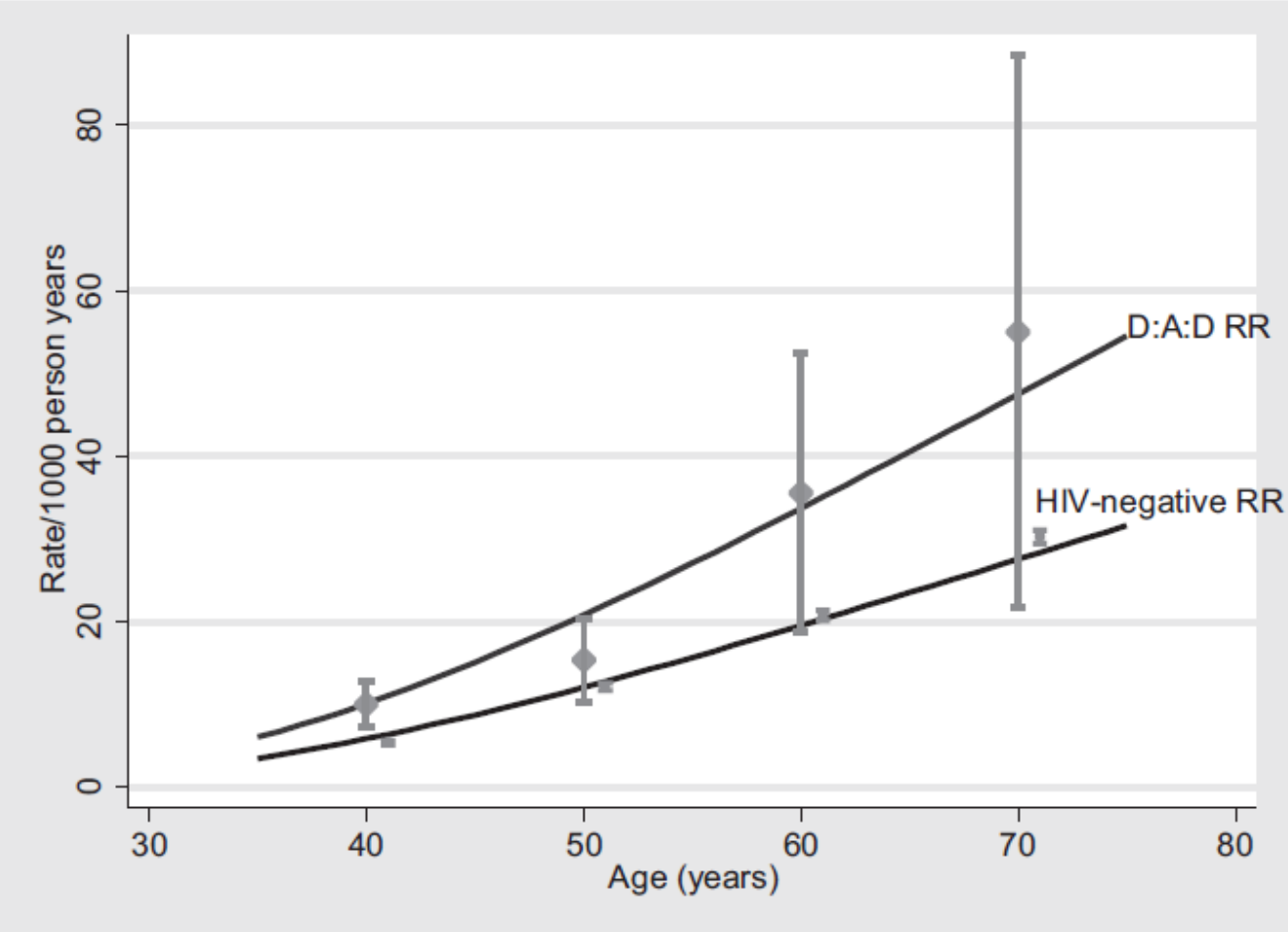
# Lipid Profile *due to* HIV Infection



# Lipid Profile *due to* Several ARTs



# Increased Risk for CVD with Age in HIV




Petoumenos et al., HIV Med 2014

# HAART and Cardiovascular Disease

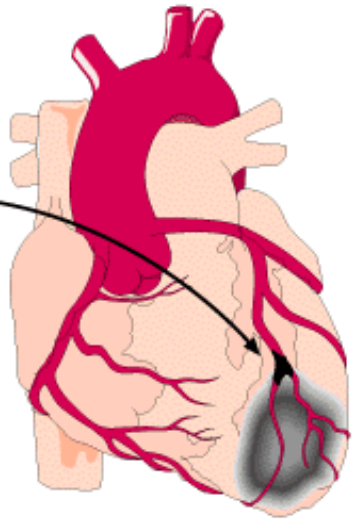
HAART

Insulin resistance
Type 2 diabetes

Dyslipidemia
High FFA
Small dense LDL
