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## RESEARCH ARTICLE

# A STUDY OF METABOLIC SYNDROME IN ANTIRETROVIRAL THERAPY TREATMENT NAIVE HIV PATIENTS

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**ABSTRACT**

The Metabolic syndrome has been known to occur in several chronic infections like HIV. Several studies have documented increased prevalence of metabolic syndrome in HIV patients on antiretroviral therapy. However, sparse data exists about metabolic syndrome in treatment naive HIV patients. We studied the prevalence and components of metabolic syndrome in treatment naive HIV patients.

**Study protocol:** This cross sectional study included 134 HIV patients and controls. Different aspects of metabolic syndrome along with CD4 count was quantified.

**Results:** Incidence of MeTS was significantly higher (34% against 7.5%) in HIV patients as compared to the control group. HIV patients had significantly higher triglycerides (163 (IQR 117-221.25) mg/dl vs 105.5( IQR 87.75 - 141.25)mg/d, lower HDL-C (23.1mg/dl ( IQR 16.8-30.30) mg/dl vs.37.2 ( IQR 31.18-44.62)mg/dl) ,lower waist circumference and BMI as compared to controls ($p<0.001$) along with higher fasting blood glucose levels. There was no significant difference in the values of blood pressure and uric acid. Higher incidence of metabolic syndrome was seen in HIV patients with CD4 count > 350/µl and WHO stages 1 and 2.

**Conclusion:** MeTS was present in treatment naive HIV patients which is more often seen with CD4 count> 350/ µl and earlier stages of the infection

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## INTRODUCTION

Metabolic syndrome (MeTS) is defined by a constellation of interconnected physiological, biochemical, clinical, and metabolic factors that directly increases the risk of cardiovascular disease, type 2 diabetes mellitus, and all cause mortality. MetS started as a concept rather than a diagnosis (Shaw *et al*., 2003). Owing its origin in 1920 when Kylin, a Swedish physician, demonstrated the association of hypertension, hyperglycemia and gout. The field moved forward significantly following the 1988 Banting lecture given by Reaven. He described "a cluster of risk factors for diabetes and cardiovascular disease" and named it "Syndrome X" (Reaven, 1988). With the introduction of Highly Active Antiretroviral Therapy (HAART), the treatment of HIV has undergone a paradigm shift as HIV patients live longer with improved quality of life. Several studies have described the increasing incidence of MeTS among patients on HAART. Over the last few years, chronic infection like HIV has been implicated in the pathogenesis of MeTS.

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However, limited data exist on prevalence of MeTS on treatment naive HIV patients. The present study was done to study MeTS in treatment naive HIV patients and to understand its determinants

## MATERIAL AND METHODS

This was a cross-sectional evaluation of metabolic syndrome in newly diagnosed treatment naive HIV patients.

### Place and Duration of Study

The study was conducted over a period of 18(eighteen) months from Jan 2013 to June 2014 involving newly diagnosed HIV patients attending Department of Medicine of Silchar Medical College

### Methodology

The study was conducted on HIV patients > 18 years of age, attending outpatient and inpatient departments of Medicine of Silchar Medical College. Inclusion criteria were 1) confirmed HIV infection done at Integrated Counselling and Testing

Centre (ICTC) , Laboratory of Silchar Medical College where tests were done as per National Aids Control Organisation (NACO) guidelines 2) men and women > 18 years of age. Participation was voluntary and all patients who gave formal consent were included in the study. Exclusion criteria included 1) patients who were seriously ill or had associated chronic inflammatory conditions like Hepatitis B and C, 2) Chronic diseases like Rheumatoid arthritis, SLE 3) Diseases associated with lipid abnormalities like hypothyroidism, familial dyslipidemia 4) pregnant and lactating women, 6) metabolic diseases like chronic kidney disease, cholestatic liver disease and 6) patients on drugs that affect lipid and carbohydrate metabolism. All patients included in the study were subjected to comprehensive physical examination with special attention to anthropological features, blood pressure measurement and HIV related opportunistic diseases. All literate patients were given a set of questionnaire for information regarding age, sex, family history, substance abuse, characteristics related to HIV infection and use of medications. Patients who were illiterate and unable to answer the questionnaires were helped by departmental staff. The study was approved by the ethics committee of the College A control population of 134 was taken from HIV negative medical patients attending the MOPD using simple random sampling from a frame of 321 patients stratified on age and sex to allow frequency matching with HIV-positive subjects. Exclusion criteria were the same as the HIV patient group. All patients included in the study were subjected to comprehensive physical examination with special attention to anthropological features, blood pressure measurement and HIV related opportunistic diseases.

