

# Insulin resistance and apolipoprotein B100 (Apo-B) kinetics: a comparison of protease inhibitor, efavirenz or nevirapine containing antiretroviral regimens.

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## Abstract

### Background

Insulin resistance and apolipoprotein B (Apo-B) kinetics: a comparison of protease inhibitor, efavirenz or nevirapine containing antiretroviral regimens. M. Shahmanesh<sup>1\*</sup>, S Das<sup>1</sup>, M Stolinski<sup>2</sup>, W Jefferson<sup>2</sup>, N Jackson<sup>2</sup>, G Gilleran<sup>2</sup>, R Cramb<sup>1</sup>, and M Umpleby<sup>2</sup>  
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### Results

Insulin resistance is seen in HIV patients taking protease inhibitor (PI) containing regimens but little information is available in non-PI containing antiviral regimens.

We performed a cross sectional 9-hour tracer kinetic study with 13C-leucine to measure VLDL and IDL Apo-B absolute secretion rate (ASR) and fractional catabolic rate (FCR). Insulin resistance was calculated by the homeostatic model (HOMA). Subjects were HIV negative (control, n=12), treatment naïve HIV positive patients (n=15) or taking HAART containing PI (n=14), efavirenz (EFV, n=14) or nevirapine (NVP, n=12). All subjects underwent a whole body DEXA scan. Comparison between groups was by Mann-Whitney test.

NVP-treated subjects has significantly lower glucose than those on PI or EFV and also had lower HOMA compared to PI but not EFV. On a linear regression model HOMA correlated with VLDL cholesterol, free fatty acid and trunk fat but not with peripheral fat, VLDL and IDL ASR or FCR. Patients on antiretroviral drugs had similar peripheral fat or trunk fat but significantly lower peripheral fat than controls.

### Conclusion

Nevirapine containing regimens have a more favourable glucose-insulin profile than antiviral regimens containing efavirenz or protease inhibitors.

## Introduction

- Insulin resistance is seen in HIV patients taking protease inhibitor (PI) containing regimens
- Little information is available in non-PI containing antiviral regimens
- We studied insulin resistance in HIV-negative control and 3 HIV-positive patient groups and related this to apolipoprotein B-100 (Apo-B) kinetics

## Methods

- We performed a cross sectional 9-hour tracer kinetic study with 13C-leucine
- We measured VLDL and IDL Apo-B absolute secretion rate (ASR) and fractional catabolic rate (FCR)
- We calculated Insulin resistance by the homeostatic model (HOMA)
- Subjects were HIV negative (control, n=11), treatment naïve HIV positive patients (n=16) or taking HAART containing PI (n=14), efavirenz (EFV n=14) or nevirapine (NVP n=12)
- All subjects underwent a whole body DEXA scan
- Comparison between groups was by Mann-Whitney test

## Results Summary

- HAART regimens containing PI, NVP or EFV are associated with peripheral fat loss (Table 1) and reduced clearance of VLDL and IDL ApoB (Table 3 and Figs 1 and 2)
- Insulin resistance (HOMA) correlated with trunk fat but not peripheral fat (Fig 3)
- HOMA correlated with VLDL cholesterol and VLDL triglyceride (Fig 4) and VLDL cholesterol/Apo-B ratio (Fig 5)
- On a forward linear logistic regression model HOMA was predicted by trunk fat (p=0.001), age (p=0.005), VLDL cholesterol (p=0.001), and FFA (p=0.05)
- HOMA does not correlate with VLDL or IDL Apo-B secretion or clearance
- Nevirapine containing regimens have a more favourable glucose-insulin profile than antiviral regimens containing efavirenz or protease inhibitors (table 4)

## Conclusion

- Insulin resistance correlated with trunk fat, VLDL cholesterol, serum FFA but not with peripheral fat or VLDL and IDL Apo-B kinetics
- Nevirapine containing regimens have a more favourable glucose-insulin profile

Table 1: Baseline Demography (Mean+/- SD)

