HIV, bone and body composition

Findings from studies in Soweto (Johannesburg) and Cape Town

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Sub-Saharan **A**frican **M**u**S**cul**O**skeletal **N**etwork (SAMSON)

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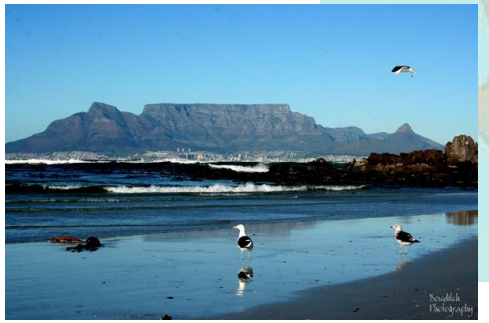
Introduction

- Anti-retroviral therapy (ART) has **increased life expectancy** of HIV-infected individuals;
- Increased risk of chronic **NCDs**
- **Body composition**: metabolic complications include changes in body fat distribution (**lipodystrophy**).
- **Bone**: the prevalence of low **BMD** and risk of associated **fractures** are higher in HIV-infected patients compared to the general population.

Two SA studies …..



BODY COMPOSITION

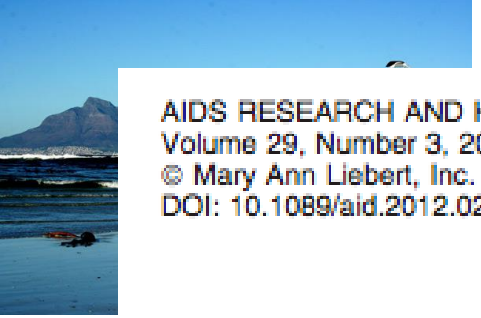
What is **lipodystrophy**?

- Includes lipoatrophy and lipohypertrophy;

Increased abdominal VAT, dorsocervical fat pad (buffalo hump) and/or breast enlargement

Subcutaneous fat wasting of the face, extremities, and/or buttocks

- Occur with differing frequency and severity in patients using ART;
- Can occur separately or overlap in the same patient;
- Prevalence differs according to definition and examination;
- ? relevance of findings from studies done in HICs.
- Few studies from Africa have distinguished between lipoatrophy and lipohypertrophy;
- ART dependent



AIDS RESEARCH AND HUMAN RETROVIRUSES
Volume 29, Number 3, 2013

DOI: 10.1089/aid.2012.0252

Effect of Different Antiretroviral Drug Regimens on Body Fat Distribution of HIV-Infected South African Women

Julia H. Goedecke,[1,2] Lisa K. Micklesfield,[1,3] Naomi S. Levitt,[4] Estelle V. Lambert,[1] Sacha West,[1] Gary Maartens,[5] and Joel A. Dave[4]

First African study to use DXA, and report on body fat composition in patients on second-line (PI based) ART

AIDS PATIENT CARE and STDs
Volume 30, Number 10, 2016

DOI: 10.1089/apc.2016.0183

First longitudinal study in SSA to document changes in body composition using DXA in patients starting ART

Changes in Body Fat Distribution on Dual-Energy X-Ray Absorptiometry in Black South Africans Starting First-Line Antiretroviral Therapy

Zulfa Abrahams,[1] MPH, Naomi Levitt, PhD,[1] Maia Lesosky, PhD,[2] Gary Maartens, PhD,[3] and Joel Dave, PhD[1]

AIM: To compare body composition, using DXA and anthropometry, in HIV infected black South African women received SA DOH first line ART, SA DOH second-line ART, and ART-naïve.

BODY FAT AND ART IN SOUTH AFRICAN WOMEN

TABLE 1. PARTICIPANT CHARACTERISTICS OF ART-NAIVE, ART1, AND ART2 WOMEN

	ART-naive	*ART1*	*ART2*
N	309	344	91
Age (years)	31 (27–38)[A,B]	33 (29–40)[A]	35 (30–40)[B]
Housing density (persons/room)	2.0 (1.3–3.0)[a]	1.7 (1.0–3.0)[a,c]	2.0 (1.3–3.0)[c]
CD4 start (cells/μl)		113 (54–157)	115 (48–154)
CD4 current (cells/μl)	271 (185–436)[A,B]	336 (225–478)[A,C]	505 (315–667)[B,C]
Time on d4T (months)		13 (8–19) (n=296)[C]	14 (10–23) (n=80)[C]
Time on AZT (months)		12 (7–20) (n=132)[C]	19 (9–29) (n=78)[C]
Total time on ART (months)		16 (10–25)[C]	33 (26–47)[C]
Time on ART2 (months)			18 (10–27) (n=83)

