Lipodystrophy in HIV infected patients on long term Antiretroviral therapy in western Kenya.

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Introduction

- Changes in fat distribution has been observed in patients on highly active antiretroviral therapy.
- The frequently reported drugs that cause fat redistribution are stavudine and protease inhibitors.
- Stavudine also causes a high incidence of metabolic complications and peripheral neuropathy.

Background

- Stavudine therapy is mostly associated with lipoatrophy or loss of subcutaneous fat.
  - Prominent in the extremities and in the face
- Less commonly stavudine and protease inhibitors can cause fat accumulation syndromes
  - Abdominal obesity
  - A buffalo hump
  - Isolated breast enlargement.

Background

- HIV associated lipodystrophy is multifactorial and the leading hypothesis include:
  - Host related factors such as diet and gene mutations.
  - Viral factors such as cytokine synthesis or depletion of polyunsaturated fatty acids.

Background

- Pharmacological or drug induced
  - Mitochondrial DNA-polymerase inhibition
  - Lipolysis inhibition
  - Adiponectin (involved in lipid metabolism)synthesis reduction
- Reduced levels of adiponectin has been reported in HIV infected patients especially those receiving stavudive.

Background

- Lipodystrophy is more common in women
- Other high risk factors cited in literature include:
  - Low CD4 counts
  - Higher CDC/WHO stage
  - Low body mass index
  - High viral load
  - Previous use of other ARVs

Background

- Pattern of distribution is different in men and women
  - Men: more peripheral lipoatrophy
  - Women: mixed lopoatrophy and lipohypertrophy.

Background.

- In AMPATH clinics some patients were noted to have wasting of the extremities and face.
- Changes mainly noted by patients, family members and the clinicians.
- To describe and estimate the frequency of lipodystrophy in our setting we conducted a survey on 200 patients on long term ARV and their care providers.

Research question

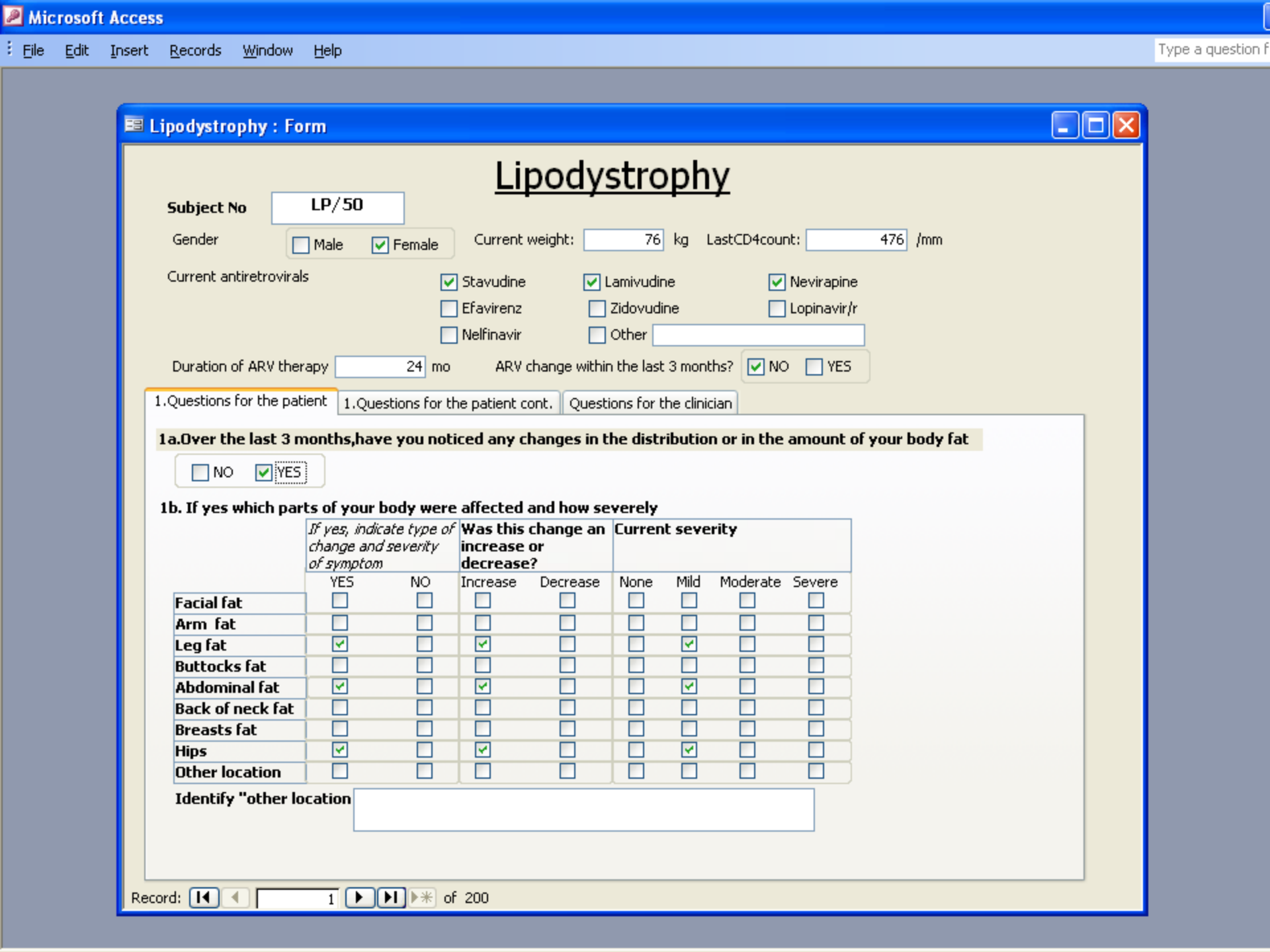
- What is the pattern and frequencies of fat redistribution in a population of HIV infected patients in western Kenya, who have received at least 6 months of antiretroviral therapy?