	Control (12)	Rx naïve (15)	PI (14)	EFV (14)	NVP (12)
Age (years)	30.7+/- 10.5	38.1+/- 10.7	44.1+/- 9.4	36.9+/- 8.9	39.7+/- 12.7
Months on Treatment	0	0	47.1	***24.1	40.8
BMI (Kg/m <sup>2</sup> )	22.9 +/- 3.8	24.4 +/- 2.9	24.4+/- 3.7	22.7 +/- 3	23.5 +/- 3.2
Peripheral fat (g) / BMI	386.6***	317.0	254.0	268.8	243.4
Trunk fat (g) / BMI	303.3	302.8	333.3	352.5	295.0

\*p=0.04, vs. Rx naïve and \*p=0.006, vs. PI  
\*\*p=0.000 vs. PI and \*\*p=0.003 vs. NVP  
\*\*\* p <0.02 vs. HIV treatment groups

Table 3: VLDL and IDL Apo-B Absolute Secretion Rate (ASR) and Fractional Clearance Rate (FCR) Mean+/- SD

	VLDL Apo-B ASR mg/kg/day	VLDL Apo-B FCR pools/day	IDL Apo-B ASR mg/kg/day	IDL Apo-B FCRpools/day
Control (12)	7.4* +/- 5.1	13.7** +/- 4.9	5.2 +/- 3.0	10.1*** +/- 4.4
Rx naïve (16)	6.3 +/- 3.6	10.1 +/- 6.5	4.2 +/- 4.2	7.1 +/- 6.0
PI (14)	7.8 +/- 5.1	6.3+/- 2.8	6.7 +/- 10.9	4.2 +/- 3.0
EFV (14)	5.1 +/- 2.7	6.3 +/- 3.6	2.3 +/- 1.6	4.1 +/- 3.4
NVP (12)	5.9 +/- 3.5	6.3 +/- 2.1	1.8 +/- 1.5	3.5 +/- 2.8

\* p < 0.02 vs NVP and EFV \*\*p=0.003, vs. Treatment groups  
\*\*\* p= 0.003, 0.016 & 0.008 compared to PI, NVP and EFV

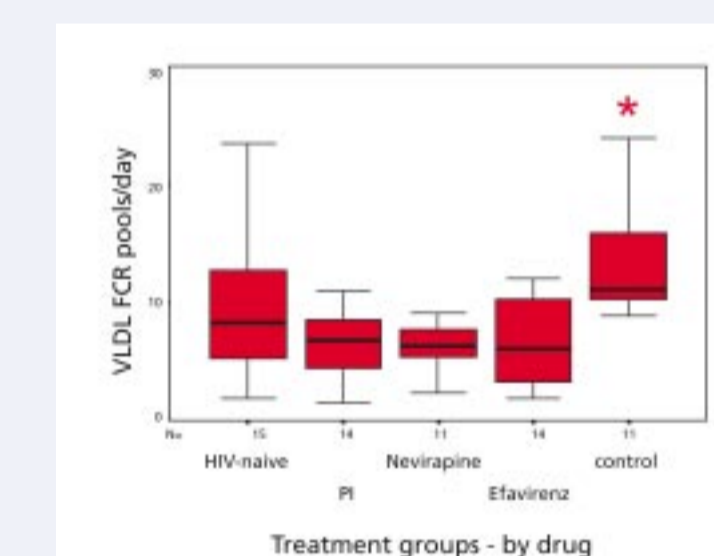
Table 2: Baseline Lipids and Free Fatty Acids (FFA)

	Total cholesterol mmol/l	HDL Cholesterol mmol/l	Triglyceride mmol/l	FFA mmol/l
Control (12)	4.7 +/- 1.1	1.8 +/- 0.4	1.1 +/- 0.5	0.6 +/- 0.3
Rx naïve (16)	4.3 +/- 0.9	1.1 +/- 0.3	1.4 +/- 1	0.5 +/- .3
PI (14)	5.9 +/- 2.2	1.3 +/- 0.5	2.2 +/- 1.3	0.5 +/- 0.2
EFV (14)	4.8 +/- 1	1.2 +/- 0.2	1.7 +/- 1.1	0.4 +/- 0.3
NVP (12)	5 +/- 0.7	1.2 +/- 0.2	1.7 +/- 1.1	0.5 +/- 0.2

