

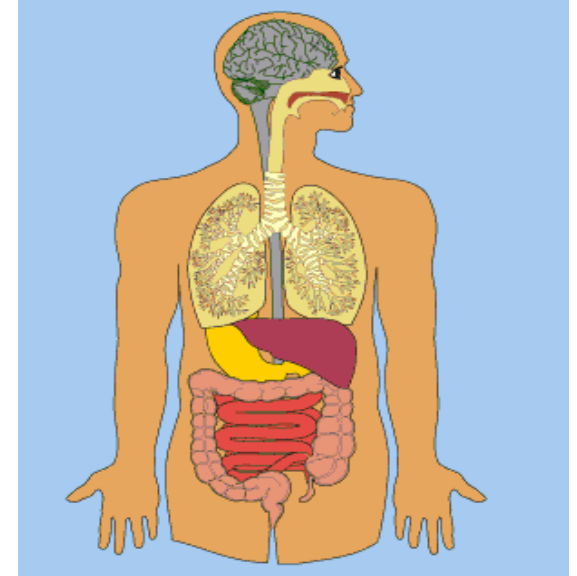
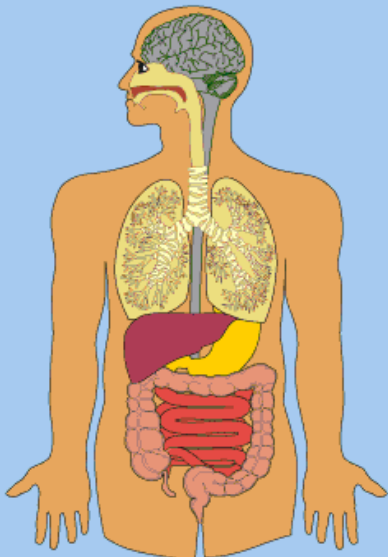


Dave Spencer Head Infectious  
Diseases Helen Joseph Hospital  
And the University of the Witwatersrand  
Johannesburg  
September 2014



## **WEIGHT LOSS ON ANTIRETROVIRAL THERAPY.**

The Metropolitan Health Symposium:  
Clinical HIV for the Busy Health Worker



# Ms RU 22yr. Weight Loss in a Woman on Antiretroviral Therapy

## Medical History

**Admission: 25 June 2014**

### **PAST MEDICAL HISTORY**

Zimbabwean

**Infected at birth**

Parents deceased

Lives with a sister

Unemployed

### **Adherence to ART:**

Took ART 2009-2010

Defaulted ART

2010-2014 April

Admitted to hospital April

2014 with end-stage

lung disease

Presenting complaint:

Shortness of breath

Cough

Right-sided c/p

Weakness

Known RVD+ve

ART since 2009

Current ART: ZDV+3TC+LPV/r

PTB 2007/ 2009

## **Ms RU 22yr. Weight Loss in a Woman Who is on Antiretroviral Therapy.**

### **Examination**

**Admission: 25 June 2014**

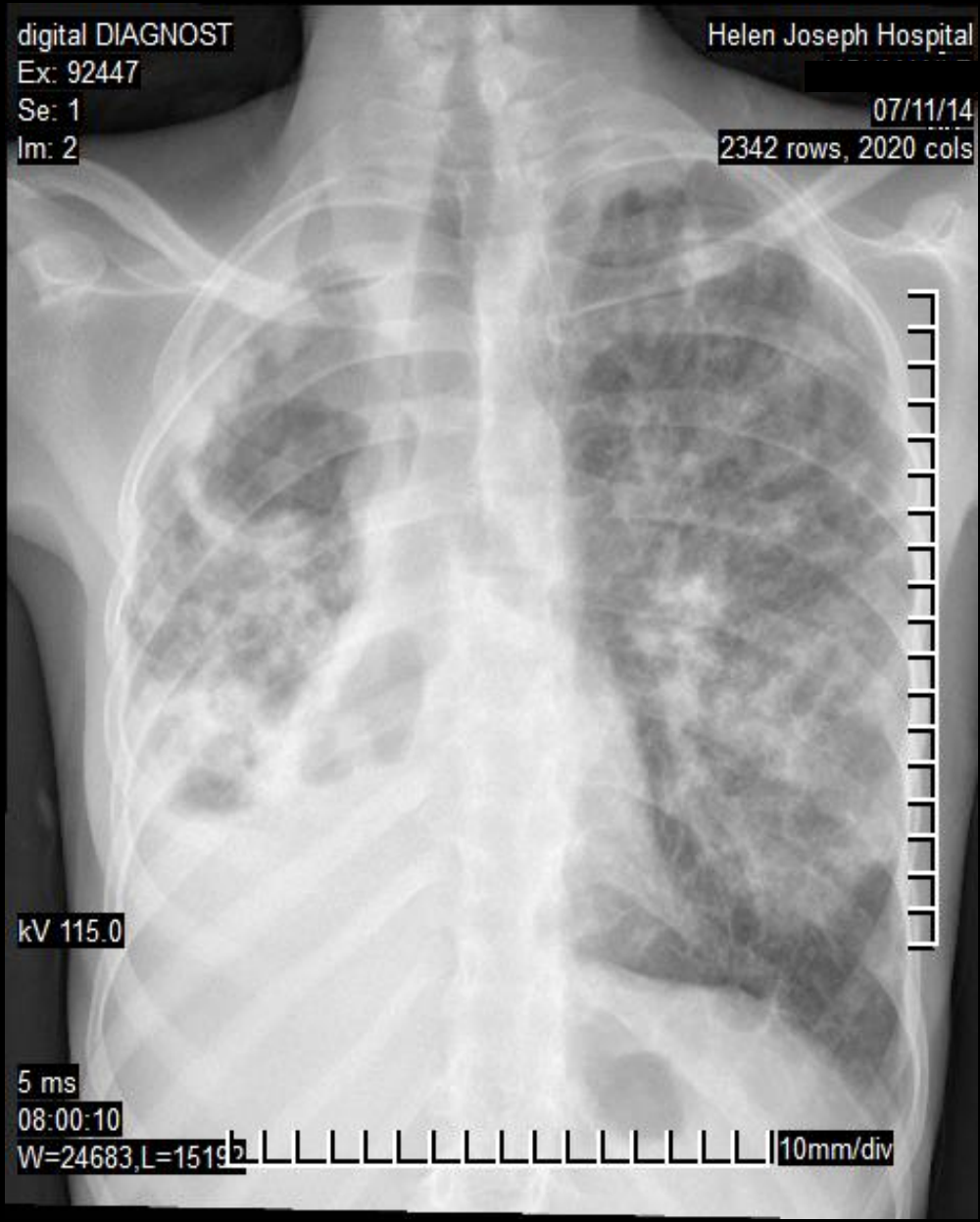
**CD4 = 10**  
**VL = 341 590 cp/ml**  
(on ZDV+3TC+LPV/r)

