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Effects of Different Interventions to Improve ART-associated Dyslipidemia

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on behalf of DAD study group

Introduction

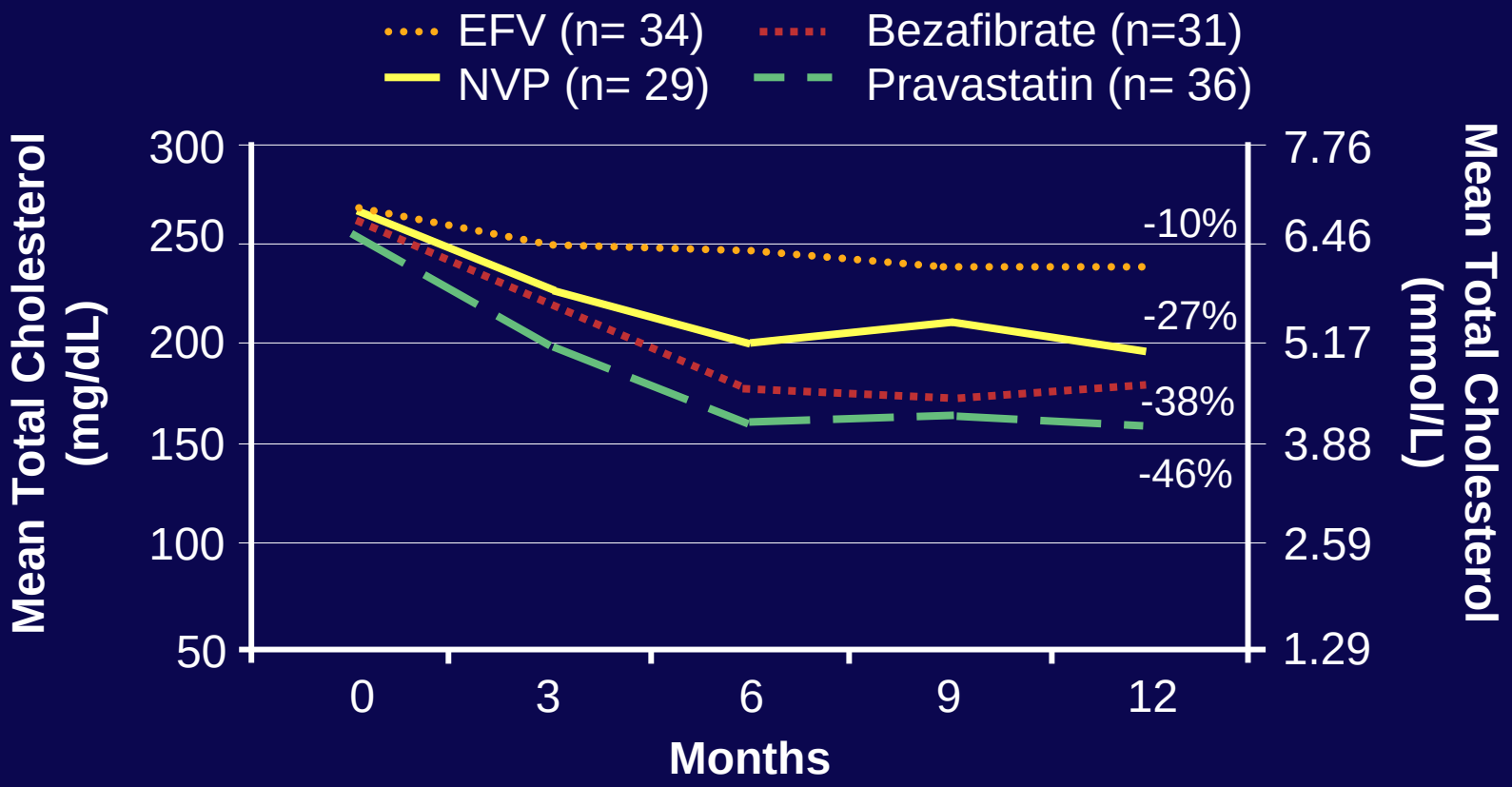
- Best strategy to treat ART-related hyperlipidemia is uncertain
- Lipid lowering therapy is unable to achieve NCEP guidelines [1]
- Replacing PI with NNRTI or abacavir results in significant improvements in plasma lipids [2]

[1] Aberg et al; ACTG 5087 fenofibrate versus pravastatin AIDS Clinical Trials Group Study 5087 AIDS Res Hum Retroviruses. 2005 Sep;21(9):757-67

[2] Fisac et al; Metabolic benefits 24 months after replacing PI with ABC, EFV or NVP; AIDS 2005 Jun 10;19(9):917-25

Dyslipidemia: Lipid-Lowering Agents vs PI to NNRTI Switch

effects on total cholesterol



Calza L, et al. AIDS. 2005;19:1051-1058.