**Blood Pressure Assessment and Anthropometric Measurements**

Blood pressure (BP) recording was done on both upper limbs with the patient in sitting position using LED sphygmomanometer. An average of two readings taken at 5 minutes interval was recorded. Weight and height were recorded to the nearest 0.1 kg and 0.1 cm, respectively, to calculate Body mass index (BMI). Height was measured with the patient standing upright with both heels together, without shoes, with back against the wall and eyes directed forward. Height was measured against a fixed tape-board on the wall using a movable headboard. Height was recorded in centimetres. Weight was measured using a weighing machine of aneroid type. The person was asked to wear light clothing while measurement of weight. BMI was calculated as weight in kilograms (Kg) divided by the Square of the height in meters. A non-stretchable measuring tape was used for measurement of waist circumference. Subjects were asked to stand in a relaxed position with both feet together. Waist circumference was measured at the midpoint between the lower costal margin and upper border of the iliac crest. It was measured in centimetres. Hip circumference was measured at the level of the greater trochanter and recorded in centimetres.

**Laboratory Analysis**

All HIV patients included in the study were investigated as per the protocol developed by NACO, which is the apex body formulating care of HIV patients in India. Blood glucose and lipid profiles were estimated in every patient as per standard methods.CD4 count was done at diagnosis in every patient. Depending on the presenting features, investigations were also done to diagnose any co-existing opportunistic infections and other associated diseases.

**Diagnosis of Metabolic Syndrome**

Though several criteria exist for diagnosis of MeTS, the present study adopted the US National Cholesterol Education Program Adult Treatment Panel III (ATP III) NHLBI updated definition 2005 for defining metabolic syndrome in the study group [4]. Metabolic syndrome was said to be present if patient fulfil any three or more of the following criteria:

- Elevated waist circumference- ≥102 cm (≥40 inches) in men and ≥88 cm (≥35 inches) in women.
- Elevated triglycerides ≥150 mg/do (1.7 mol/L) Or On drug treatment for elevated triglycerides
- Reduced HDL-C- ≤40 mg/dl (≤1.03 mol/L) in men and ≤50 mg/dl (≤1.3 mmol/L) in women or on drug treatment for reduced HDL-C
- Elevated blood pressure- ≥130 mm Hg systolic blood pressure or ≥85 mm Hg diastolic blood pressure or On antihypertensive drug treatment in a patient with a history of hypertension
- Elevated fasting glucose ≥100 mg/dl or on drug treatment for elevated glucose.

**Statistical Methods**

Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0 and GraphPad InStat. Continuous variables were presented as mean ± SD, and categorical variables were presented as absolute numbers and percentage. The comparison of normally distributed continuous variables between the groups was performed using Student's t test; otherwise Mann Whitney U test was used. Nominal categorical data between the groups were compared using Chi-squared test or Fisher's exact test as appropriate. For all statistical tests, a P value less than 0.05 was considered statistically significant.

## RESULTS AND OBSERVATIONS

The patients included in the study were investigated to identify the components of MetS.

**Socio-Demographic, HIV-Related Characteristics of the Study Population**

Of the 134 patients included in the study, male patients were in greater numbers 79.1%, (n= 106 men) and 20.9%, (n= 28) women. The highest number of patients was in the age group of 31-40 years (59 patients; 44%) and the next common age group was 21-30 years (41 patients; 30.6%). There were no patients below 20 years and above 50 years of age. The details of demographic, anthropological and components of MeTS of the study group is show in Table 1. Both groups had almost similar sex distribution. The HIV infected group comprised of 26 females (19.4%) and 108 male patients (80.6%), whereas the control group had 28 females (20.9%) and 106 male

patients (79.1%). The number of HIV patients with a history of smoking and drinking was 48.5% (n=65) and 47.3% (n=63) while the corresponding figures in the control group were 46.3 %( n=62) and 38.8% (n= 52). The difference was not statistically significant. p=0.175. MetS was seen in (34.3%, n= 46) HIV patients against (7.5%, n= 10) of the control group (p < 0.001) when using NCEP-ATP III criteria (NHLBI updated 2005. Elevated fasting blood glucose levels were seen in 32.1% (n=43) HIV patients against 7.5% (n=10) controls (p< 0.001).