**Hospital stay:**  
**25 June-19 July**  
**(24 days)**

#### **EXAMINATION:**

**Vitals: Wt 30kg BMI = 16.4 kg/m<sup>2</sup>**  
**p116 BP 90/45**  
**rr 34 Afebrile**  
**Wasted and frail**  
**Distressed: dyspnoeic**  
**Sitting upright in bed**  
**On Oxygen**  
**Chest: bilateral crackles**  
**bronchial breathing R base posteriorly**  
**CVS: Right heart failure + edema**  
**CNS: intermittent confusion.**

# Ms RU 22yr. Weight Loss in a Woman Who is on Antiretroviral Therapy



## Ms RU 22yr. Weight Loss in a Woman Who is on Antiretroviral Therapy.

### Laboratory

Test	25/6	2/7	12/7	19/7 [D/C]	20/7/2014
WBC	12.8	17.0	12.3	Discharged from hospital on home O2/ medication	Patient died at home while eating lunch. Severe coughing accompanied by vomiting of a large amount of blood. Died within a few seconds. Certified DOA in the ER at 16h45 that afternoon.
Hb	7.8	6.5	5.8		
Plate	250	219	97		
Creat	50	46	44		
Ferritin	3688	<b>Blood gas 25/6/2014</b> pCO2 32.8 pO2 23.1 pH 7.25 BE 3.6 Sat 65.4%			
ALP	158				
ALT	10				
AST	40				
Urine	NAD				

**Sputum AFB stain: Negative TB GXP: NegativeX2 TB Bactec culture: Negative**

**Sputum culture: *Aspergillus fungoides***

**Blood culture: negative**

**Tx. Piperacillin-Tazobactam: Azithromycin and ethambutol; Amphotericin B and stavudine + 3TC+ lopinavir/ritonavir (aluvia)**

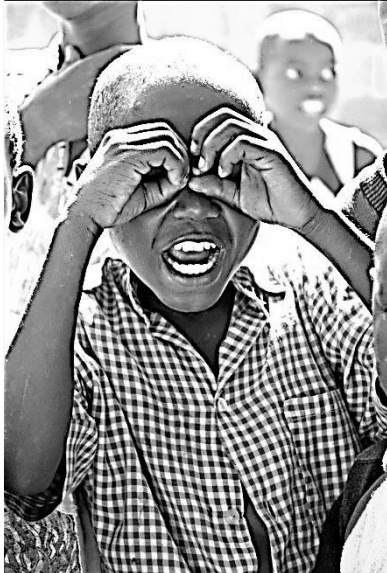


# Ms RU 22yr. Weight Loss in a Woman Who is on Antiretroviral Therapy.

## VIRAL GENOTYPE RESISTANCE TEST

Ms. RU

Date:  
27.06.14




All Mutations Detected (HXB2 reference Sequence) Resistance mutations in bold based on Stanford v7.0 (mutation score ≠ 0)

Reverse transcriptase K22R, V35T, T39E, S48T, T69D, K103N, D123N/S, T139A/wt, K173T, Q174K, I178L, T200A, Q207E, R211K, V245Q, E248D, K275R, R277K, Q278Y/H, T286wt/A, E291D, V292I, I293V, D324E/wt, R356K, M357T, G359T, T376A, T377M, K390R, E399D, T400I, E404D, V435A

