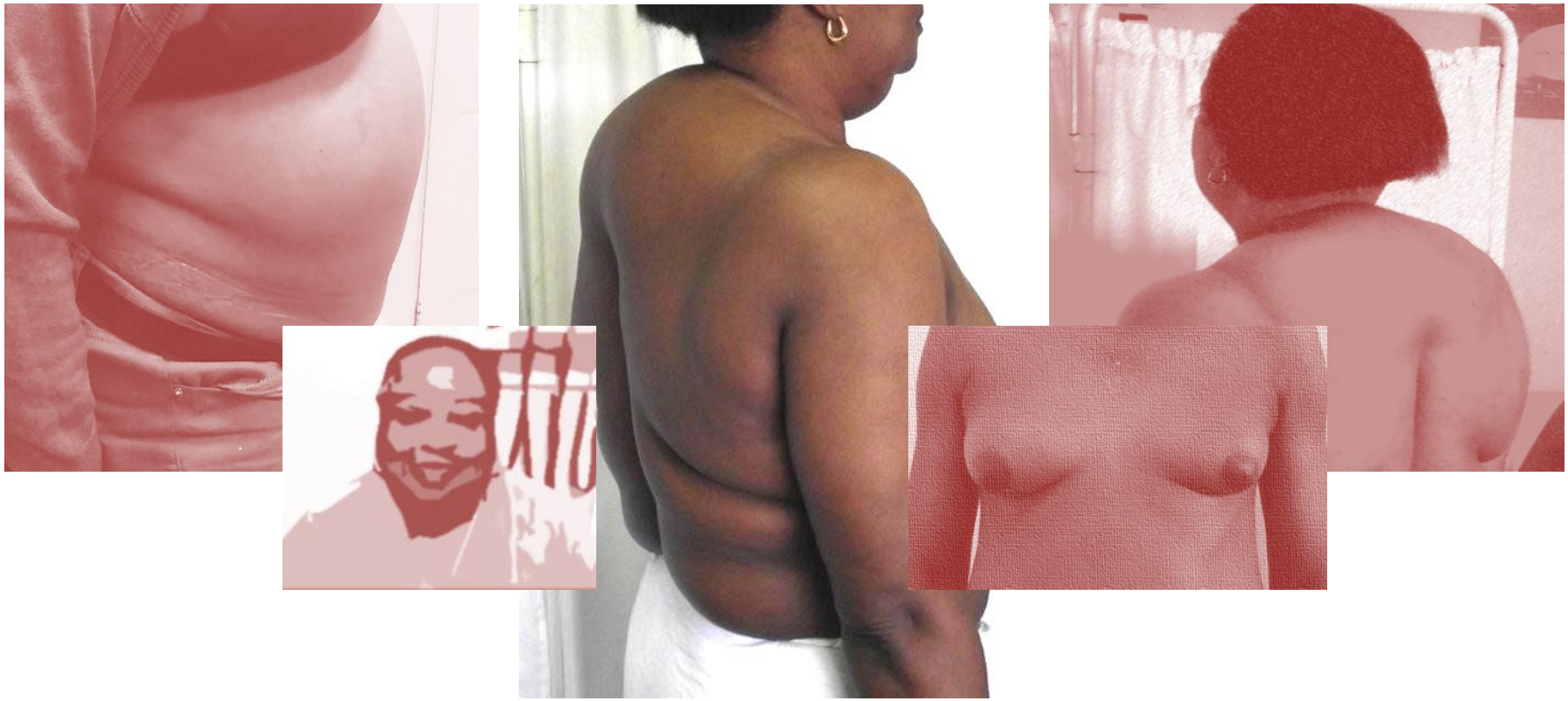
MANAGING COMORBID DISEASE IN HIV-INFECTED PATIENTS IN AFRICA IN 2014. Diabetes, Hypertension, Cholesterol.

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

Ismail-Beigo F. Glycemic Management of Type 2 Diabetes Mellitus.
N Engl J Med 2012; 366: 1319-27