## DISCUSSION

The study assessed the prevalence of MeTS in treatment naive HIV patients. Our findings show that MetS was seen in higher number of HIV patients than in controls (34.3% vs. 7.5%), which was statistically significant (p < 0.001. This finding is similar to other studies among ART naive HIV patients which ranged from 18 % to 45 % (Gupta *et al*., 2003 and Daniyam, 2013).

**Table 1. Demographic, Anthropological and components of Metabolic Syndrome in the Study Population**

| Variables | HIV group n = 134 | Control group n =134 | p value |
|---|---|---|---|
| Gender | | | |
| Male | 106 (79.1%) | 108 (80.6%) | |
| Female | 28(20.9%) | 26 (19.4%) | |
| Mean Age ± SD (years) | 35.12 ± 7.4323 | 36.13 ± 9.6 | |
| Age groups | | | |
| 20-30 yrs | 41 (30.6%) | 41 (30.6%) | |
| 31-40 yrs | 59 (44.0%) | 45 (33.6%) | |
| 41-50 yrs | 30 (22.4%) | 43 (32.1%) | |
| Smokers | 65 (48.5%) | 62 (46.3%) | |
| Alcoholconsumption | 63 (47.0%) | 52 (38.8%) | |
| Metabolic Syndrome | 46 (34%) | 10 (7.5%) | <0.001 |
| BMI (Kg/m$^2$) | 18.93 ± 3.47 | 22.69 ± 2.20 | <0.001 |
| Weight (kg) | 47.48 ± 10.45 | 57.40 ± 6.57 | <0.001 |
| Waist Circumference (cm) | 76.88 ± 11.51 | 84.51 ± 5.33 | <0.001 |
| Waist Hip Ratio | 0.90 ± 0.04 | 0.91 ± 0.05 | Ns |
| Fasting blood glucose (mg/dl) | Median 96 | 82 | <0.001 |
| IQR | 84 – 107 | 73 - 89.25 | |
| Triglyceride levels (mg/dl) | Median 163.5 | 105.5 | < 0.001 |
| IQR | 117.0 - 212.25 | 87.75 - 141.25 | |
| HDL levels < 0.001 | Median 23.1 | 37.2 | <0.001 |
| IQR | 16.8 - 30.30 | 31.18 - 44.62 | |
| Uric acid (mg/dl) | Median 4.08 | 4.71 | Ns |
| IQR | 3.22 - 5.23 | 3.58 - 6.09 | |
| Blood pressure (mm Hg) | | | |
| SBP | 117.13 ± 15.37 | 119.76 ± 12.83 | ns |
| DBP | 76.63 ± 10.22 | 75.72 ± 8.70 | ns |

*ns = not significant*

The median (IQR) triglycerides were higher in HIV positive patients than in controls 163 (117-221.25) mg/dl vs. 105.5(87.75 - 141.25) mg/dl p< 0.001. HIV-positive patients also had significantly lower HDL-C -23.1mg/dl (16.8-30.30) mg/dl vs.37.2 (31.18-44.62) mg/dl, P < 0.001. The study found a significant difference in weight, BMI and waist circumference between the control group and the HIV group. There were no significant differences in waist-hip ratio in HIV patients (p = 0.117) over controls, but waist circumference and BMI was significantly lower in the HIV groups (p < 0.001).