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Study objective

Comparison of the impact of lipid lowering therapy (LLT) versus switching to a NNRTI on plasma lipids in the D:A:D study

International collaboration of 11 cohorts (33.389 HIV-1 infected patients included)

Inclusion criteria

- PI > 6 months
- NNRTI naive
- Total cholesterol > 6 mmol/l (230 mg/dl) on two consecutive occasions

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Three groups studied:

1. **LLT group: start lipid lowering therapy**
2. **Switch group: PI → NNRTI**
3. **Control group: No changes to therapy**

- Follow up 12 months
- No other changes to ART allowed in any group; no additional interventions allowed

- No information on specific LLT used, or whether samples were drawn fasting

Baseline characteristics

	LLT	Switch	Control	p-value
N	221	208	1463	
Male	86%	82%	79%	0.08
Age (yrs)	45 (27-74)	45 (26-78)	41 (20-83)	0.0001
BMI (kg/m2)	23.1 (16.7-36.1)	23.6 (17.4-43.5)	23.5 (14.8-41.1)	0.93
Baseline CD4	484 (30-1370)	534 (56-1473)	488 (0-2126)	0.0003
Any CVD	4.5%	0%	1.2%	0.0005
CVD drugs *	15%	8%	7%	0.0004
Current smoker	28%	33%	24%	0.80
Ever smoker	46%	53%	35%	0.35
Diabetes	10%	4%	2%	0.0001
PI exposure (yrs)	3.7 (0.5-8.8)	3.8 (0.6-9.3)	2.7 (0.6-9.1)	0.0001
Baseline PIs				
Ritonavir	53%	40%	36%	0.0001
Indinavir	29%	48%	37%	0.0002
Lopinavir	12%	3%	5%	0.0001
Nelfinavir	27%	28%	34%	0.08
Saquinavir	20%	14%	18%	0.35

•anti-platelets, anti-hypertensive therapy; all data expressed in median (range) or mean %

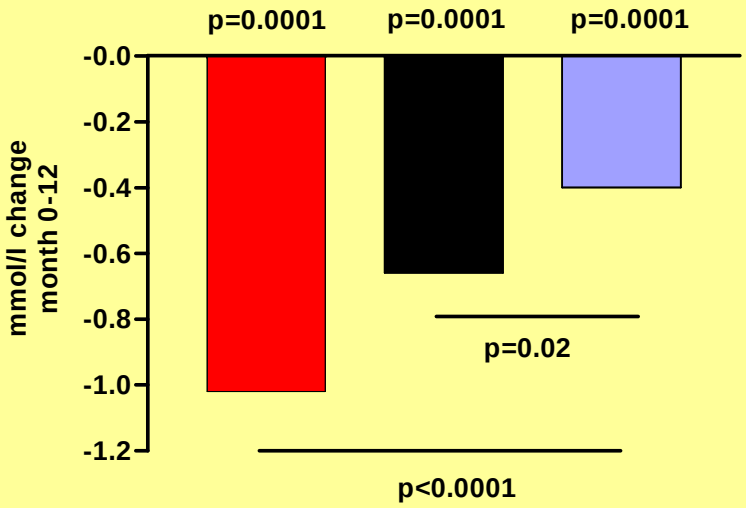
Baseline plasma lipids (mmol/l)

	LLT	Switch	Control	p-value
Total cholesterol	7.6 (6.0 -14.9)	7.1 (6.0-10.6)	6.7 (6.0-21.6)	0.0001
LDL-cholesterol	5.4 (1.5-9.5)	5.1 (2.5-7.7)	4.9 (3-7.5)	0.0001
Triglycerides	3.6 (0.8-29.8)	2.6 (0.3-19.7)	2.6 (0.3-57.7)	0.0001
HDL-cholesterol	1.1 (0.4-2.1)	1.1 (0.4-3.0)	1.2 (0.1-3.1)	0.003
TC : HDL cholesterol	6.6 (3.6-17.1)	6.1 (2.5-17.5)	5.8 (2.1-58.2)	0.001

