HUG
Hôpitaux Universitaires de Genève

Lipides, métabolisme des hydrates de carbonne et maladies cardio-vasculaires

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Effect of estrogens on glucose metabolism : Fasting Glucose, HbA1c and C-Peptide in subjects with NIDDM after treatment with estradiol and placebo according to (8)

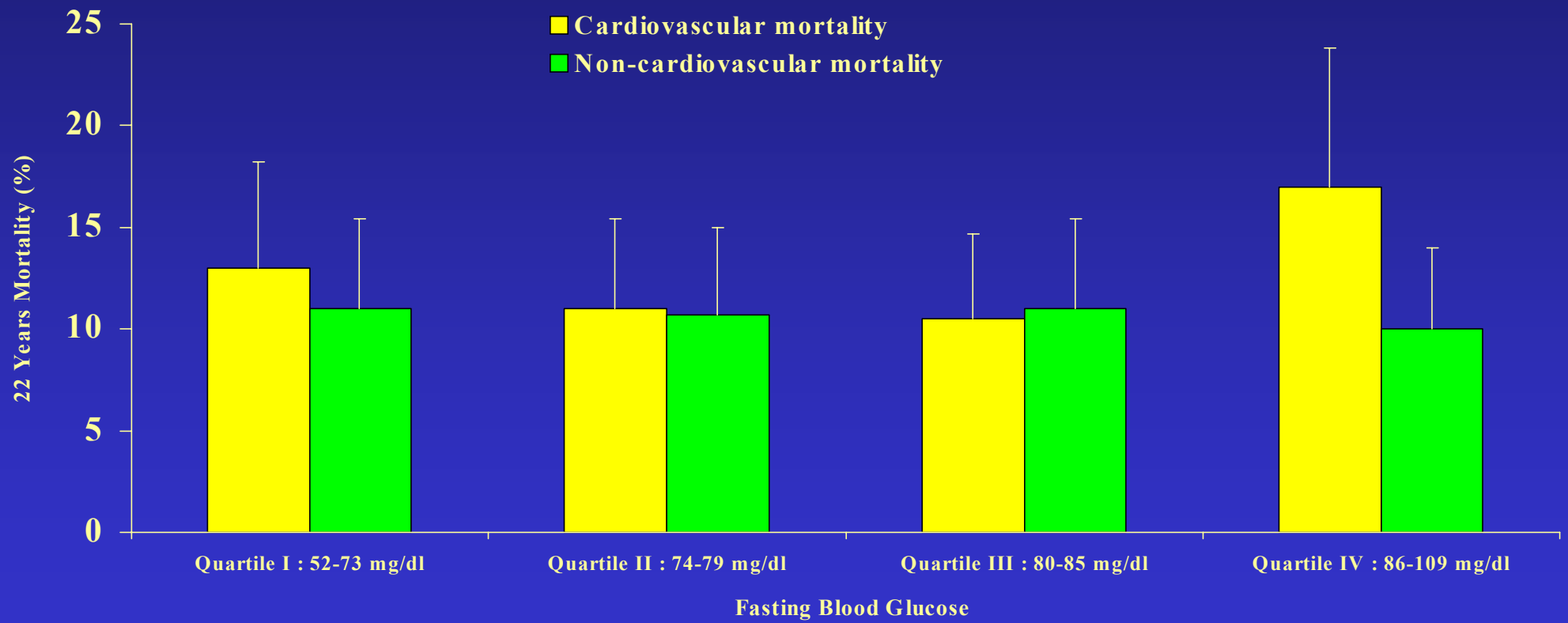
Variable	Baseline	After treatment	*p*-value
Glucose (mmol/l)			
Estradiol	12.1 ± 0.4	0.9 ± 0.4	P <0.001
Placebo	12.2 ± 0.5	12.8 ± 0.4	
HbA1c (%)			
Estradiol	8.7 ± 0.2	7.5 ± 0.2	P < 0.001
Placebo	8.5 ± 0.2	9.0 ± 0.3	
C-Peptide (nmol/l)			
Estradiol	1.29 ± 0.11	1.09 ± 0.11	P < 0.001
Placebo	1.21 ± 0.11	1.27± 0.13	

Glucose level and coronary heart disease rates in the Honolulu Heart Study (12-Year Follow-up)*

Postchallenge Glucose Level	Fatal Coronary Heart Disease	Total Coronary Heart Disease
mmol/L	%	
2.2-6.3	9.3	35.6
6.4-7.4	12.2	40.0
7.4-8.7	17.1	48.9
8.7-10.5	20.7	52.6
10.5-29.5	30.3	59.9

* The study included 6394 Japanase-American men (exclusion criteria were previous cardiovascular disease, treated hypertension, and known diabetes) and had a 12-year, age-adjusted incidence rate per 1000.

Crude 22 years cardiovascular and noncardiovascular mortality according to fasting blood glucose quartiles. Error bars indicate 95 % CI



	n	Mean
All subjects	3220	90.12
		5.01
Men	1560	92.80
		5.16
Women	1660	87.62
		4.87
Non menopausal	1207	86.41
		4.80
Menopausal	453	90.82
		5.05

Men

Age	*n*	Mean
20-29	479	88.72
		4.93
30-39	462	92.15
		5.12
40-50	270	94.54
		5.25
+50	349	97.94
		5.44

All subjects

Age	*n*	Mean
20-29	854	86.32
		4.80
30-39	855	89.54
		4.97
40-50	673	90.89
		5.05
+50	838	94.01
		5.22

Women

Age	*n*	Mean
20-29	375	83.25
		4.63
30-39	393	86.47
		4.80
40-50	403	88.45
		4.91
+50	489	91.20
		5.07

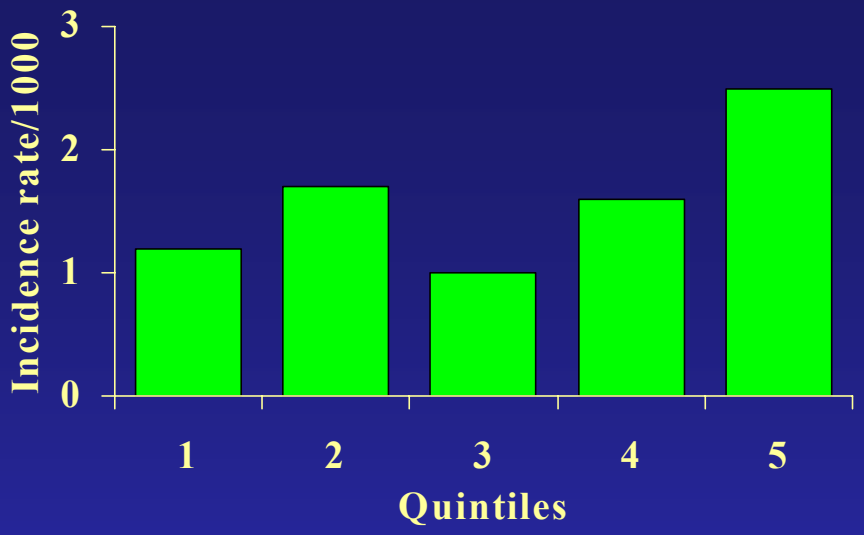
Anthropometric variables and blood pressure before and after treatment with estradiol and placebo (mean ± SEM; n = 25)

