# Trends and risk factors for obesity among HIV positive Nigerians on antiretroviral therapy

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## Abstract

*Introduction* The increased access to antiretroviral therapy has changed the once deadly infection to a chronic medical condition, resulting in a dramatic change in causes of morbidity and mortality among HIV infected individuals. Obesity and its cardiovascular sequelae are increasingly reported in the literature. However, data on the burden, trends and risk factors for obesity are sparse in countries worst hit by the epidemic.

*Objectives* To investigate the trend and risk factors for obesity among a cohort of HIV infected adults on antiretroviral therapy.

*Methods* We analysed prospectively collected data in an ongoing longitudinal observational study conducted at the HIV treatment centre, Nigerian Institute of Medical Research, Lagos, Nigeria. Patients who started treatment between June 2004 and December 2009, and completed a five year follow up were included in the analysis. Multivariate analysis was used to determine the risk factors for obesity among the cohort.

*Results* A total of 12 585 adults were enrolled in the treatment programme during the study period. Of which, 8819 (70.1%) met the inclusion criteria. At the start of treatment, 27.0% were either overweight (19.6%) or obese (7.4%) compared to 62.2% that were either overweight (35.7%) or obese (26.5%) at the end of 5 years. The observed differences were statistically significant ($p$<0.01). Female gender (aOR: 2.2; 95% CI: 1.81-2.67), low baseline BMI less than 20 (aOR: 1.9; 95% CI: 1.3-2.2) and baseline CD4 count less than 350/μl (aOR: 2.51; 95% CI: 2.13 – 3.09) were associated with the development of obesity at multivariate analysis. Type of antiretroviral drug, age, marital status, viral load and haemoglobin level were not associated with obesity after controlling for confounding variables.

*Conclusions* Obesity is common among HIV infected Nigerians on antiretroviral therapy and is associated with female gender, low baseline BMI, and CD4 count less than 350/μl. Programmes targeted at prevention of obesity and its sequelae should be integrated into routine HIV care with emphasis on those with the identified risk factors.


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## Introduction

The increased access to antiretroviral therapy has changed the once lethal HIV infection to a chronic and manageable medical condition, resulting in a dramatic change in causes of morbidity and mortality among HIV infected individuals [1,2]. Obesity and its cardiovascular complications are being increasingly reported among stable HIV infected patients [3,4]. They contribute significantly to the growing number of ill health and death due to non-communicable diseases among stable HIV patients [2-5].

Obesity is a notable risk factor for cardiovascular diseases and several publications have reported a steady rise of obesity among the general population [5-9], and recently, among stable HIV positive patients [2-5]. Despite this reported increase in non-communicable diseases among HIV positive population, data on weight trends among HIV infected individuals are sparse [1,10]. This is especially so in the sub-Saharan African countries which bear the greatest burden of HIV infection globally [1,10]. The data from the available studies are challenged by significant limitations of design, sample size and focus on wasting alone [10-13]. With the improved access to highly active antiretroviral therapy (HAART), HIV-infected persons are living longer and experiencing lower rates of acquired immunodeficiency syndrome (AIDS)-related wasting syndrome, and may become overweight or obese at a rate similar to that of the general population [1,2,12-14].

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Recent publications show a growing number of overweight and obese HIV positive individuals while on treatment, raising the possibility that HIV and its treatment may be associated with obesity [10,11]. However, such studies are from countries outside sub-Saharan Africa with small HIV positive populations [13,14]. Another potential challenge is the paucity of studies that evaluated the risk factors for the emergence of obesity among HIV positive individuals in countries with a high burden of HIV [10-14]. Nigeria has the second largest pool of HIV infected persons globally as well as a large number of persons on antireoviral therapy. The aim of our study was to identify the trends and risk factors for obesity among a cohort of HIV infected Nigerian adults on antiretroviral therapy.