Protease V3I, T12S, I15V, L19I/T, E35D, M36I, S37N, R41K, K45R, R57K, D60E, Q61E, L63P, H69K, V82wt/I, L89M, I93L

Interpretation genotypic (Stanford-v7.0)

Class	Drug	STAN  (1) v7.0 27/02/2014
NRTI	Zidovudine	S
	Didanosine	I
	Stavudine	S
	Lamivudine	S
	Emtricitabine	S
	Abacavir	S
	Tenofovir	S
NNRTI	Nevirapine	R
	Efavirenz	R
	Etravirine	S
	Rilpivirine	S
PI	Indinavir/r	S
	Saquinavir/r	S
	Nelfinavir	S
	Fosamprenavir/r	S
	Lopinavir/r	S
	Atazanavir/r	S
	Tipranavir/r	S
Darunavir/r	S	

not available

 S

 I

 R

**Ms RU 22yr. Weight Loss in a Woman Who is on Antiretroviral Therapy.**

**Death caused by massive hemoptysis secondary to chronic lung infection (Aspergillus) and poor control of the underlying HIV infection**

**WEIGHT LOSS**

- ❑ **POOR VIRAL CONTROL**
- ❑ **CHRONIC OPPORTUNISTIC INFECTION**
  - ❑ **ANOREXIA, POOR NUTRITION**
  - ❑ **GENERALISED WEAKNESS**

# **NUTRITIONAL ASSESSMENT and the DIAGNOSIS OF MALNUTRITION**

**Loss of weight and loss of lean body mass  
are both independent predictors of  
mortality in HIV-infected patients**


Chang E, Sekhar R et al. *CID* 2007;44:1509-17



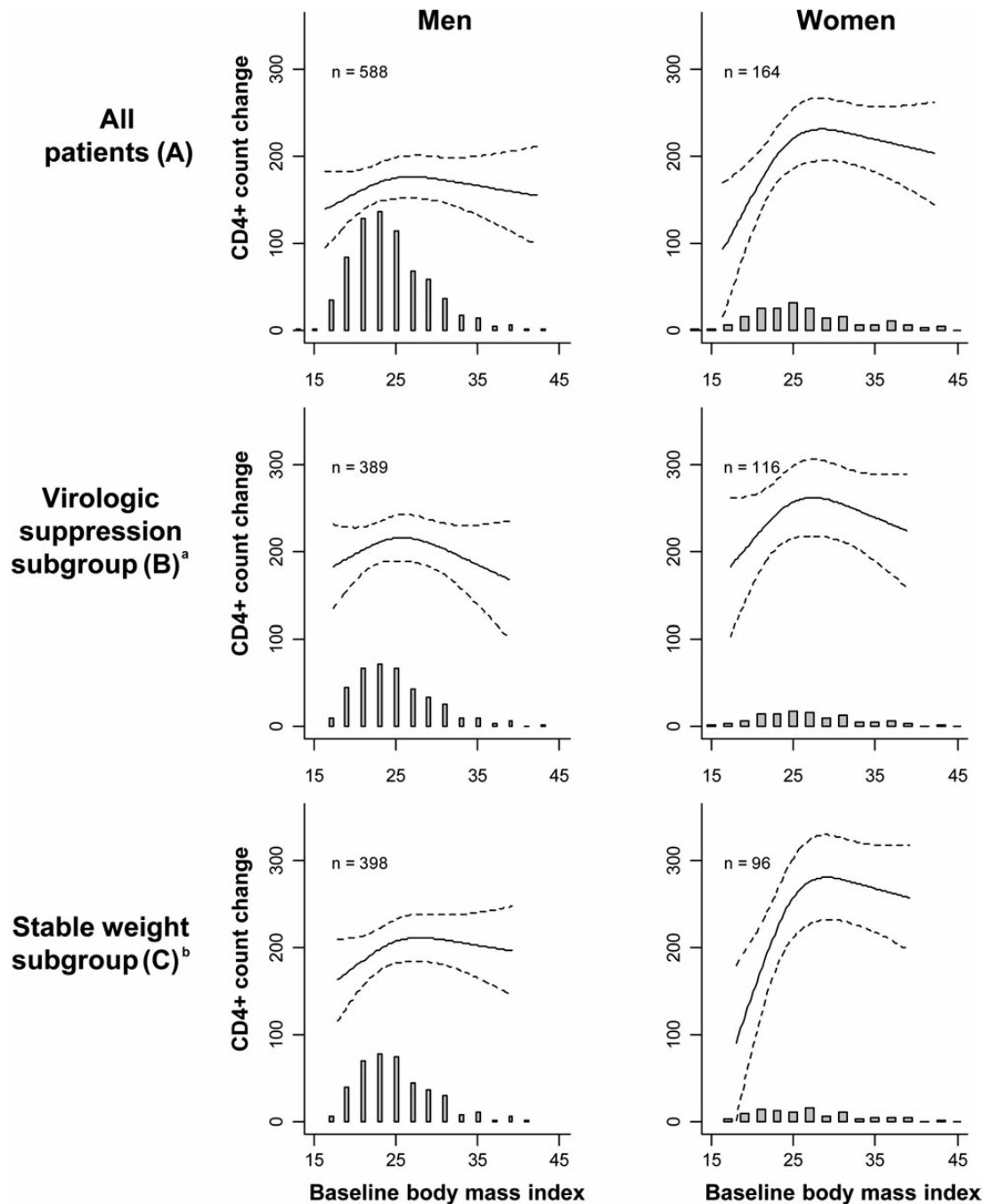
# **OPTIMAL BODY MASS INDEX (BMI) and improved immune reconstitution in HIV-infected adults.**