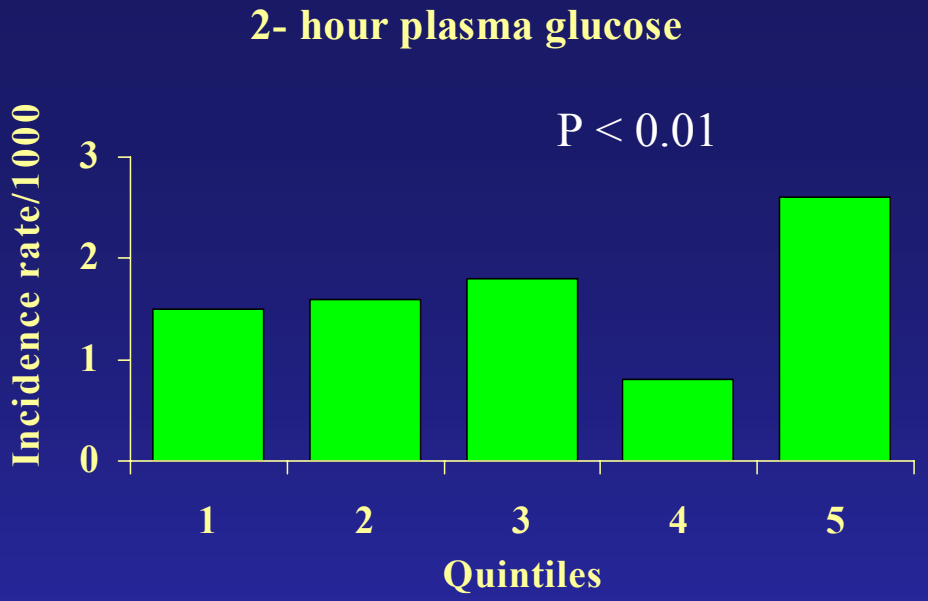
2 mg 17β-estradiol 3 months - 1 mg norethisterone acetate 10*d*

Variables	Baseline	After treatment	*P* - val
Body weight (kg)			
Estradiol	82.1 ± 3.1	83.4 ± 3.2	P < 0.001
Placebo	83.5 ± 3.2	83.2 ± 3.2	
Body fat (kg)			
Estradiol	38.0 ± 2.0	38.4 ± 2.0	P < 0.005
Placebo	40.1 ± 2.2	38.5 ± 2.2	
Lean body mass (kg)			
Estradiol	43.9 ± 1.4	44.7 ± 1.4	ns
Placebo	43.5 ± 1.3	44.5 ± 1.4	
Waist/hip ratio			
Estradiol	0.96 ± 0.02	0.96 ± 0.02	ns
Placebo	0.96 ± 0.02	0.96 ± 0.02	
SBP (mmHg)			
Estradiol	139 ± 3	136 ± 3	ns
Placebo	140 ± 4	139 ± 3	
DBP(mmHg)			
Estradiol	73 ± 2	72 ± 72	ns
Placebo	74 ± 42	74 ± 2	

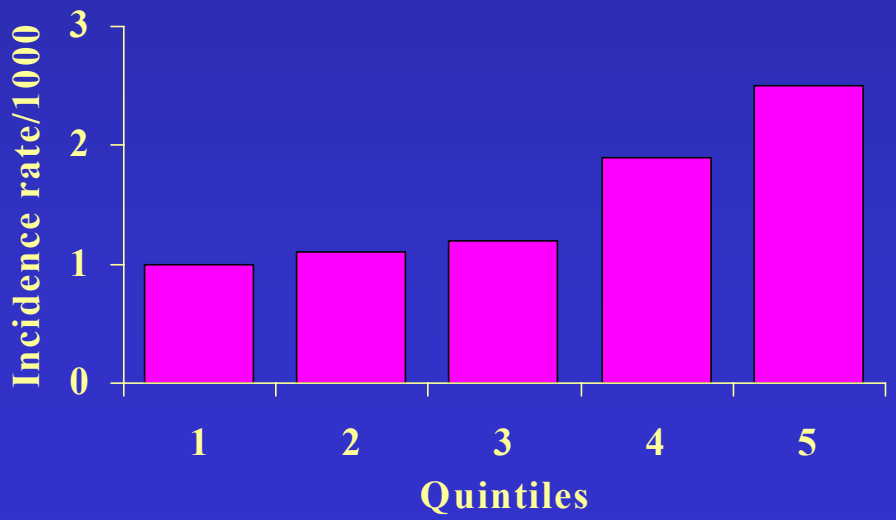
SBP, Systolic blood pressure; DBP, diastolic blood pressure, ns, not significant

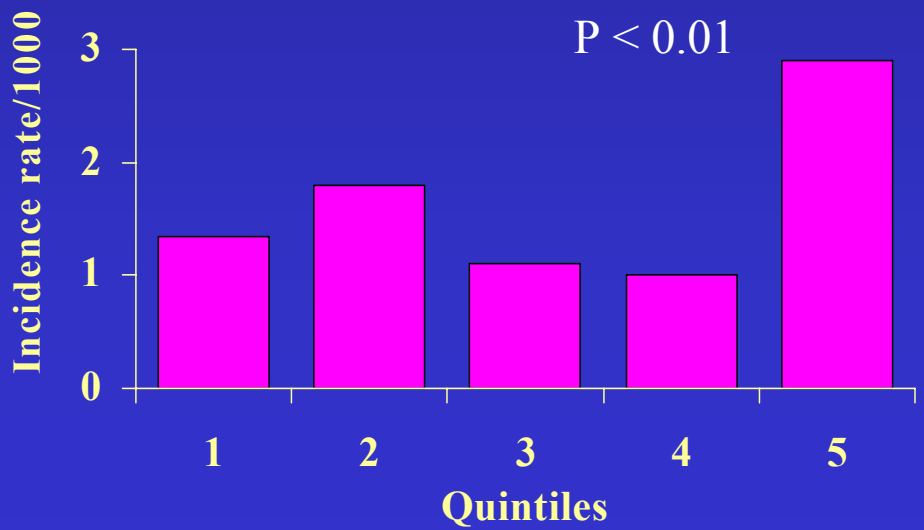
p-values for comparison between changes during estradiol treatment vs. placebo treatment



