Obesity and HIV

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INFECTIOUS DISEASES SOCIETY OF SOUTHERN AFRICA

Obesity is <u>not</u> restricted to the 1st world

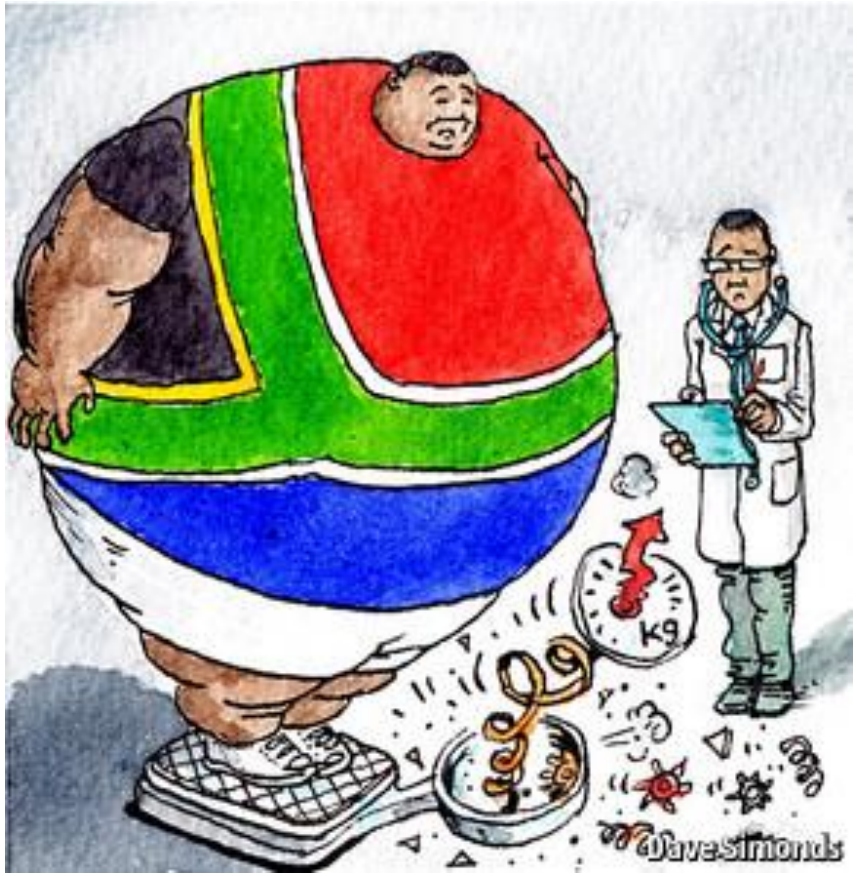
It was previously thought that obesity, a risk factor for cardiovascular disease and certain malignancies, was restricted to developed countries in the first world

Urbanization and globalization have led to changing eating and behaviour patterns

Mayosi et al, Lancet (09)61087-4, 2009
Kruger, Puoane et al, Public Health Nutrition 8(5) 491-500, 2005

Obesity is endemic in South Africa

- Obesity is more common in women, and rising in adolescents and children
- In 1998 there was a 27% prevalence of overweight BMI and a third (32%) of obese BMI amongst all population groups
- Black women had the highest prevalence of obesity and overweight
- Another study from 2005 showed that 36% of urban black women and 25% of rural black women were obese



Mayosi et al, Lancet (09)61087-4, 2009
Kruger, Puoane et al, Public Health Nutrition 8(5) 491-500, 2005

A COLLISION OF EPIDEMICS

Know Your BMI?

$$BMI = \frac{\text{Weight in Kg}}{(\text{height in m})^2}$$

< 18,5	18,5 - 24,9	25 - 29,9	30 - 34,9	35 >
UNDERWEIGHT	NORMAL	OVERWEIGHT	OBESE	EXTREMELY OBESE

- Obesity is a well-known risk factor for cardiovascular disease and certain malignancies

- In the context of HIV, this is confounded by the inflammatory effect of HIV, and the use of ART, such as PIs and NRTIs, which cause metabolic side effects, dyslipidaemia, insulin resistance and lipodystrophy

What factors influence BMI in PLWH?

