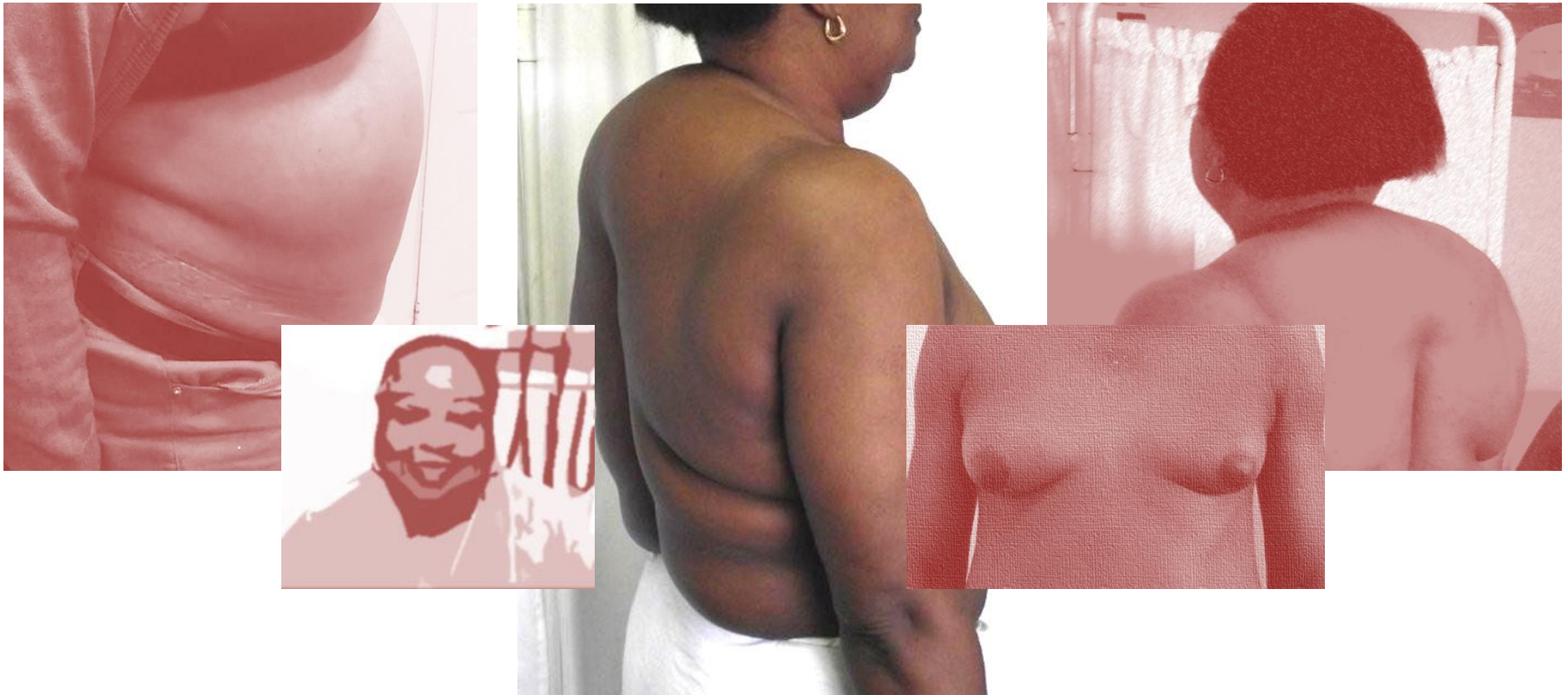


**MANAGING COMORBID DISEASE IN  
HIV-INFECTED PATIENTS IN AFRICA IN 2014.  
Diabetes, Hypertension, Cholesterol.**

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 (7.0mmol/L) or more
- or a
- 2-hour plasma glucose level of 200mg/dL (11.1mmol/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**

**AGE**

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

**BMI**

**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**

Stanifer JW, Jing B, Tolan S, et al. The epidemiology of chronic kidney disease  
in sub-Saharan Africa: a systematic review and meta-analysis.  
*Lancet Glob Health* 2014 March; 2: e174-181

# **DIABETES in HIV CARE**

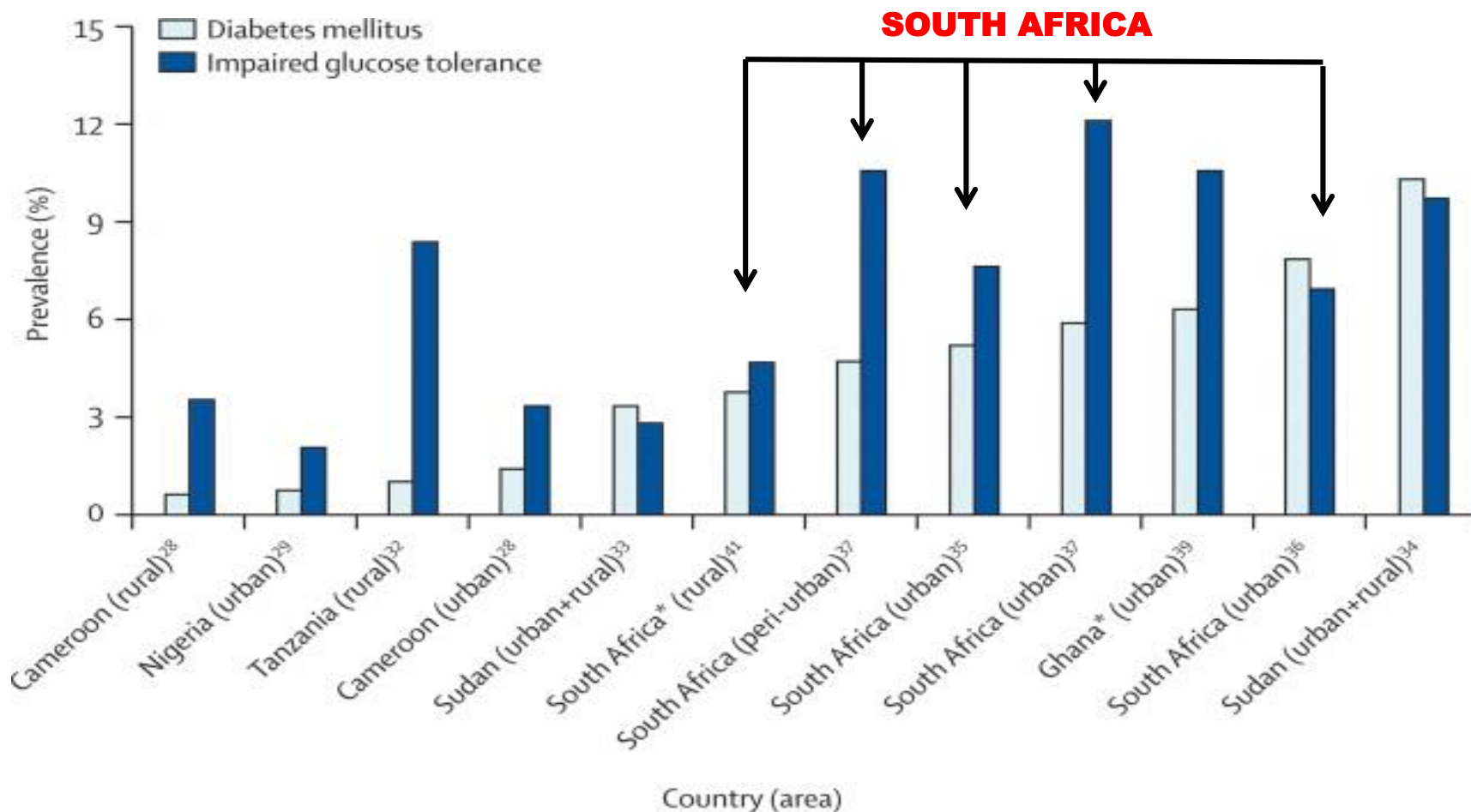
**The projected growth of type II DM in sub-Saharan Africa between the years 2010 and 2030 is 98%.**