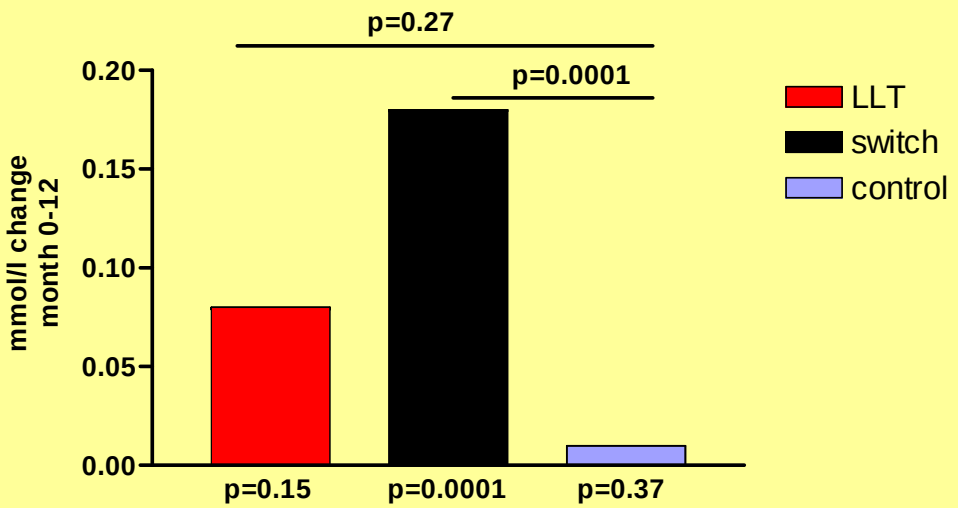
All data expressed as median (range)