Low HDL
High TG

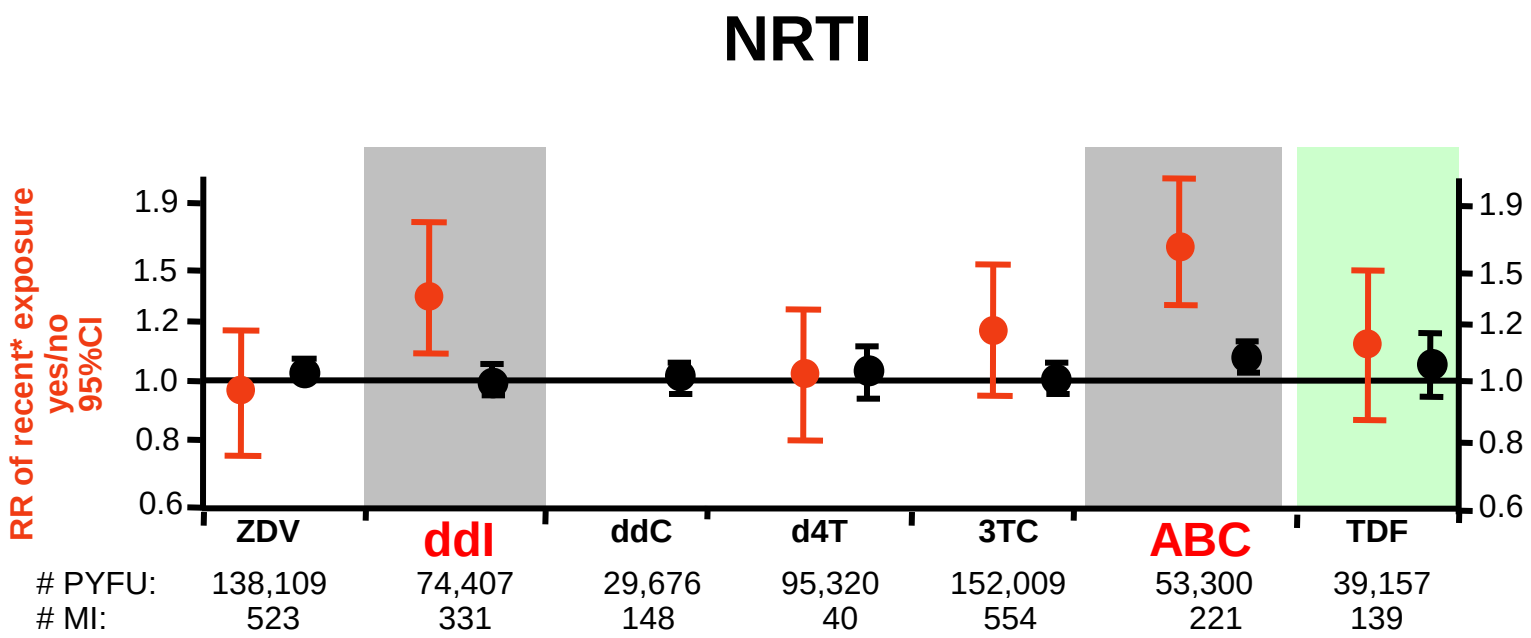
Central obesity

CVD



**Age, genetics, diet, hypertension, sedentery life style, renal disease…**

# D:A:D: Recent and/or Cumulative Antiretroviral Exposure and Risk of MI




*Current or within last 6 months. †Approximate test for heterogeneity: *P* = 0.02

Lundgren JD, et al. CROI 2009. Abstract 44LB.