**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.**

Mbanya JCN, Motala AA, Sobngwi E, Assah FK, Enoru ST. Diabetes in sub-Saharan Africa. *Lancet* 2010; 375: 2254-66

# DIABETES. HIV. AFRICA

Mbanya JCN, Motala AA, Sobngwi E, Assah FK, Enoru ST.  
Diabetes in sub-Saharan Africa. Lancet 2010; 375: 2254-66

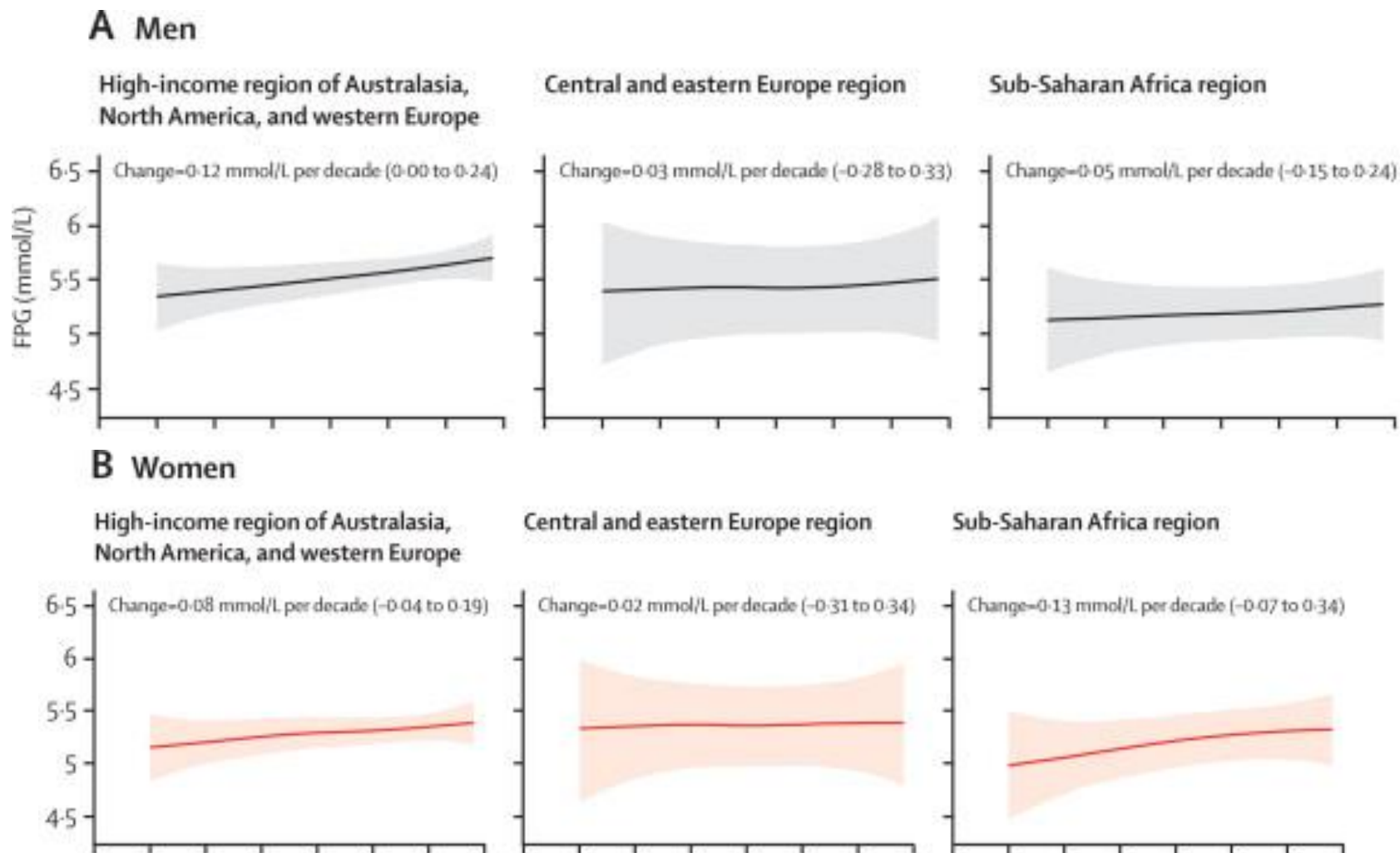


**Figure. Prevalence of diabetes mellitus and impaired glucose tolerance in community surveys in Africa. \*1998 WHO criteria**