There was no statistically significant difference in the BP recordings and uric acid levels between the groups. In the study majority of the patients were in the later stages of HIV infection – WHO Stage 3 and 4. In 34 patients in Stage 1 and 2 (Table 2), MeTS was present in 67.64% of patients while in the 100 patients in Stage 3 and 4, MeTS was present in 23% of HIV infected patients . Prevalence of MeTS in patients with CD4 count <350/ µl was 29.90 %, while it was 51.81 % in patients with CD4 count >350/ µl. In the HIV subgroup with MeTS, among the components of MeTS, low HDL and high TG were the abnormalities present at all ranges of CD4 count. CD4 count> 400/µl was associated with raised BP though the number of patients in this range of CD4 count was 13. (Table 3)

Various Indian studies have reported an incidence of MetS in the general population to be between 3% and 25 % (Nguemaïm, 2010 and Vittorio, 2010) and the incidence of MeTS in the control population was in accordance with earlier studies. In the present study, Waist circumference and BMI was lower in the HIV group than in the controls (p< 0.001).Among the other parameters of MetS, HIV infected patients had higher triglyceride levels and lower HDL levels (p <0.001). Similar findings of low HDL-C and high triglycerides have been found in other studies around the globe (Patel, 2013 and Walker, 2006). The present study did not find any difference in the Blood pressure recordings between HIV infected patients and controls. In the HERMES study (Mondy, 2007), there was no significant difference in BP readings between HIV patients and controls though HIV patient had significant nocturnal dip in BP. The study found no statistically difference in uric acid levels between the HIV group and controls. The mean serum uric acid was low 4.08mg/dl in the HIV infected group. Data regarding serum uric acid levels in HIV patients are sparse. Both low and high uric acids have been described in HIV population (patients (Sobieszczyk, 2008). Low uric acid levels have been attributed to increased renal tubular loss. The study found that patients with CD4 count > 350/µl had higher incidence of MetS Previous reports on the association between CD4+ T-cell count

and the risk of MetS are conflicting. Two cross-sectional studies found that a higher CD4+ T-cell count is associated with a higher risk of MetS (Mbunkah, 2014 and Lauda *et al*., 2011).

expression of VEGF-induced endothelial markers and this might play an instrumental role in vessel damage and in the atherosclerotic lesions observed in HIV infection (Gibellini D, 2012).

**Table 2. HIV patient with metabolic syndrome and relation with CD4 count and stage of HIV infection**

| Variables | Metabolic Syndrome (n = 46) | No Metabolic syndrome (n= 88) |
|---|---|---|
| WHO stage | | |
| Stage 1 | 6 (60%) | 4 (40%) |
| Stage 2 | 17 (70.83%) | 7 (29.17%) |
| Stage 3 | 15 (23.80%) | 48 (76.2%) |
| Stage 4 | 8 (26.62%) | 29(73.38%) |
| CD4 count | | |
| < 350 / µl | 32(29.9%) | 75(70.1%) |
| >350/ µl | 14(51.85%) | 13 (48.15%) |

**Table 3 Components of MeTS in relation to CD4 count in the HIV infected group**

| CD count | | MeTS | | | | | No MeTS |
|---|---|---|---|---|---|---|---|
| | | Elevated Waist Circumference | Low HDL | Elevated Triglycerides | Elevated Fasting Blood Glucose | Elevated Blood Pressure | |
| 0-100 | 16 | 4.35% | 95.65% | 56.52% | 34.78% | 30.43% | 32 |
| 101-200 | 14 | 3.70% | 85.19% | 55.55% | 37.04% | 22.22% | 40 |
| 201-300 | 2 | 0% | 100% | 71.43% | 0% | 28.57% | 5 |
| 301-400 | 1 | 0% | 100% | 71.43% | 14.29% | 28.57% | 6 |
| 401-500 | 8 | 18.18% | 100% | 72.73% | 36.36% | 90.91% | 3 |
| >501 | 5 | 11.11% | 77.78% | 56.52% | 22.22% | 55.56% | 4 |

In contrast, in a cross-sectional study of 293 subjects, a CD4+ T-cell count less than 100 cells/µl was associated with a higher risk of MetS. The significance of higher CD4 count with increased prevalence of MeTS is not clear as different studies have come up with contrasting results. The reason may be due to physiological response to HIV at an earlier stage of infection leading to viral suppression and maintaining of immune response which in some unknown way lead to MetS. Higher incidence of MetS was seen in the later stages of HIV infection. Similar observations were made in the HERMES study where the higher prevalence of abnormal levels of triglycerides, HDL cholesterol and blood glucose was seen than those at a less advanced stage. However, Mbunkah *et al* did not find any relation to the prevalence of MS with HIV disease stage (Kalantari, 2008).