Table 4: Baseline Glucose and HOMA (Mean+/- SD)

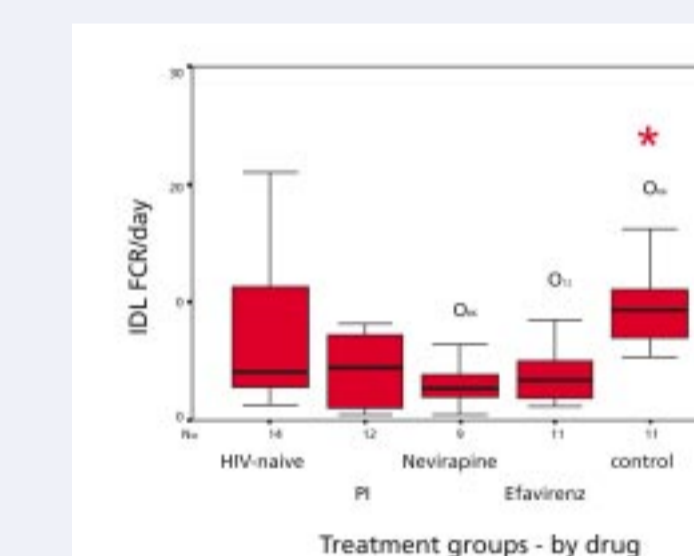
	Glucose mmol/l	HOMA
Control (12)	5.0 +/- 0.4	1.0 +/- 0.4
Rx naïve (16)	4.9 +/- 0.4	1.4 +/- 0.7
PI (14)	5.2 +/- 0.4	2.5 +/- 2.1
EFV (14)	5.2 +/- 0.6	1.7 +/- 1.2
NVP (12)	*4.7 +/- 0.5	**1.0 +/- 0.7

Figure 1: VLDL Apo-B Fractional Clearance Rate (FCR)



Median, 50th percentile (box) and 75th and 25th percentile (brackets) \* P= 0.003, 0.016 & 0.008 compared to PI, Nevirapine and Efavirenz

Figure 2: IDL Apo-B Fractional Clearance Rate (FCR)



\* P <0.0003 ( control vs. PI, NVP and EFV )