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

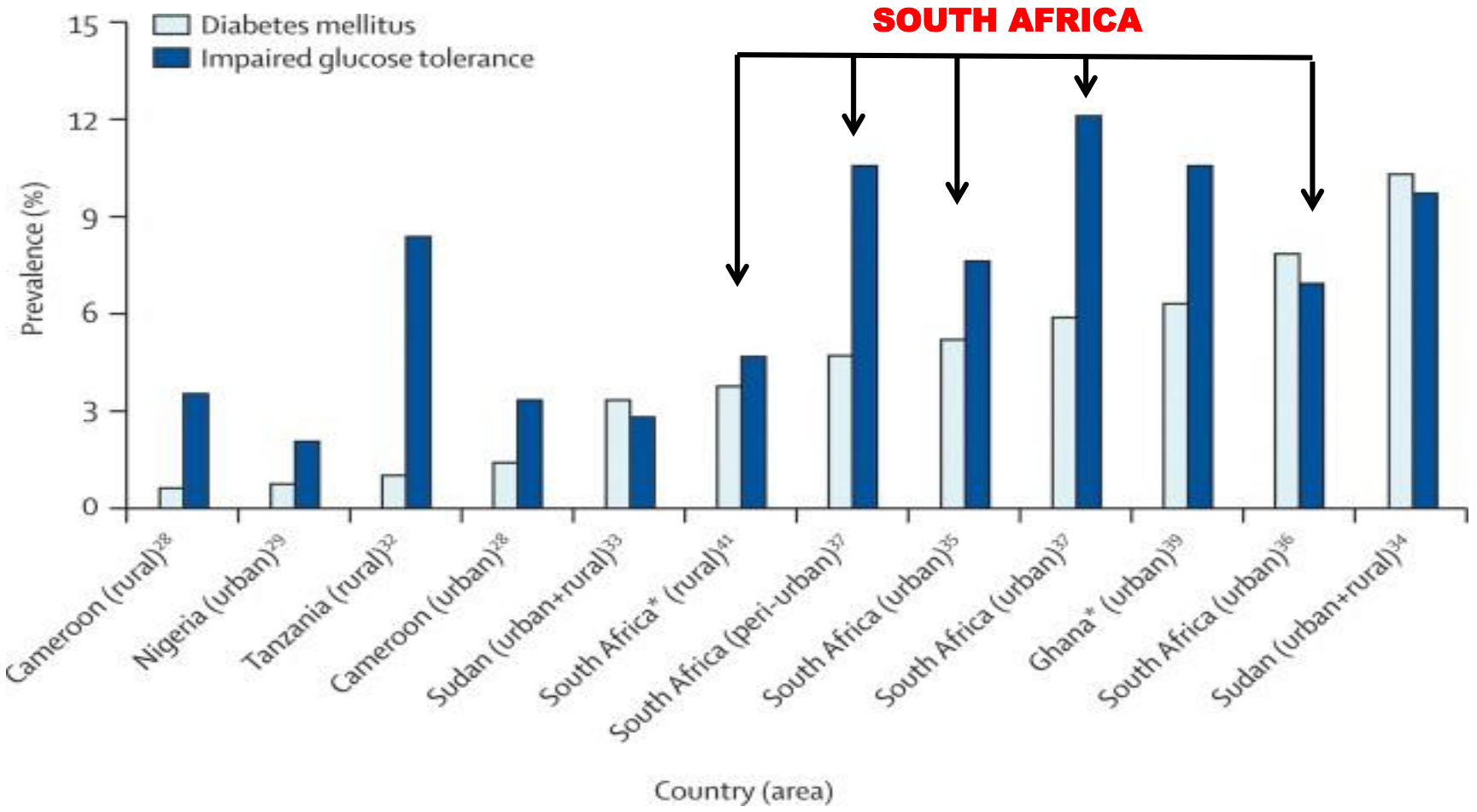


Figure. Prevalence of diabetes mellitus and impaired glucose tolerance in community surveys in Africa. *1998 WHO criteria

Reported prevalence of Type II DM in Africa:

COUNTRY	PREVALENCE
Benin	3%
Mauritania	6%
Cameroon	6.1%
Congo	7.1%
Zimbabwe	10.2%
DRC	14.5%

SOUTH AFRICA URBAN	PREVALENCE	
Investigator	DM	GTT impaired
Omar (1993)	5.3%	7.7%
Levitt (1993)	8.0%	7.0
Mollentze (1995)	6.0%	12.2%
Mollentze: peri-urban (1995)	4.8%	10.7%