## Methods

This is a cohort review of prospectively obtained data of adult HIV positive Nigerian men and women enrolled in a study to determine long term efficacy of the Nigerian national antiretroviral treatment programme. The programme started in 2002, and continues to recruit participants. The study setting was the HIV treatment centre, Nigerian Institute of Medical Research, Lagos, Nigeria. The centre is one of the 25 tertiary health institutions in the country that started the Federal Government of Nigeria ARV access programmes in 2002. In 2004 it became one of the centres supported by the Harvard School of Public Health (HSPH), Boston. The centre currently provides comprehensive HIV care, treatment and support for over 23000 patients. Sixty five percent of the patients come from Lagos, and the rest from the other five states of south-west Nigeria, as well as from north-central, south-south and south-eastern Nigeria. Approximately 0.03% comes from the neighbouring West African countries. Patients are enrolled into the HIV treatment programme following a referral from the HIV Counselling and Testing Centre, Nigerian Institute of Medical Research Lagos, or transfer from other government approved HIV treatment centres.

Participants in this study were adult HIV positive Nigerians enrolled in the Nigerian national HIV treatment programme. They were on antiretroviral drugs and aged over 16 years. Those enrolled between January 2004 and December 2009 and followed up for five years were included in the analysis. Antiretroviral drug regimen used was according to Nigerian national ART treatment guideline. Eligibility for treatment changed three times during the study period from CD4 less than 200 cells/μl to less than 350 cells/μl and to less than 500 cells/μl. The choice of first-line regimen has also changed from Nevirapine, lamivudine and Stavudine/Zidovudine to Efavirenz, Emtricitabine and Tenofovir.

At enrolment into the treatment programme, information on sociodemographic, medical, reproductive and HIV treatment history were recorded by the attending physician. Patients' height, weight and vital signs were measured. Blood samples were then collected for the determination of CD4 count, viral load, hepatitis B screen, full blood count, lipid profile, electrolytes, urea and creatinine level. The laboratory investigations and physical examination (except hepatitis B screening and height) were repeated three monthly and thereafter six monthly. The data were transferred into the programme database by trained data entry clerks and verified by two senior data managers.

For this cohort review, study-specific data were extracted from the programme database. For each patient, information on age at enrolment, sex, height, weight marital status, education status, WHO stage, oppourtunisitic infections, ARV status, type of ARV drug regimen, CD4 count, haemoglobin level, viral load, cholesterol level, at enrolment and at 12 , 24, 36, 48 and 60 monthly visits were extracted. The extracted data were analysed with SPSS for windows version 20.0. Frequency distributions were generated and then trends in body mass index (BMI) were determined. BMI was classified as wasted (moderate and severe underweight) <16.99, underweight (mild underweight) 16.99-18.49, normal weight 18.5-24.9, overweight 25-30 and obesity > 30. Univariate analysis using relevant statistics were performed to identify factors associated with obesity. Multivariate logistic regression was further used to identify independent risk factors for obesity, while controlling for potential confounding variables. The variables were entered into the model in a stepwise manner irrespective of their *p* value on univariate analysis but starting with the variable with weakest *p* value. In the analysis, the comparison group was non-obese adult HIV positive patients. $P< 0.05$ was considered to be statistically significant. Odds ratios (OR) and 95% confidence intervals (CI) for the OR were also calculated.

Approval for the study was obtained from the Institutional Review Board, Nigerian Institute of Medical Research, Lagos, Nigeria. All patients gave written, informed consent to use their de-identified data for research.

## Results

A total of 12 585 individuals were enrolled into the programme and followed up during the study period. However only 8 819 (70.1%) met the inclusion criteria and were used for the analysis.

The sociodemographic characteristics of the 819 patients are shown in Table 1. The mean age of the patients was 35.5 ± 7.1 years (range 16 - 82 years). Majority were in the age group 30-49 years (64.8%). Female patients were in the majority (64.2%). Married (57.9%), having at least secondary education (73.3%) and presented at a late WHO disease stage (67.2%) were in the majority. Over 80% of the patients reported heterosexual route as the possible route of HIV infection (82.4%). The baseline laboratory parameters of the patients are shown in Table 2. The CD4 cell counts ranged from 3 – 1 736 cells/μl with a mean of 256.9±164.5. Majority of the patients had CD4 cell counts

less than 500 cells/μl (86.3%). Most of the patients had a haemoglobin value above 10g/dl (61.3%), viral load above 100 000 copies (53.9%), low density lipoprotein (LDL) less than 160 (90.4%), high density lipoprotein (HDL) greater than 40 (51.0%) and total cholesterol/HDL ratio greater than 4.0 (51.8%).

