

# Increased baseline body weight is a risk factor associated with virological failure while on antiretroviral treatment



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## Objectives

Few studies have specifically addressed the association of body weight and the risk of virological failure. The metabolism of non nucleoside reverse-transcriptase inhibitors is known to be positively correlated with body weight and sub-therapeutic drug levels are associated with virological failure. We assessed the association between body weight and virological failure.

## Methods

The study was conducted in two urban public health centers (Kinyinya and Kimironko HC) in Kigali, Rwanda where > 3000 patients have been started on antiretroviral treatment (ART) since 2003 (~90% with a regimen containing stavudine, lamivudine and nevirapine). Viral load measurement was routinely performed after 1 year of treatment, and virological failure defined as a viral load >1000 copies/ml. Risk factor analysis was performed using a multivariate logistic regression model.

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**Table 1: Baseline characteristics of patients with lipotrophy prior to substitution with stavudine**

Risk factor	Virological failure	OR	P-value	Adjusted OR	P-value
<b>Sex</b>					
Male	32/276 (10.4)	1		1	
Female	67/791 (7.8)	0.76 (0.49-1.16)	0.205	0.70 (0.42-1.17)	0.180
<b>Age</b>					
≤ 35 years	51/474 (9.7)	1		1	
> 35 years	48/593 (7.5)	0.76 (0.51-1.13)	0.175	0.68 (0.43-1.09)	0.113
<b>Baseline body weight<sup>b</sup></b>					
< 55 kg	34/506 (6.3)	1		1	
55-65 kg	37/391 (8.6)	1.35 (0.84-2.16)	0.218	1.54 (0.91-2.60)	0.109
> 65 kg	26/164 (13.7)	2.25 (1.32-3.81)	0.003	2.90 (1.59-5.27)	0.001
<b>Baseline CD4 count (cells/μl)<sup>c</sup></b>					
< 100	40/296 (11.9)	1		1	
100-200	32/394 (7.5)	0.56 (0.35-0.91)	0.018	0.54 (0.32-0.90)	0.019
> 200	21/317 (6.2)	0.49 (0.29-0.84)	0.009	0.38 (0.20-0.69)	0.002
<b>Time on ART</b>					
≤ 1.5 years	55/664 (7.6)	1		1	
> 1.5 years	44/403 (9.8)	1.37 (0.92-2.04)	0.123	1.20 (0.76-1.89)	0.446
<b>Baseline WHO clinical stage</b>					
I	4/40 (9.1)	1		1	
II/III/IV	95/1026 (8.5)	1.14 (0.40-3.22)	0.805	1.01 (0.32-3.20)	0.990
<b>NNRTI at start of treatment</b>					
Efavirenz	10/71 (12.3)	1		1	
Nevirapine	89/996 (8.2)	0.55 (0.30-1.00)	0.051	1.22 (0.49-3.02)	0.673
<b>NRTI at start of treatment</b>					
Zidovudine	12/64 (15.8)	1		1	
Stavudine	87/1003 (8.0)	0.55 (0.31-0.99)	0.045	0.46 (0.21-1.01)	0.052
<b>NNRTI change</b>					
No	90/950 (8.6)	1		1	
Yes <sup>d</sup>	9/117 (7.1)	0.78 (0.38-1.58)	0.487	0.67 (0.31-1.47)	0.323
<b>NRTI change</b>					
No	83/903 (8.4)	1		1	
Yes <sup>d</sup>	16/164 (8.9)	1.10 (0.65-1.88)	0.716	1.05 (0.57-1.94)	0.874
<b>Adherence<sup>e</sup></b>					
100 %	31/486 (6.0)	1		1	
95-99 %	23/250 (8.4)	1.71 (0.99-2.92)	0.052	1.38 (0.76-2.51)	0.293
<95 %	45/331 (12.0)	2.33 (1.46-3.71)	0.001	1.99 (1.18-3.36)	0.009

<sup>a</sup> data represent N (%) unless otherwise stated

<sup>b</sup> median (interquartile range)

<sup>c</sup> within 6 months prior to substitution; missing for 5 individuals

## Results

We analyzed the data of 1166 adult patients who had been on ART for at least one year. In bivariate analysis, low baseline CD4 count, poor adherence, the use of zidovudine and a baseline body weight over 65 kg were associated with virological failure (OR 2.25; P=0.003).

Increased body weight remained an independent risk factor for treatment failure in multivariate analysis, after controlling for differences in clinico-immunological parameters, ART regimen/toxicity, adherence and other baseline characteristics (OR 2.90; P=0.001). The same was true if mean on-treatment body weight or body mass index (BMI) (significantly increased risk of failure for BMI > 25 kg/m<sup>2</sup>) was entered as the main risk factor (instead of baseline body weight), although the association tended to be less strong.

## Conclusions

These data show "high baseline body weight" to be a risk factor for ART failure and this finding might suggest the consequences of sub-therapeutic drug levels for patients with higher body weight. The relevance of weight-adjusted dosing needs to be explored.