## Reported prevalence of Type II DM in Africa:

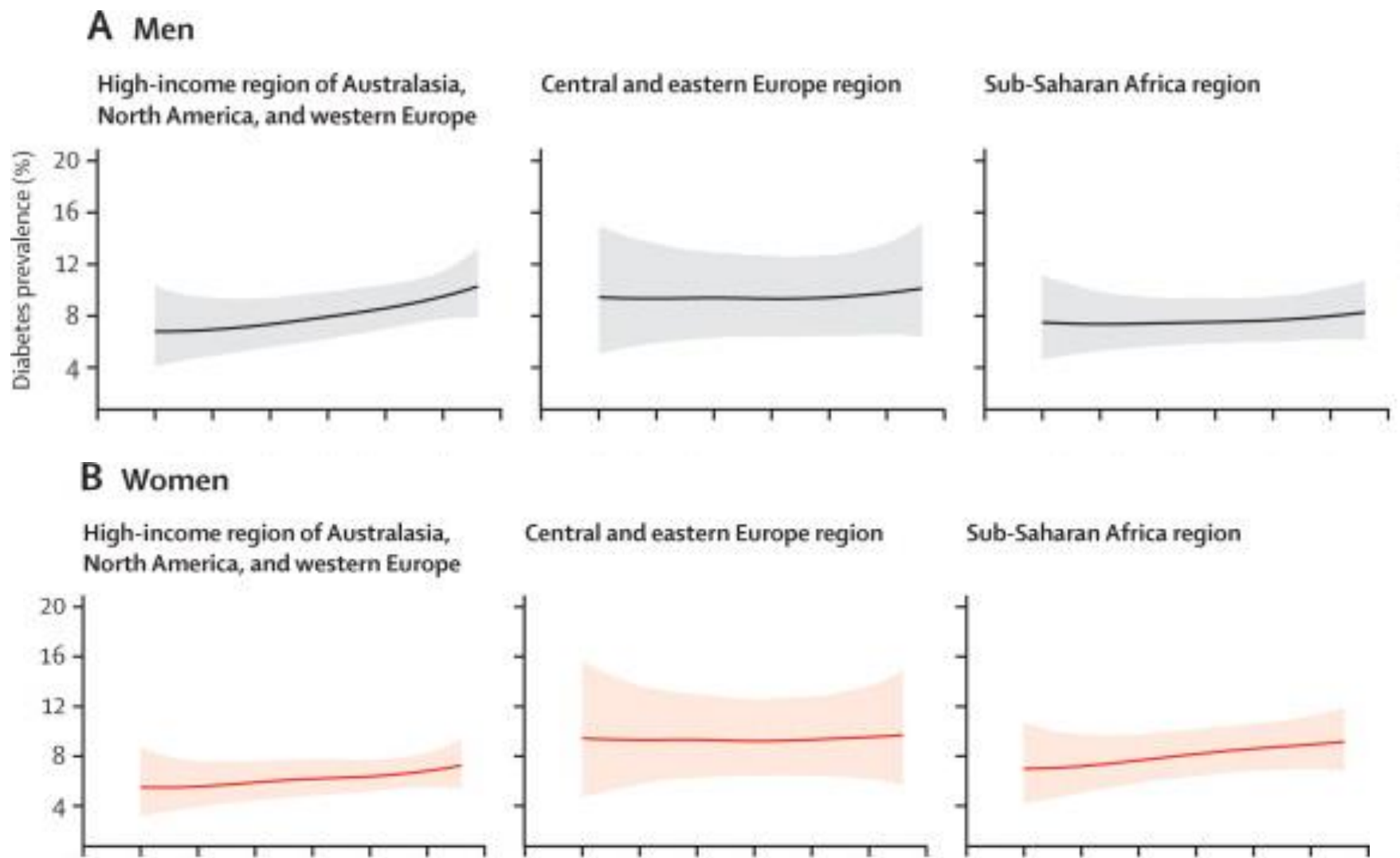
COUNTRY	PREVALENCE	SOUTH AFRICA URBAN	PREVALENCE	
<b>Benin</b>	<b>3%</b>	<b>Investigator</b>	<b>DM</b>	<b>GTT impaired</b>
<b>Mauritania</b>	<b>6%</b>	<b>Omar (1993)</b>	<b>5.3%</b>	<b>7.7%</b>
<b>Cameroon</b>	<b>6.1%</b>	<b>Levitt (1993)</b>	<b>8.0%</b>	<b>7.0</b>
<b>Congo</b>	<b>7.1%</b>	<b>Mollentze (1995)</b>	<b>6.0%</b>	<b>12.2%</b>
<b>Zimbabwe</b>	<b>10.2%</b>	<b>Mollentze: peri-urban (1995)</b>	<b>4.8%</b>	<b>10.7%</b>
<b>DRC</b>	<b>14.5%</b>			

Mbanya JCN, Motala AA, Sobngwi E, Assah FK, Enoru ST. Diabetes in sub-Saharan Africa. *Lancet* 2010; 375: 2254-66



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

Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, et al, on behalf of the Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Blood Glucose). National, regional and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 3270 country-years and 2.7 million participants. *Lancet* 2011; 378: 31-40

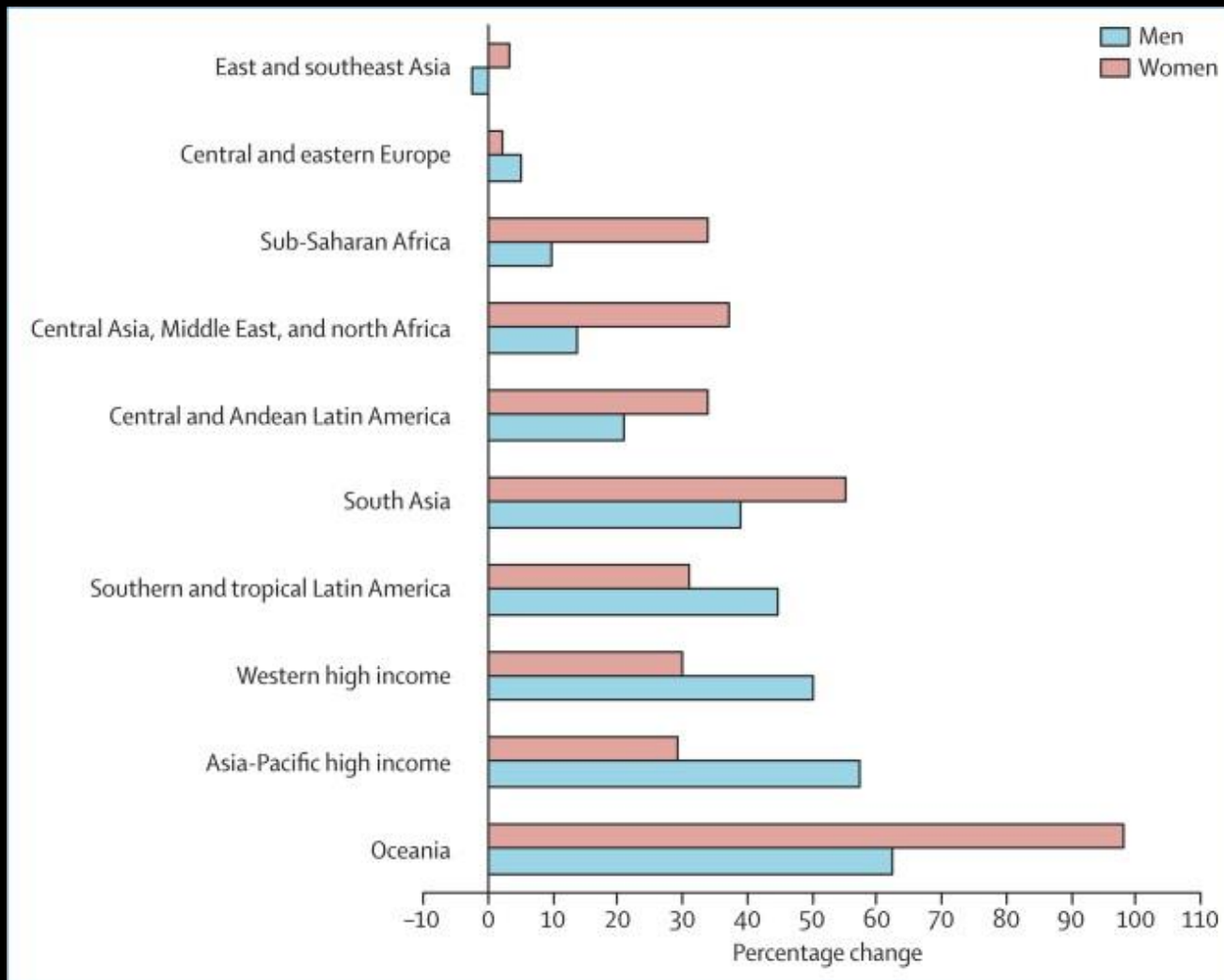


**Figure. Trends in Age-standardised diabetes prevalence by region between 1980 and 2008 for (A) men and (B) women.**

Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, et al, on behalf of the Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group (Blood Glucose). National, regional and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 3270 country-years and 2.7 million participants. *Lancet* 2011; 378: 31-40