- Antiretroviral side effects
  - PIs, INSTIs
- Immunological recovery on ART
- Perceptions of body image

ART side effects and BMI

- When ART is started there is a rise in adiposity and change in distribution of fat deposition[1,2]
  - High prevalence of dysglycaemia, increased visceral adiposity and dyslipidaemia on cART
- SCOLTA cohort: significant increase in BMI in patients treated with DTG (p=0.004), RTG (p=0.0004), Elvitegravir (p=0.004) and Darunavir (p=0.0006)[3]
  - In early HIV (CDC A/B): BMI gain correlated with low baseline BMI and older age, while in more advanced HIV (CDC C): BMI gain correlated with low BMI and CD4 count<200
- In a retrospective observational cohort, VL suppressed patients switched from EFV/TDF/FTC to an INSTI-containing regimen gained ~2.9kg at 18 months compared to 0.9kg in those that didn't switch (p=0.003)[4]

1. Levitt et al, Am J Clin Nutr, 2011
2. Hurley et al, SAMJ; 101:645-650, 2011
3. Taramasso et al, Open Forum Infectious Diseases IDSA (1-3), 2017
4. Norwood et al, JAIDS: 76:527-531, 2017

Immune recovery and BMI gain

- Weight gain observed in patients soon after ART initiation is believed to be due in part to
  - A reduction in basal metabolic rate after suppression of plasma viraemia
  - Improved appetite (lower inflammatory cytokine effects on the hypothalamus)
  - Reduction in rate of protein turnover

- Sub-study of Temprano RCT in Abidjan (early ART and IPT), BMI measured at baseline and after 24 months
  - Among the 597 patients at follow up, being overweight increased from 20.4-24.8% (p=0.01) and being obese increased from 7.2-9.2% (p=0.03). An associated factor was immunological response, measured as increase in CD4 count +50 cells/mm3: aOR 1.01; 95% CI 1.05-1.13, p=0.01