Only >30,000 PY of follow up

# HIV Drug-Specific Associations to CVD

HAART

**Abacavir**
**Didanosine**
**Indinavir**
**Lopinavir**

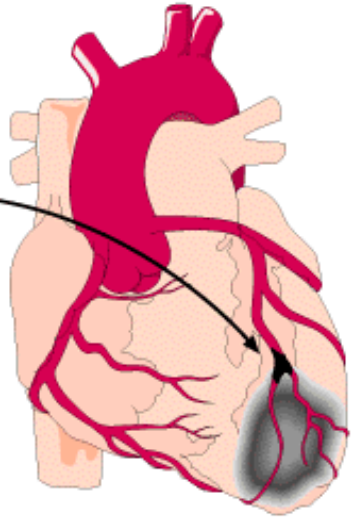
Insulin resistance
Type 2 diabetes

Dyslipidemia
High FFA
Small dense LDL
Low HDL
High TG

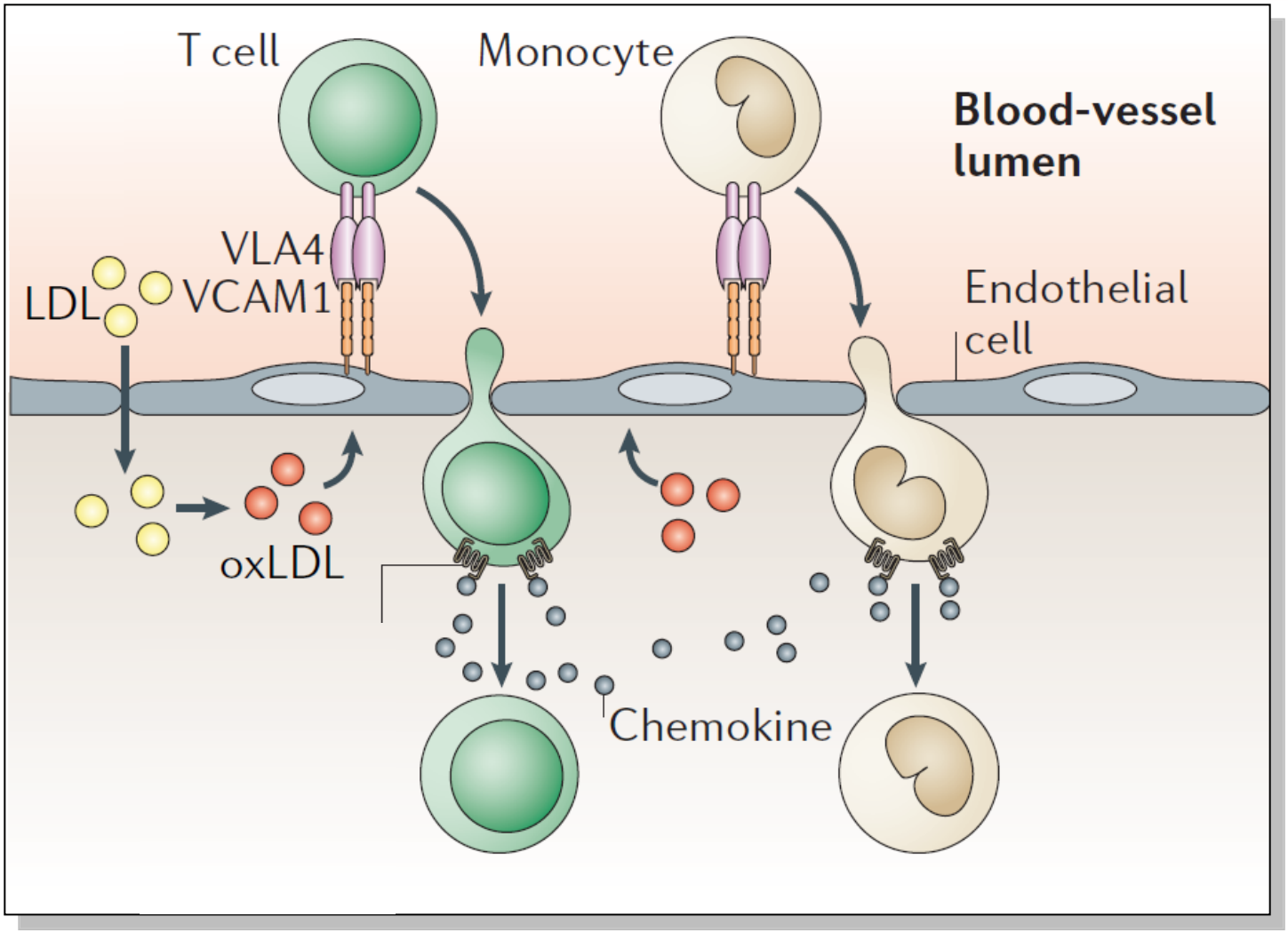
Central obesity

Inflammation ?