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

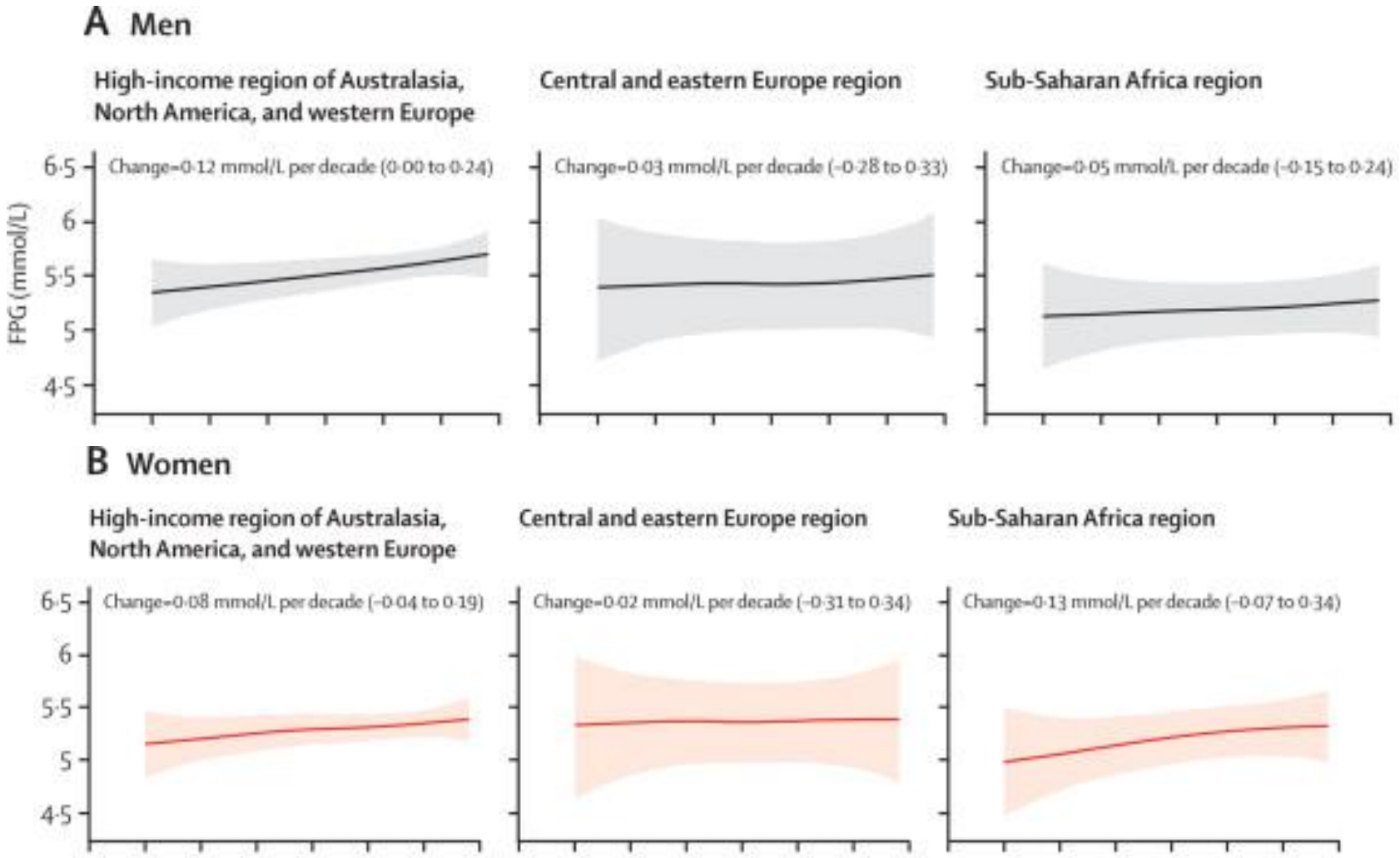
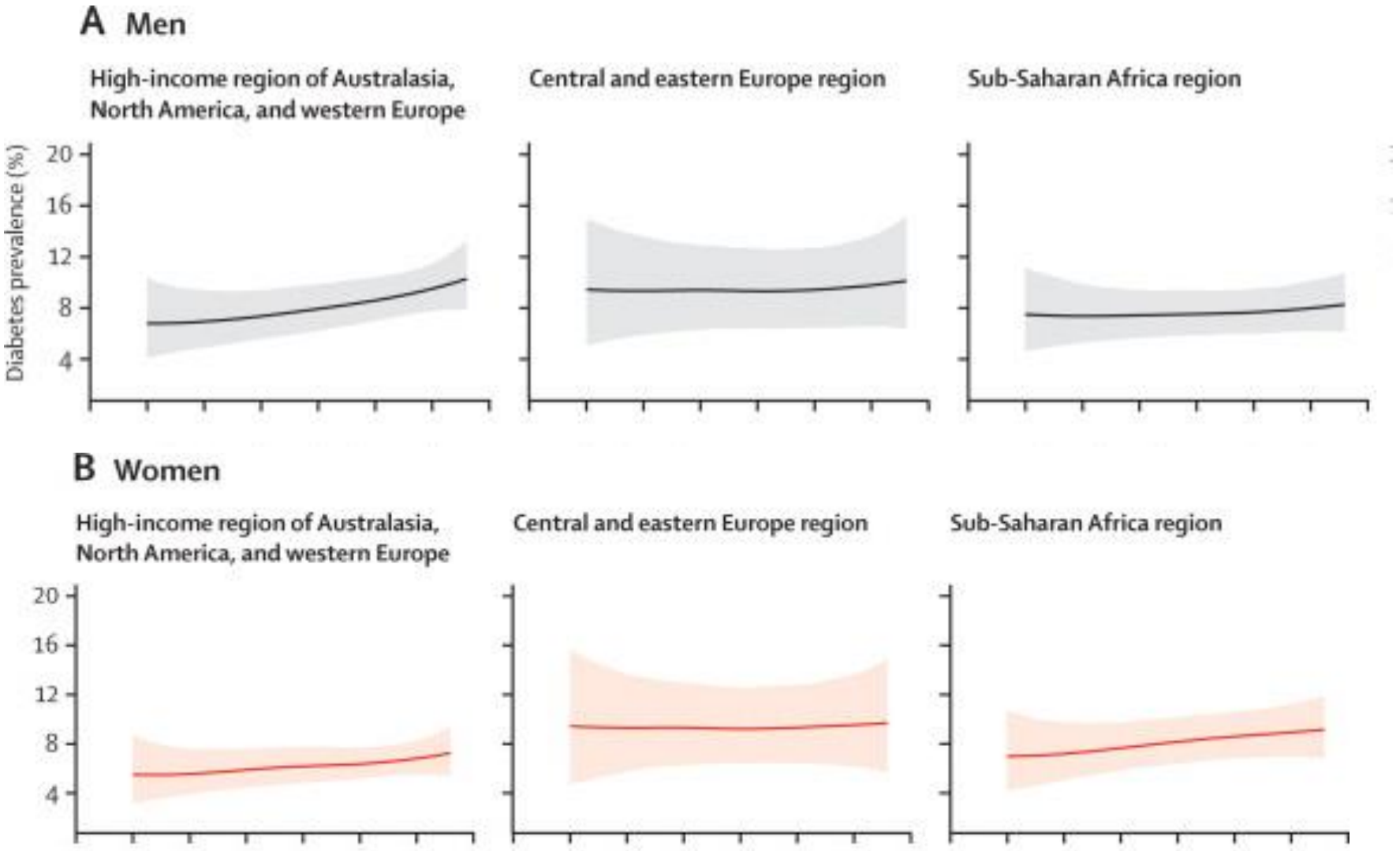


Figure. Trends in age-standardised mean fasting plasma glucose (FPG) by region between 1980 and 2008 for (A) men and (B) women.