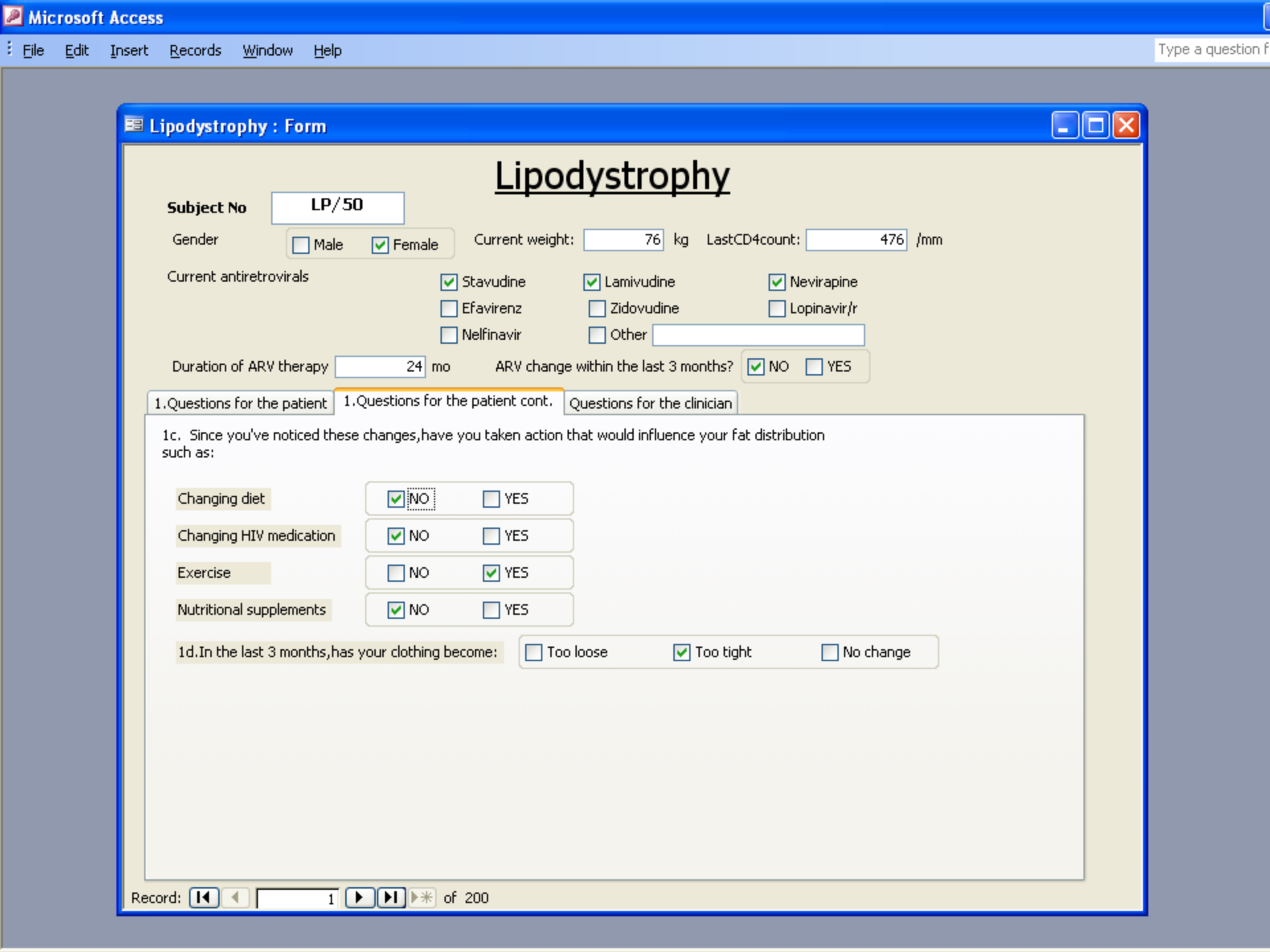
Objectives

- To estimate the frequency of fat redistribution as perceived by the patients on ARV therapy
- To estimate the frequency of fat redistribution in those same patients as perceived by the care providers.

Methods

- Cross sectional survey of patients on ARV therapy followed up in AMPATH clinics.
- Survey instrument used was modified from the one used by the Multicenter AIDS Cohort Study (MACS) in the USA.
- Consecutive patients were recruited as they presented to the clinic.
- Research assistant asked the set of questions to both the patient and provider.