**Tobias M. Global control of diabetes: information for action. Lancet 2011; 378: 3-4**



**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.**

# Swiss HIV Cohort Study

## DESCRIPTION:

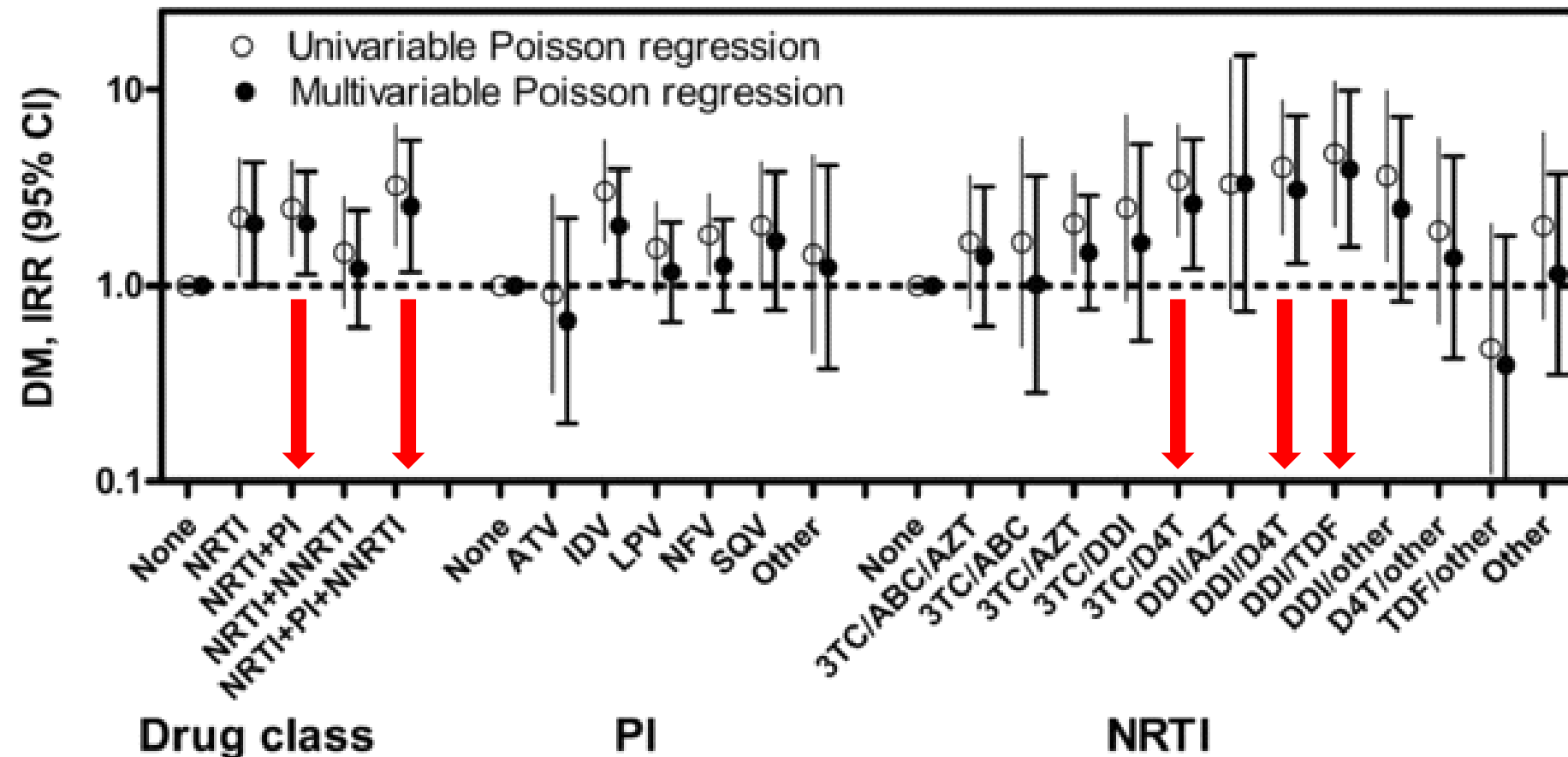
Prospective cohort-study, clinic based. Started in 1988

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**

Ledergerber B, Furrer H, Rickenbach M, Lehmann R, et al. and the Swiss HIV Cohort Study.  
Factors Associated with the Incidence of Type 2 Diabetes Mellitus in HIV-Infected  
participants in the Swiss HIV Cohort Study. Clin Infect Dis 2007; 45: 111-9



**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.

Ledergerber B, Furrer H, Rickenbach M, Lehmann R, et al. and the Swiss HIV Cohort Study. Factors Associated with the Incidence of Type 2 Diabetes Mellitus in HIV-Infected participants in the Swiss HIV Cohort Study. *Clin Infect Dis* 2007; 45: 111-9

<b>DRUG CLASS</b>	<b>ADVERSE METABOLIC EFFECT</b>	<b>IMPACT ON CORONARY HEART DISEASE</b>
<b>PROTEASE INHIBITOR</b>		
<b>LOPINAVER/r</b>	<b>Dyslipidemia+++; insulin resistance++</b>	Cumulative exposure= an independent risk for MI
<b>ATAZANAVER/r</b>	Dyslipidemia+; insulin resistance+	No data available: insufficient patients (numbers) exposed
<b>DARUNAVER/r</b>	Dyslipidemia+; insulin resistance+	No data available: insufficient patients exposed
<b>RITONAVER</b>	<b>Dyslipidemia+++; insulin resistance+++</b>	This drug is never used on its own i.e. a used as a pharmacological 'booster'.
<b>SAQUINAVER</b>	Dyslipidemia+; insulin resistance+	No associated risk for MI
<b>INDINAVER</b>	<b>Dyslipidemia and insulin resistance+++</b>	Controversial results
<b>AMPRENAVER/r</b>	Dyslipidemia+; insulin resistance+	No data available: insufficient numbers exposed
<b>TIPRANAVER/r</b>	Dyslipidemia++; insulin resistance+	No data available: insufficient numbers exposed
<b>NELFINAVER</b>	Dyslipidemia+; insulin resistance+	No associated risk for MI

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

Bocara F, Lang S, Meuleman C, Ederhy S, Mary-Krause M, et al.  
HIV and Coronary Heart Disease.  
JACC 2013; 61: 511-23

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

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

Bocara F, Lang S, Meuleman C, Ederhy S, Mary-Krause M, et al.  
HIV and Coronary Heart Disease.  
*JACC* 2013; 61: 511-23