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



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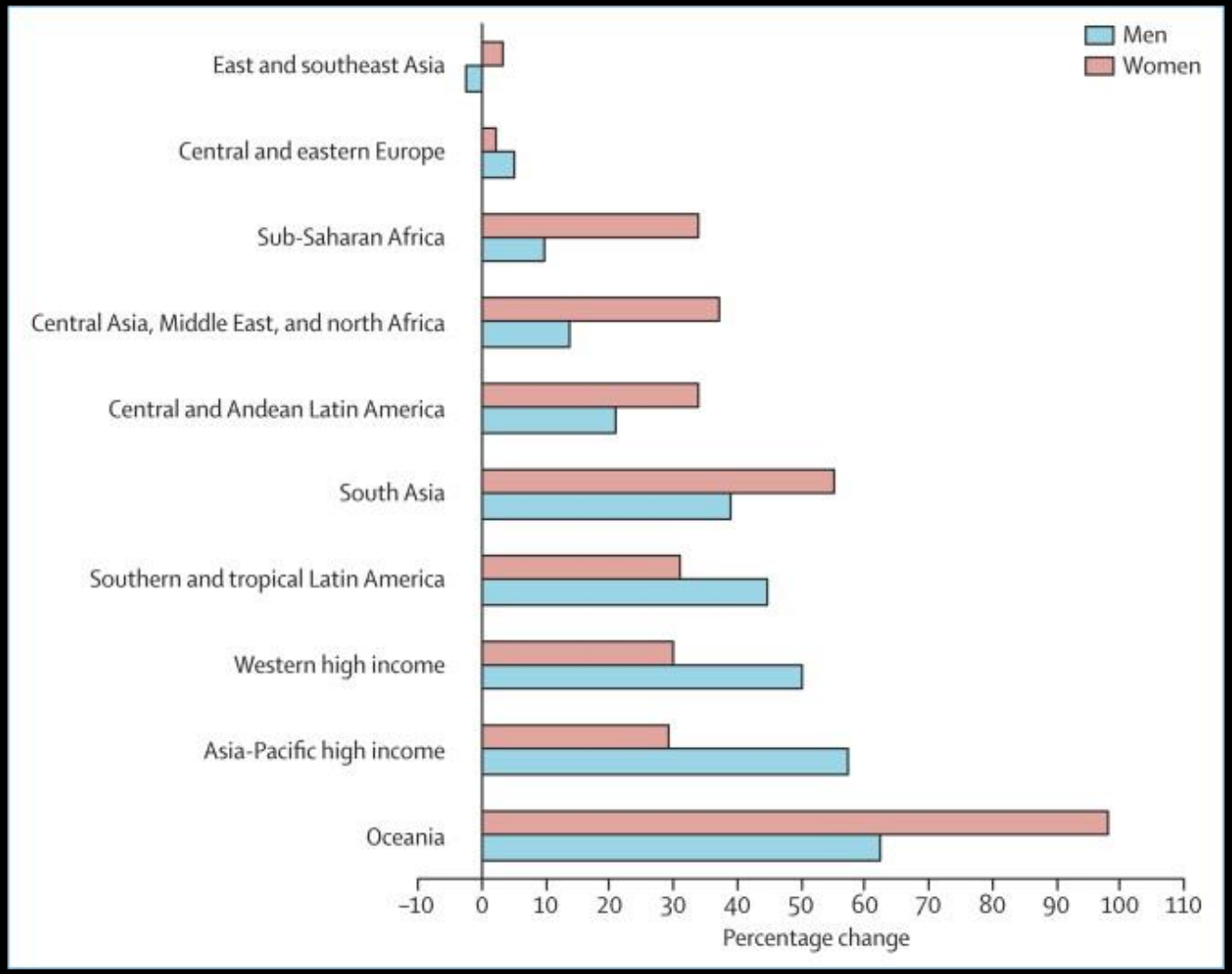


Tobias M. Global control of diabetes: information for action. Lancet 2011; 378: 3-4

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

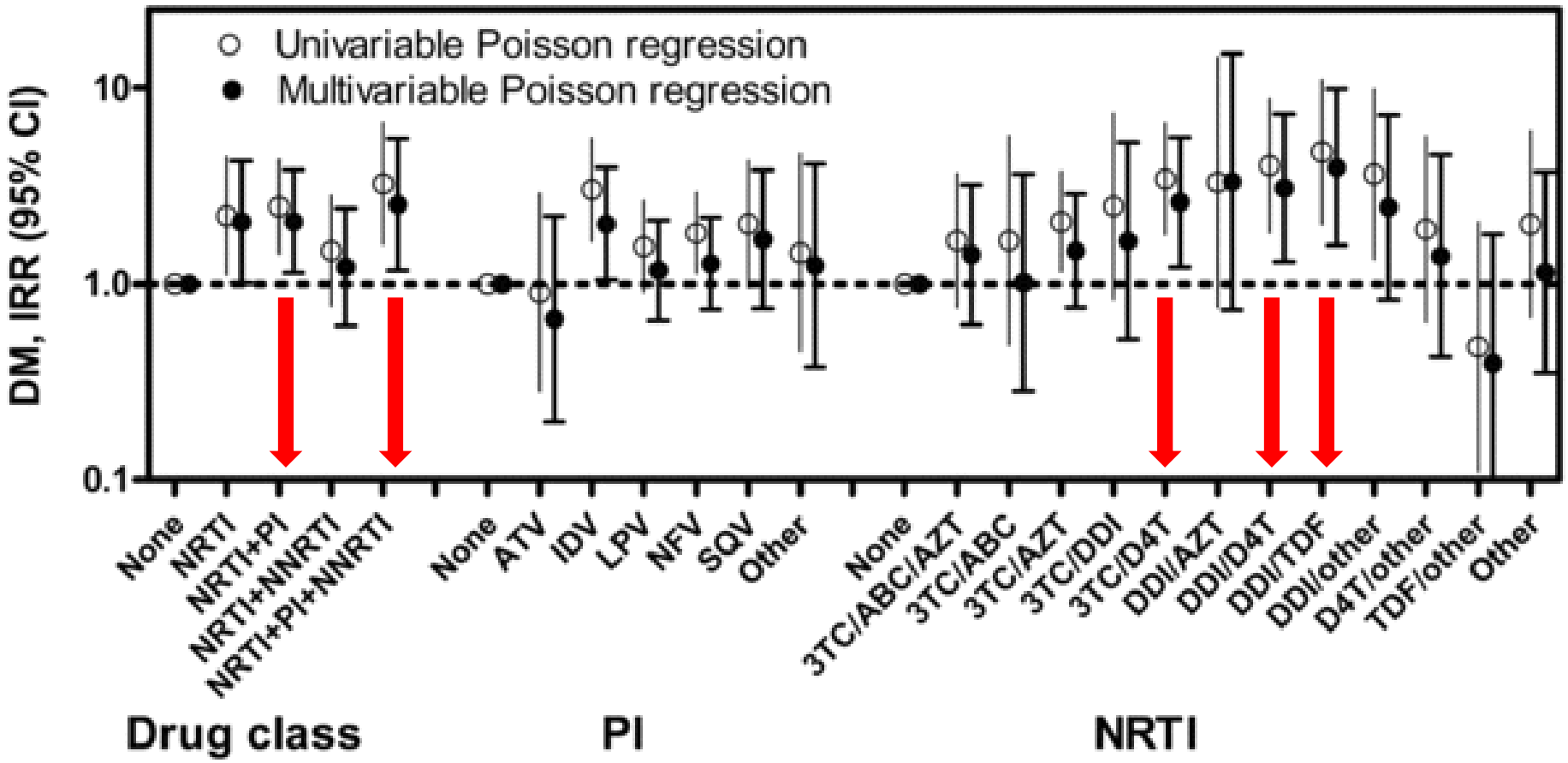


Figure. Incidence rate ratios (IRRS) for the development of new-onset type 2 diabetes mellitus (DM) based on 123 events among 6513 participants with 27,798 person-years of follow-up. Shown are associations with current receipt of specific drug classes and individual protease inhibitor (PI) and nucleoside 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