**Table 1. Baseline characteristics of the study participants**

| *Characteristic* | *Number (%)* |
|---|---|
| **Age (years)** | |
| Less than 30 | 2425 (27.5) |
| 30 – 49 | 5714 (64.8) |
| 50 and above | 679 (7.7) |
| Range | 16 – 82 |
| Mean | 35.5 ± 7.1 |
| **Sex** | |
| Female | 5660 (64.2) |
| Male | 3159 (35.8) |
| **Marital status** | |
| Married | 5102 (57.9) |
| Single | 2347 (26.6) |
| Divorced/Separated | 486 (5.5) |
| Widowed | 883 (10.0) |
| **Education** | |
| Less than secondary (<12 years) | 2351 (26.7) |
| Secondary and above (≥12 years) | 6468 (73.3) |
| **Identifiable risk for HIV transmission** | |
| Heterosexual | 7263 (82.4) |
| Intravenous drug use | 12 (0.1) |
| Men having sex with men | 56 (0.6) |
| Mother to child | 7 (0.08) |
| Blood transfusion | 342 (3.9) |
| Unknown | 1138 (12.9) |
| **WHO disease stage** | |
| 1 and 2 | 2893 (32.8) |
| 3 and 4 | 5926 (67.2) |
| **BMI** | |
| <16.99 | 1394 (15.8) |
| 16.99 - 18.49 | 1140 (12.7) |
| 18.5 - 24.99 | 3754 (44.4) |
| 25 - 30 | 1664 (19.7) |
| >30 | 668 (7.4) |

The distribution of the patients by their body mass index at enrolment is shown in Table 3. The prevalence of obesity ranged from 7.1% among patients enrolled in year 2004 to 7.9% among these enrolled in year 2009, with lowest (6.9%) and highest (8.0%) prevalence among those enrolled in years 2006 and 2007. The slight differences in prevalence across the years were not statistically significant ($p$>0.05). Similar trends were also observed for other BMI categories (Table 3).

**Table 2. Baseline biological characteristics of the study participants**

| *Characteristic* | *Number (%)* |
|---|---|
| **Haemoglobin (g/dl)** | |
| ≤ 10 | 3410 (38.7) |
| >10 | 5409 (61.3) |
| Range | 4.8 – 19.9 |
| Mean | 10.5 ± 4.5 |
| **CD4 count (cells/μl)** | |
| <200 | 4244 (48.1) |
| 200 – 499 | 3369 (38.2) |
| ≥500 | 1208 (13.7) |
| Range | 3 – 1736 |
| Mean | 256.9 ± 164.5 |
| **Viral load** | |
| <10,000 | 1972 (22.4) |
| 10,000 – 100,000 | 2097 (23.8) |
| >100,000 | 4749 (53.9) |
| **Total cholesterol (mg/dl)** | |
| <240 | 8192 (92.9) |
| ≥ 240 | 627 (7.1) |
| Mean | 164.8 ± 38.9 |
| **LDL cholesterol (mg/dl)** | |
| <160 | 7971 (90.4) |
| >160 | 848 (9.6) |
| Mean | 100.6 ± 37.0 |
| **HDL cholesterol (mg/dl)** | |
| <40 | 4322 (49.0) |
| >40 | 4497 (51.0) |
| Mean | 43.3 ± 17.7 |
| **Total cholesterol/HDL ratio** | |
| <4.0 | 4254 (48.2) |
| >4.0 | 5465 (51.8) |
| Mean | 5.7 ± 3.1 |

The trend in distribution of body mass index among the patients over the 5 year follow up is shown in Figure 1. The prevalence of obesity at baseline was 7.4% among the cohort. This increased to 13.9% at the end of two years and to 26.5% at the end of 5 years. Also the proportion of patients that were overweight increased from 19.6% at baseline to 35.7% after five years. The proportion of patients that were wasted and underweight decreased over the years. At the end of the fifth year, the number of patients with normal weight decreased from 44.4% to 37.1%. The differences were statistically significant ($p$< 0.01).