Norwood et al, JAIDS: 76:527-531, 2017
Guehi et al, AIDS Res Ther 13:12, 2016

Perceptions of Body Image

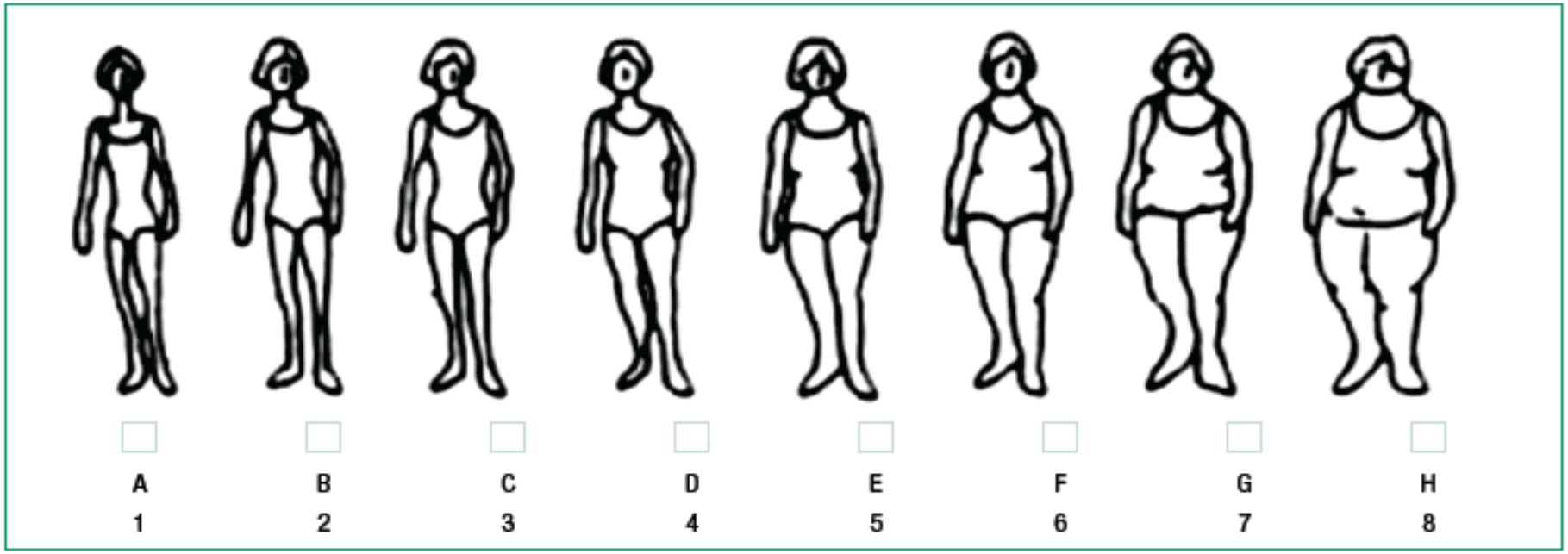


Figure1: Figures representing body image

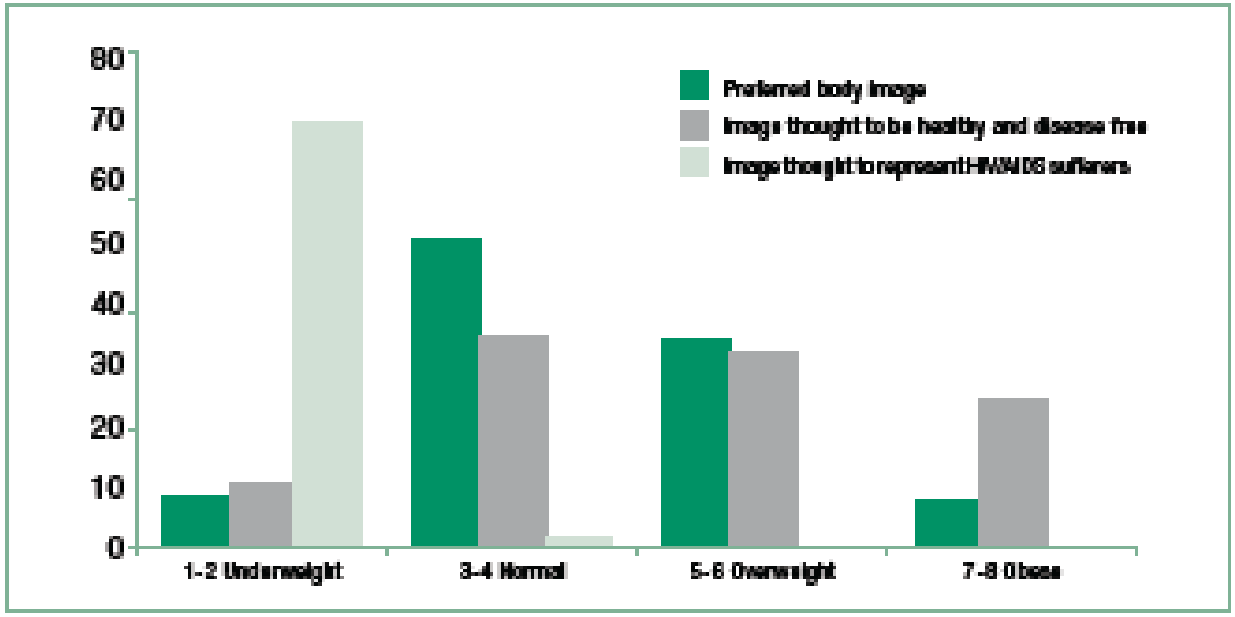


Figure 2: The participants' preferences and perceptions regarding body image, presented as choice of figures in percentages

Matoti-Mvalo, Puoane, S Afr J Clin Nutr 24(1):40-45, 2011

Would you prefer to be overweight and at risk of acquiring cardiovascular diseases, or would you rather be thin with people believing that you have HIV?

The participants confirmed that they would rather be overweight, and once again the point was made that people gossip and spread unkind rumours about people who are losing weight. It is often suggested that they have AIDS and have been promiscuous and this shames and embarrasses the person.

Would you say that people would prefer to be overweight, rather than lose weight and be associated with carrying the HIV infection or with having AIDS?

This group felt that being overweight protected them from being stigmatised in the community, and that it was desirable to be overweight rather than thin and believed to be infected with HIV or having AIDS.

"Yes, because it is not pleasant when rumours and gossip go around the neighbourhood that you are positive," said one participant. Many others nodded as she spoke.

Why are people afraid of others thinking that they may be infected with HIV or that they have AIDS?