d4T=stavudine
AZT=zidovudine
3TC=lamivudine
dDI-didanosine

NRTIs

ART1=SA DOH first line ART regimen: d4T or AZT, 3TC, efavirenz or nevirapine

ART2=SA DOH second line ART regimen: lopinavir/ritonavir, AZT, didanosine

Goedecke et al., 2013

DXA of ART-Naïve, ART1 and ART2 women

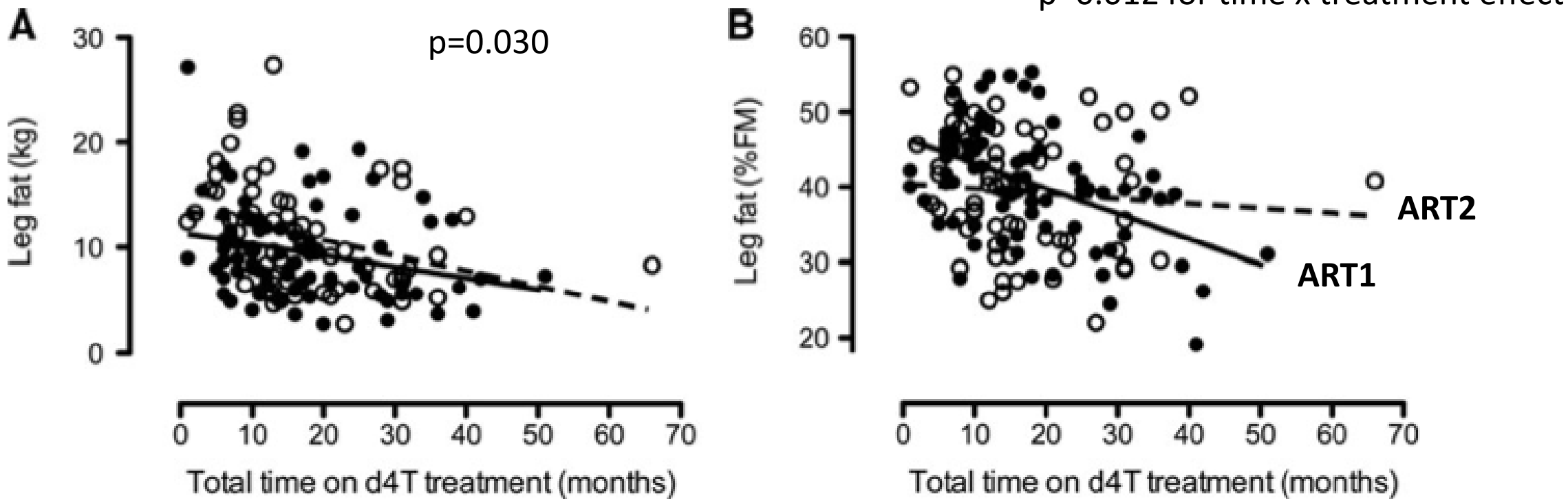
Confirmed by anthropometry measures

	Unadjusted values		
	ART-naive	*ART1*	*ART2*
N	143	103	70
Fat mass (kg)	22.4 (15.9–33.0)	23.9 (17.6–30.4)	24.3 (19.0–35.9)
Fat mass (%)	37.1 (30.6–43.3)	36.3 (30.6–41.5)	36.8 (32.1–43.2)
Trunk fat (kg)	9.2 (6.0–14.2)[b]	10.7 (6.8–15.0)	11.5 (8.4–17.6)[b]
Trunk fat (%FM)	41.1 (36.3–45.2)[A,B]	44.2 (39.4–50.1)[A]	46.9 (39.3–52.8)[B]
Limb fat (kg)	12.7 (8.5–17.7)	11.9 (8.7–15.7)	12.5 (9.1–18.4)
Limb fat (%FM)	55.0 (51.7–58.8)[A,B]	52.4 (46.8–56.3)[A]	50.0 (44.6–57.5)[B]
Arm fat (%FM)	11.1 (9.8–12.5)	10.8 (9.9–12.4)	10.7 (9.9–11.9)
Leg fat (%FM)	43.9 (39.3–48.1)[A,B]	41.2 (34.8–45.8)[A]	40.2 (32.9–45.7)[B]
Trunk/limb fat	0.75 (0.62–0.87)[A,B]	0.85 (0.69–1.06)[A]	0.93 (0.68–1.18)[B]
Trunk/leg fat	0.94 (0.77–1.14)[A,B]	1.07 (0.85–1.43)[A]	1.16 (0.85–1.56)[B]
FFSTM (kg)	37.7 (34.0–42.8)[b]	39.0 (34.9–45.4)	40.0 (35.8–46.8)[b]