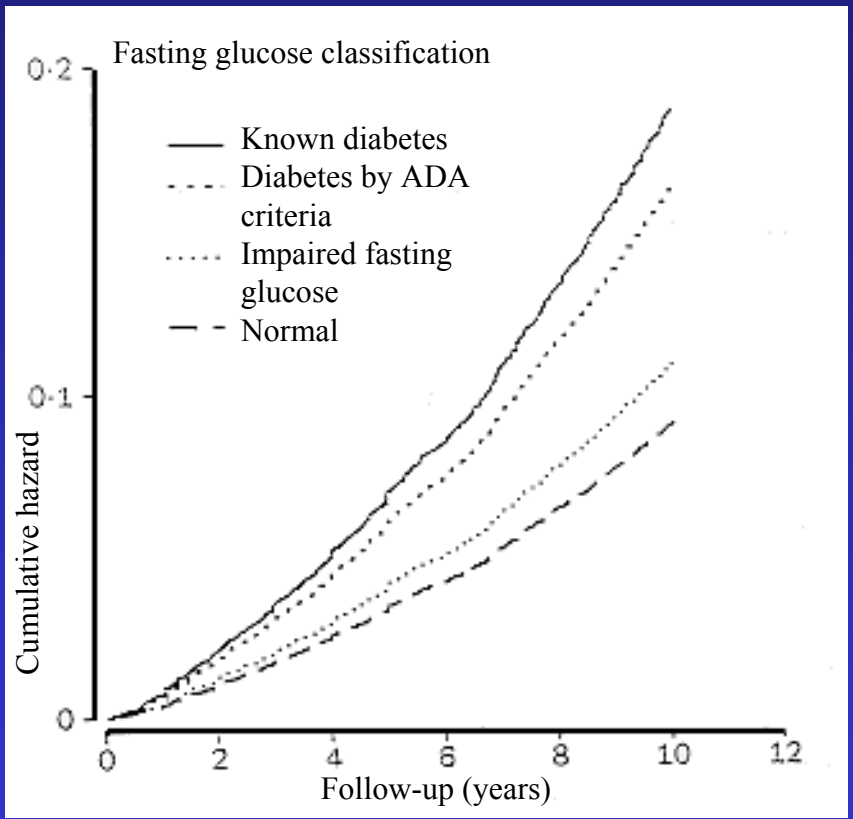


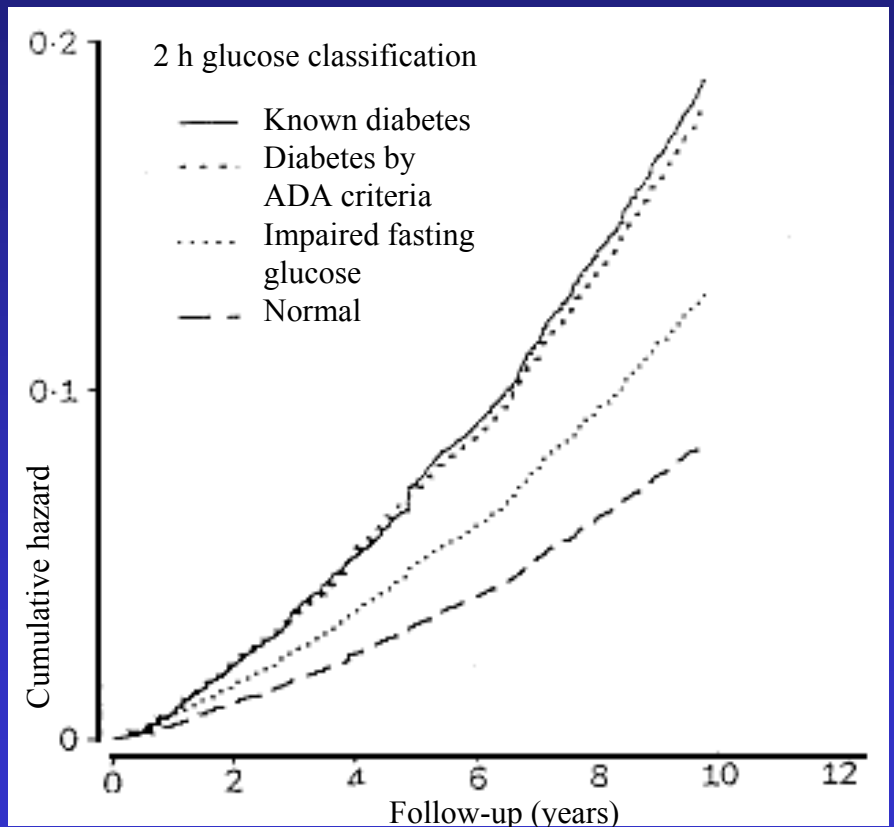
Incidence of CVD according to fasting and 2-hour plasma glucose and insulin concentrations