Figure 3: Correlation of HOMA with peripheral fat/BMI and trunk fat/BMI ratios

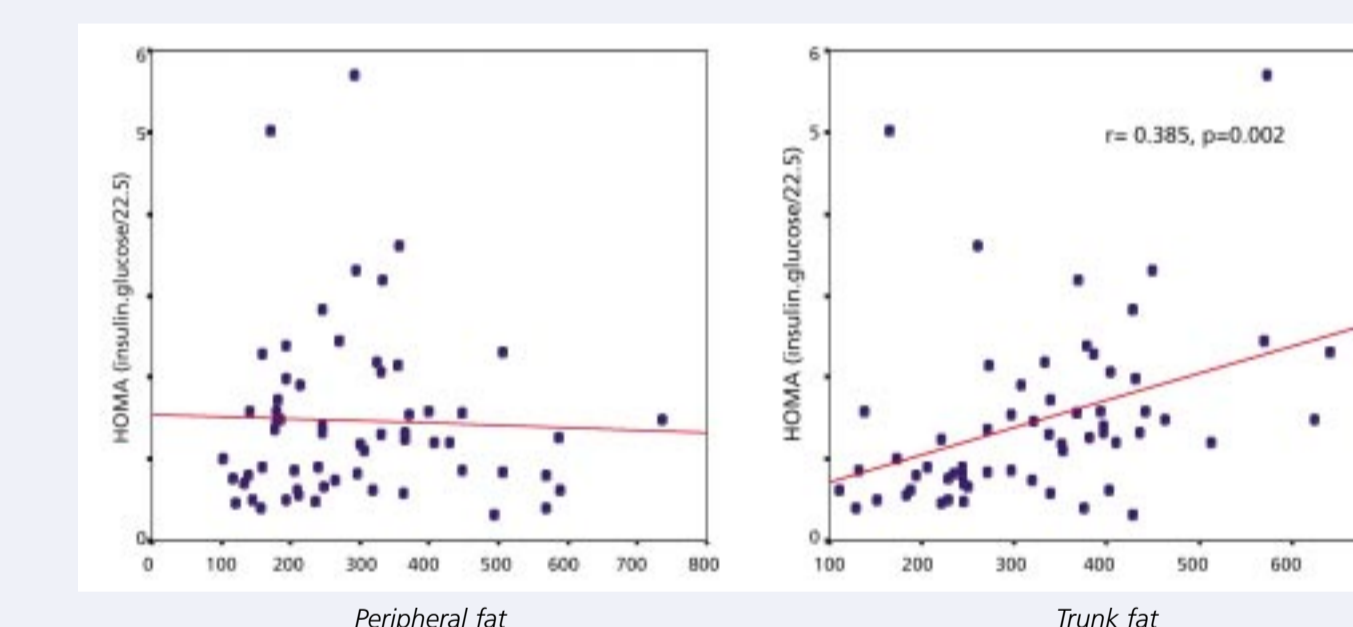


Figure 4: Correlation of HOMA with VLDL cholesterol and VLDL triglyceride

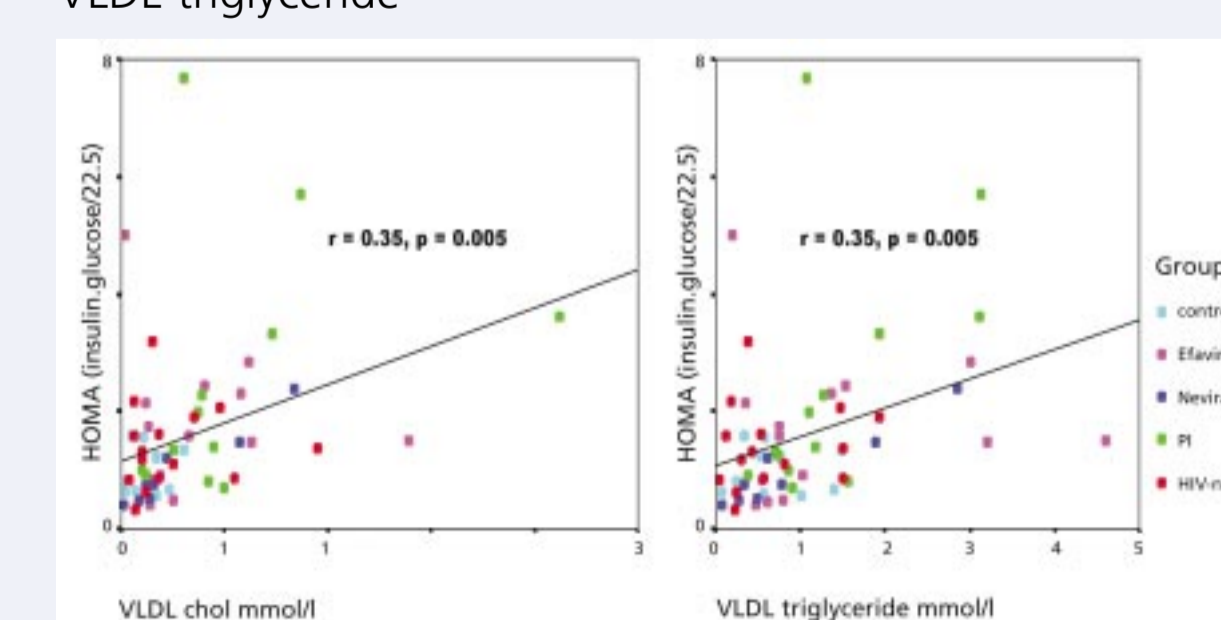


Figure 5: Correlation of HOMA with VLDL cholesterol ApoB ratio