CVD



# Atherosclerosis and Immune Cells




Modified from Hansson & Libby.
The immune response in atherosclerosis: a double-edged sword. Nat Rev Immunol 2006

# HIV and Cardiovascular Risk

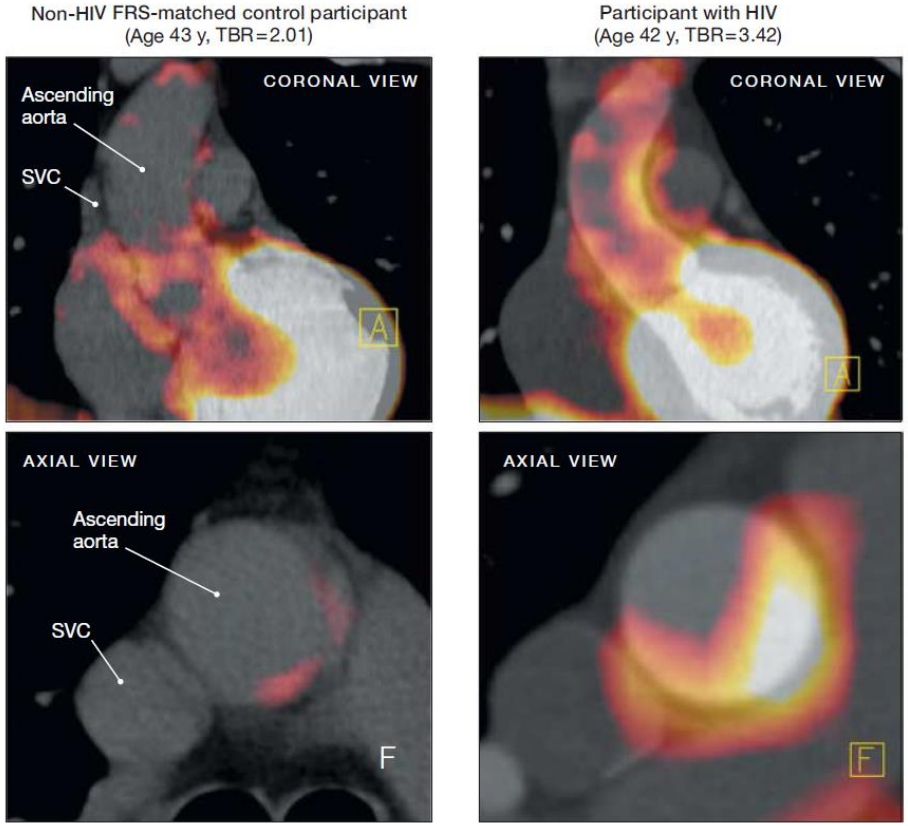
**HIV induces**

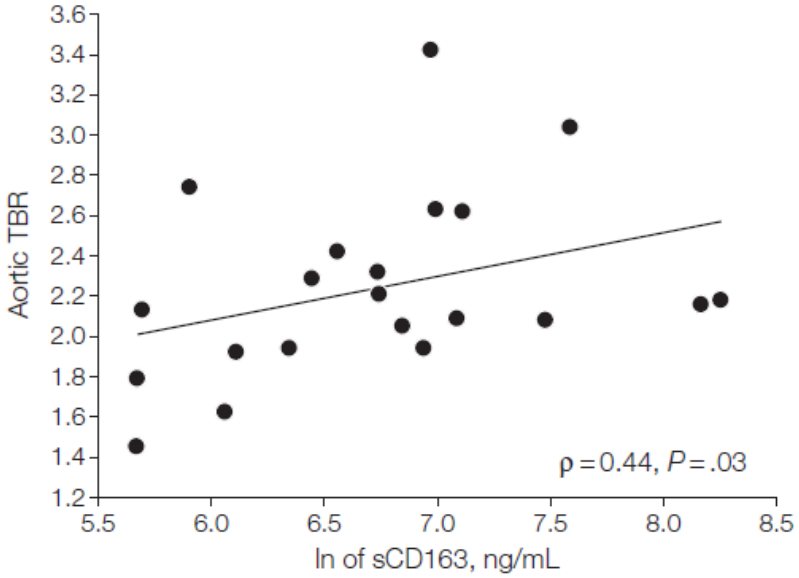
- Apoptosis ↑ in endothelial cells (gp120, Tat)[1-3]
- Endothelial dysfunction[4]
- Leukocyte activation[5]
- HDL ↓, IL-6 ↑, sICAM ↑, D-dimer ↑
- MCP-1-CCR2 axis activation[6]
- MCP-1 polymorphism associated with atherosclerosis in HIV[7]
- a distinct (inflammatory) atherosclerosis process?[8]