n=1069 patients  
ART-naïve patients in a retrospective observational cohort (USA)  
Baseline and 12-month CD4 assessments n = 753 patients

**A BMI of 20kg/m<sup>2</sup> when compared with  
the reference group was associated with  
a reduced 12-m CD4+ gain as was a  
BMI of 40kg/m<sup>2</sup> when cp. With the reference.**



Koethe JR, Jenkins CA, Shepherd BE, Stinnette SE, Sterling TR. An optimal Body Mass Index range Associated With Improved Immune Reconstitution Among HIV-Infected Adults Initiating Antiretroviral Therapy. Clin Infect Dis 2011; 53(9): 952-960

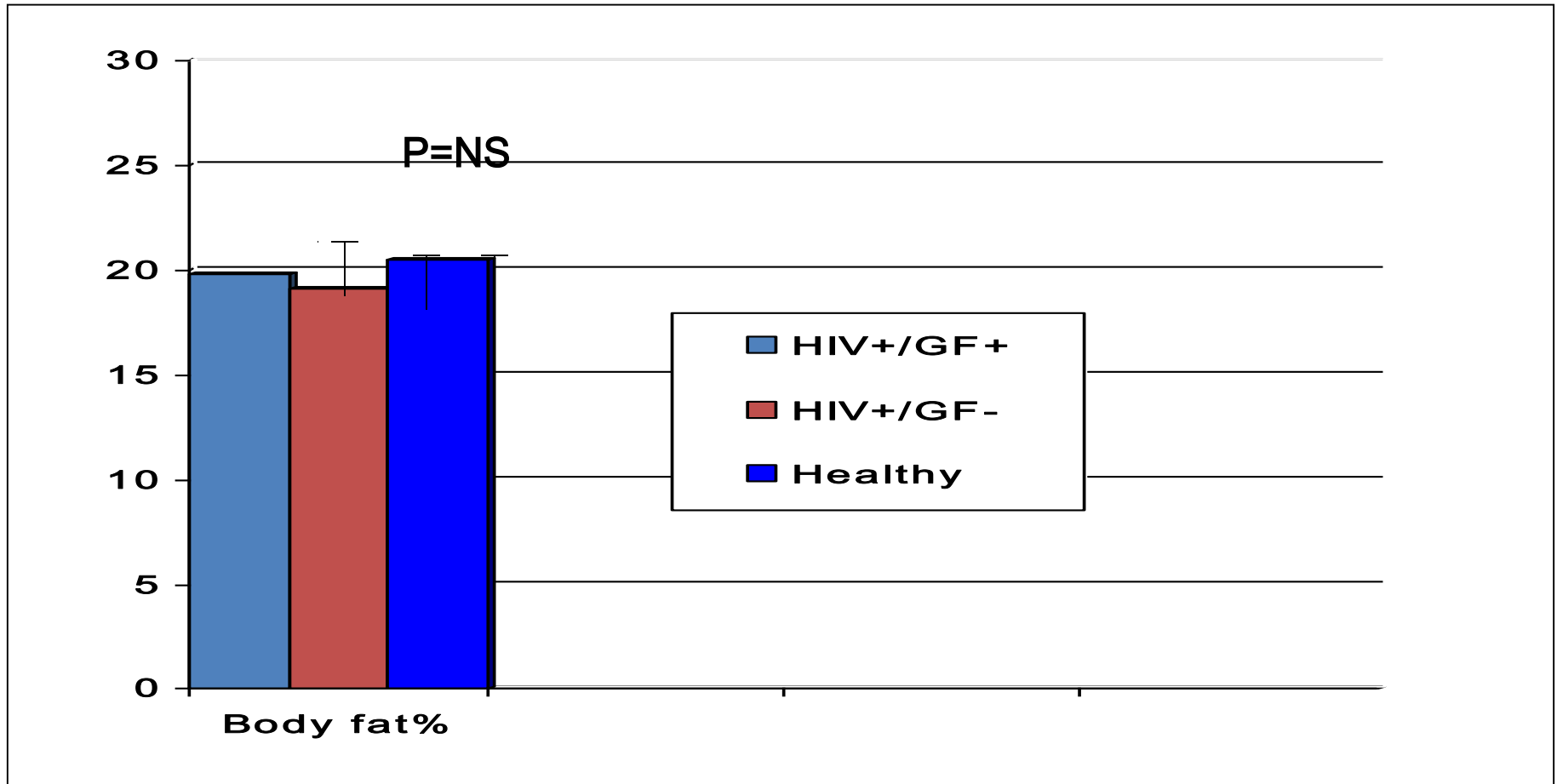


**Figure. BMI and CD4+ recovery after initiating ART.**

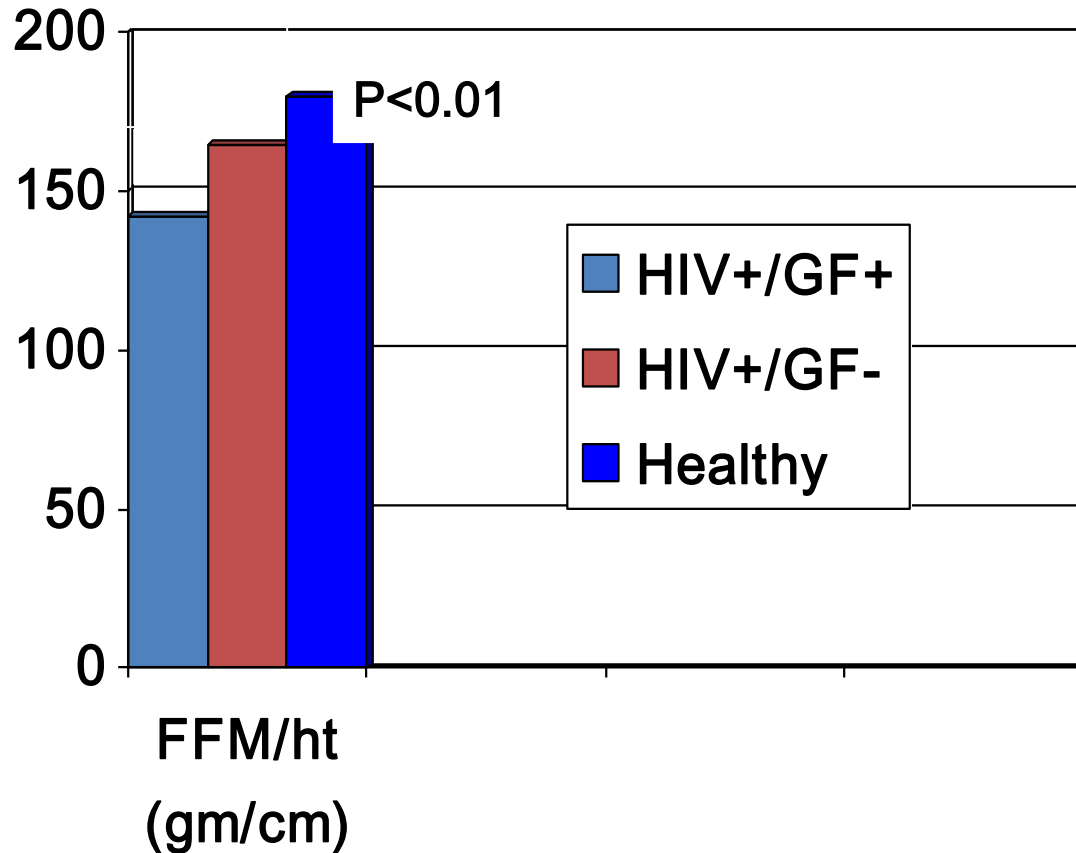
Baseline body mass index (BMI) and change in CD4+ lymphocyte count at 12 months stratified by sex, for all patients (A), the virologic suppression group (B), and the stable weight subgroup (C). Regression lines are adjusted for age, race, protease inhibitor use, year of antiretroviral therapy (ART) start, and baseline CD4+ lymphocyte count and plasma HIV-1 RNA level ( $\log_{10}$  transformed): dashed lines represent 95% confidence intervals. Shaded histogram shows the number of patients contributing data. Each bar represents a 2kg/m<sup>2</sup> BMI interval.

Koethe JR, Jenkins CA, Shepherd BE, Stinnette SE, Sterling TR. An optimal Body Mass Index range Associated With Improved Immune Reconstitution Among HIV-Infected Adults Initiating Antiretroviral Therapy. *Clin Infect Dis* 2011; 53(9): 952-960

# Body fat is spared in HIV-infected children with growth failure



# Lean tissue (fat-free mass) is reduced in HIV infection even in absence of growth failure



A low BMI at the start of ART is an independent predictor of early mortality in several reports from sub-Saharan Africa.

In Zambia, we found that patients starting **ART with a BMI <16.0 kg/m<sup>2</sup> had a higher mortality rate in the first 90 days** (adjusted hazard ratio, 2.4 [95% CI, 1.83-3.2]), compared to patients starting ART with a BMI >16.0 kg/m<sup>2</sup>.