# LIFESTYLE MODIFICATION

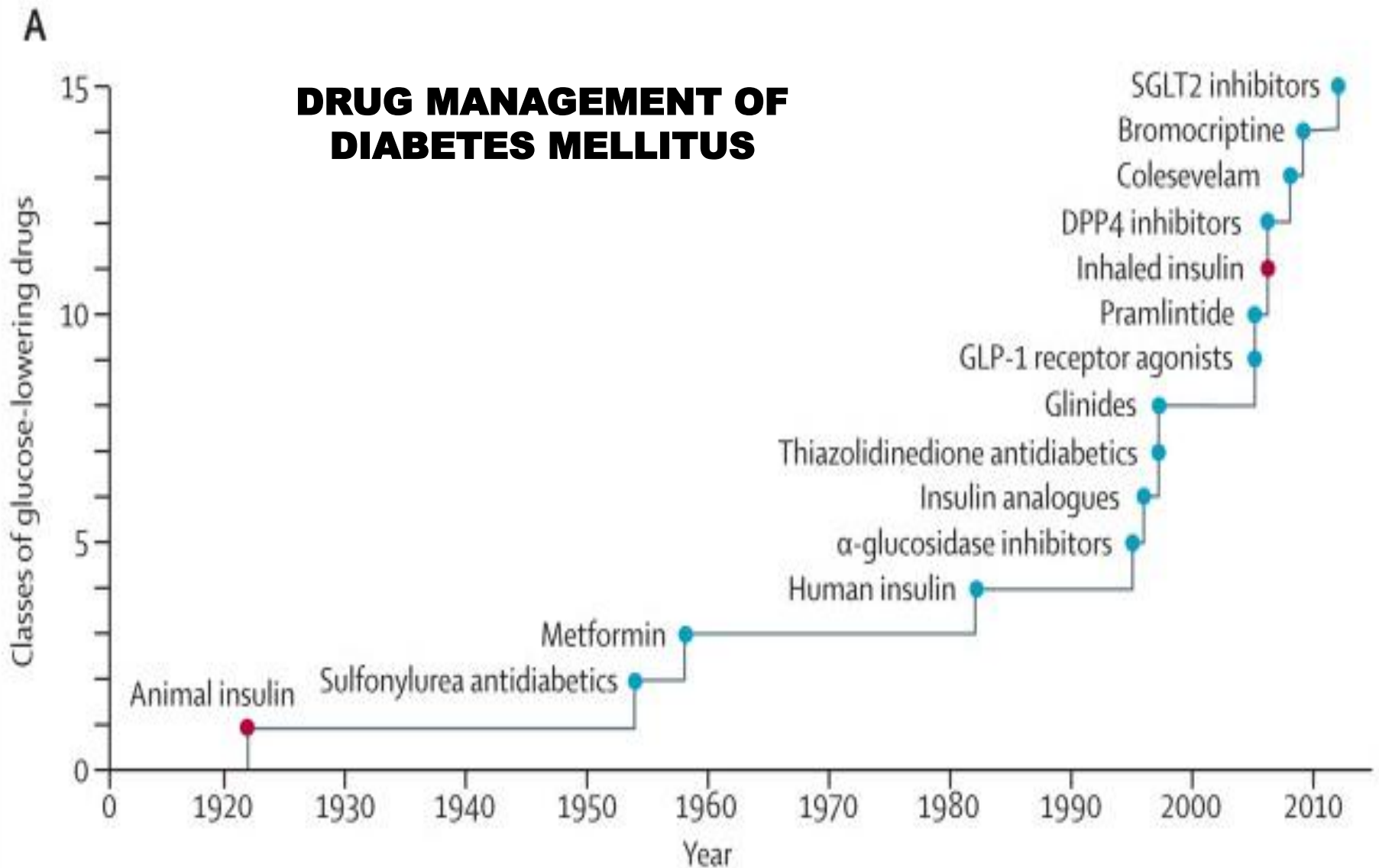
## Weight loss/diet:

**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.  
*N Engl J Med* 2012; 366: 1319-27



**Figure. Increasing complexity of the drug management of diabetes mellitus over time.**

Khan SE, Cooper ME, Del Prato S. Pathophysiology and treatment of type 2 diabetes: perspectives on the past, present and future.

*Lancet* 2014; 383: 1068-83

**Second-generation sulfonylureas: Glibenclamide; Gliclazide; Glimeriride; Glipizide**

**Biguanide: Metformin**

**Peroxisome proliferator-activated receptor  $\gamma$  agonists: Thiazolidinediones:  
Pioglitazone; Rosiglitazone**

**$\alpha$ -Glucosidase inhibitors: Acarbose; Miglitol; Voglibose**

**DPP4 inhibitors: Alogliptin; Linagliptin; Saxagliptin; Sitagliptin; Vildagliptin**

**SGLT2 inhibitors: Canagliflozin; Dapagliflozin**

**Glinides: Nateglinide; Repaglinide**

**Bile-acid-binding resins: Colesevelam**

**Dopamine-receptor agonists: Bromocriptine**

**Oral drugs approved for treatment of hyperglycemia in type 2 diabetes.**

Khan SE, Cooper ME, Del Prato S. Pathophysiology and treatment of type 2 diabetes: perspectives on the past, present and future. *Lancet* 2014; 383: 1068-83



**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**

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

**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.**

# **HYPERTENSION. HIV. AFRICA**

# THE HEART OF SOWETO STUDY

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

Sliwa K, Wilkinson D, Hansen C, et al. Spectrum of heart disease and risk factors in a black urban populations in South Africa (the Heart of Soweto Study): a cohort study. *Lancet* 2008; 371: 915-22