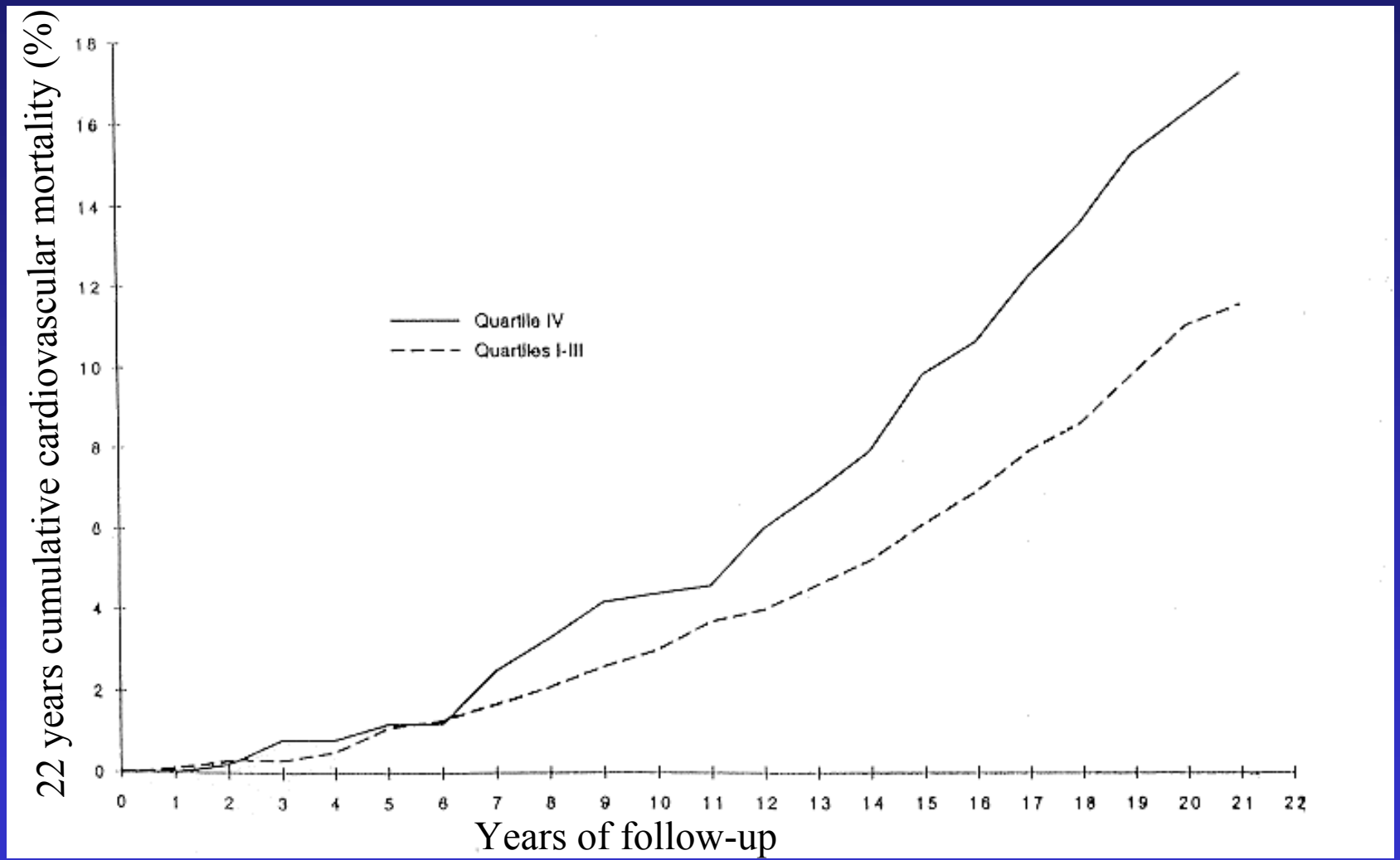


Cumulative hazard curves for ADA fasting glucose criteria and WHO 2h glucose criteria adjusted by age, sex, and study center