Mean change in lipids month 0 - 12

Total cholesterol



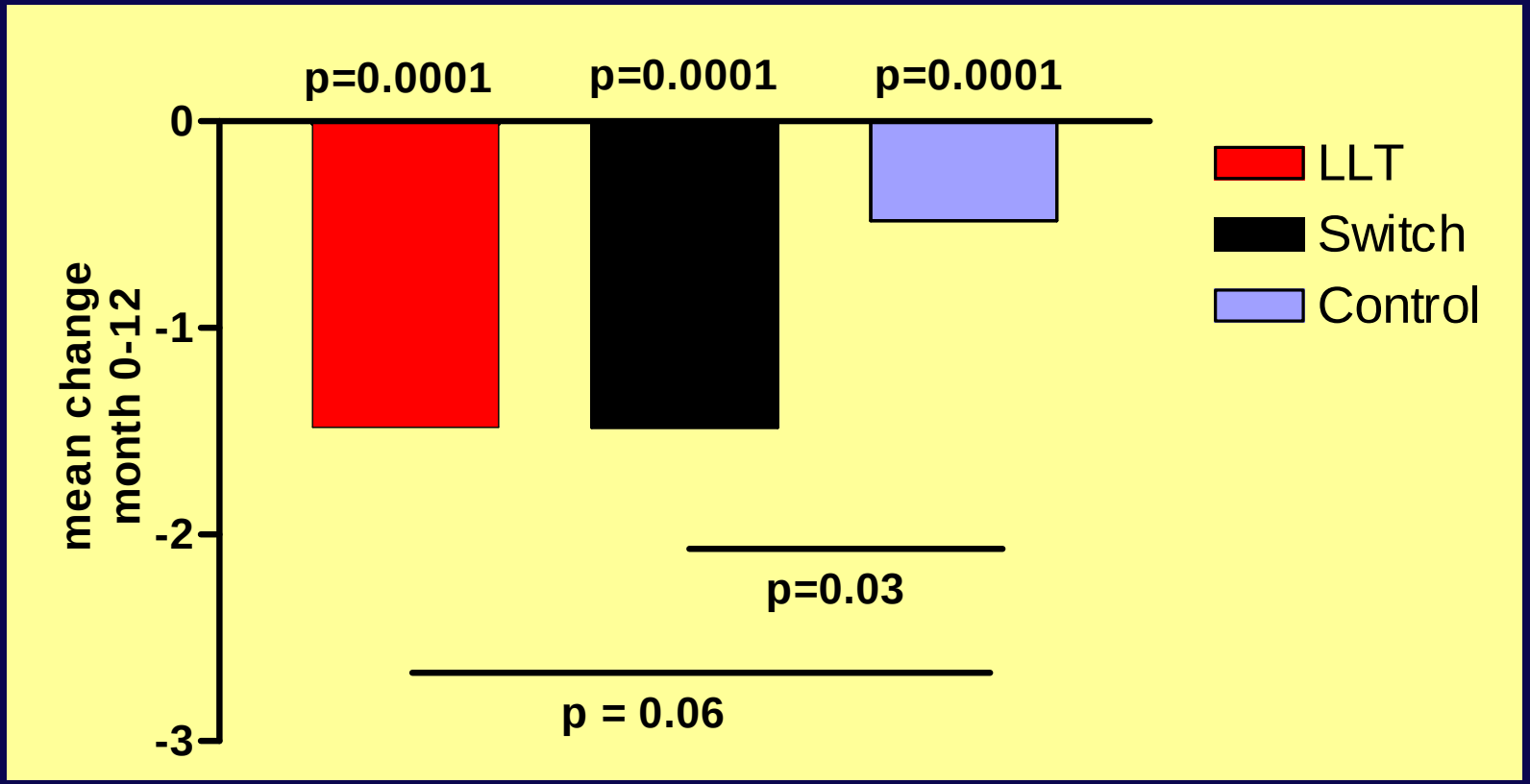
HDL cholesterol



p value in between arms represents result from multiple regression analyses of changes in lipid measurements adjusted for sex, age, ethnicity, BMI, smoking status, diabetes, previous CHD, baseline CD4 and HIV RNA, number of PIs previously received, duration of PI exposure, number of drugs received, and current use of LPV, RTV, IDV and NFV

Mean change in lipids month 0 - 12

TC: HDL cholesterol



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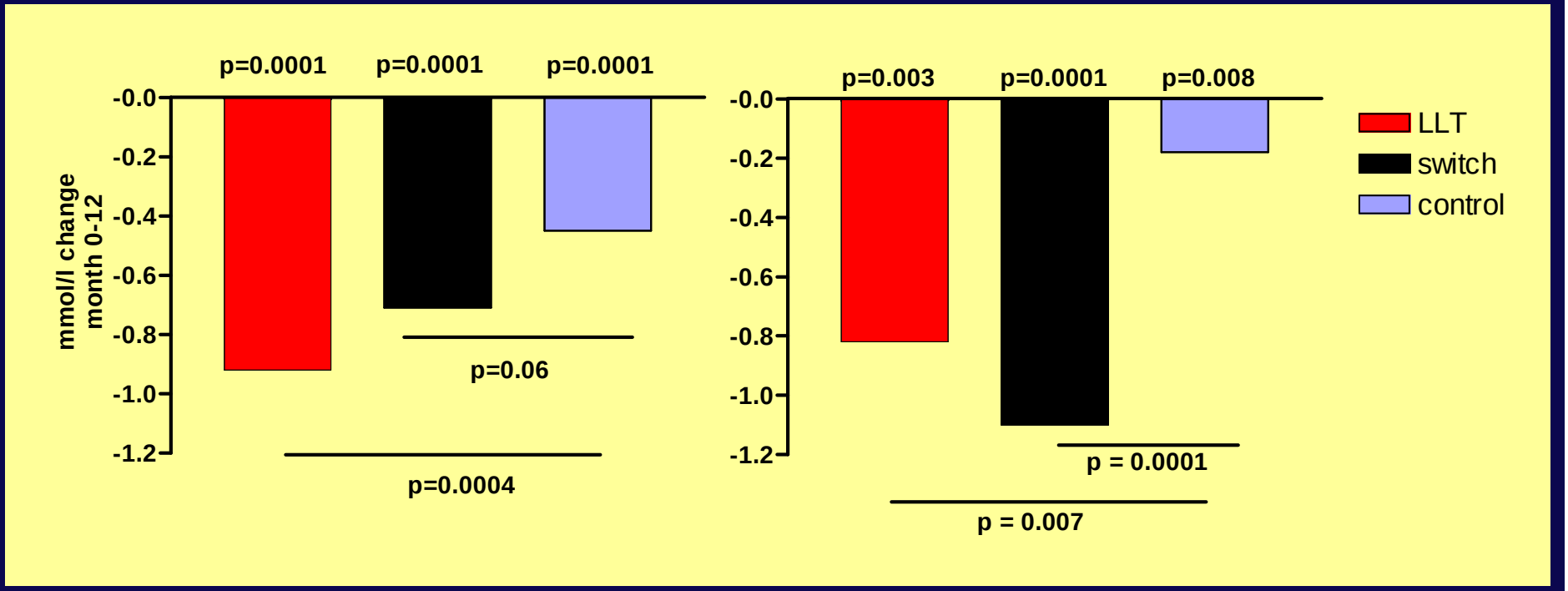
Mean change in lipids month 0 - 12