Microsoft Access
File Edit Insert Records Window Help
Type a question f
Lipodystrophy : Form
Lipodystrophy
Subject No
LP/50
Gender
Male
Female
Current weight:
76
kg
LastCD4count:
476
/mm
Current antiretrovirals
Stavudine
Lamivudine
Nevirapine
Efavirenz
Zidovudine
Lopinavir/r
Nelfinavir
Other
Duration of ARV therapy
24
mo
ARV change within the last 3 months?
NO
YES
1.Questions for the patient
1.Questions for the patient cont.
Questions for the clinician
1a.Over the last 3 months,have you noticed any changes in the distribution or in the amount of your body fat
NO
YES
1b. If yes which parts of your body were affected and how severely
If yes, indicate type of change and severity of symptom
Was this change an increase or decrease?
Current severity
YES
NO
Increase
Decrease
None
Mild
Moderate
Severe
Facial fat
Arm fat
Leg fat
Buttocks fat
Abdominal fat
Back of neck fat
Breasts fat
Hips
Other location
Identify "other location
Record:
1
of 200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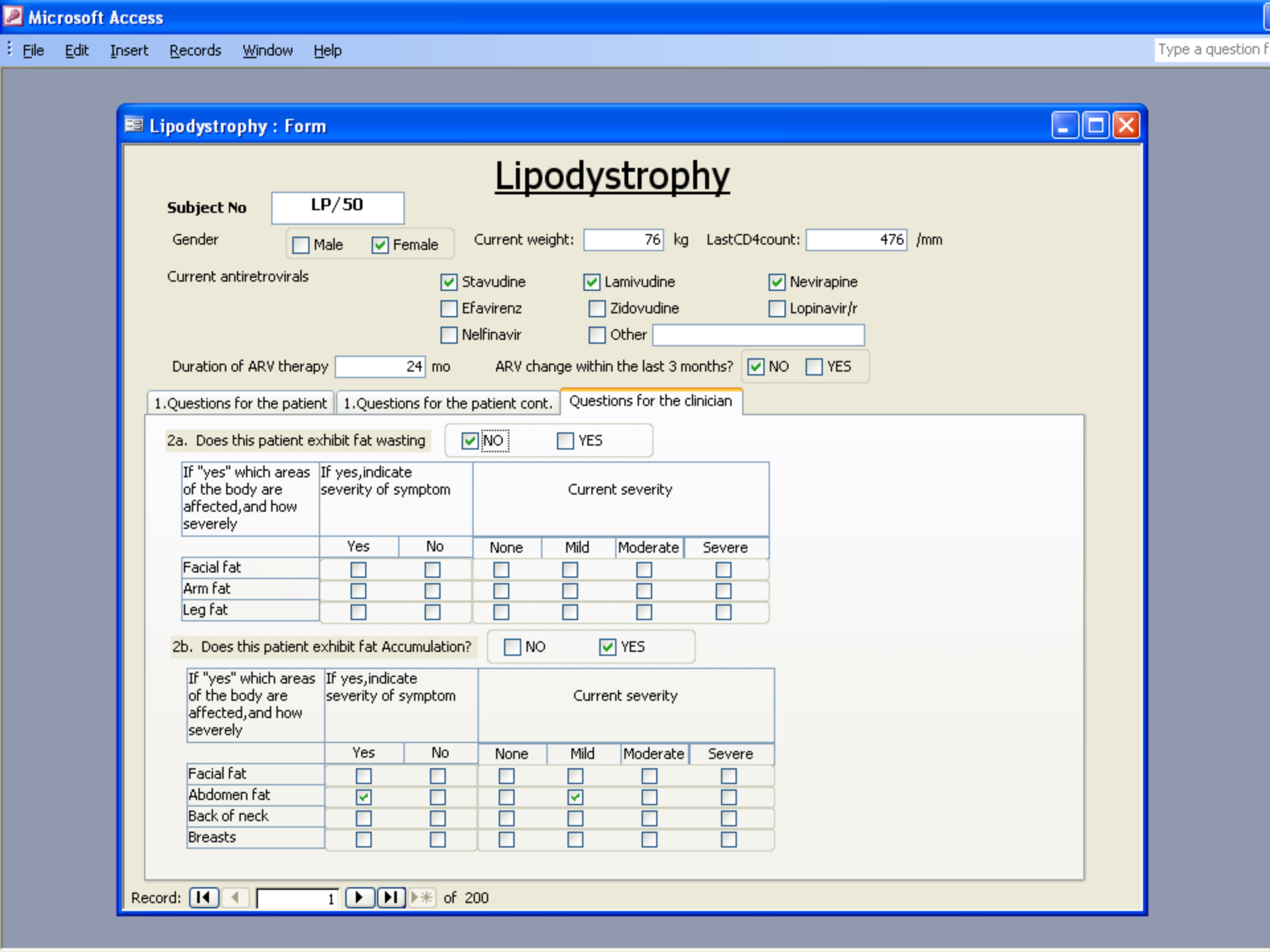
Duration of ARV therapy
24
mo
ARV change within the last 3 months?
NO
YES
1.Questions for the patient
1.Questions for the patient cont.
Questions for the clinician
1c. Since you've noticed these changes,have you taken action that would influence your fat distribution such as:
Changing diet
NO
YES
Changing HIV medication
NO
YES
Exercise
NO
YES
Nutritional supplements
NO
YES
1d.In the last 3 months,has your clothing become:
Too loose
Too tight
No change
Record:
1
of 200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Current antiretrovirals
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Lamivudine
Nevirapine
Efavirenz
Zidovudine
Lopinavir/r
Nelfinavir
Other
Duration of ARV therapy
24
mo
ARV change within the last 3 months?
NO
YES
1.Questions for the patient
1.Questions for the patient cont.
Questions for the clinician
2a. Does this patient exhibit fat wasting
NO
YES
If "yes" which areas of the body are affected,and how severely
If yes,indicate severity of symptom
Current severity
Yes
No
None
Mild
Moderate
Severe
Facial fat
Arm fat
Leg fat
2b. Does this patient exhibit fat Accumulation?
NO
YES
If "yes" which areas of the body are affected,and how severely
If yes,indicate severity of symptom
Current severity
Yes
No
None
Mild
Moderate
Severe
Facial fat
Abdomen fat
Back of neck
Breasts
Record:
1
of 200

Methods

- Inclusion criteria
  - Age 18 years or more
  - History of ARV treatment for at least 6 months
  - Willingness to answer survey questions
- Exclusion criteria
  - Lack of willingness to participate
  - Previous participation in the study.