DRUG CLASS	ADVERSE METABOLIC EFFECT	IMPACT ON CORONARY HEART DISEASE
PROTEASE INHIBITOR		
LOPINAVIR/r	Dyslipidemia+++; insulin resistance++	Cumulative exposure= an independent risk for MI
ATAZANAVIR/r	Dyslipidemia+; insulin resistance+	No data available: insufficient patients (numbers) exposed
DARUNAVIR/r	Dyslipidemia+; insulin resistance+	No data available: insufficient patients exposed
RITONAVIR	Dyslipidemia+++; insulin resistance+++	This drug is never used on its own i.e. a used as a pharmacological 'booster'.
SAQUINAVIR	Dyslipidemia+; insulin resistance+	No associated risk for MI
INDINAVIR	Dyslipidemia and insulin resistance+++	Controversial results
AMPRENAVIR/r	Dyslipidemia+; insulin resistance+	No data available: insufficient numbers exposed
TIPRANAVIR/r	Dyslipidemia++; insulin resistance+	No data available: insufficient numbers exposed
NELFINAVIR	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
NUCLEOTIDE/SIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTIs)		
NRTIs	Insulin resistance+: stavudine>zidovudine; dyslipidemia with didanosine and stavudine	Two NRTIs viz. abacavir and didanosine have been associated with an increased risk for MI but results 'controversial'
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTIs)		
NNRTIs	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	No association with an increased risk for MI
INTEGRASE INHIBITORS (RALTEGRAVIR) and CCR5 CO-RECEPTOR INHIBITOR (MARAVIROC)		
	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

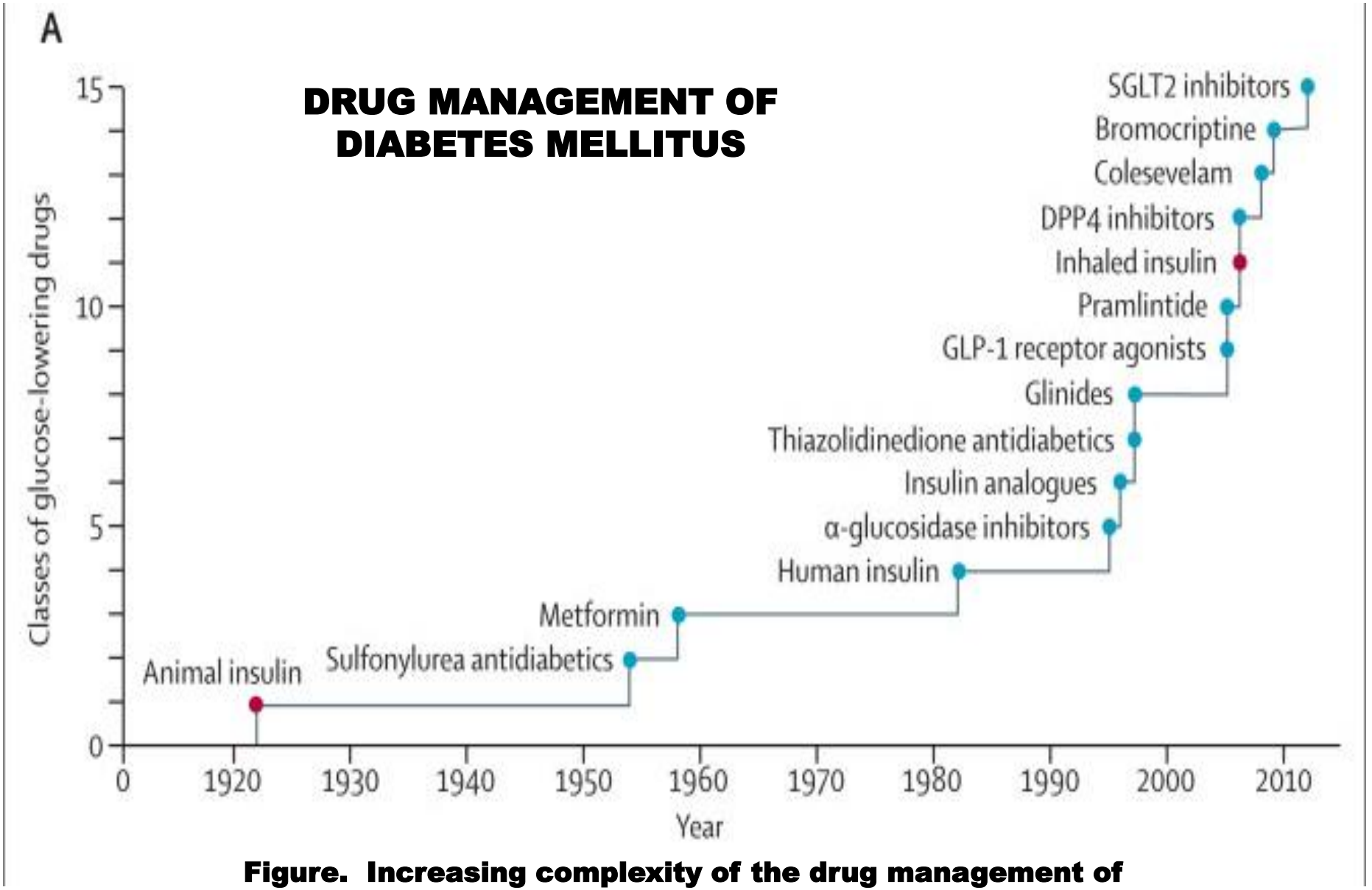


Figure. Increasing complexity of the drug management of diabetes mellitus over time.