It was suggested that people tend to spread gossip and malicious rumours about people who are losing weight. They will imply that they have AIDS and have been promiscuous, and this brings shame on the person and the family name. One participant added:"If you have AIDS and suddenly gain weight, people believe that you are well again. I know a girl who is fat and pretty. Now you cannot say she was sick".

Matoti-Mvalo, Puoane, S Afr J Clin Nutr 24(1):40-45, 2011

Table II: Comparison of perceived body image with participants' calculated BMI results expressed as percentages

Parameter	Calculated BMI categories [n(%)]				
Perceived body image	Underweight BMI< 18.5 kg/m^2	Normal weight BMI 18.5-24.9 kg/m^2	Overweight BMI 25-29.9 kg/m^2	Obese BMI >30 kg/m^2	Total*
Underweight	**2 (0.4%)**	3 (0.6%)	16 (3.1%)	23 (4.5%)	44 (8.6%)
Normal	7 (1.4%)	**44 (8.6%)**	96 (18.7%)	110 (21.4%)	257 (50.0%)
Overweight	3 (0.6%)	21 (4.1%)	**77 (15.0%)**	71 (13.8%)	172(33.5%)
Obese	2 (0.4%)	7 (1.4%)	18 (3.5%)	**13 (2.5%)**	41(8.0%)
Total	14 (2.7%)	75 (14.6%)	207 (40.3%)	217 (42.3%)	513 (100.0%)

* Percentages may not add up to 100%, as some variables areunavailable.

41 participants were obese, but only 13 (~1 in 3) perceived themselves as being obese

Matoti-Mvalo, Puoane, S Afr J Clin Nutr 24(1):40-45, 2011

What are the risks associated with BMI in PLWH?

DOI: 10.1111/hiv.12294
HIV Medicine (2016), 17, 255–268

ORIGINAL RESEARCH

Short-term weight gain after antiretroviral therapy initiation and subsequent risk of cardiovascular disease and diabetes: the D:A:D study*

AC Achhra,[1] A Mocroft,[2] P Reiss,[3] C Sabin,[2] L Ryom,[4] S de Wit,[5] CJ Smith,[2] A d'Arminio Monforte,[6] A Phillips,[2] R Weber,[7] J Lundgren[8] and MG Law[1] for the D:A:D Study Group

Short term BMI gain after ART assoc with increased risk of diabetes, increase in CVD risk only if baseline BMI was normal

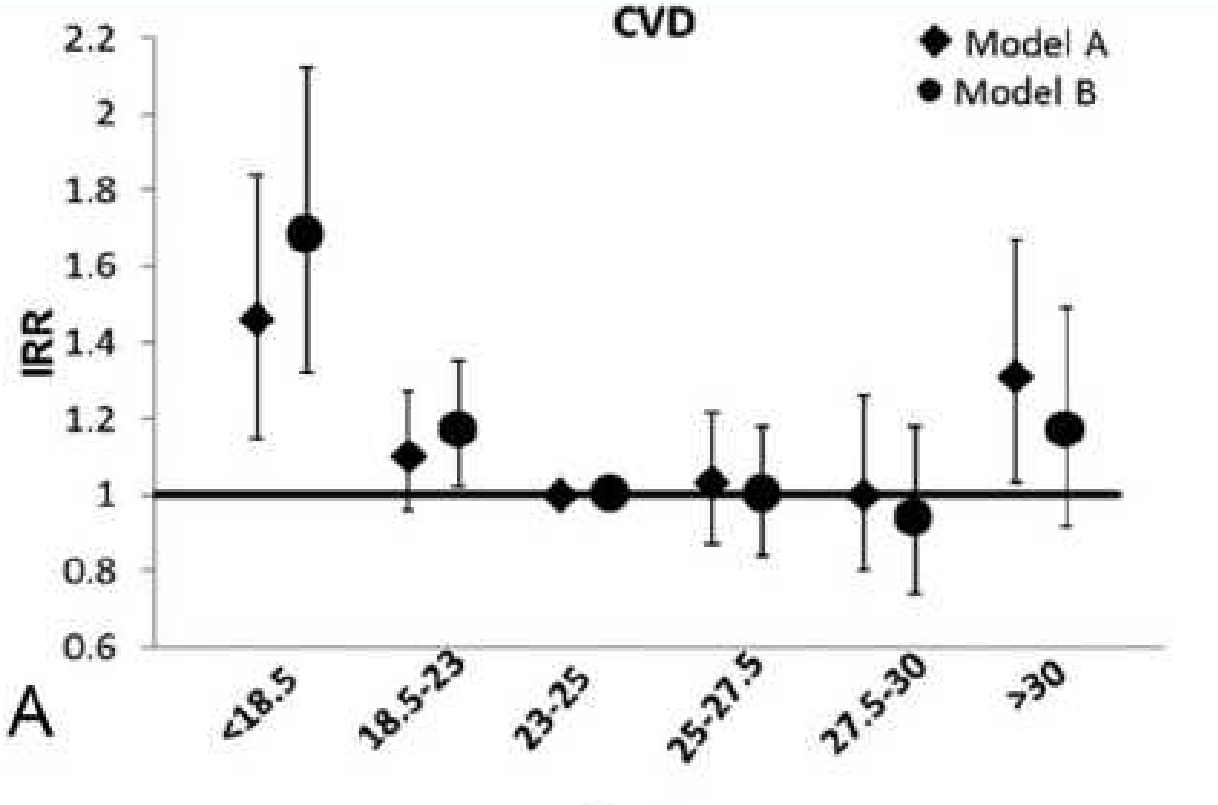
Body Mass Index and the Risk of Serious Non-AIDS Events and all-cause Mortality in Treated HIV-Positive Individuals