LDL cholesterol*

Triglycerides



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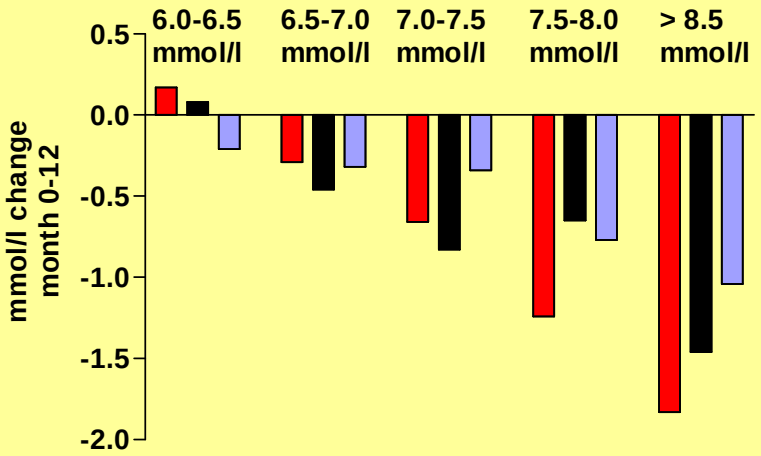
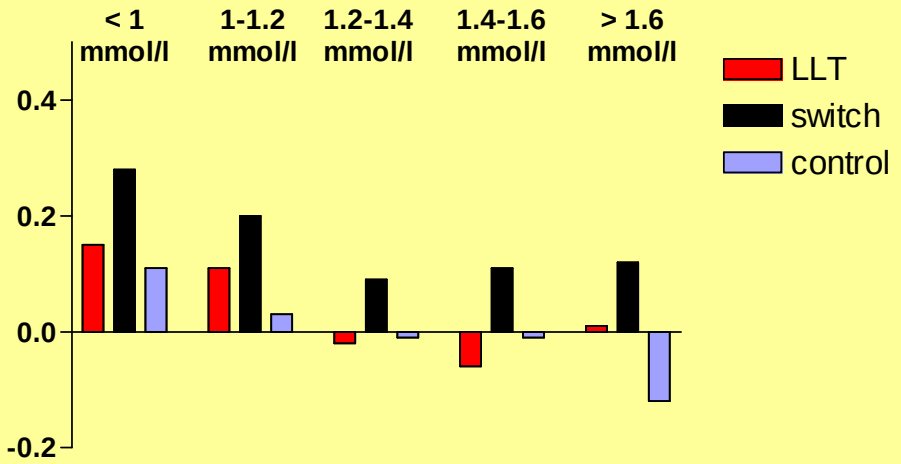
* Calculated using Friedewald formula