**Table 3. Distribution of body mass index of the patients by year of enrolment (2004-2009)**

| *BMI category (kg/m²)* | *Year of enrolment and number of patients enrolled* | | | | | | |
|---|---|---|---|---|---|---|---|
| | *2004 n = 383 (%)* | *2005 n = 1256 (%)* | *2006 n = 1518 (%)* | *2007 n = 1914(%)* | *2008 n = 1993 (%)* | *2009 n = 1755 (%)* | *Total n = 8819 (%)* |
| Wasted (< 16.9 ) | 63 (16.4) | 200 (15.9) | 234 (15.4) | 308 (16.1) | 315 (15.8) | 274 (15.6) | 1394 (15.8) |
| Underweight (16.99 - 18.49) | 55 (14.3) | 165 (13.1) | 203 (13.4) | 234 (12.2) | 239 (12.0) | 244 (13.9) | 1140 (12.7) |
| Normal (18.5-24.99) | 168 (43.9) | 515 (41.0) | 525 (44.5) | 869 (45.4) | 903 (45.3) | 774 (44.1) | 3754 (44.4) |
| Overweight (25-30) | 71 (18.6) | 252 (20.1) | 294 (19.4) | 350 (18.3) | 372 (19.3) | 325 (18.5) | 1664 (19.7) |
| Obesity (>30) | 27 (7.1) | 87 (6.9) | 111 (7.3) | 153 (8.0) | 151 (7.6) | 139 (7.9) | 668 (7.4) |

Underweight = mild underweight; Wasted = moderate and severe underweight

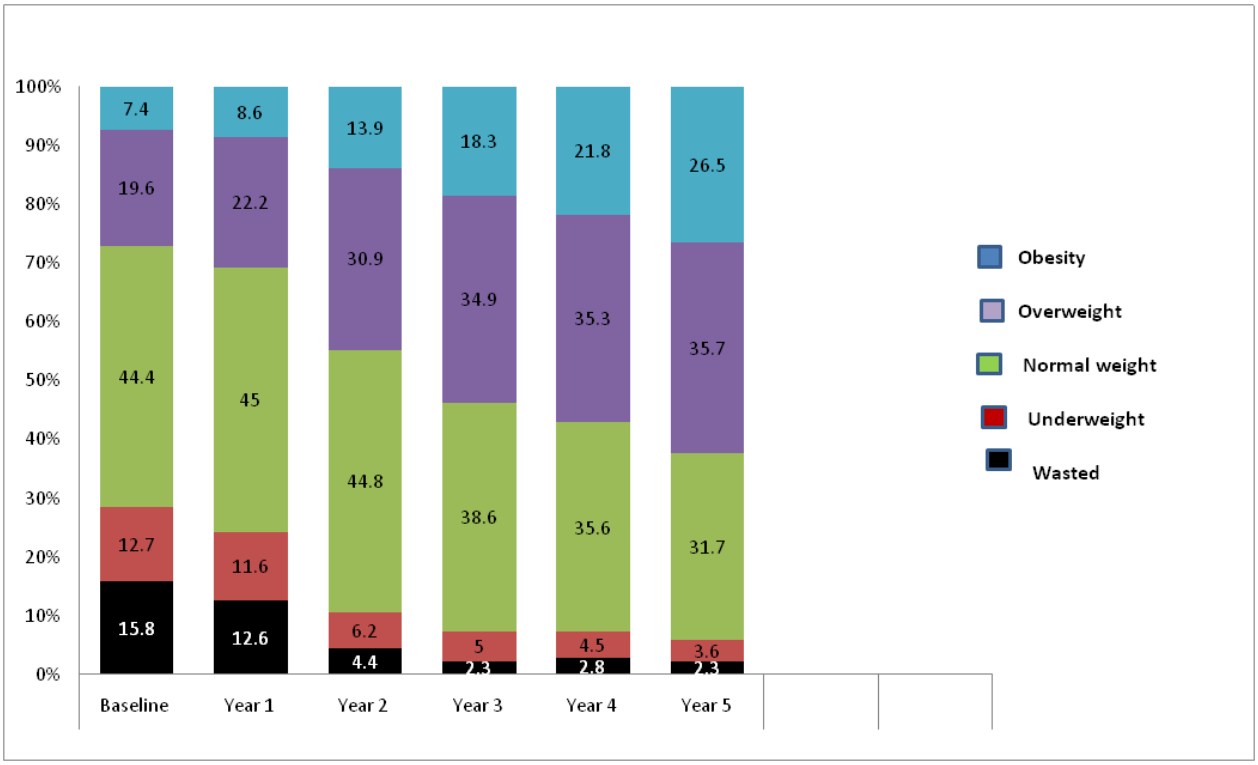


Figure 1. **Trend in nutritional status of the participants over 5 year period.**