MCP-1: Monocyte chemotactic protein-1

[1]Sudano, Am Heart J 2006; [2]Huang, J AIDS 2001; [3]Jia, Biochem Biophys Res Commun 2001; [4]Solages, CID 2006; [5]de Gaetano, Lancet Infect Dis 2004; [6]Park Blood 2001; [7]Alonso-Villaverde Circulation 2004; [8]Mehta, Angiology 2003, Baker CID 2010

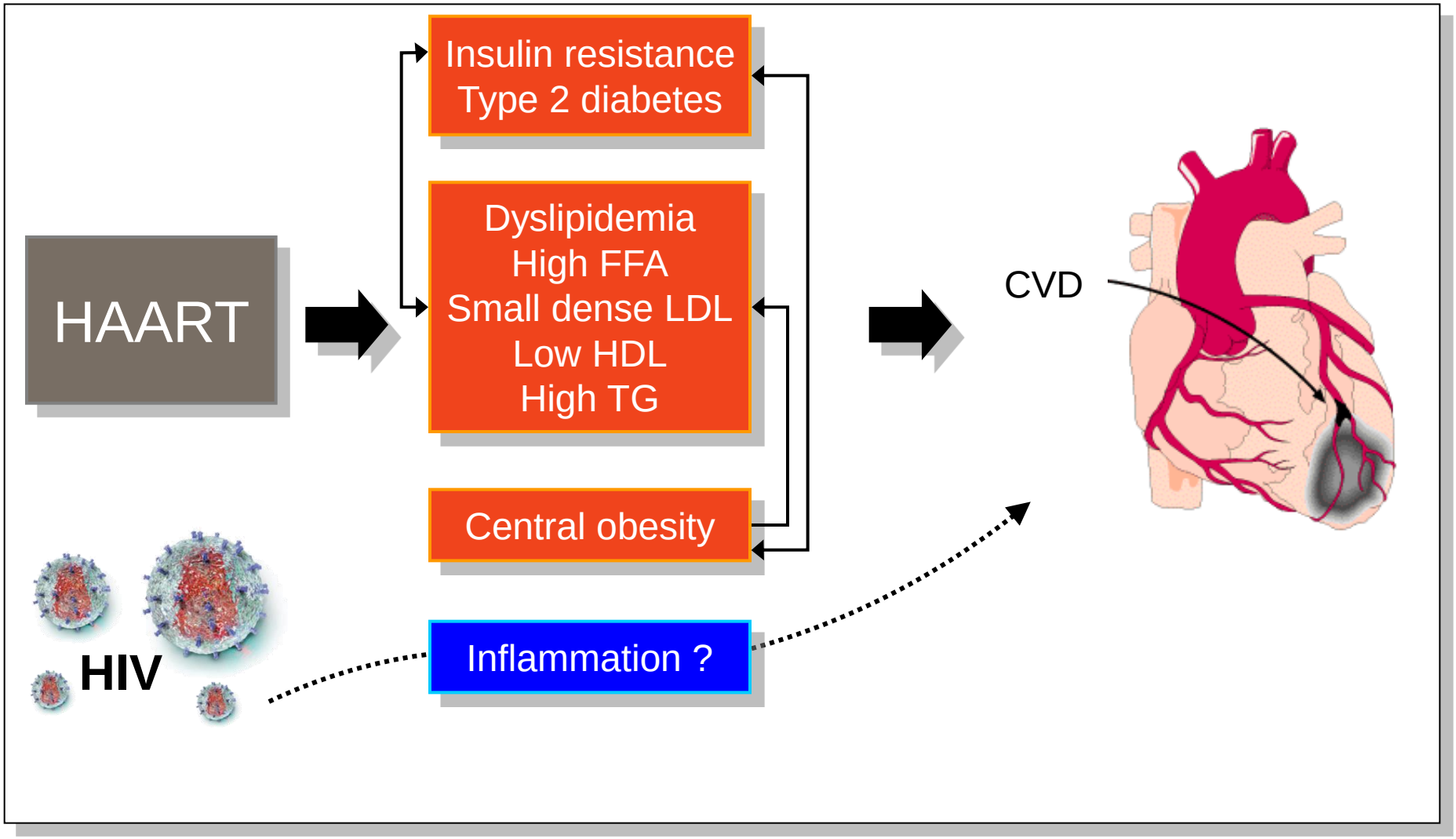
# Arterial Inflammation in Patients With HIV