Plasma lipids stratified according to baseline values

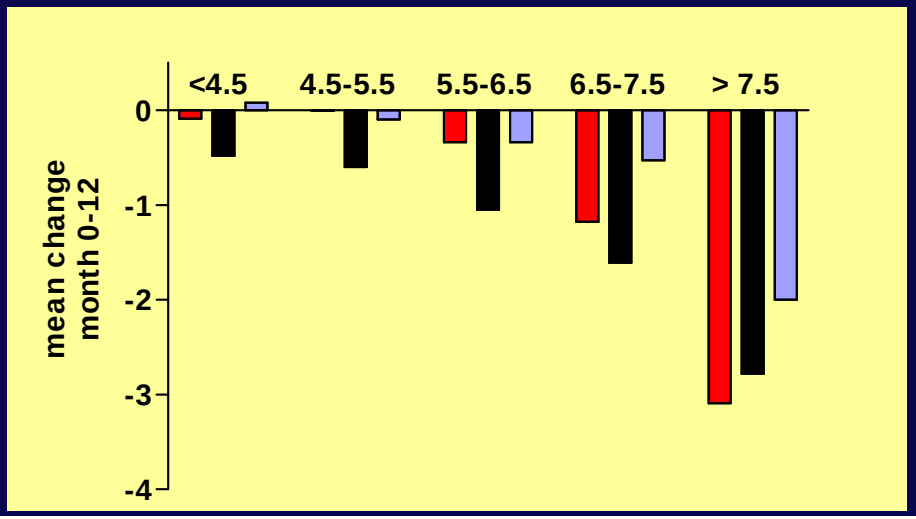
Total cholesterol



HDL cholesterol



TC:HDL cholesterol



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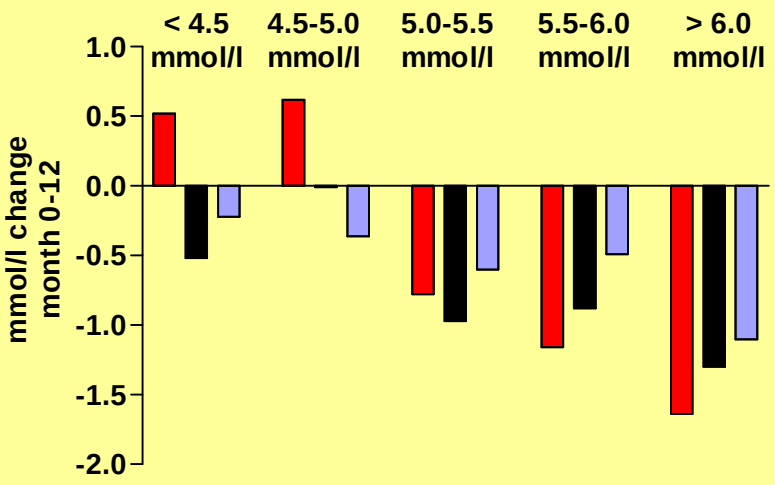
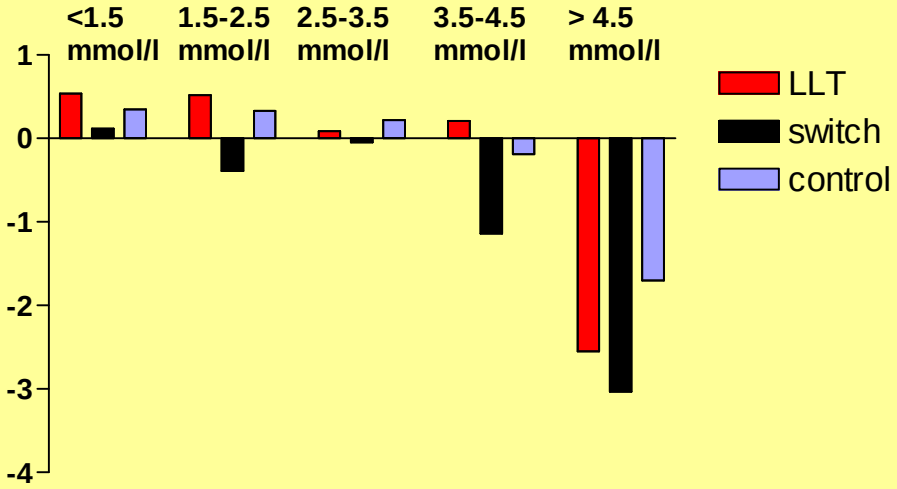
Plasma lipids stratified according to baseline values

LDL cholesterol*



Triglycerides



*** Calculated using Friedewald formula**

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Conclusions

- LLT resulted in most pronounced decreases in TC and LDL-c, particularly in those with highest baseline values
- Effects of LLT on HDL-c were minimal
- Switching to a NNRTI resulted in greater increases in HDL-c, irrespective of baseline values
- Both strategies resulted in similar decreases in the ratio of TC/HDL-c

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Further considerations

- Selection bias (sensitivity analysis)
- Possible regression to the mean effect
- No information regarding lifestyle changes
- No information on specific LLT used

Acknowledgements

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