D: A: D Cohort Analysis

Amit C. Achhra, MBBS, MPH, PhD; Caroline Sabin, PhD; Lene Ryom, MD, PhD; Camilla Hatleberg, MD, PhD; Monforte Antonella d'Aminio, MD, PhD; Stephane de Wit, MD; Andrew Phillips, PhD; Christian Pradier, MD; Rainer Weber, MD; Peter Reiss, MD, PhD; Wafaa El-Sadr, MD, PhD; Fabrice Bonnet, MD; Amanda Mocroft, PhD; Jens Lundgren, MD, PhD; Matthew G. Law, PhD

Cohort of 41 149 individuals 73% male, baseline mean age 40, all had at least one BMI measurement and followed up at least 1 year

J Acquir Immune Defic Syndr. 2018;78(5):579-588.



Figures show incidence rate ratios [IRRs or relative risk (RR)] for all outcomes by time-updated BMI category. BMI category of 23–25 was the reference category in all models. Overall BMI was a significant predictor for all outcomes (overall $P < 0.05$ for the BMI variable in all models). The relationship of BMI was *J* or *U*-shaped with the risk of all SNAEs except DM

Model A: adjusted for known confounders (race, sex, age, age, CD4 count), Model B further adjusted for SBP & lipids

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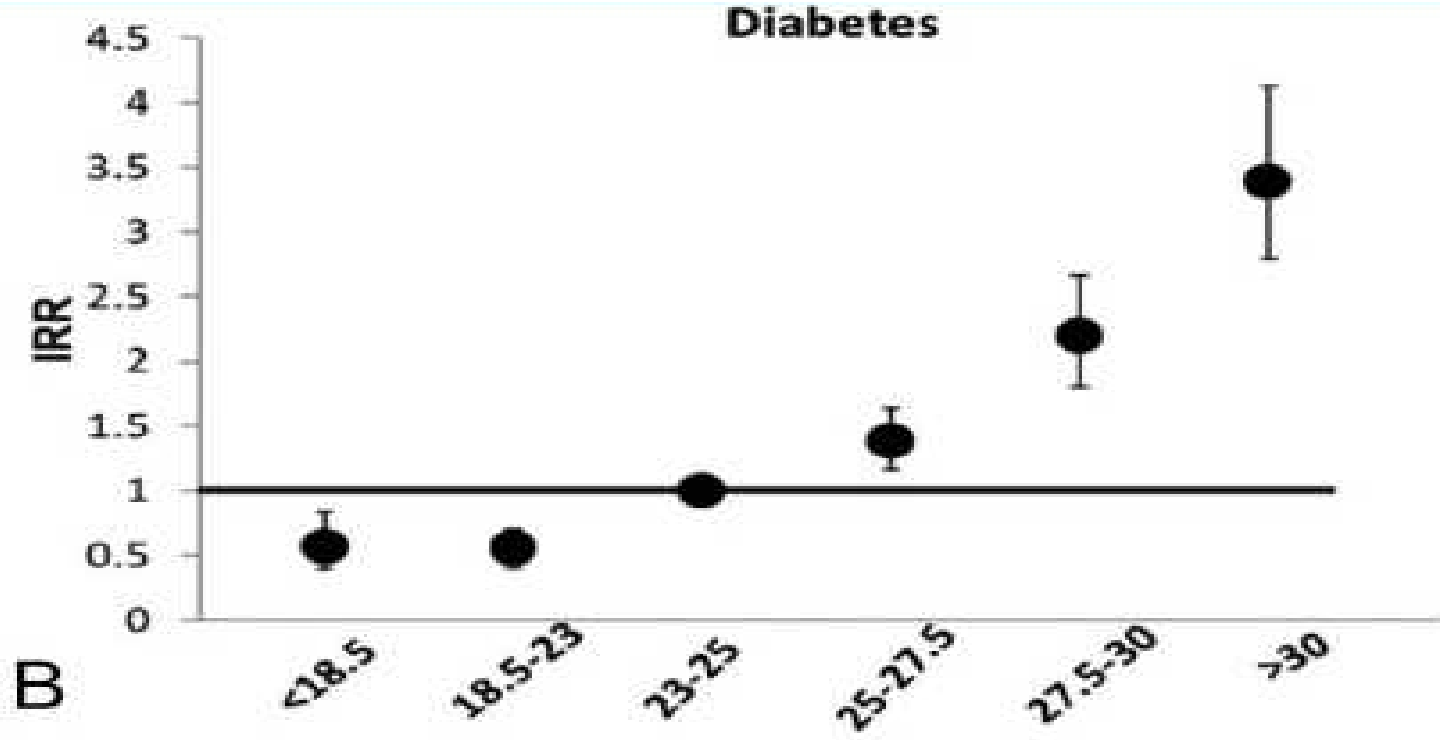
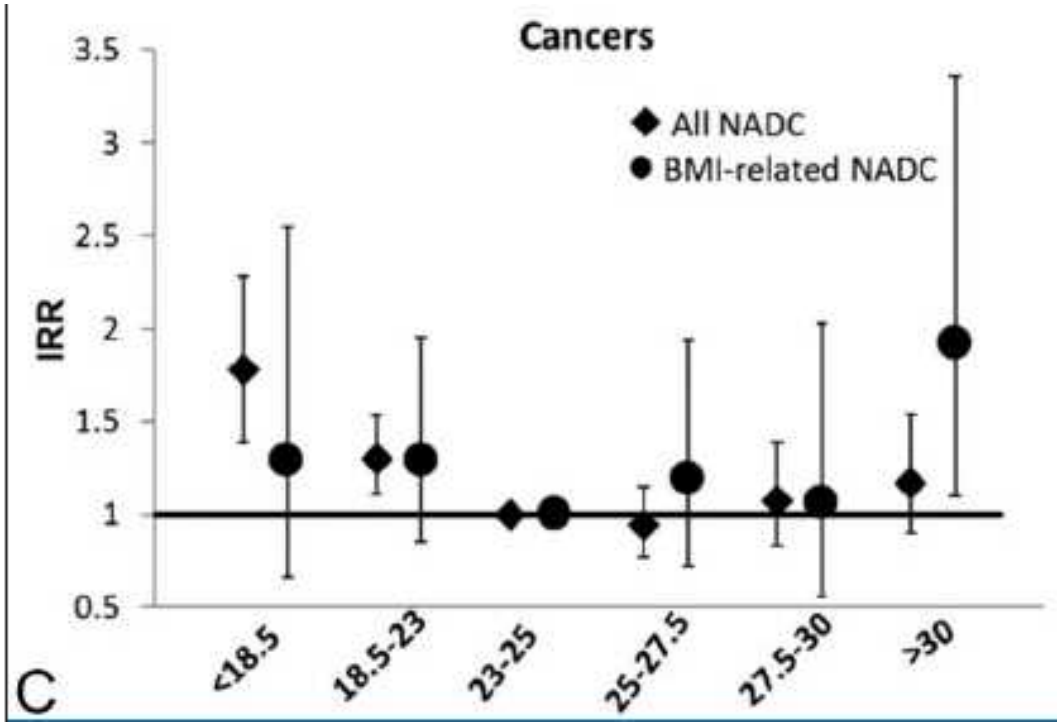


For DM, the relationship with BMI was linear, ie, increasing risk with increasing BMI, with RR nearly 3.5 times (IRR 3.39, 95% CI: 2.79 to 4.12) for BMI > 30 vs BMI of 23–25

J Acquir Immune Defic Syndr. 2018;78(5):579-588.