Despite a similar BMI, those on ART weighed more and had a greater central and lower peripheral distribution of fat compared to ART-naïve women

Goedecke et al., 2013

Associations between total time on stavudine (d4T) and leg fat mass in women on ART1 and ART2

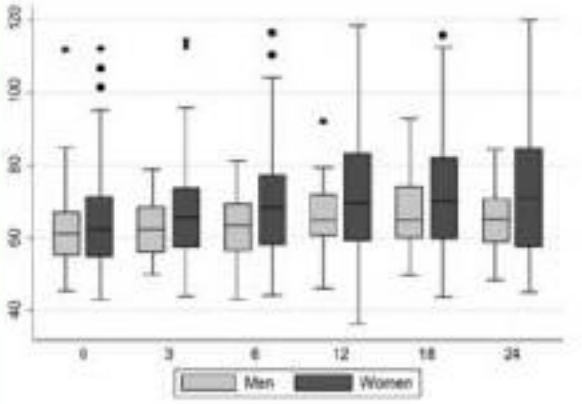


The effects of ART on peripheral body fat distribution were largely mediated by the effects of the first-line ART treatment.

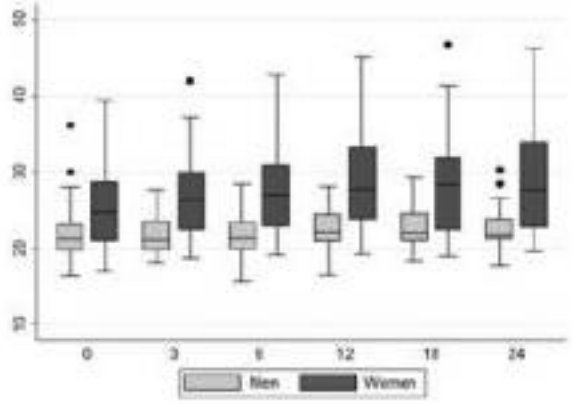
Goedecke et al., 2013

AIM: To use DXA scans to describe the changes in fat distribution over a 24-month period in a population of black SA men and women initiated on ART

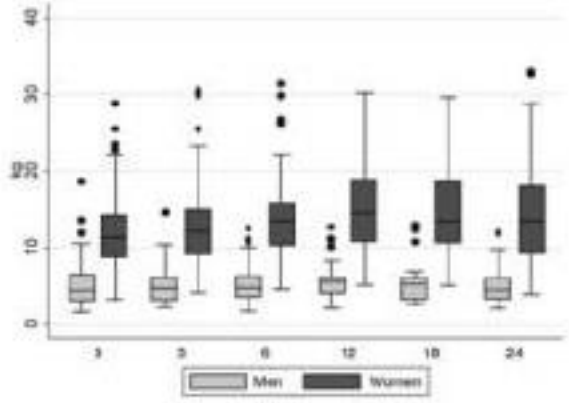
A Weight (kg)
Men p=0.009; Women p<0.001



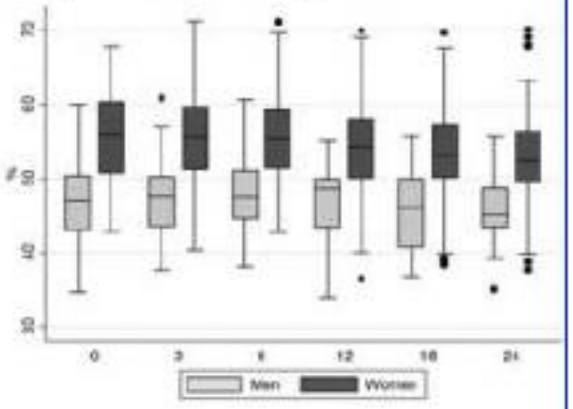
B BMI
Men p=0.002; Women p<0.001



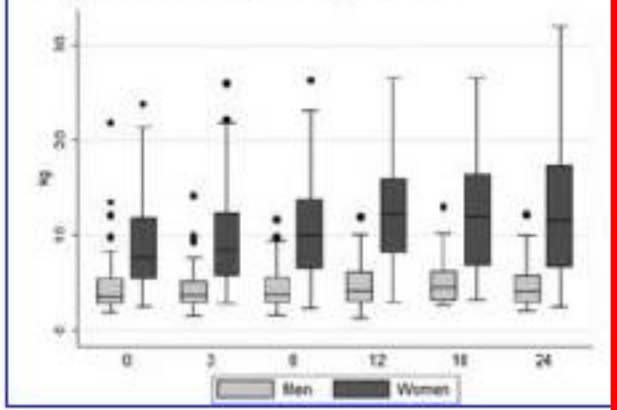
C Limb fat (kg)
Men p=0.211; Women p<0.001