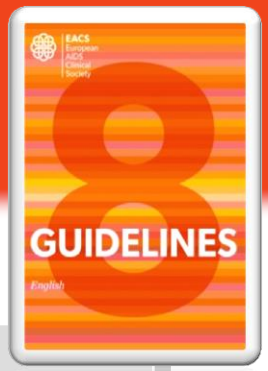




Subramanian et al JAMA 2012

# Inflammation and Cardiovascular Disease



# EACS Guidelines




Assess CVD risk in the next 10 years

↓

Advise on diet and lifestyle in all patients
Consider ART modification, if 10 year CVD risk ≥20%

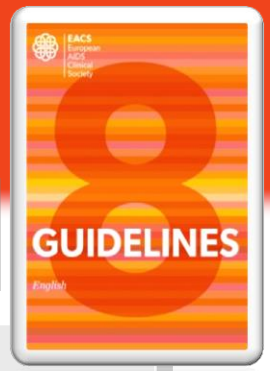
↓

Smoking ← Identify key modifiable risk factors

↓

| Blood pressure | Coagulation | Glucose | Lipids |
|---|---|---|---|
| ↓ | ↓ | ↓ | ↓ |
| **Drug treatment if:** SBP≥140 or DBP≥90 mmHg (especially if 10 year CVD risk ≥20%) | **Drug treatment if:** Established CVD or Age ≥ 50 and 10 year CVD risk ≥20% | Confirm DM and treat | **Drug treatment if**: Established CVD or T2D or 10 year CVD risk ≥20% |

# EACS Guidelines




Assess CVD risk in the next 10 years

Advise on diet and lifestyle in all patients
Consider ART modification, if 10 year CVD risk ≥20%

Smoking

Identify key modifiable risk factors

## Blood pressure

| Target | |
|---|---|
| If T2D or prior CVD or CKD + proteinuria | Others |
| SBP<130 | <140 |
| DBP<80 | <90 |