## Study population:

N = 4162 confirmed with cardiovascular disease

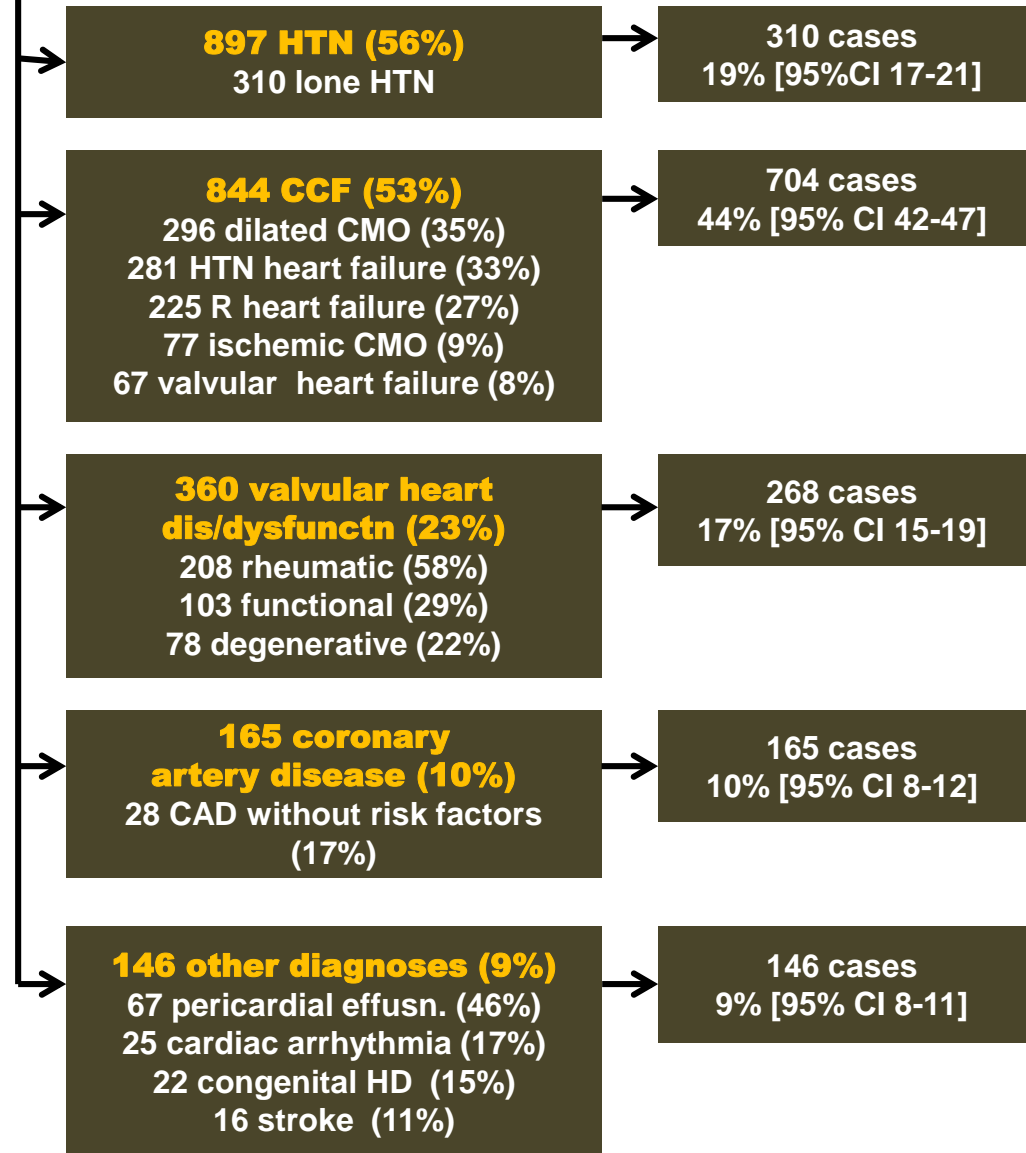
**N = 1593 (38%) newly diagnosed**

N = 2569 (62%) previously diagnosed and on treatment

N = 74 (5%) HIV-positive

1593 new cases of cardiac disease

## Primary diagnosis



**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.**

Sliwa K, Wilkinson D, Hansen C, et al. Spectrum of heart disease and risk factors in a black urban population in South Africa (the Heart of Soweto Study): a cohort study. Lancet 2008; 371: 915-22

## THE HEART OF SOWETO STUDY (2006)

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

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

Sliwa K, Wilkinson D, Hansen C, et al. Spectrum of heart disease and risk factors in a black urban population in South Africa (the Heart of Soweto Study): a cohort study. *Lancet* 2008; 371: 915-22

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

## **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 > 90 mmHg  
and characterized as mild (140-159.9/90-99.9)  
or moderate/severe ( $\geq 160/\geq 100$ )**

**Brennan AT, Fox MP, Maskew M, Sanne I, et al. Predictors of incident hypertension in HIV-positive adults over 24 months on ART in South Africa. CROI Boston, February 2014, Poster #79**

**HIV AND HYPERTENSION: HELEN JOSEPH HOSPITAL**

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

<b>Age</b>	<b>HR for HTN at 24m [95%CI]</b>	<b>HR for mild HTN at 24m [95%CI]</b>	<b>HR for mod/severe HTN at 24m [95%CI]</b>
<b>40-49.9y</b>	1.6 [1.4-1.7]	1.5 [ 1.4-1.7]	1.7 [1.2-2.3]
<b>≥50y</b>	2.5 [2.2-2.9]	2.3 [2.0-2.6]	4.3 [3.1-6.0]
<b>BMI at ART start</b>			
<b>25-29.9</b>	1.5 [1.3-1.7]	1.5 [1.3-1.7]	1.6 [1.2-2.3]
<b>30-34.9</b>	1.8 [1.5-2.2]	1.8 [1.5-2.2]	1.9 [1.1-3.3]
<b>≥35-39.9</b>	2.8 [2.0-3.8]	2.5 [1.8-3.5]	4.4 [2.1-9.2]

**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.**

Brennan AT, Fox MP, Maskew M, Sanne I, et al. Predictors of incident hypertension in HIV-positive adults over 24 months on ART in South Africa. CROI Boston, February 2014, Poster #79