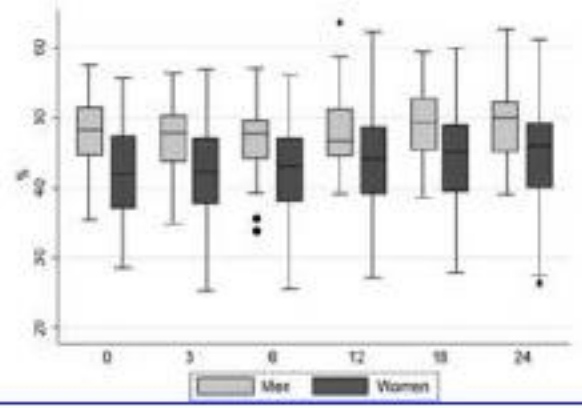
D Limb fat (% of body fat)
Men p=0.248; Women p<0.001



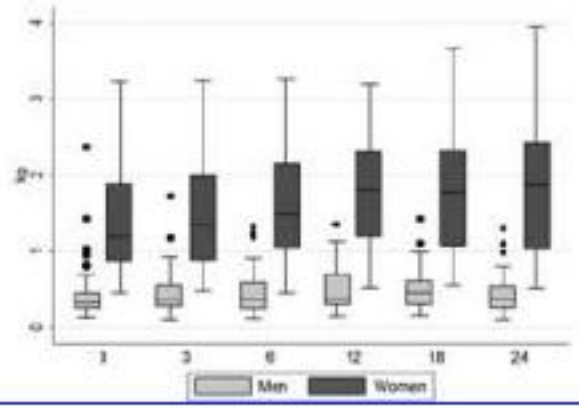
E Trunk fat (kg)
Men p=0.027; Women p<0.001



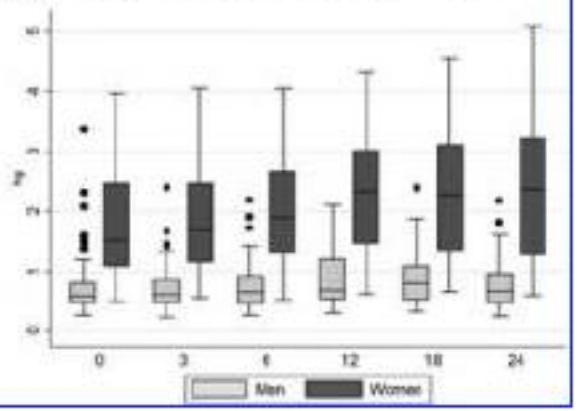
F Trunk fat (% of body fat)
Men p=0.085; Women p<0.001



G Abdominal Subcutaneous Adipose Tissue (kg) Men p=0.049; Women p<0.001



H Abdominal Visceral Adipose Tissue (kg) Men p=0.032; Women p<0.001



Abrahams et al., 2016

Osteoporos Int
DOI 10.1007/s00198-013-2373-y

ORIGINAL ARTICLE

Bone mass, body composition and vitamin D status of ARV-naïve, urban, black South African women with HIV infection, stratified by CD_4 count

M. M. Hamill · K. A. Ward · J. M. Pettifor · S. A. Norris · A. Prentice

ORIGINAL ARTICLE

JBMR®

Changes in Bone Mineral Density, Body Composition, Vitamin D Status, and Mineral Metabolism in Urban HIV-Positive South African Women Over 12 Months

Matthew M Hamill,[1,2] John M Pettifor,[2] Kate A Ward,[1] Shane A Norris,[2] and Ann Prentice[1,2]

AIM: To describe BMD, **body composition** and vitamin D status in SA women with and without HIV infection

Table 1 Subject characteristics, anthropometric measurements and vitamin D status as measured by serum 25(OH)D