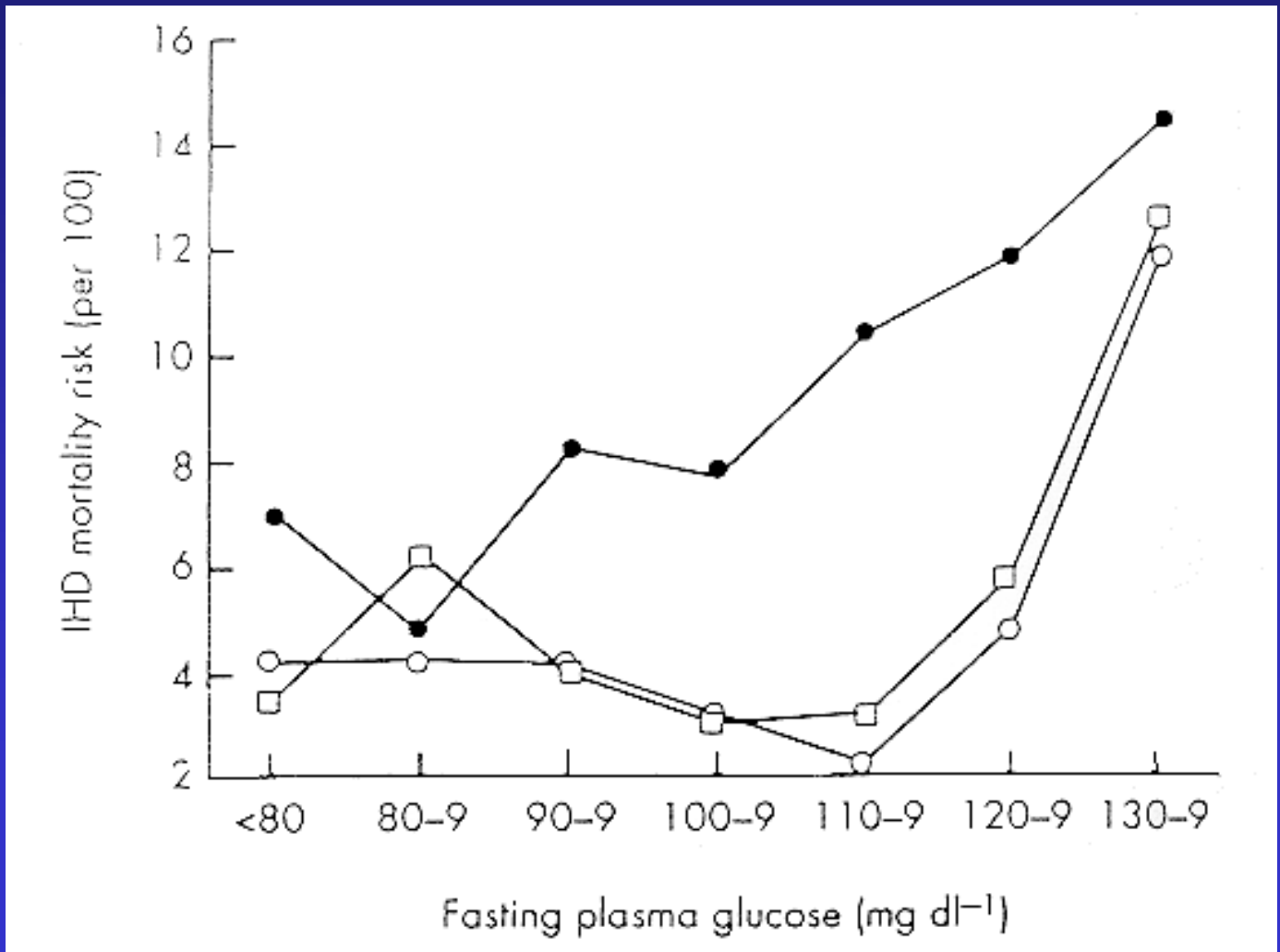




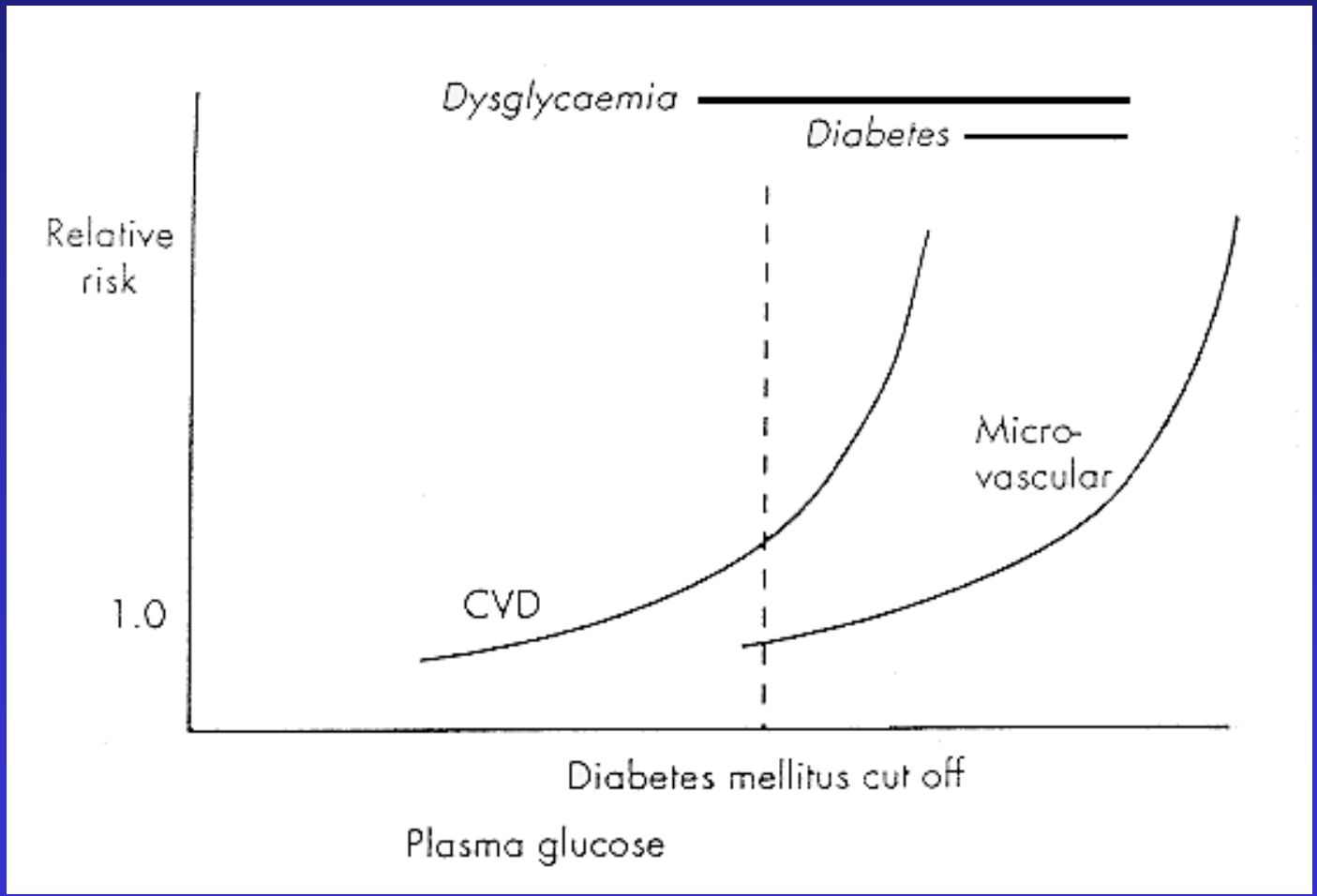
Age adjusted 22 years cumulative cardiovascular mortality comparing fasting blood glucose quartiles I-III (≤ 85 mg/dl) with quartile IV (> 85 mg/dl)



The relationship between non-diabetic glycemia and ischaemic heart disease (IHD) mortality in men (●); premenopausal women (○); and postmenopausal women (□). Non-diabetic men and women aged 40-79 years were followed for an average of 14 years. ***(Schwidt-Nave et al. Am J Epidemiol 1991; 133: 565-76)***



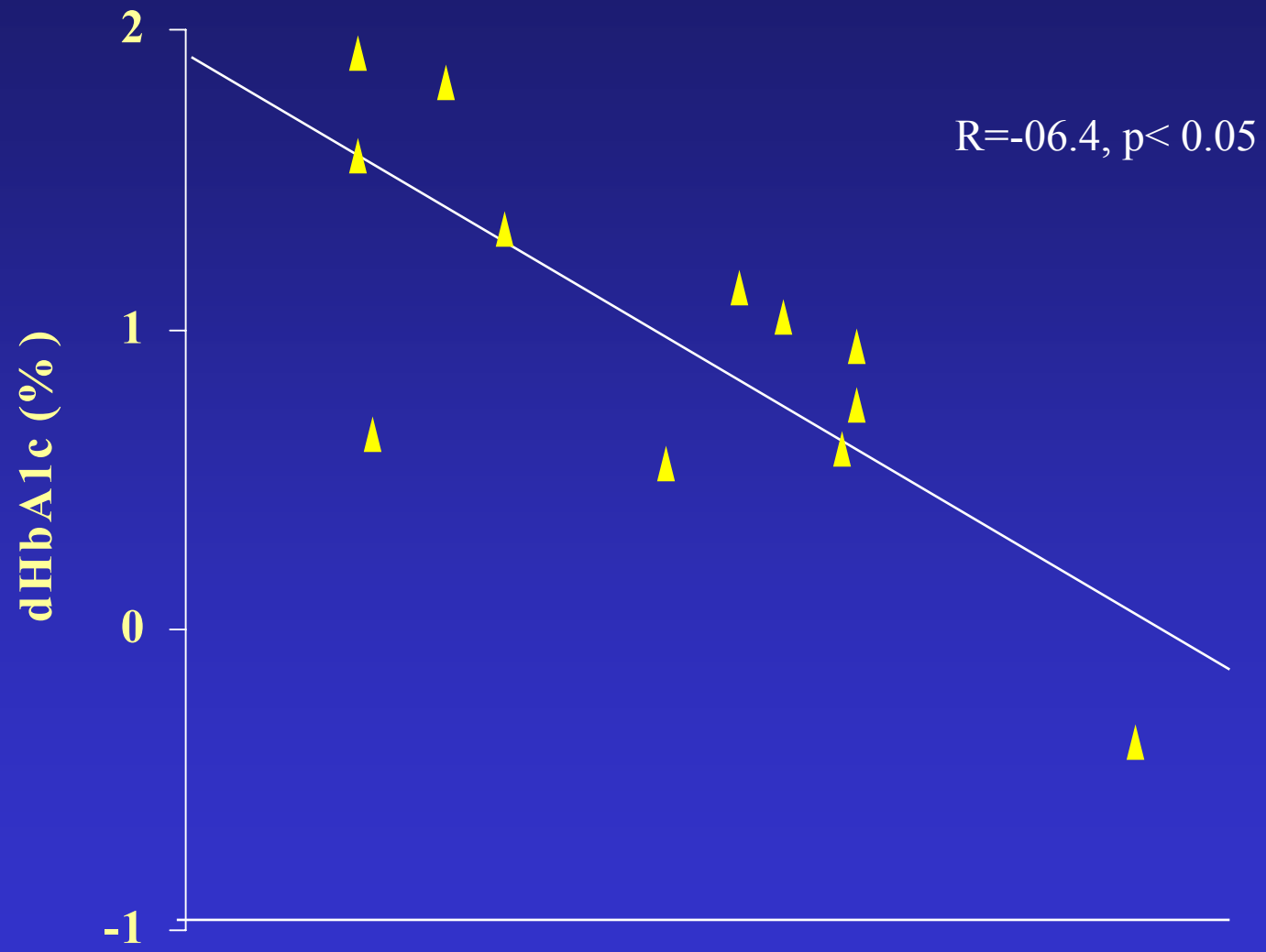
The significance of glucose concentrations as a risk factor for chronic disease. Plasma glucose concentrations above the diabetic cut off are associated with an increasing risk of cardiovascular and microvascular disease; levels above the IGT cut off are associated with an increasing risk of diabetes; and elevated levels above some, as yet undefined, "dysglycaemic" cut off are associated with an increasing risk of cardiovascular disease.