At the end of the five year follow up period 2 337 of the 8 819 patients (26%) in the cohort were found to be obese (95% CI: 17.9 - 30.5%). Table 4 shows the univariate and multivariate analysis of selected patient characteristics and obesity. Age at enrolment of less than 35 years (cOR: 1.3; 95% CI: 1.1 -1.7), female gender (cOR: 2. 1; 95% CI: 1.8 -2.5), having less than secondary education (cOR: 1.3; 95% CI: 1.1 - 1.6) and WHO disease stage 1 and 2 (cOR: 1.3; 95% CI: 1.1 - 1.5) were found to be associated with obesity at univariate analysis. Also baseline CD4 count less than 350 (cOR:1.4; 95% CI: 1.2 - 1.8), haemoglobin less than 10g/dl (cOR:1.3; 95% CI: 1.1-1.5), viral load greater than 100, 000 copies (cOR:1. 3; 95% CI:1.1- 1.5), cholesterol/ HDL ratio greater than 4.0 (cOR: 1.4; 95% CI: 1.1 -1.9) and low baseline BMI (cOR: 2.4; 95% CI: 1.5 -2.9) were found to be associated with obesity at univariate analysis. Patient's marital status (cOR: 0.76; 95% CI: 0.65 - 0.90), social class (cOR: 2.11; 95% CI: 0.1 - 8.3), presence of opportunistic infection (cOR: 0.7; 95% CI: 0.5 -1.1) and type of antiretroviral drugs (cOR: 0.8; 95% CI: 0.4 -1.4) were not found to be associated with the development of obesity. After controlling for possible confounding variables, only female gender (aOR: 2.2; 95% CI: 1.8 -2.7), baseline CD 4 count less than 350 cells/µl (aOR: 2.5; 95% CI: 2.1 -3.1) and low baseline BMI (aOR: 1.9; 95% CI: 1.3-2.2) retained their independent association with obesity.

**Table 4. Risk factors for obesity (BMI >30)**

| *Characteristic* | *Unadjusted* | | *Adjusted*[α] | |
|---|---|---|---|---|
| | *OR [95% CI]* | *p value* | *OR [95% CI]* | *p value* |
| **Age (years)** | | | | |
| Less than 35 | 1.33 (1.13 - 1.56) | 0.001 | 1.01 (0.76 - 2.01) | 0.06 |
| ≥ 35 | 1.0 | | 1.0 | |
| **Gender** | | | | |
| Female | 2.09 (1.75 - 2.50) | 0.000 | 2.2 (1.81 - 2.67) | 0.007 |
| Male | 2.0 | | | |
| **Marital status** | | | | |
| Married | 1.0 | | 1.0 | |
| Unmarried | 0.76 (0.65 - 0.90) | 0.001 | 0.54 (0.43 - 1.23) | 0.09 |
| **Education status** | | | | |
| Less than secondary | 1.31 (1.07 - 1.60 | 0.01 | 1.5 (0.84 - 2.56) | 0.21 |
| Secondary and above | 1.0 | | 1.0 | |
| **Social class** | | | | |
| Low | 2.11 (0.13 - 8.32) | 0.03 | 1.9 (0.87 - 6.73) | 0.34 |
| Middle | 1.0 | | 1.0 | |
| Upper | 0.63 (0.22 - 1.65) | 0.09 | 0.35 (0.19 - 3.21) | 0.63 |
| **BMI** | | | | |
| < 20 | 2.4 (1.5 -2.9) | 0.01 | 1.9 (1.3-2.2) | 0.02 |
| ≥20 | 1.0 | | 1.0 | |
| **WHO stage** | | | | |
| 1-2 | 1.26 (1.05 - 1.52) | 0.01 | 2.31 (0.56 - 2.39) | 0.06 |
| 3-4 | 1.0 | | 1.0 | |
| **Opportunisitic infections** | | | | |
| Yes | 1.0 | 1.0 | | |
| No | 0.72 (0.49 - 1.07) | 0.09 | 0.51 (0.72 - 2.32) | 0.15 |
| **Type of ARV drugs** | | | | |
| d4T based regimen | 0.75 (0.41 - 1.36) | 0.31 | 0.63 (0.53 - 2.22) | 0.54 |
| AZT based Regimen | 1.0 | | 1.0 | |
| **CD4 count** | | | | |
| <350 cells/ μl | 1.44 (1.18 - 1.76) | 0.0002 | 2.51 (2.13 - 3.09) | 0.006 |
| ≥ 350 cells/ μl | 1.0 | | 1.0 | |
| **Haemoglobin** | | | | |
| <10 g/ dl | 1.0 | 0.04 | 1.0 | 0.09 |
| ≥ 10 g/ dl | 1.28 (1.08 - 1.53) | | 1.49 (0.95 - 2.34) | |
| **Viral load** | | | | |
| <100.000 | 1.0 | 0.003 | 1.0 | 0.63 |
| ≥100,000 | 1.27 (1.08 - 1.50) | | 1.33 (0.98-2.76) | |
| **Cholesterol/HDL ratio** | | | | |
| <4.0 | 1.0 | 0.01 | 1.0 | 0.67 |
| ≥4.0 | 1.43 (1.09 - 1.86) | | 2.13 (0.73 - 3.17 | |