	Group 1 HIV-negative *n*=98	Group 2 HIV-positive, non-ARV *n*=74	Group 3 HIV-positive, pre-ARV *n*=75	Group effect ANOVA *p*
Age (years)	30.0 (8.1)	33.5 (6.1)[a]	33.4 (6.5)[a]	0.001
HIV status	Negative	Positive	Positive	
Current CD_4 count $\times 10^6$ cells/l	ND	412 (91)	161 (69)[b]	<0.001
Median (IQR)		420 (127;409)	175 (120;165)	
Min	NA	240	18	
Max	NA	604	275	
Gravidity median (IQR)	1 (0;2)	2 (2;3)[a]	2 (1;3)[a]	
Range	0–5	0–6	0–6	
Current hormonal contraceptive use (%)	34 (35.4)	26 (36.6)	25 (33.3)	0.9
Current smoking (%)	10.2	13.5	8	0.2
Height (cm)	157.6 (5.9)	159.4 (5.9)	159.2 (5.3)	0.06
Weight (kg)	69.7 (17.0)	72.0 (17.4)	62.3 (15.2)[c,d]	<0.001
BMI (kg/m^2) Median (IQR)	27.3 (23.1;31.7)	27.8 (23.3;32.3)	23.5 (20.5;27.0)[d,e]	<0.001
Overweight BMI >24.9 kg/m^2, <30 kg/m^2 (%)	35	28	28	
Obese BMI >30 kg/m^2 (%)	30	37	16	
Underweight BMI <18.5 kg/m^2 (%)	4	1	11	
WBLH Fat (kg)	26.1 (11.5)	26.1 (9.8)	19.7 (9.3)[b,e]	<0.0001
WBLH Lean (kg)	38.3 (60.8)	39.5 (62.4)	36.4 (48.1)[d]	0.005
Fat/lean^2 (kg/kg^2)*	17.32 (4.80)	15.92 (4.56)	14.58 (5.47)[a,f]	0.002

Hamill et al., 2013

AIM: Follow up women for 12 months…

Hamill et al., 2017

Body composition results…

- Nref and Plow gained significant amounts of weight and body fat over the 12 months
- However Plow still lighter with less fat mass than Nref

Hamill et al., 2017

BODY MINERAL DENSITY

Osteoporos Int
DOI 10.1007/s00198-013-2373-y

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AIM: To describe **BMD**, body composition and vitamin D status in SA women with and without HIV infection

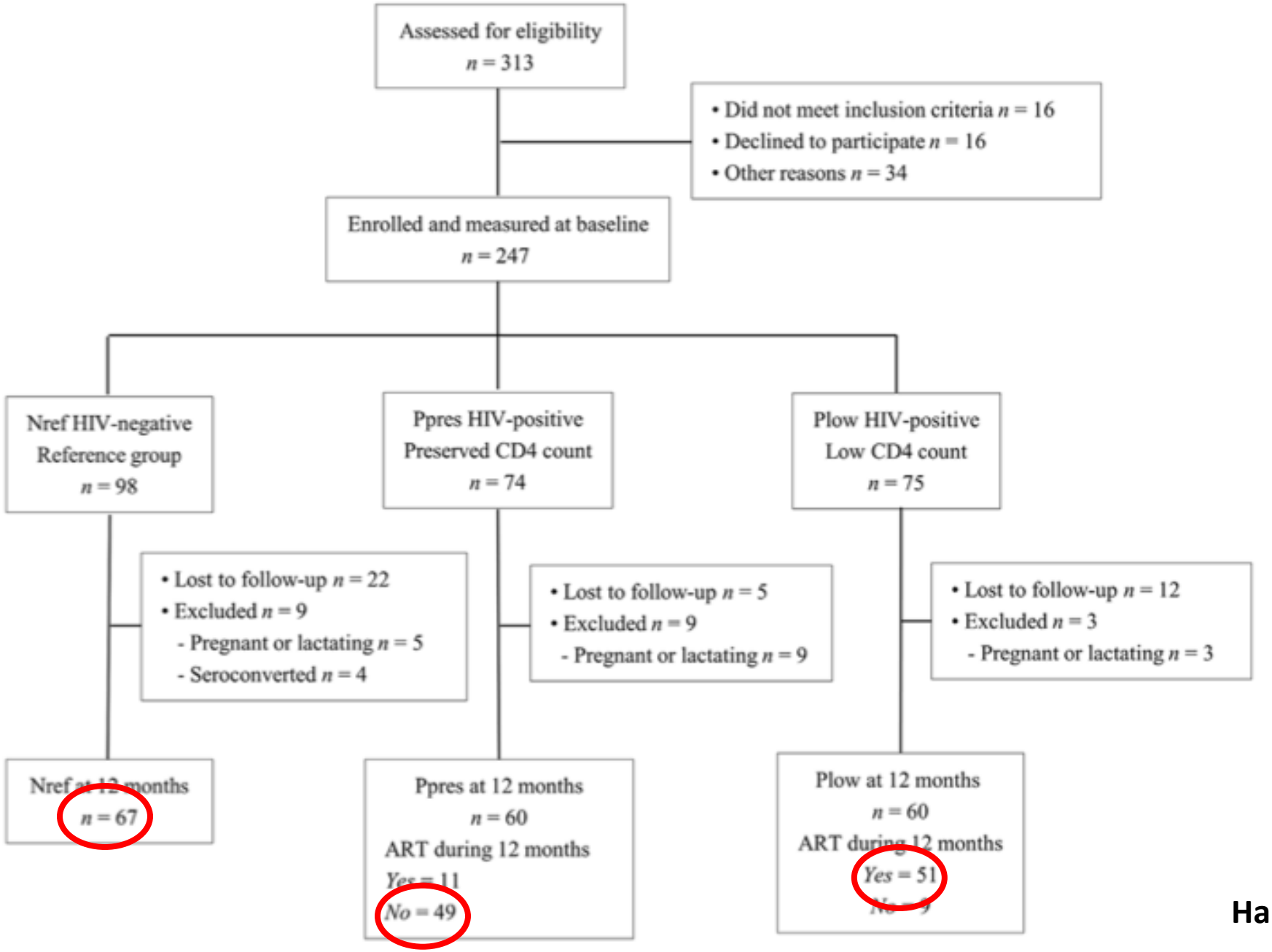
Table 2 BMD of the three groups of South African women