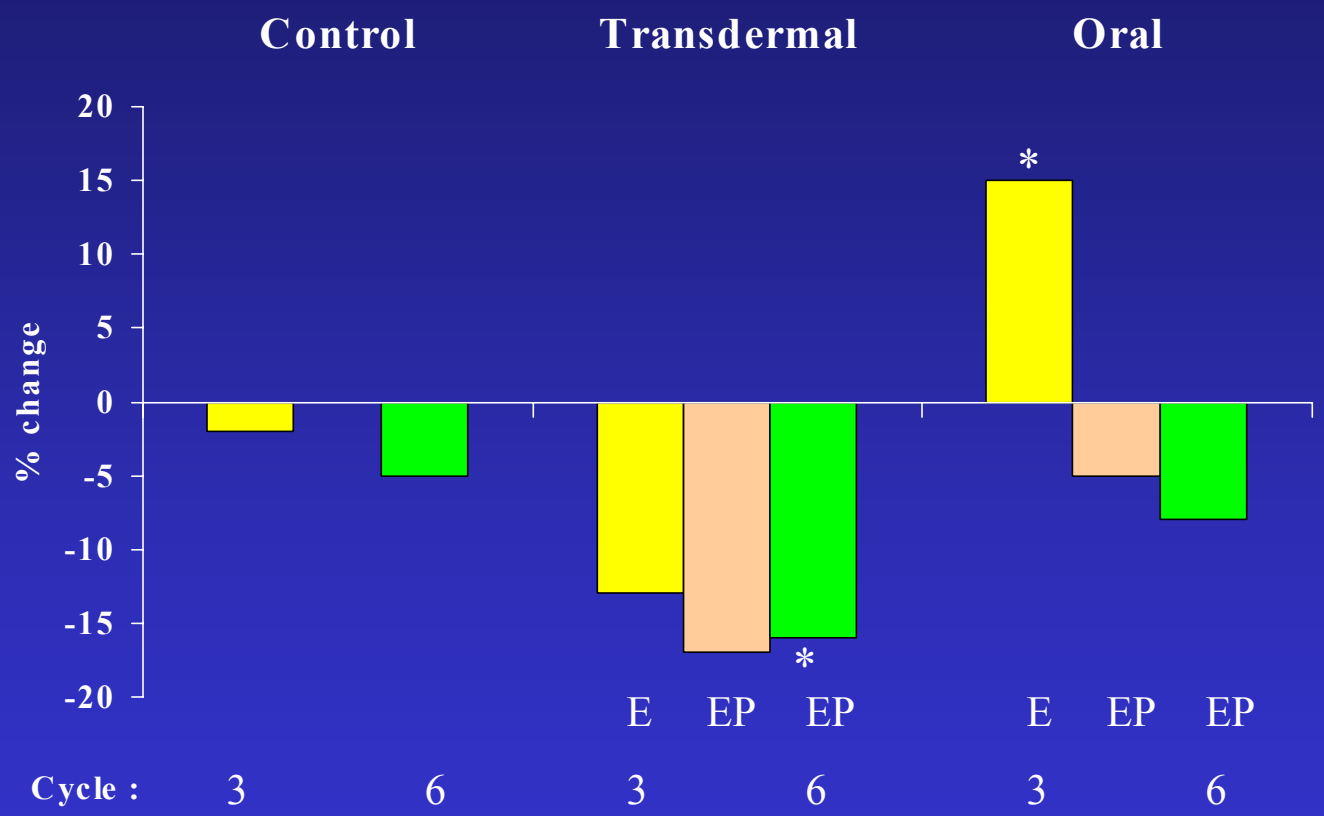
Blood lipids before and after treatment with estradiol and placebo (mean ± SEM; n = 25)

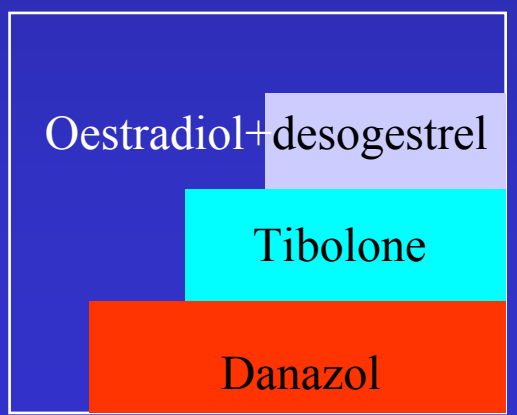
Variables	Baseline	After treatment	*P* - val
Cholesterol (mmol/L)			
Estradiol	5.7 ± 0.2	5.2 ± 0.1	P < 0.01
Placebo	5.9 ± 0.2	5.8 ± .2	
HDL-C (mmol/L)			
Estradiol	1.10 ± 0.05	1.33 ± 0.06	P < 0.001
Placebo	1.11 ± 0.06	1.11 ± 0.05	
LDL-C (mmol/L)			
Estradiol	3.74 ± 0.17	2.86 ± 0.14	P < 0.001
Placebo	3.54 ± 0.19	3.72 ± 0.15	
Triglycerides (mmol/L)			
Estradiol	2.04 ± 0.16	2.28 ± 0.17	ns
Placebo	2.39 ± 0.25	2.36 ± 0.26	

HDL-C, High density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol
p-values for comparison between changes during estradiol treatment vs. placebo treatment