**HIV AND HYPERTENSION: HELEN JOSEPH HOSPITAL**

# **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%)**

**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**

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

**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:  
HR1.4 [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

**HIV AND HYPERTENSION: HELEN JOSEPH HOSPITAL**

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

**OUTCOME**

**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

**HIV AND HYPERTENSION: HELEN JOSEPH HOSPITAL**

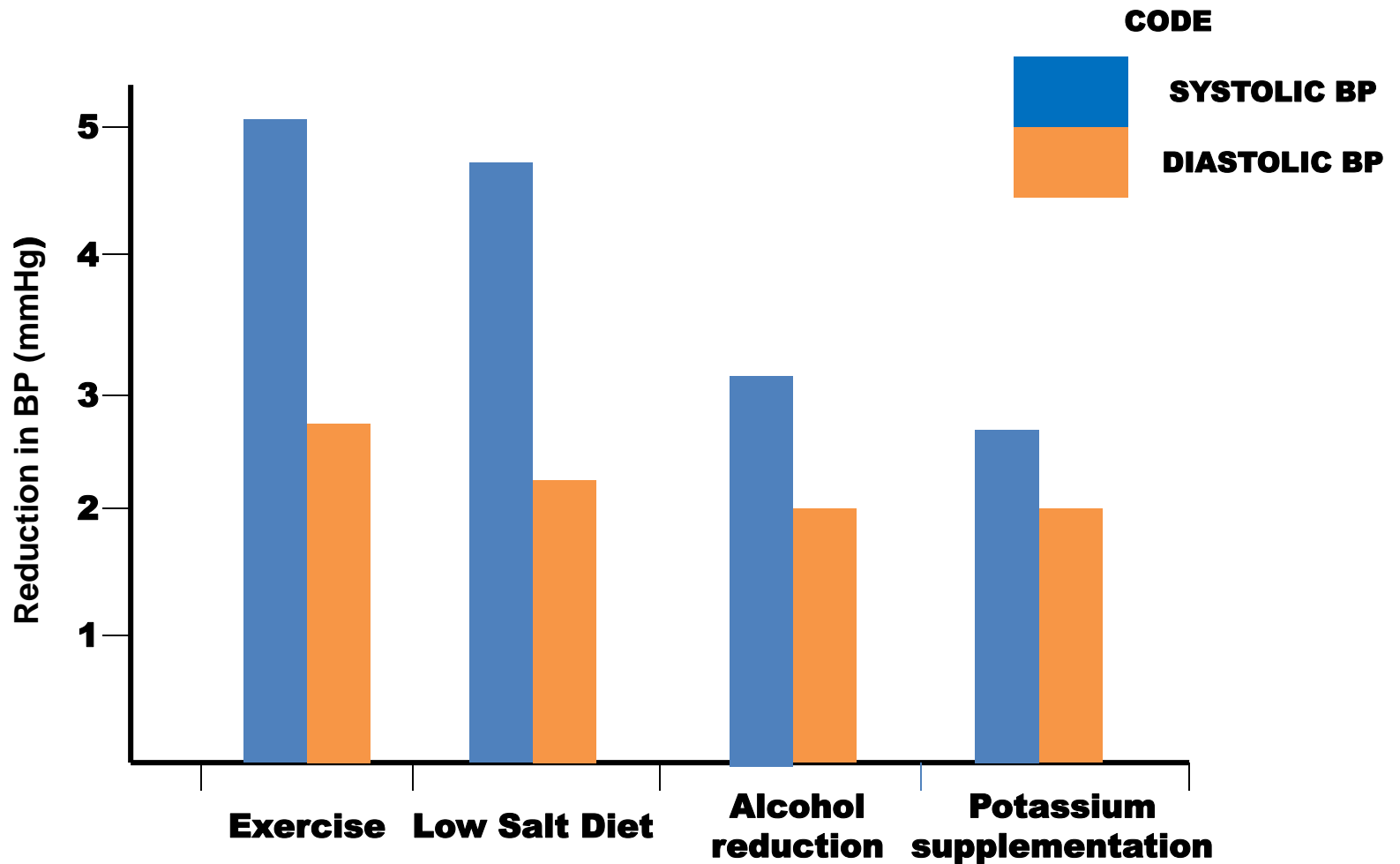


Figure. Estimated decrease in blood pressure mediated by non-pharmacological anti-hypertensive interventions.

**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**

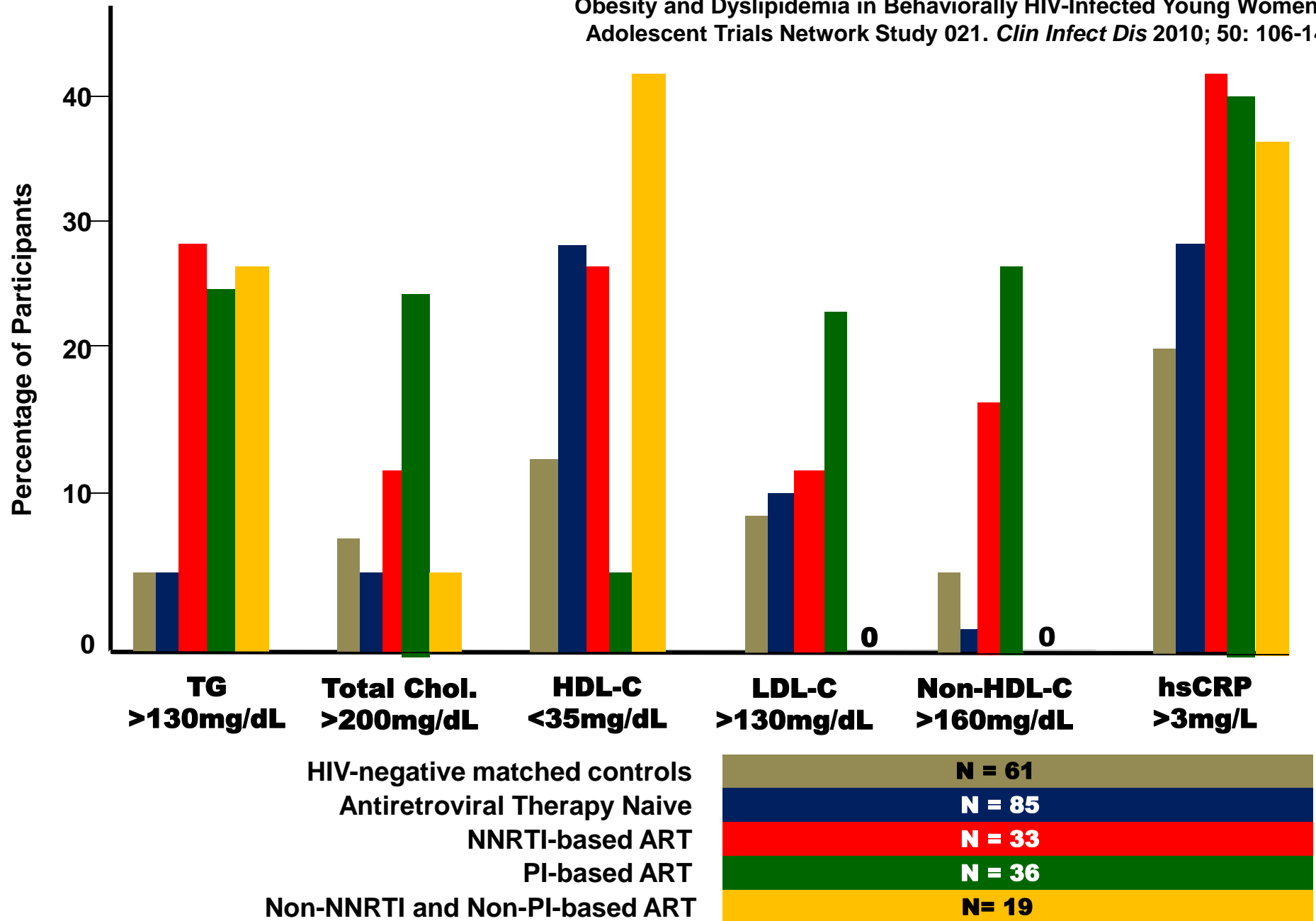
**ON PI-BASED  
ART  
N = 36**

**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**

Mulligan K, Harris DR, Monte D, Stoszek S, et al., for the Adolescent Trials Network 021 Protocol Team. Obesity and Dyslipidemia in Behaviorally HIV-Infected Young Women: Adolescent Trials Network Study 021. *Clin Infect Dis* 2010; 50: 106-14





## **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.**

**HMG-Co-A Reductase Inhibitor**

**Antiretroviral Agent:**

**Dosing Recommendations**

**ATOVASTATIN**

**All PIs**

**Use lowest possible starting dose and monitor carefully: rhabdomyolysis**

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

**NNRTI**

**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**

Corbett AH, Sheffield CI. Key Pharmacologic Principles and Drug-Drug Interactions in HIV Patient Care. Accessed on 24.12.2011 at [www.clinicaloptions.com/inPractice/HIV/Antiretroviral%20Therapy/ch19](http://www.clinicaloptions.com/inPractice/HIV/Antiretroviral%20Therapy/ch19)

<b>HMG-Co-A Reductase Inhibitor</b>	<b>Antiretroviral Agent:</b>	<b>Dosing Recommendations</b>
<b>PRAVASTATIN</b>	<b>PIs</b>	
<p><b>Etravirine has no effect on pravastatin levels but efavirenz will decrease pravastatin area under the curve by 44%</b></p>	<b>Darunavir/r</b>	Potential for signif. increase in prava level: start with lowest dose and monitor closely
	<b>Lopinavir/r</b>	Prava conc. increases: monitor carefully
	<b>NNRTI</b>	
	<b>Efavirenz</b>	<b>Adjust prava dose accord 2 lipid response</b>
	<b>Etravirine</b>	<b>No interaction</b>
	<b>Nevirapine</b>	<b>No data</b>
<b>Rilpivirine</b>	<b>No data</b>	

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**

Corbett AH, Sheffield CI. Key Pharmacologic Principles and Drug-Drug Interactions in HIV Patient Care. Accessed on 24.12.2011 at [www.clinicaloptions.com/inPractice/HIV/Antiretroviral%20Therapy/ch19](http://www.clinicaloptions.com/inPractice/HIV/Antiretroviral%20Therapy/ch19)

HMG-Co-A Reductase Inhibitor	Antiretroviral Agent:	Dosing Recommendations
<b>Simvastatin</b>	<b>PIs</b>	<b>CONTRAINDICATED</b>
<p><b>NNRTIs reduce the atorvastatin, simvastatin and lovastatin blood levels by 40-80%</b></p>	<b>NNRTI</b>	
	Efavirenz	Adjust dose of simvastatin according to lipid response
	Etravirine	Do not exceed maximum recommended dose
	Nevirapine	
	Rilpivirine	

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

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

Corbett AH, Sheffield CI. Key Pharmacologic Principles and Drug-Drug Interactions in HIV Patient Care. Accessed on 24.12.2011 at [www.clinicaloptions.com/inPractice/HIV/Antiretroviral%20Therapy/ch19](http://www.clinicaloptions.com/inPractice/HIV/Antiretroviral%20Therapy/ch19).