	BMD (g/cm^2) Mean (SD)			Group effect[a] *p*
	Group 1 HIV-negative *n*=98	Group 2 HIV-positive, non-ARV *n*=74	Group 3 HIV-positive, pre-ARV *n*=75	
Total Hip	1.013 (0.131)	0.985 (0.124)	0.988 (0.125)	0.3
Femoral Neck	0.930 (0.114)	0.916 (0.125)	0.923 (0.131)	0.8
Lumbar Spine	1.018 (0.118)	1.021 (0.109)	1.006 (0.128)	0.7
WBLH	0.958 (0.079)	0.943 (0.071)	0.947 (0.080)	0.4

No significant differences in BMD at the TH, FN, LS and WBLH were found, and age and size adjustment did not reveal any differences between groups.

Hamill et al., 2013

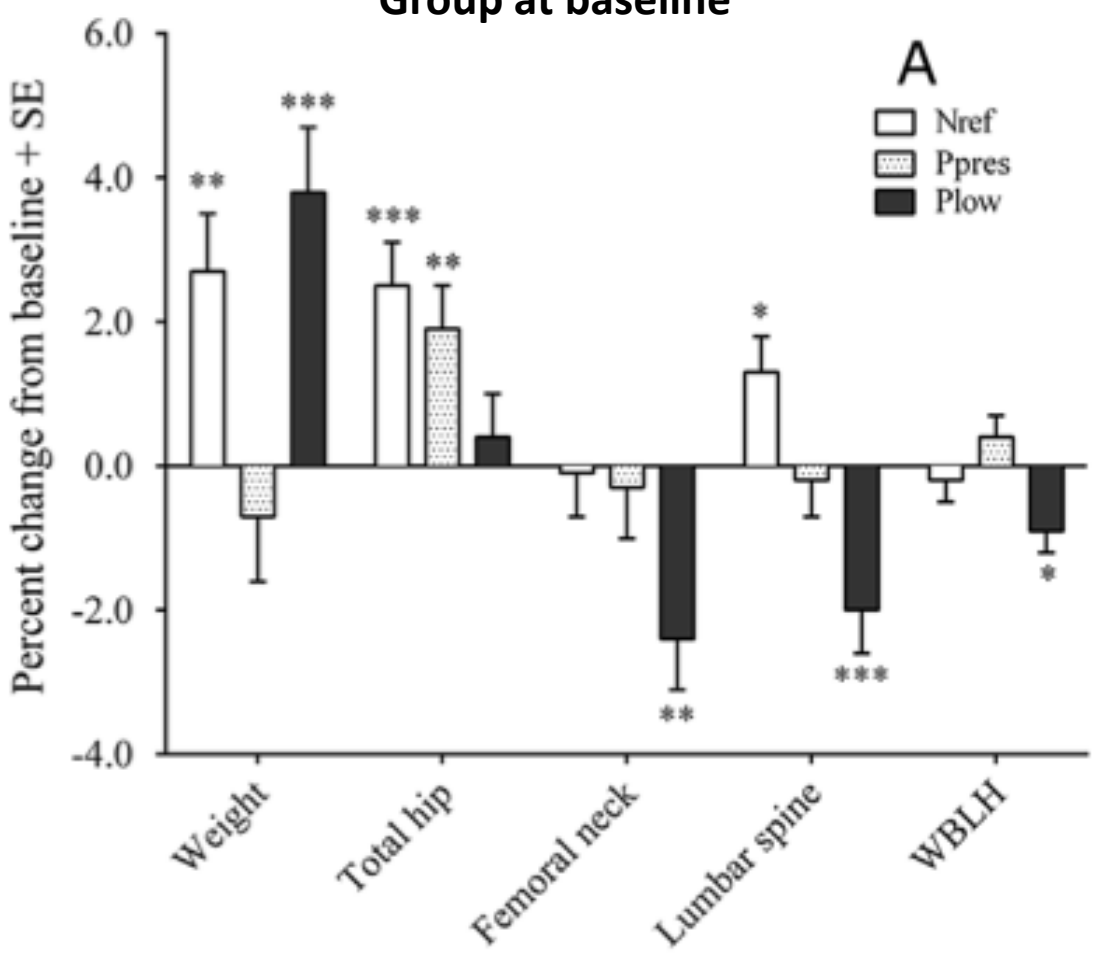
AIM: Follow up women for 12 months…



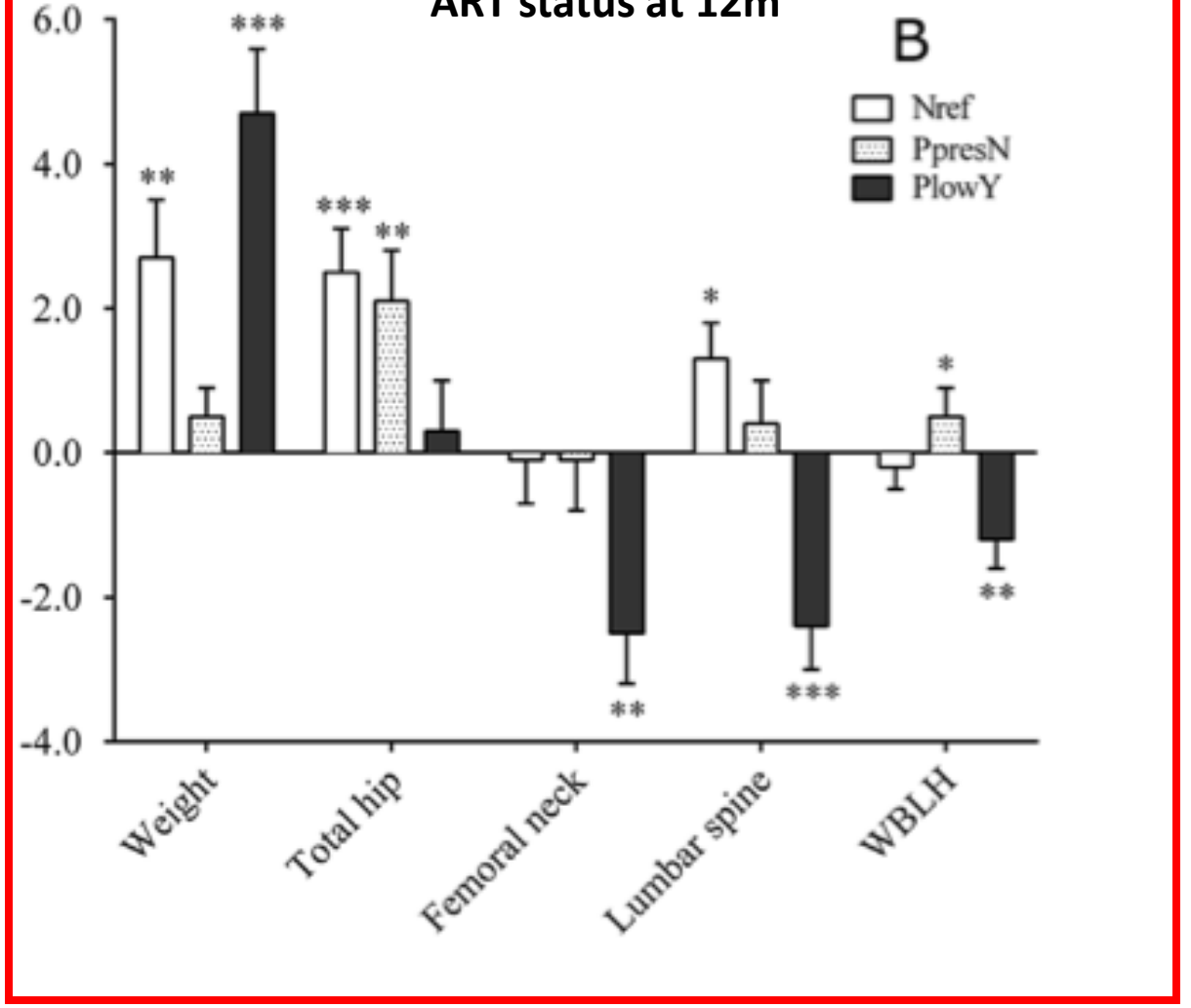
Hamill et al., 2017

BMD results…

Group at baseline



ART status at 12m



Hamill et al., 2017

n=444
Median age = 35 years
ART vs. ART naive

PLOS | ONE

RESEARCH ARTICLE

Antiretroviral Therapy, Especially Efavirenz, Is Associated with Low Bone Mineral Density in HIV-Infected South Africans