# HIV-associated wasting:

one feature that was observed in the pre-HAART period and has persisted despite the use of HAART, is **increased resting energy expenditure.**

Chang E, et al. Dysregulated Energy Expenditure in HIV-Infected Patients: A Mechanistic Review. *CID* 2007;44:1509-17

## Total energy expenditure

HIV-uninfected

Activity-related Energy Expenditure – (AEE)

Resting Energy Expenditure ( $\alpha$ BMR)

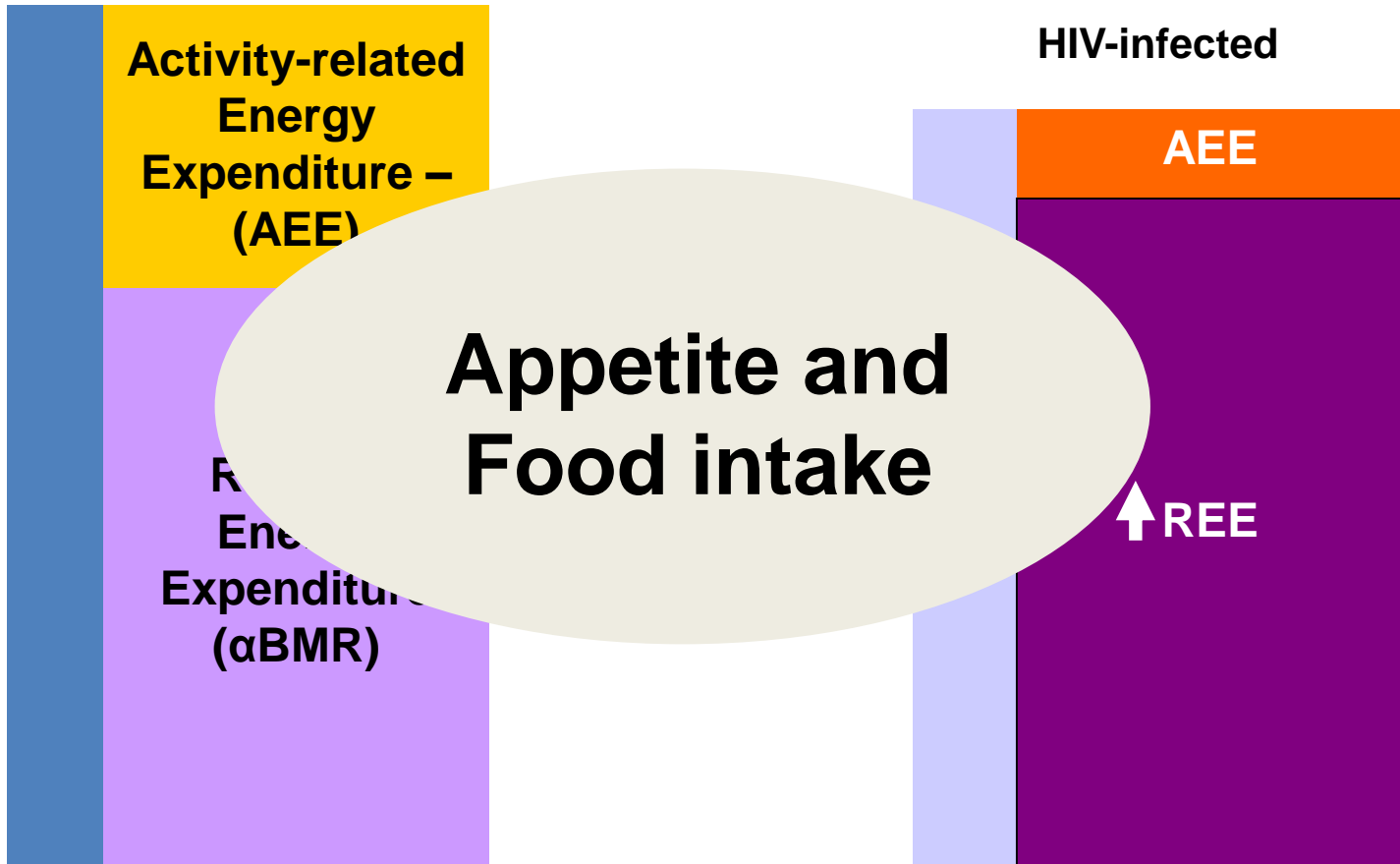
Appetite and Food intake

HIV-infected

AEE

↑ REE

Rollins N  
WHO 2006



# CAUSES OF INCREASED RESTING ENERGY EXPENDITURE

## Elevated levels of pro-inflammatory cytokines

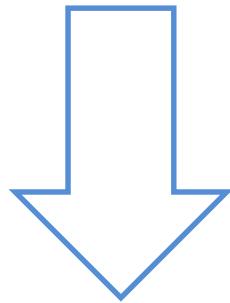
- TNF- $\alpha$  and IL-1 $\beta$  implicated in several studies
- TNF- $\alpha$  is also associated with decrease in lean body mass
- Increased REE correlates with levels of CRP, ESR, Ferritin level, IL-6 level, and soluble TNF receptor type I level
- Of these, CRP is an independent predictor of REE per kg FFM

## Altered regulation of anabolic and adipocyte hormones

- Altered regulation of hormonal axes eg Thyroid, leptin, catecholamines, adiponectin, resistin could potentially result from chronic immune activation



**Episodes of opportunistic infection usually accompanied by fatigue and decreased physical activity, thus overall decrease in TEE**