## Coagulation

**Target**

N/A

Consider to treat with acetylsalicylic acid 75-150mg

## Glucose

**Target**

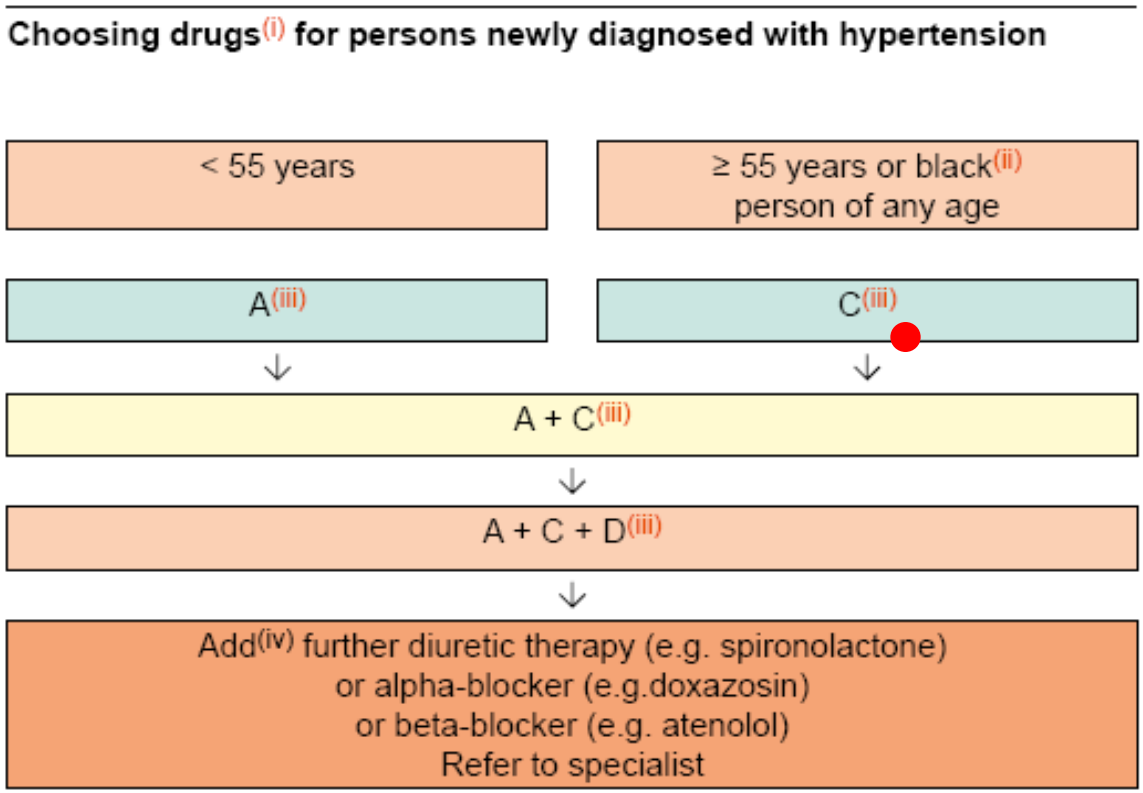
HbA1c <6.5-7%

## Lipids

**Target**

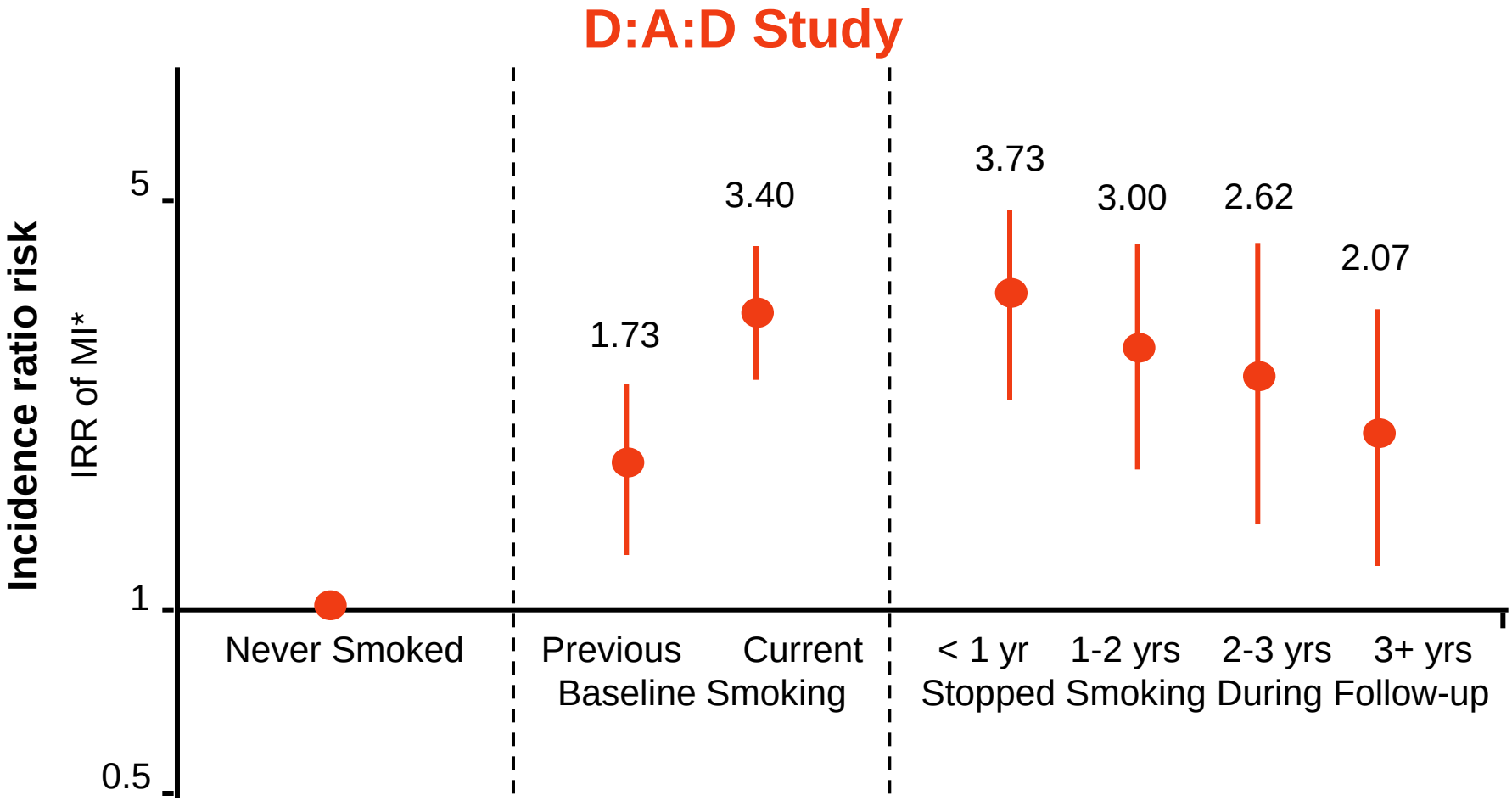
| | Best | Standard |
|---|---|---|
| TC | ≤4 (155) | ≤5 (190) |
| LDL | ≤2 (80) | ≤3 (115) |