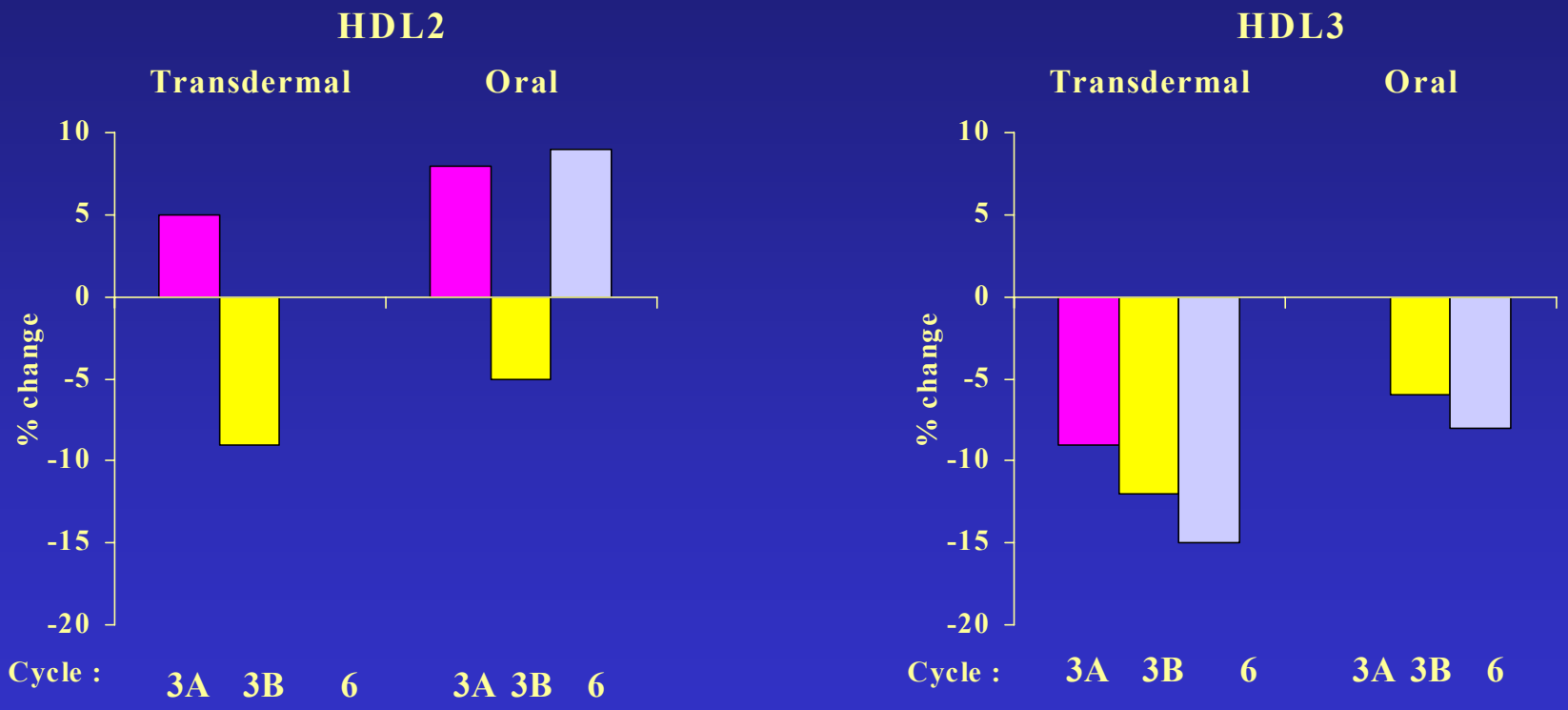

2
1
0
-1
dHbA1c (%)
R=-06.4, p< 0.05

Changes in triglycerides in post-menopausal women receiving either no treatment, transdermal oestradiol-17β 0.05 mg daily with cyclical transdermal norethisterone acetate 0.25 mg daily, or oral conjugated equine oestrogens 0.625 mg daily with cyclical oral dl-norgestrel 0.15 mg daily. 3A, oestrogen alone phase; 3B, combined phase, 6, combined phase. (*p < 0.05).





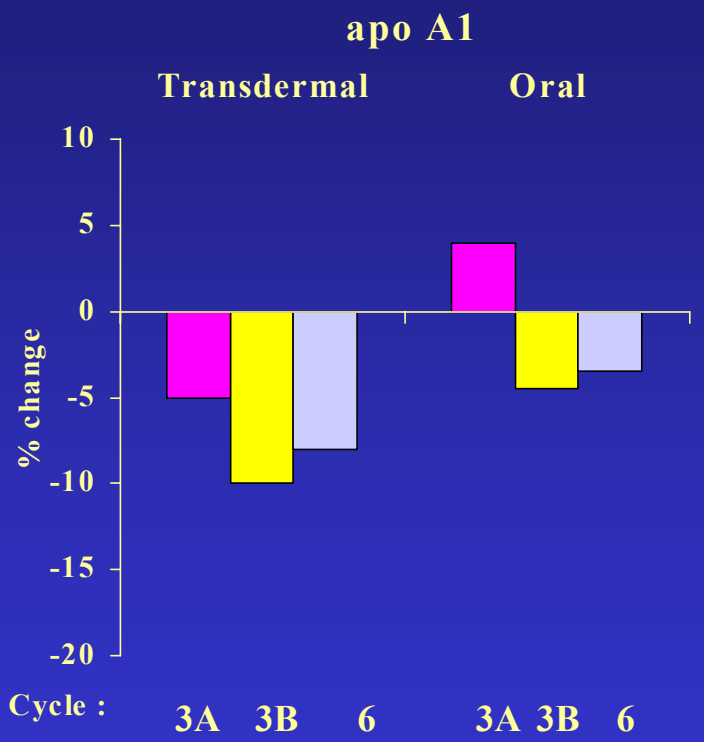
Changes in high density lipoprotein (HDL) subfractions and apolipoproteins AI and AII in post-menopausal women receiving either transdermal oestradiol-17β 0.05 mg daily with cyclical transdermal norethisterone acetate 0.25 mg daily,or oral conjugated equine oestrogens 0.625 mg daily with cyclical oral *dl*-norgestrel 0.15 mg daily