In the present study, low HDL and high triglyceride was present in all ranges of CD4 count among the HIV group and were the main components responsible for MeTS. This finding is similar to that of Lauda *et al* from Brazil (Grunfeld, 1992). However, some other studies have found higher contributions from elevated BP and altered blood glucose as the major components of MeTS (Hansen BR, 2009). MetS is a state of chronic low grade inflammation as a consequence of the complex interplay between genetic and environmental factors. Studies on the central role of inflammation have recently unearthed many rather unexpected nodes of interaction with various infectious diseases like HIV. HIV infection is associated with deregulated inflammatory response. HIV-infected monocytic cells have down regulated expression of the tyrosine kinase RON, a negative regulator of the inflammatory process and HIV transcription as well, via ubiquitin-proteosome degradation. Tat, a key molecule in HIV replication and pathogenesis can affect both mesenchymal stem cells survival and differentiation by down regulating the

The natural course of HIV infection is associated with particular unbalances in lipid levels. The dynamics of HIV infection determine an initial decrease in HDL-c followed by a decrease in LDL-c levels. In more advanced stages, there is an increase in TG and in VLDL-c levels with a strong correlation between serum IFN-α levels and TG clearance time. (Grunfeld, 1992).These declines in TC, LDL-C and HDL-C observed after HIV sero-conversion are consistent with a chronic inflammatory state. Our study was not without limitations. Physical activity was not considered in the study group. Considering that the study design was cross-sectional, it was not possible to determine the temporal relationship between acquisition of HIV infection and development of MeTS. Also some of the findings were from small number of patients for which statistical significance could not be determined.

## Conclusion

The study concludes that metabolic syndrome is present in treatment naive HIV patients. Some components of metabolic syndrome like low-HDL and high triglycerides were present in all ranges of CD4 count. Also higher CD4 count and earlier stages of HIV infection was associated with higher prevalence of metabolic syndrome.

**Conflict of Interest:** None

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Departmental staff of Medicine, Silchar Medical College

## REFERENCES

Bonfanti, P., De Socio, G.L., Marconi, P., Franzetti, M., Martinelli, C., Vichi, F., Penco, G., Madeddu, G., Orofino, G, Valsecchi, L., Vitiello, P., Menzaghi, B., Magni, C., Ricci, E. Curr Is metabolic syndrome associated to HIV

infection per se? Results from the HERMES study. *Curr HIV Res.,* 2010 Mar; 8(2):165-71. [PubMed] [Ref list

Daniyam, C.A. and Iroezindu, M.O. 2013. Lipid Profile of Anti-Retroviral Treatment-Naïve HIV-Infected Patients in Jos, *Nigeria Ann Med Health Sci Res.* Jan-Mar; 3(1): 26–30

Deepa, R., Shantiram, C.S., Premlalitha, G., Shanti, N.G., Mohan, V. 2002. Prevalence of insulin resistance syndrome in a selected south Indian population-the Chennai urban population study-7 [CUPS-7] *Indian J Med Res*. 115:118–27. [PubMed]

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 285 : 2486 –2497,2001.

Gibellini D, Miserocchi A, Tazzari PL, Ricci F, Clo A, Morini S, Ponti C, Pasquinelli G, Bon I, Pagliaro P, et al: Analysis of the effects of HIV-1 Tat on the survival and differentiation of vessel wall-derived mesenchymal stem cells. *J Cell Biochem* 2012, 113:1132–1141.

Grunfeld, C., Pang, M., Doerrler, W., Shigenaga, J.K., Jensen, P., Feingold, K.R., Lipids, lipoproteins, triglyceride clearance, and cytokines in human immunodeficiency virus infection and the acquired immunodeficiency syndrome. *J Clin Endocrinol Metab* 1992*, 74:1045-1052*

Gupta, A., Gupta, R., Sarna, M, Rastogi S, Gupta VP, Kothari K, *et al*. 2003. Prevalence of diabetes, impaired fasting glucose and insulin resistance syndrome in an urban Indian population. *Diab Res Clin Pract*. 61:69–76. [PubMed]

Hansen, B.R., Petersen, J., Haugaard, S.B., Madsbad, S., Obel, N., Suzuki, Y. *et al*. 2009. The prevalence of metabolic syndrome in Danish patients with HIV infection: the effect of antiretroviral therapy. HIV Med. 10(6):378-87