The IRR (95% CI) for NADC was highest for those with a BMI of ≤18.5: 1.78 (1.39 to 2.28) and for those with a BMI of 18.5–23: 1.30 (1.11 to 1.53)

However, for the BMI-cancers, BMI >30 was associated with nearly twice the risk compared with BMI 23–25 (IRR 1.90, 1.11 to 1.36)

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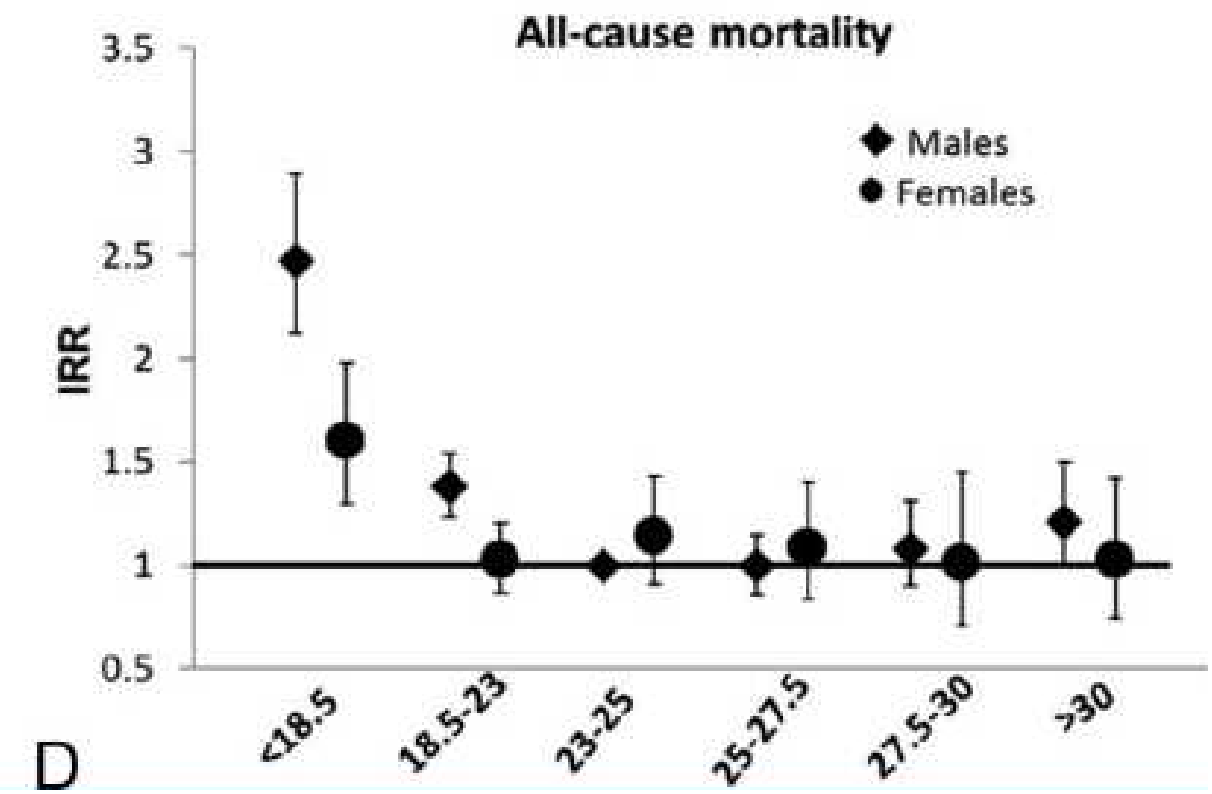


The effect of BMI on all-cause mortality tended to vary by sex (P for interaction between BMI and sex for all-cause mortality: <0.001), but not for all other outcomes

