

# Active surveillance of body fat changes and metabolic abnormalities in HIV-infected children and adolescents in Europe: first round results

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## Introduction

Lipodystrophy Syndrome (LS), referring to body fat alterations (loss of fat from the face, limbs, and/or buttocks and/or fat accumulation around the trunk, on the dorso-cervical region and/or the breasts) usually accompanied by metabolic disturbances, was first identified in children in 2000<sup>1</sup>.

While several studies have investigated prevalence among HIV-infected adults<sup>2-3</sup>, this has been mostly overlooked in child and juvenile populations. The metabolic changes in LS may be important in the development of cardiovascular disease or diabetes<sup>4</sup>. Children with lipodystrophy and dyslipidemia possibly have an increased risk of developing cardiovascular disease or diabetes.

Prospective data on fat distribution and dyslipidemia are needed;

- To better understand factors associated with the emergence, persistence and progression/regression of body fat alterations and metabolic abnormalities

- To elucidate the associations between body fat alterations and metabolic abnormalities

Building on a previous cross-sectional study, we have established an active multi-centre surveillance cohort study to explore these issues

## Definition of a Lipodystrophy Syndrome (LS) case

Any sign of body fat redistribution (mild, moderate or severe)  
 Hypercholesterolemia (according to age and sex adjusted thresholds)  
 Hypertriglyceridemia (according to age and sex adjusted thresholds)  
 Impaired glucose tolerance (fasting plasma glucose < 126 mg/dl and a 2-hour value (mg/dl) during OGTT between 140 and 199)

## Methods

Recruitment from HIV-infected children identified from attendees at 15 collaborating sites from Belgium, Italy and Poland over a 3-4 month period

Clinicians completed a questionnaire to allow for collection of variables pertaining to demographics, blood chemistry, treatment, clinical progression, and body fat alterations

Children classified as LS cases or non-LS cases

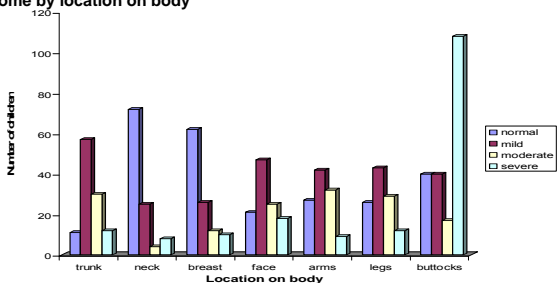
Surveillance continues with follow-up evaluation every 6 months, and further screening process to identify new incident cases.

Data stored in a Microsoft Access database and analysis conducted in STATA version 9.

## Results 1

403 children under the age of 18 years were identified. Data was also collected on 86 individuals over the age of 18 (not presented)

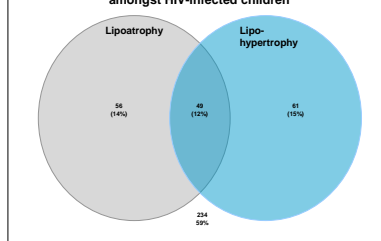
### Degree of fat redistribution amongst HIV- infected children with lipodystrophy syndrome by location on body



## Demographic and baseline characteristics of HIV-infected children

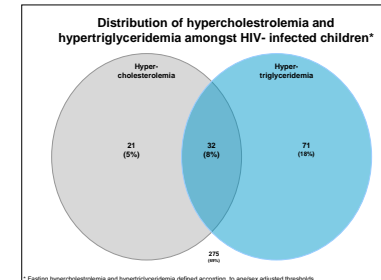
	n (%)
<b>Sex</b>	
Male	176 (47)
Female	202 (53)
<b>Ethnicity</b>	
White	259 (69)
Black	99 (27)
Other	14 (4)
<b>Age in years (median and IQR)</b>	12.2 [9.1-15.0]
<b>Tanner scale for physical development</b>	
Stage I	47 (36)
Stage II-IV	138 (38)
Stage V	92 (26)
<b>Hepatitis C co-infected</b>	27 (7)
<b>Mother to child transmission of HIV</b>	362 (94)
<b>Current CDC clinical stage</b>	
N	244 (69)
A	79 (22)
B	19 (5)
C	11 (3)
<b>Current CD4% (median and IQR)</b>	32 [25-39]
<b>Current HIV-RNA level</b>	
Undetectable (RNA≤250 copies ml <sup>-1</sup> )	281 (70)
HIV-RNA in those with RNA>250 copies ml <sup>-1</sup> (median and IQR)	9570 [18889-30122]
<b>Ever HAART use</b>	357 (89)

### Distribution of lipodystrophy and lipohypertrophy amongst HIV-infected children



- 166 (42%; 95% confidence interval; 37%, 47%) children had clinically determined signs of fat redistribution
- There was no predominant area for fat gain in children with dyslipidemia with comparable numbers of children gaining weight in the trunk, neck and breasts. This was also true of the "severe" cases
- Most fat loss, including severe cases, occurred in the buttocks as opposed to the face, arms and legs.
- Classifications of severe fat loss of body areas outnumbered severe fat gain by a ratio of 3:1

## Results 2

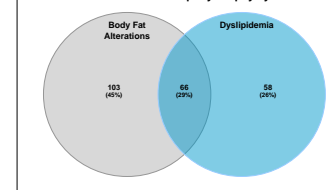


Dyslipidemia was present in 124 (31% 95% confidence interval; 27, 36) of children

### Blood glucose and triglyceride levels in HIV-infected children with dyslipidemia (unadjusted for sex and age)

	Underlying metabolic state	Median	Inter quartile range	n
Fasting blood glucose (mg/dL)	Hypercholesterolemia	226.4	205-248	37
Fasting blood triglyceride (mg/dL)	Hypertriglyceridemia	185	140- 263	59

### Body fat alterations and dyslipidemia frequency in HIV-infected children with lipodystrophy syndrome



- 227 (56%; 95% confidence interval; 51%, 60%) children had LS, using the definition illustrated
- Of the 227 children with LS, 66 (29%; 95% confidence interval; 23%, 35%) children had both dyslipidemia and body fat alterations
- There was a statistically significant difference between the number of children with dyslipidemia and the number of children with body fat alterations; p<0.005
- 6 (1.5%) of the children had impaired glucose tolerance

## Conclusions

- Overall prevalence of LS in the cohort was high at 56%.
- 42% of all children had clinical signs of fat redistribution.
  - Severe fat loss was three times more common as severe fat gain.
- Dyslipidemia was present in 31% of all children.
- Of the 227 children with Lipodystrophy Syndrome, 29% had both dyslipidemia and body fat alterations.
- Follow up of this European multi-centric cohort will allow risk factors to be described in a large study population, and evaluate the progression and the management of this syndrome.

## References

1. Jaquet D et al. Clinical and metabolic presentation of the lipodystrophy syndrome in HIV-infected children. AIDS, 2000 14; 2123-2128  
 2. Heath KV et al. Lipodystrophy-associated morphological, cholesterol and triglyceride abnormalities in a population-based HIV/AIDS treatment database. AIDS, 2001 15: 231-239  
 3. Mutamura E et al. Metabolic function and the prevalence of lipodystrophy in a population of HIV-infected African subjects receiving highly active antiretroviral therapy. J Acquir Immune Defic Syndr 2007 46(4): 451-455  
 4. Bays HE. "Sick Fat," Metabolic Disease, and Atherosclerosis. Am J Med, 2009 122 (1A) s26 -s37

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