[α]Adjusted for age, education, sex, social class, haemoglobin, opportunistic infection, viral load, CD4 count, cholesterol, LDL, HDL, type of ARV and WHO stage

## Discussion

Our study found a low prevalence of obesity among newly diagnosed HIV patients and progressive increase in the prevalence of overweight and obesity after commencement of antireoviral therapy. The number of obese persons in our HIV cohort increased from 7.4% to 26.5% in five years. Although there is a reported increase in obesity among the general population in Nigeria, the reported 26.5% increase after five years of treatment is not likely to be a reflection of the growing obesity epidemic in the country's general population, which is in the range of 3.5-8.5% [6-9]. It is likely to be due to the effect of HIV treatment with antiretroviral drugs [5,11]. However, the prevalence of obesity in this cohort is similar to two Nigerian studies that found a high prevalence of obesity (21-26%) among Nigerians [15,16]. But the two studies had a small sample size consisting of mainly urban dwellers. These two are the only studies reporting such a high prevalence. Therefore it is fair to assume that the increased obesity was more likely to reflect the effect of antiretroviral therapy than changing trends in the general population. Also the non-significant differences in the proportion of patients that were obese at baseline in different years supports the observation that progressive increase in weight was due to antiretroviral therapy.

Low baseline BMI was found to be associated with obesity among our study cohort. Although the explanation for this finding is not immediately obvious, the underweight and wasted patients at the time of enrolment had more advanced disease and may have become healthier and gained weight over time with recovery and clearance of opportunisitic infections. Patients in this category also tend to adhere better to their drug regimen and hence faster recovery [17]. Another possible explanation for the observed association of low baseline BMI and obesity may be that the stigma associated with wasting in AIDS patients encourage eating to gain weight in an attempt to obscure the diagnosis of AIDS [18]. The observed association between female gender and obesity in this study is in agreement with previous studies in both the general and HIV infected populations [6-9,19]. The observed association between low baseline CD4 count less than 350/μl and obesity is in agreement with previous studies showing a correlation between immune reconstitution and increased gain in weight [20,21]. The explanation for this observation is similar to that of the association between low BMI and obesity. Patients with low CD4 counts are sicker and are likely to adhere better to their treatment enhancing their recovery [17].

This study is not without limitations as we did not include patients not on antiretroviral drugs. Also our study was conducted in Lagos and it may not be generalisable to the entire HIV population. Lagos is a cosmopolitan city and has been described as mini Nigeria, as all ethnic groups and social classes are represented. Hence results of studies conducted in the city are more likely to be generalised to the HIV population than studies conducted in other cities. The lack of an HIV-negative control group for comparison in this study is another limitation. The BMI that was used to assess the patients weight gain does not capture information on body habitus and may overestimate the prevalence of obesity [22,23]. This study however have strengths as it provides important data on weight trends among HIV-infected persons on therapy which were hitherto not available. Our study has the advantage of being a longitudinal study involving a large sample which makes generalisation of results possible.

In conclusion, the prevalence of obesity and overweight is high among HIV-infected persons on antiretroviral therapy. Female gender, low baseline BMI and CD4 count less than 350/μl were associated with development of obesity during antiretroviral therapy. Programmes targeted at prevention of obesity and its sequelae among HIV infected patients on therapy should be integrated into routine HIV care with special focus on women and those with advanced disease.

## Conflicts of interests

There are no conflicts of interest.

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