## 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.



**ATAZANAVIR**

## 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

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

## ANTIRETROVIRAL 'SWITCH' REGIMENS

Avoid thymidine NRTIs and ddl; 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

## **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.**

**Estrella MM, Moosa MR, Nachega JB. Risks and Benefits of Tenofovir in the  
Context of Kidney Dysfunction un Sub-Saharan Africa.  
*Clin Infect Dis* 2014 (15 May); 58(10): 1481-3**

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

**N=302 patients**

**Age (mean) = 47y  $\pm$ 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/1.73m<sup>2</sup> in 50.6% of cohort**

**Risk factors associated**

**with eGFR<30 =**

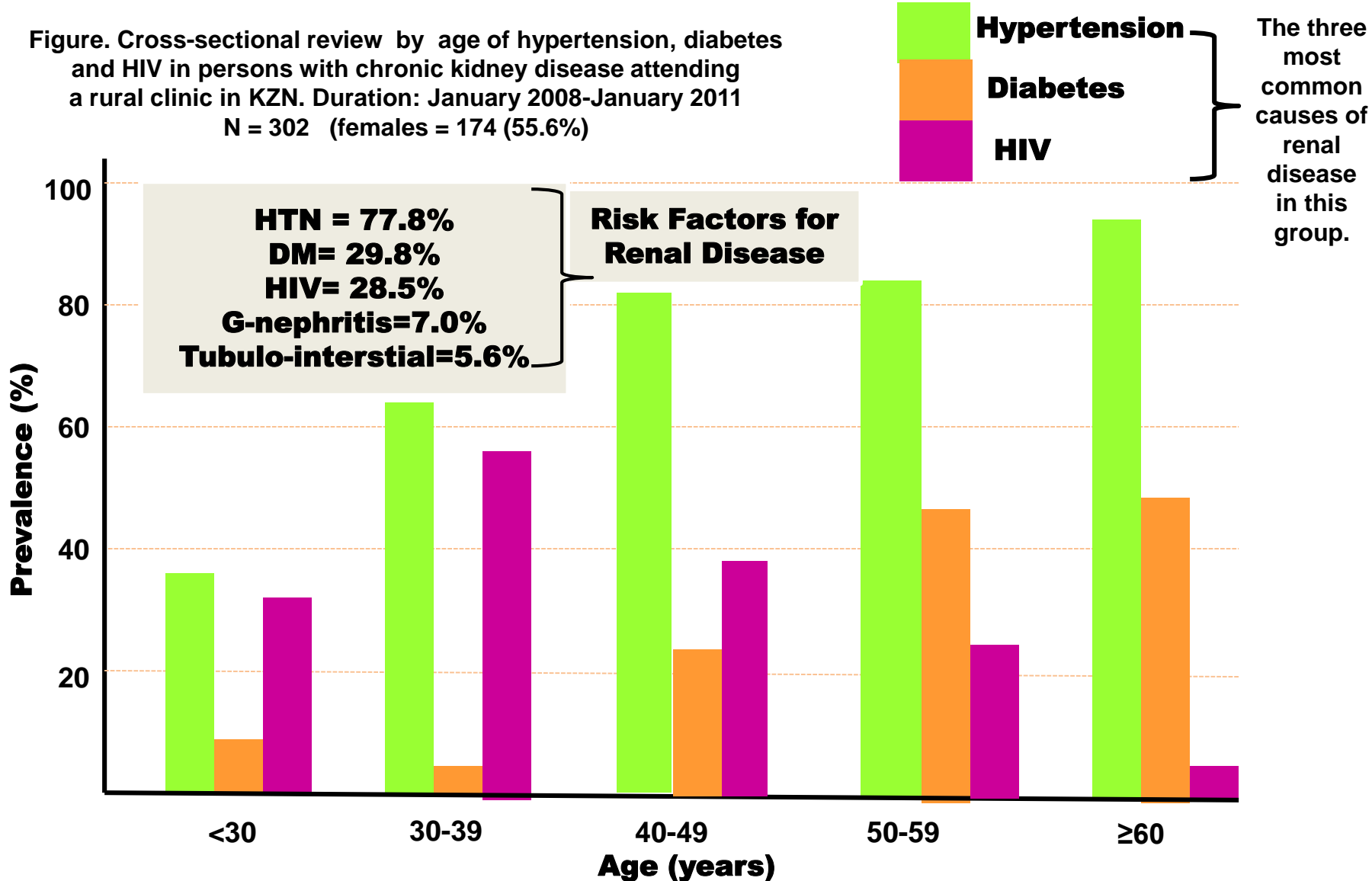
**HIV: OR 2.4 (1.3-3.4, p=.004)**

**HTN: OR 2.3 (1.3-4.2, p=.007)**

**Madala ND, Thusi GP, Assounga AGH, Naicker S. Characteristics of South African patients presenting with kidney disease in rural KwaZulu-Natal: a cross sectional study. BMC Nephrology 2014, 15:61**  
<http://www.biomedcentral.com/1471-2369/15/61> Accessed on August 22, 2014



Figure. Cross-sectional review by age of hypertension, diabetes and HIV in persons with chronic kidney disease attending a rural clinic in KZN. Duration: January 2008-January 2011  
 N = 302 (females = 174 (55.6%))



### RISK FACTORS FOR CHRONIC RENAL DISEASE IN RURAL KZN

Madala ND, Thusi GP, Assounga AGH, Naicker S. Characteristics of South African patients presenting with kidney disease in rural KwaZulu-Natal: a cross sectional study. BMC Nephrology 2014, 15:61

<http://www.biomedcentral.com/1471-2369/15/61> Accessed on August 22, 2014

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

**HIV age (mean)  $39.5 \pm 11.9$ yr vs cohort (mean)  $47.1 \pm 17.0$ yr**

**KWA-ZULU NATAL: Ngwelazana Hospital  
Rural South Africa**

Madala ND, Thusi GP, Assounga AGH, Naicker S. Characteristics of South African patients presenting with kidney disease in rural KwaZulu-Natal: a cross sectional study. BMC Nephrology 2014, 15:61  
<http://www.biomedcentral.com/1471-2369/15/61> Accessed on August 22, 2014



**END**