Results

- Overall 200 patients were interviewed
- 144(72%) were women (typical of our patient population)
- The median duration of antiretroviral therapy was 15 months (range 6-61months)
- The median weight was 60kg (range 38-97)

Results

- Median CD4 was 265 (1-1026).
- All patients were on HAART (2 NRTIS +1NNRTI or PI).
- 55 (27.5%) patients reported change in fat distribution over the last 3 months
- Clinicians reported that 41(20.5%) patients had evidence of fat wasting or accumulation.

Table 1: Patient demographics

Variable	**Total**	**Male (%) N=56(28.0%)**	**Female N=144(72%)**	**P-value**
Weight Median(range)	60(38-97)	65(48-95)	59(38-97)	0.0016
CD4 count Median(Range)	265(1-1026)	216.5(1-728)	280(40-1026)	0.0088
ARV duration in months Median(Range)	15(6-61)	14.5(6-48)	15(6-61)	0.9826
ARV change Yes No	14(7.0%) 186(93.0%)	3(5.36%)	11(7.64%)	0.2197
ARVs Stavudine Lamivudine Nevirapine Efavirenz Zidovudine Lopinavir_r	 181(90.5%) 191(95.5%) 157(78.5%) 33(16.5%) 15(7.5%) 5(2.5%)	 52(92.86%) 54(96.43%) 42(75.00%) 11(19.64%) 4(7.14%) 2(3.57%)	 129(89.58%) 137(95.14%) 115(79.86%) 22(15.28%) 11(7.64%) 3(2.08%)	

Table 2a: Changes in fat distribution (patient perceptions)

Variable	Frequency (%)	Male (%) N=56(28.0%)	Female N=144(72%)	P-value
Noticed change over last 3 months				
Yes	55(27.50%)	13(23.21%)	42(29.17%)	0.3973
No	145(72.50%)	43(76.79%)	102(70.83%)	
Changes in fat distribution				
Fat accumulation (Increase)	43(21.50%)	11(19.64%)	32(22.22%)	
Wasting (Decrease)	2(1.00%)	0(0.00%)	2(1.39%)	
Accumulation +Wasting (Both)	9(4.50%)	2(3.57%)	7(4.86%)	
No change	146(73.00%)	43(76.79%)	103(71.53%)	
Action taken				
Yes	47(23.50%)	16(28.57%)	31(21.53%)	0.2915
No	153(76.50%)	40(71.43%)	113(78.47%)	
Change in clothing				
Too loose	16(8.21%)	3(5.45%)	13(9.29%)	0.5753
Too tight	43(22.05%)	11(20.00%)	32(22.86%)	
No change	136(69.74%)	41(74.55%)	45(67.86%)	

Table 2b: Changes in fat distribution (clinician's perception)

Variable	Frequency (%)	Male (%) N=56(28.0%)	Female N=144(72%)	P-value
Patient exhibit changes in fat distribution				
Fat accumulation (Increase)	29(14.50%)	9(16.07%)	20(13.89%)	
Wasting (Decrease)	7(3.50%)	0(0.00%)	7(4.86%)	
Accumulation +Wasting (Both)	5(2.50%)	0(0.00%)	5(3.47%)	
No change	159(79.5%)	47(83.93%)	112(77.78%)	

Results

- None of the risk factors such as weight, gender, CD4, type of ARV or duration of therapy were significantly related to the development of lipodystrophy in both univariate and multivariate analysis.

Conclusions

- Subjective lipodystrophy by patient or clinician survey was not uncommon
- Since most of our patients gain weight after starting ARVs, this probably represents a minimal estimate of lipoatrophy.
- Objective measures of fat loss such as DEXA scans and CT scans may yield higher estimates.

Conclusions

- The pattern of fat redistribution may be different in our setting as compared to the USA or Europe due to:
  - Predominance of women among our cohort
  - Prevalent malnutrition
  - Heterosexual mode of HIV transmission
- More studies are needed to identify the factors that are associated with lipodystrophy in our setting.