Kalantari, P., Harandi, O.F., Hankey, P.A., Henderson, A.J. 2008. HIV-1 Tat mediates degradation of RON receptor tyrosine kinase, a regulator of inflammation. *J Immunol*, 181:1548-1555

Krishnan, Supriya DSc[*]; Schouten, Jeffrey T. MD[†]; Atkinson, Benjamin MS[‡]; Brown, Todd MD, PhD[§]; Wohl, David MD[‖]; McComsey, Grace A. MD[¶]; Glesby, Marshall J. MD, PhD[#]; Shikuma, Cecilia MD[**]; Haubrich, Richard MD[††]; Tebas, Pablo MD[‡‡]; Campbell, Thomas B. MD[§§]; Jacobson, Denise L. PhD, *MPH JAIDS Journal of Acquired Immune Deficiency Syndromes*: 1 November 2012 - Volume 61 - Issue 3 - p 381–389

Lauda., L.G. Aline Brandão Mariath., Grillo, L.P. Rev. Assoc. Med. Bras. vol.57 no.2 São Paulo Mar./Apr. 2011

Mbunkah, H.A., Meriki, H.D. Anthony Tufon Kukwah AT, Nfor, O. and Nkuo-Akenji, T.N., Prevalence of metabolic syndrome in human immunodeficiency virus - infected patients from the South-West region of Cameroon, using the adult treatment panel III criteria Diabetology & Metabolic Syndrome 2014, 6:92

Mondy, K., Overton, E.T., Grubb, J., *et al*. 2007. Metabolic syndrome in HIV-infected patients from an urban, midwestern US outpatient population. CID. 2007; 44(5):726–734. Epub Jan 22. [PMC free article][PubMed

Nguemaïm, N.F., Mbuagbaw, J., Nkoa, T., Alemnji, G., Této, G., Fanhi, T.C., Asonganyi, T., Samé-Ekobo, A. 2010. Serum lipid profile in highly active antiretroviral therapy-naïve HIV-infected patients in Cameroon: a case-control study. *HIV Med.* Jul 1; 11(6):353-9.

Patel, N.J., Sheth, H.S., Rajan, R. and Espinoza, L.R., Hyperuricemia, its Prevalence and Correlation with Metabolic Syndrome in Anti-Retroviral Naive HIV Cohort: Review of the Literature *J Immunol Tech Infect Dis* 2013, 2:2

Reaven, G.M., 1988. "Role of insulin resistance in human disease," Diabetes, vol. 37, no. 12, pp. 1595–1607.

Shaw, J.E. and Chisholm, D.J., 2003. "Epidemiology and prevention of type 2 diabetes and the metabolic syndrome," *Medical Journal of Australia*, vol. 179, no. 7, pp. 379–383.

Sobieszczyk, M.E., Hoover, D.R., Anastos, K., *et al*. 2008. Prevalence and predictors of metabolic syndrome among HIV-infected and HIV-uninfected women in the Women's Interagency HIV Study. *J Acquir Immune Defic Syndr.* 2008 Jul 1;48(3):272–280. [PubMed]).

Vittorio, L.G., De Socio, Bonfanti, P., Martinelli, C., Ricci, E., Pucci, G., Marinon, Mi, Vitiello, P., MD *et al*. 2010. Negative Influence of HIV Infection on Day–Night Blood Pressure Variability *J Acquir Immune Defic Syndr* 2010;55:356–360

Walker, Ulrich Aa; Hoffmann, Christianb; Enters, Markc; Thoden, Jana; Behrens, Georgd; Mitzel, Sophie La High serum urate in HIV-infected persons: the choice of the antiretroviral drug matters AIDS: Volume 20(11) 13 July 2006 p 1556-1558.

Wand, Calmy A., Carey, D.L., *et al.* 2007. Metabolic syndrome, cardiovascular disease and type 2 diabetes mellitus after initiation of antiretroviral therapy in HIV infection. AIDS. 21:2445–2453.

Wilson, P.W.F., R. D'Agostino, B.H. Sullivan, P.L., and Meigs, J.B., 2005. "Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus," Circulation, vol. 112, no. 20, pp. 3066–3072.

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