Joel A. Dave[1]*, Karen Cohen[2], Lisa K. Micklesfield[3,4], Gary Maartens[2], Naomi S. Levitt[1]

BMD results…

	All participants	Men	Women	p value	On ART	Not on ART	p value
Lumbar spine	0.930 (0.120)	0.943 (0.123)	0.928 (0.119)	0.408	0.925 (0.125)	0.937 (0.112)	0.287
Femoral neck	0.817 (0.128)	0.820 (0.136)	0.816 (0.125)	0.798	0.795 (0.130)	0.844 (0.120)	<0.0001
Total hip	0.930 (0.125	0.973 (0.128)	0.917 (0.121)	0.0001	0.908 (0.122)	0.956 (0.124)	<0.0001

TH and FN BMD were significantly lower in ART vs ART-naïve participants;

Z-score<-2: 17% LS; 5% TH

Dave et al., 2015

Multivariate regressions – total hip BMD

	Univariate analysis		Multivariate analysis	
Variable	**Beta coefficient (95% CI)**	**p-value**	**Beta coefficient (95% CI)**	**p-value**
Age (years)**	-0.002 (-0.016 to 0.013)	0.833	-0.007(-0.021 to 0.005)	0.249
Weight (kg)**	0.028 (0.022 to 0.035)	<0.001	0.033 (0.027 to 0.039)	<0.0001
Male	0.057 (0.029 to 0.085)	<0.001	0.081 (0.055 to 0.106)	<0.0001
Vit D (nmol/L)*	0.008 (0.000 to 0.016)	0.058	0.008 (0.000 to 0.015)	0.037
ART exposure				
ART naive	referent		referent	
efavirenz–based ART	-0.071 (-0.105, -0.037)	<0.0001	-0.075(-0.105 to -0.044)	<0.0001
nevirapine-based ART	-0.025 (-0.059, 0.008)	0.141	-0.021(-0.050 to 0.008)	0.158
lopinavir–based ART	-0.057 (-0.089, -0.024)	0.001	-0.067(-0.095 to -0.038)	<0.0001

Model adjusted R^2 = 0.28.

*univariate and multivariate analyses calculated on 412 participants with complete data for all variables.

** increments of 10.

Exposure to efavirenz or lopinavir-based ART was associated with lower total hip BMD.

Dave et al., 2015

Multivariate regressions – lumbar spine BMD

	Univariate analysis		Multivariate analysis	
Variable	**Beta coefficient (95% CI)**	**p-value**	**Beta coefficient (95% CI)**	**p-value**
Age (years)**	-0.018 (-0.031 to -0.005)	0.005	-0.023 (-0.036 to -0.010)	<0.001
Weight (kg)**	0.021 (0.014 to 0.027)	<0.001	0.023 (0.017 to 0.029)	<0.001
Male	0.013 (-0.014 to 0.040)	0.339	0.039 (0.013 to 0.065)	0.003
ART exposure				
ART naive	referent		referent	
efavirenz–based ART	-0.035 (-0.067 to -0.003)	0.034	-0.032 (-0.062 to -0.001)	0.040
nevirapine-based ART	0.006 (-0.026 to 0.038)	0.722	0.007 (-0.023 to 0.037)	0.655
lopinavir–based ART	-0.017 (-0.048 to 0.014)	0.283	-0.021 (-0.050 to 0.009)	0.169

Model adjusted $R^2 = 0.13$

*univariate and multivariate analyses calculated on 423 participants with complete data for all variables. 19 participants were missing data for 1 or more variables included in the multivariate model.

**increments of 10.

Exposure to efavirenz-based ART was associated with lower total LS BMD.

Dave et al., 2015

Conclusions

- ART is associated with increased central fat and reduced peripheral fat;
- Different ART regimens have different effects on body fat distribution;
- Conflicting results on BMD differences between HIV and ARV groups;
- Longitudinal data – ART exposure results in significant bone loss, particularly at the LS
- Future work
  - Need to understand what effect changes in body fat distribution has on cardiovascular risk;
  - Establish if bone loss continues with ongoing ART and if this results in increased fracture rates.

Thank you