For males, the J-shaped relationship with BMI was more prominent. For males with a BMI of ≤18.5, the RR of mortality was about 2.5 times (IRR 2.47, 2.12 to 2.89) higher and for those with a BMI of 18.5–23, IRR was 1.38 (1.23 to 1.54) compared with those with a BMI of 23–25. The risk then tended to increase only in those with BMI > 30: 1.21, 0.98 to 1.50)

For females, a BMI <18.5 was also strongly related with the risk of mortality but at a lower RR compared with that in males (IRR 1.60, 1.30 to 1.98) and the risk did not increase at higher levels of BMI

J Acquir Immune Defic Syndr. 2018;78(5):579-588.

In a nutshell

Results were similar for all outcomes: for all SNAEs (except diabetes)

“Low BMI (≤18.5, and in some cases 18.5–23) was associated with high risk of several individual SNAEs as well as all-cause mortality.

The RR of SNAEs and mortality did not increase at intermediate/moderately high BMI (around 23–30) and only tended to increase at BMI >30.

These findings suggest that BMI of 25–30, thought to be "overweight/mildly obese" in general population, may in fact confer some survival advantage in HIV-positive individuals..”

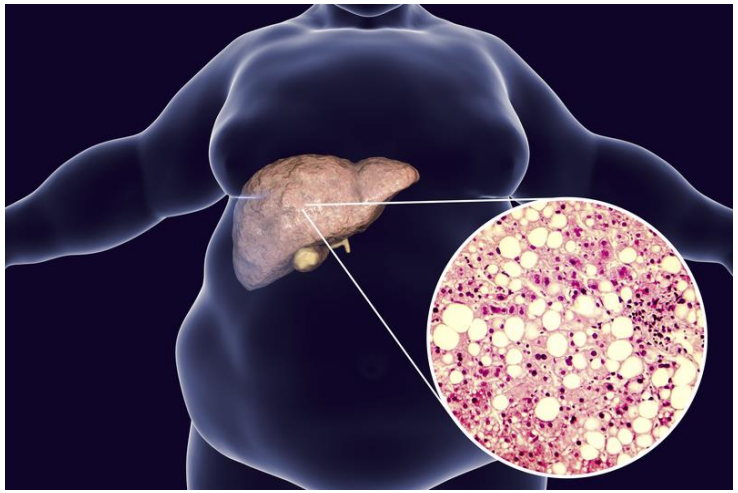
J Acquir Immune Defic Syndr. 2018;78(5):579-588.

What should clinicians be monitoring?

- Weights and heights should be measured at each visit

- High risk for diabetes: Overweight, obese, waist-hip ratio, metabolic syndrome, older generation PIs, case reports DTG

Yearly HbA1c or fasting glucose, fasting triglycerides and HDL



- High risk for fatty liver: triad of obesity, glucose intolerance and high triglycerides, also concomitant moderate-heavy ETOH use and viral hepatitis

Yearly AST/ALT, consider ultrasound liver if persistently elevated

- Low threshold to screen for BMI-NADCs

Koethe, Vanderbilt University Medical Centre, Southeast AETC Webcast Wed Series, Aug 2017
Achhra, JAIDS; 78(5):579-588, 2018

What should we be advising our patients?

- Weight loss: Goal BMI <25kg/m^2 and waist circumference <94cm (males) or <80cm (females)
- Prevention of weight gain after ART initiation: <5kg or <5cm in waist circumference
- Nutrition counseling:
  - Aim for <25% calories from fat
  - Reduce/eliminate energy dense snacks
  - Reduce/eliminate soft drinks and high sugar juices
  - Increase soluble fibre intake
- Physical activity:
  - 30 minutes of walking daily
  - 10 000 steps/day
- Address issues of stigma and body image

Koethe, Vanderbilt University Medical Centre, Southeast AETC Webcast Wed Series, Aug 2017
Achhra, JAIDS; 78(5):579-588, 2018

Summary

- Proportion of overweight and obese HIV-infected individuals is reaching parity with the general population
- Comorbid obesity and HIV is a risk factor for diabetes and fatty liver disease
- Emphasis on nutrition and exercise counseling, routine diabetes and CVD screening and treatment, and prevention of weight gain can improve health outcomes for obese persons with HIV