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

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

Biguanide: Metformin

Peroxisome proliferator-activated receptor γ agonists: Thiazolidinediones: Pioglitazone; Rosiglitazone

α-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: Bromcriptine

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

Beran D, Yudkin JS. Diabetes care in sub-Saharan Africa. *Lancet* 2006; 368: 1689-95

	Hospitals (n=176)	Health centres (n=92)	Dispensaries (n= 67)	P value	Total	P value vs HIV
At least fair knowledge						
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
Experienced						
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
Comfortable						
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.

Peck R, Mghamba J, Vanoberghen F, et al. Preparedness of Tanzanian health facilities for outpatient primary care of hypertension and diabetes: a cross-sectional survey. *Lancet Global Health* 2014; 2: e285-92

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

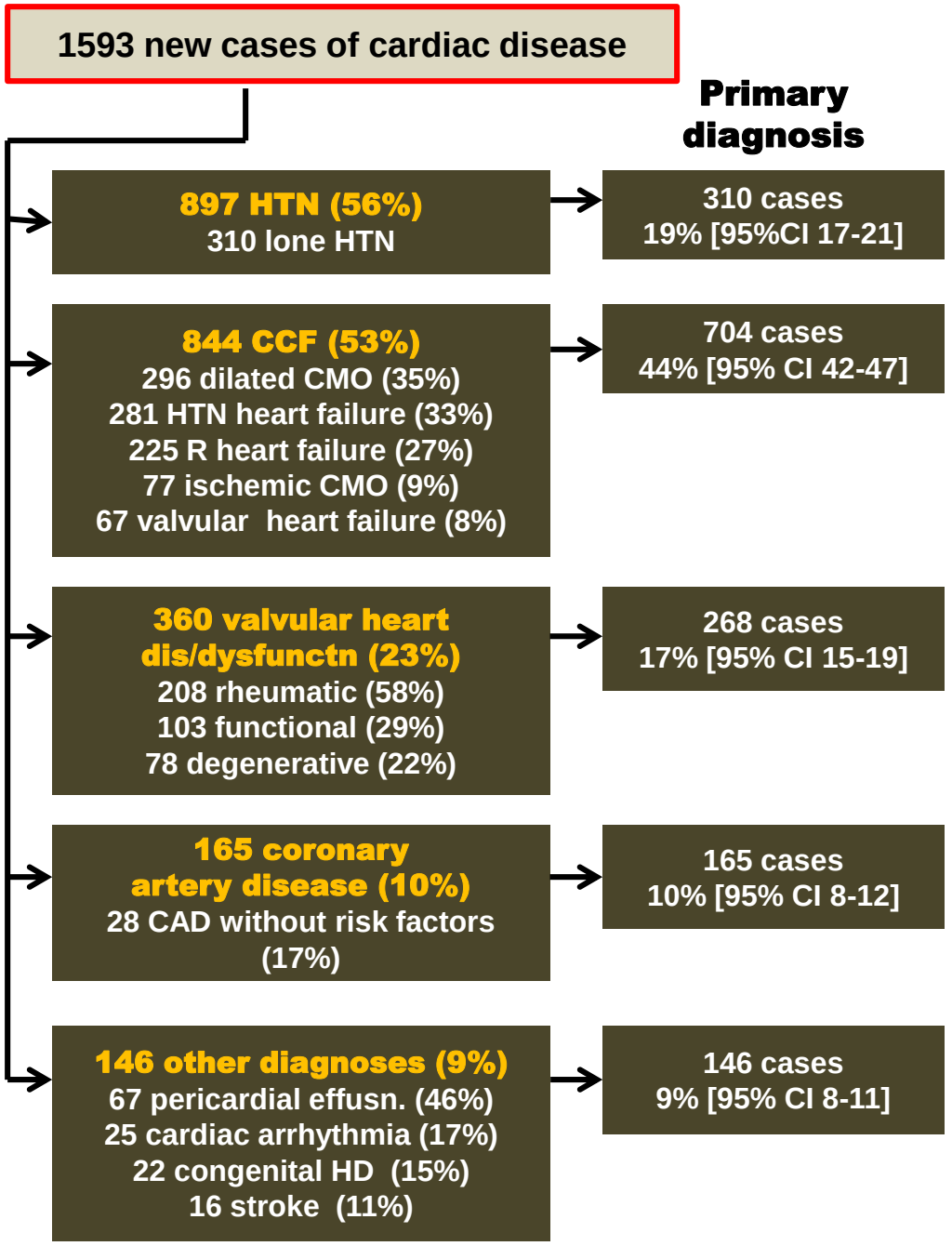
Study population:

N = 4162 confirmed with cardiovascular disease

N = 1593 (38%) newly diagnosed

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

N = 74 (5%) HIV-positive



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)
Age (yr)	**52.8 (17.1)**	**58.3 (15.3)**	**55.1 (16.2)**	**45.7 (18.2)**	**56.7 (12.4)**	**38.0 (16.6)**
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%)
High cholesterol	**159 (22%)**	**54 (38%)**	**45 (17%)**	**16 (21%)**	**37 (35%)**	**7 (20%)**
Smoker	661 (41%)	112 (36%)	327 (46%)	84 (31%)	84 (51%)	54 (37%)
Renal dysf.	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%)
Diabetes	**165 (10%)**	**41 (13%)**	**66 (9%)**	**13 (5%)**	**35 (21%)**	**10 (7%)**
HIV+ve*	**74 (5%)**	4 (1%)	35 (5%)	10 (4%)	2 (1%)	**23 (16%)**
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>90mmHg
and characterized as mild (140-159.9/90-99.9)
or moderate/severe (≥160/≥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

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

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

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

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

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 Inititation 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 Inititation 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