# Hypertension: Management




A: ACE inhibitors
C: Dihydropyridine calcium-channel blocker
D: Thiazide-type diuretics

# Smoking Cessation Decreases Risk of CVD in HIV-infected Patients



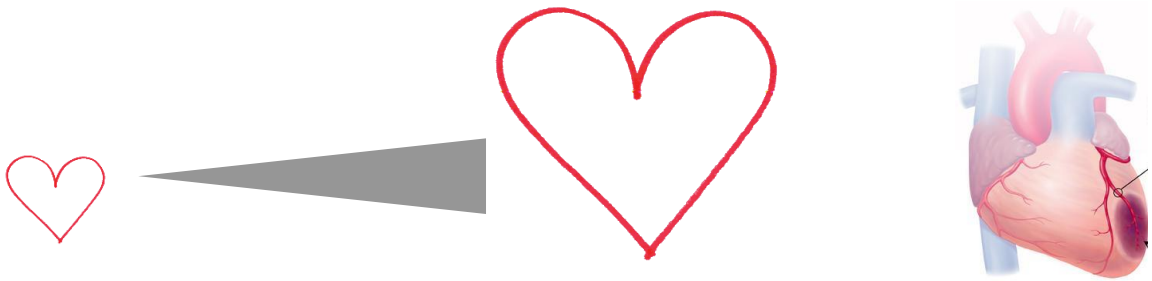

*Adjusted for: age, cohort, calendar yr, antiretroviral treatment, family history of CVD, diabetes, time-updated lipids and blood pressure assessments.

Petoumenos et al. HIV Medicine 2011

# The ART Drug Profile

- Antiviral activity
- Metabolisation
- Resistence profile
- Pharmacokinetics
- Drug-drug interaction
- $C_{max}$
- Lipid profile…

# Summary



1995 2005 2015 2025

**Drug-associated „Metabolics“**

**Inflammation**

**Clinical end points**

**Ageing**

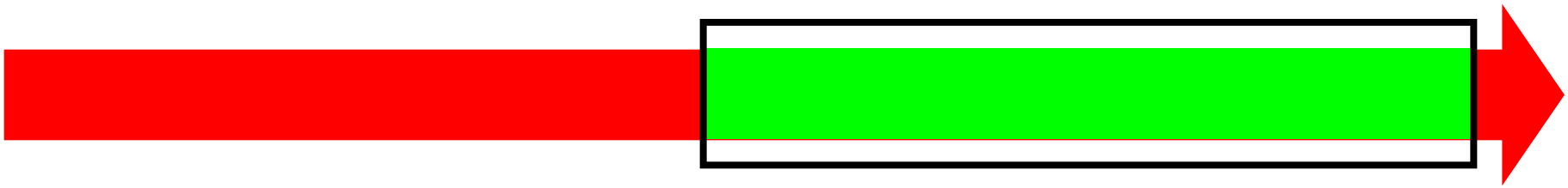
# Summary

## Early phase

**Focus on**

- **Prevent disease progression**
- **Suppress viral replication**
- **Prevent resistance mutation development**
- **Maintain adherence**

# Summary




**Focus on**

- **Long term toxicity**
- **Long-term HIV infection**
- **Co-morbidities**
- **Ageing**