**Therefore...**

**Decreased caloric intake, rather than increased REE, significantly correlates with the rate of weight loss.**

**DURING A 13,416 PERSON-YEARS FOLLOW UP, 501 TB INFECTIONS OCCURED AMONG 7536 PEOPLE.**

**This corresponds to a 10% risk in the first 4 years on ART and an overall incidence rate of 4.2 cases of TB/100 person years.**

**The highest incidence rate viz. 21.7/ 100 person years occurred in the first 3 months of ART among people with CD4 counts below 50 cells/mm<sup>3</sup>.**

Van Rie A, Westreich D, Sanne I. Tuberculosis in Patients receiving Antiretroviral Treatment. Incidence, Risk Factors and Prevention Strategies. J Acquir Immune Defic Syndr 2011; 56 (4): 349-355

Patients of the Themba Lethu Clinic, Johannesburg, South Africa. Initiating ART between April 2004-March 2007

<b>Duration of ART</b>	<b>No. At Risk</b>	<b>Person Months</b>	<b>No. Of TB cases.</b>	<b>Incidence Rates and 95% CI (range)</b>
	Total = 7281	144,749	501	4.2 (3.8-4.5)
<b>YEAR ONE</b>	7234	66,046	375	6.8 (6.1-7.5)
<b>0-90 DAYS</b>	6292	16,994	196	13.9 (11.9-15.8)
<b>91-180 DAYS</b>	5943	16,416	88	6.3 (5.0-7.7)
<b>181-365 DAYS</b>	5887	32,329	91	3.5 (2.8-4.2)
<b>YEAR TWO</b>	5277	47,585	83	2.2 (1.7-2.6)

## **TB Incidence Rate and Rate Ratios by Time after Starting ART.**

Van Rie A, Westreich D, Sanne I.  
Tuberculosis in Patients  
receiving Antiretroviral  
Treatment. Incidence, Risk  
Factors and Prevention  
Strategies. J Acquir Immune  
Defic Syndr 2011; 56 (4): 349-  
355

Covariates: Demographic Data	Incident TB Category	
	Early Incident TB	Late Incident TB
Baseline Low Hb.	2.54 (1.92-3.37)	
Baseline BMI <18.5	2.93 (1.34-3.07)	
Baseline CD4 <50	1.68 (1.03-2.74)	
Post ART: Low Hb		1.69 (1.21-2.34)
PostART: BMI <18.5		4.07 (2.53-6.57)
PostART: CD4 <50		3.80 (1.99-7.27)
PostART: CD4 51-100		3.28 (1.83-5.88)
PostART: CD4 101-200		1.94 (1.21-3.09)
Post ART: CD4 201-350		1.78 (1.17-2.70)
Most recent vl>10,000		2.52 (1.67-3.82)

Patients with prevalent TB at the time that ART was started had the most advanced HIV disease: 42% = CD4 <50., 32% = BMI < 18.5, 72% = anaemia [Hb<13 in men, and 12 in women or <11 if pregnant]

**Adjusted Hazard Ratios (95% CI) for Early and Late Incident TB in Patients Receiving Antiretroviral Treatment (ART)**

## **CO-INFECTIONS AND HIV: Adolescents**

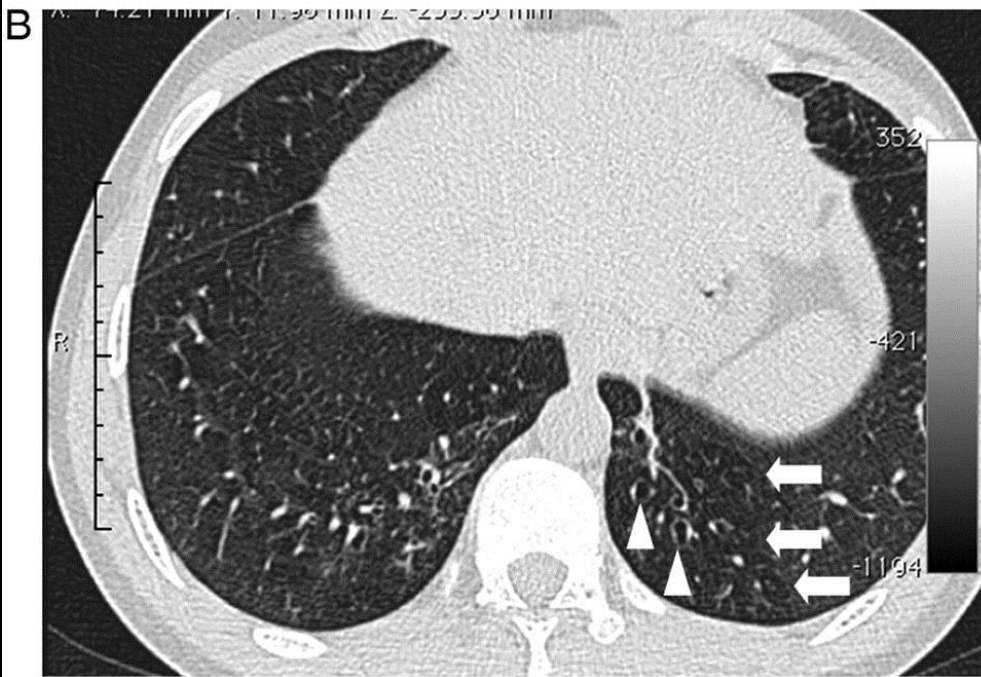
**Recently diagnosed or still undiagnosed vertically acquired HIV is now the most common cause of admission and the most common cause of in-hospital death among adolescents in Zimbabwe.**