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

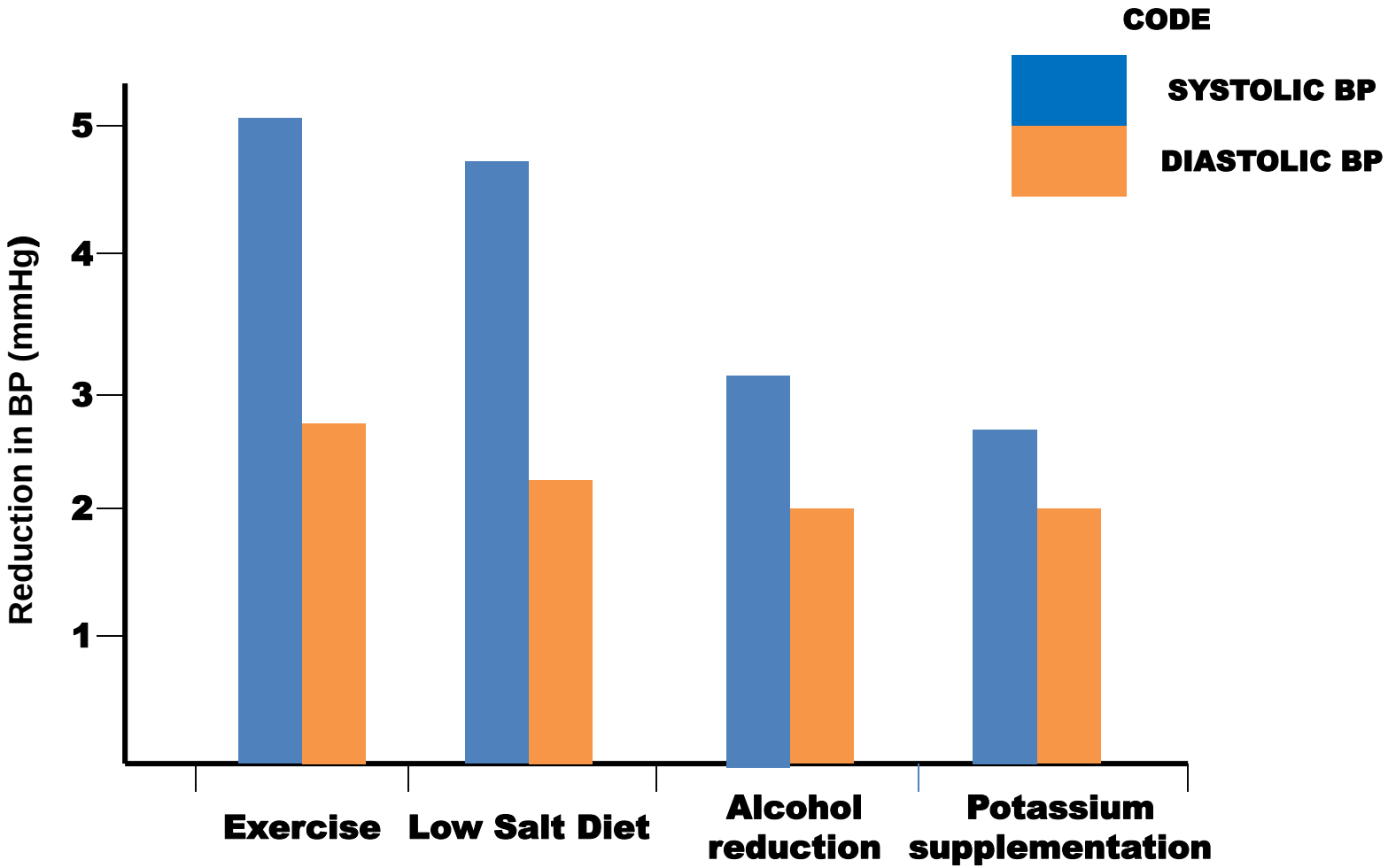


Figure. Estimated decrease in blood pressure mediated by non-pharmacological anti-hypertensive interventions.

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.

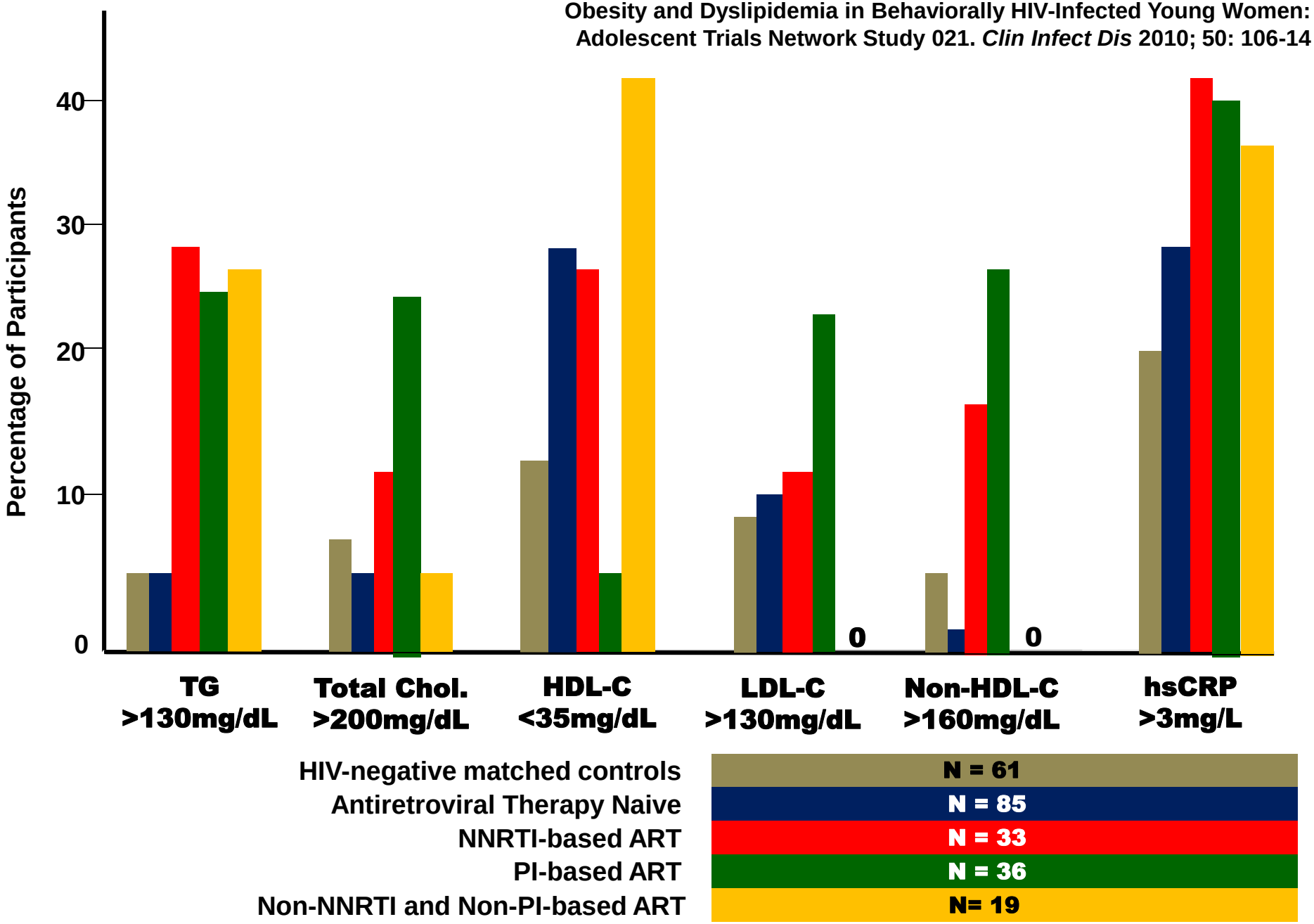
4 CATEGORIES:

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

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

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.

Goff DC, Lloyd-Jones DM, Bennet G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013 November 12 (Epub ahead of print).

HMG-Co-A Reductase Inhibitor	Antiretroviral Agent:	Dosing Recommendations
ATOVASTATIN	**All PIs**	Use lowest possible starting dose and monitor carefully: rhabdomyolysis
	NNRTI	
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

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

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

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

HMG-Co-A Reductase Inhibitor	Antiretroviral Agent:	Dosing Recommendations
Simvastatin	**PIs**	**CONTRAINDICATED**
NNRTIs reduce the atorvastatin, simvastatin and lovastatin blood levels by 40-80%	**NNRTI**	
	Efavirenz	Adjust dose of simvastatin according 2 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.

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

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 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

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

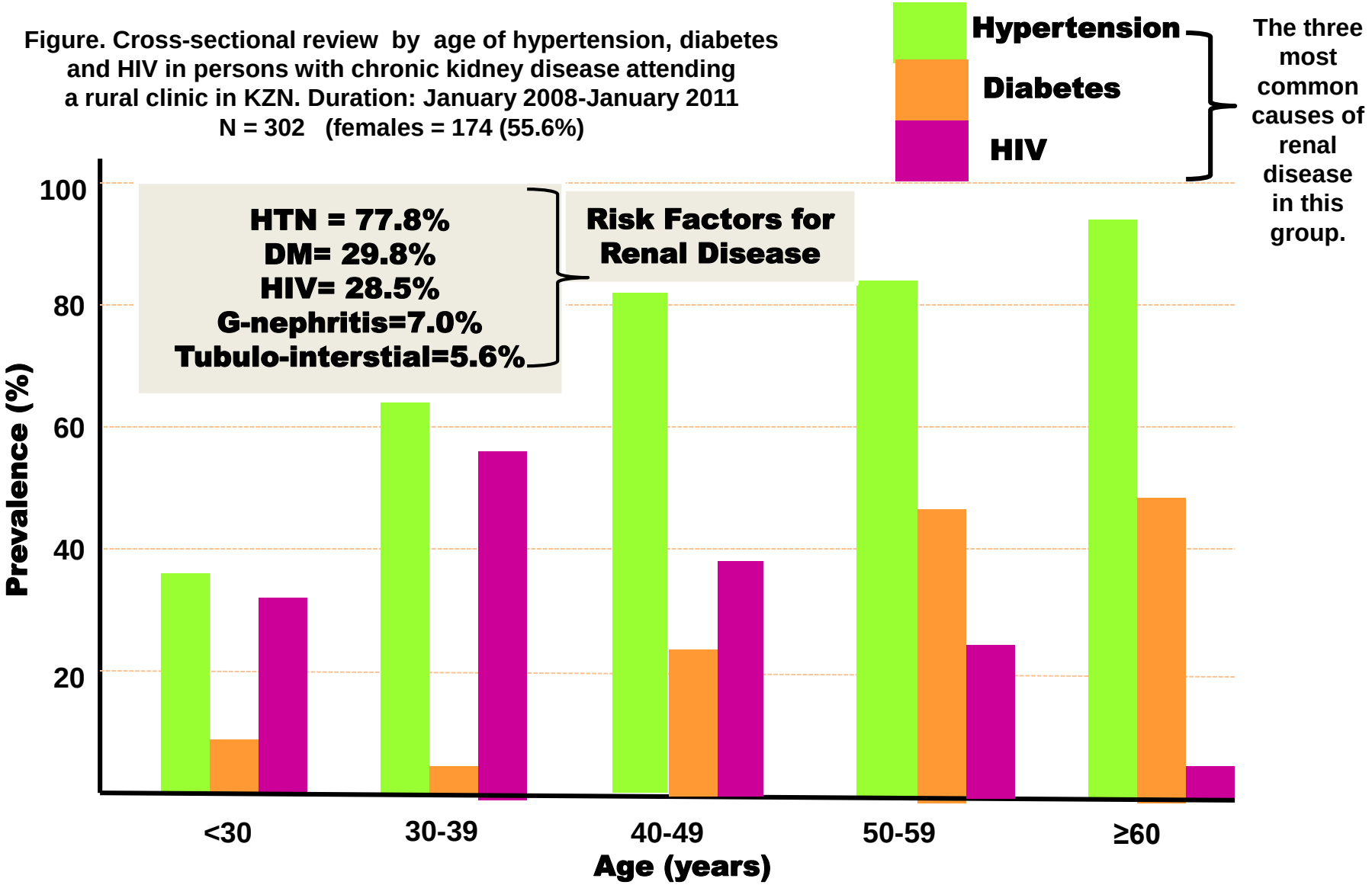
Age (mean) = 47y ±SD7y

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)

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±11.9yr vs cohort (mean) 47.1±17.0yr

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



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