Ferrand RA, Bandason T, Musvaire P, et al. Causes of acute hospitalization in adolescence: burden and spectrum of HIV-related morbidity in a country with an early-onset and severe HIV epidemic: a prospective survey. *PLoS Med* 2010; 7e1000178



## **Lung high-resolution computed tomography findings in participants.**

**A. Image section at the level of the carina in a 15-year old female. There is a clear zone of decreased attenuation in the right upper lobe and to a lesser extent, the left lung. In regions of decreased attenuation there is reduction in the calibre of pulmonary vessels. There was no bronchiectasis in this patient.**



**B. Image section in a 19-year old male through the lower zones demonstrating focal areas of decreased attenuation in both lungs (arrows) and bronchiectasis in the left lower lobe (arrowheads).**

## **CO-INFECTIONS AND HIV: Chronic Lung Disease in Adolescents**

### **Clinically suspected chronic lung disease (CLD):**

**Defn: two or more episodes of chronic cough i.e. present most days for 3 months of the year in the past 2 years, recurrent respiratory tract infections viz. > ATB courses in the last year., and moderate to severe limitation in physical activity caused by breathlessness (NYHA Class 2-4), and/or existing diagnosis and/or signs of cor pulmonale (finger clubbing, raised JVP), or hypoxia (O<sub>2</sub> sat ≤92% at rest or desat (O<sub>2</sub> sat ≥5%) on exercise.**

Ferrand RA, Desai SR, Hopkins C, Elston CM, Copley SJ, Nathoo K, et al (Elizabeth Corbett).  
Chronic Lung Disease in Adolescents With Delayed Diagnosis of Vertically Acquired HIV Infection.  
Clin Infect Dis 2012 (1 July); 55(1): 145-52

**Study: Harare, Zimbabwe**



## CO-INFECTIONS AND HIV: Chronic Lung Disease in Adolescents

Baseline Characteristics	N= 116 (%)
Age: ≤12yr; 13-15yr; 16-18yr	34 (29%); 39 (34%); 43 (37%)
Gender: male	50 (43%)
Both parents alive; one parent alive; both parents deceased	9 (8%); 51 (44%); 56 (48%)
Age at diagnosis, yr, median (IQR)	12 (10-15)
CTX prophylaxis	111 (96%)
ART; first-line (NNRTI); second-line (PI/r)	80 (69%); 72 (62%); 6 (5%)
Height-for-age z score, median (IQR)	-1.96 (-2.9 to -1.3)
Weight-for-age z score, median (IQR)	-1.74 (-2.9 to -0.79)
BMI z score, median (IQR)	-0.69 (-1.7 to 0.1)

Ferrand RA, Desai SR, Hopkins C, Elston CM, Copley SJ, Nathoo K, et al (Elizabeth Corbett).  
Chronic Lung Disease in Adolescents With Delayed Diagnosis of Vertically Acquired HIV Infection.  
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## CO-INFECTIONS AND HIV: Chronic Lung Disease in Adolescents

Respiratory Signs and Symptoms	Patients (%)
Prior diagnosis and Tx for TB	42 (36%)
Hospitalized in the past year for a LRTI	19 (16%)
≥2 courses of ATBs for LRTI during the immediate past year	48 (41%)
Recurrent cough ± purulent sputum	77 (66%)
NYHA Dyspnoea class: 1, 2, 3 and 4	72 (62%), 20 (17%), 22 (18%), 2 (2%)
Clinical: clubbing 12 (10%), bibasal crackles 37 (32%), tachycardia at rest 35 (30%), increased resting respiratory rate >25b/min 33 (28%), Resting O2 sat <92% 15 (13%), drop by ≥5% in O2 sat with exercise testing 21 (19%).	
FEV1, % predicted: 80-100 = 64 (55%); 50-79 = 40 (35%); <50 = 12 (10%)	
PEFR, % predicted: 80-100 = 83 (72%); 50-79 = 28 (24%); <50 = 5 (4%)	

Ferrand RA, Desai SR, Hopkins C, Elston CM, Copley SJ, Nathoo K, et al (Elizabeth Corbett).  
Chronic Lung Disease in Adolescents With Delayed Diagnosis of Vertically Acquired HIV Infection.  
Clin Infect Dis 2012 (1 July); 55(1): 145-52

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## **ACKNOWLEDGEMENTS**



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Helen Joseph Hospital  
Johannesburg**



**My thanks to colleagues in the Infectious Diseases Department  
for continuing to look after our patients while I and the  
others are away at the HIV Clinicians' Conference**