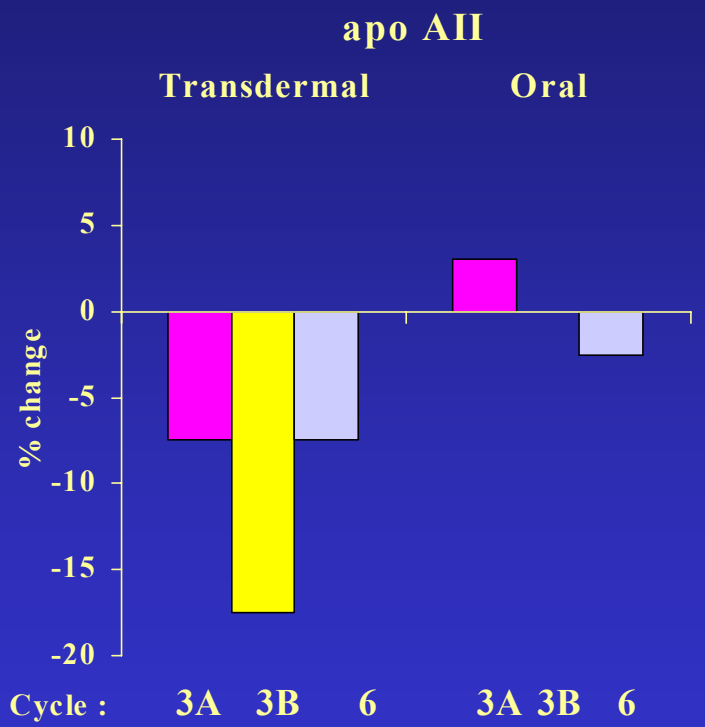


3A : oestrogen alone phase - 3B : combined phase - 6 : combined phases

** $p<0.01$; *** $p< 0.001$

Changes in high density lipoprotein (HDL) subfractions and apolipoproteins AI and AII in post-menopausal women receiving either transdermal oestradiol-17β 0.05 mg daily with cyclical transdermal norethisterone acetate 0.25 mg daily,or oral conjugated equine oestrogens 0.625 mg daily with cyclical oral *dl*-norgestrel 0.15 mg daily

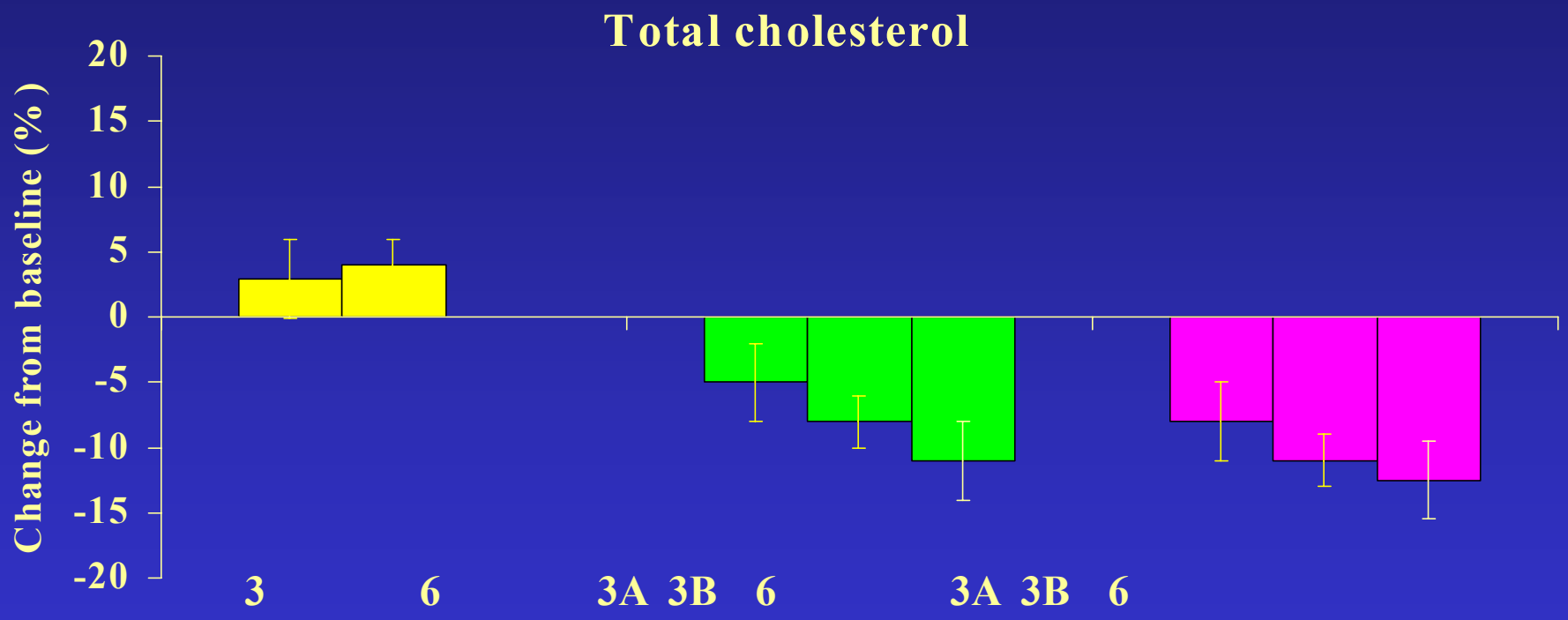




3A : oestrogen alone phase - 3B : combined phase - 6 : combined phases

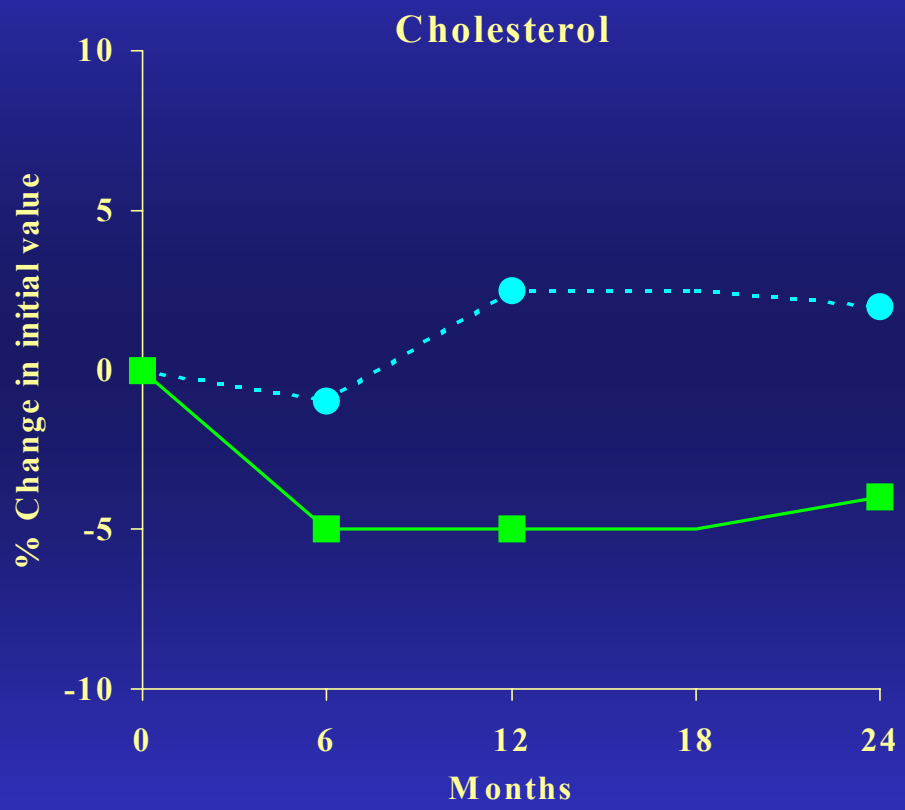
** $p<0.01$; *** $p< 0.001$

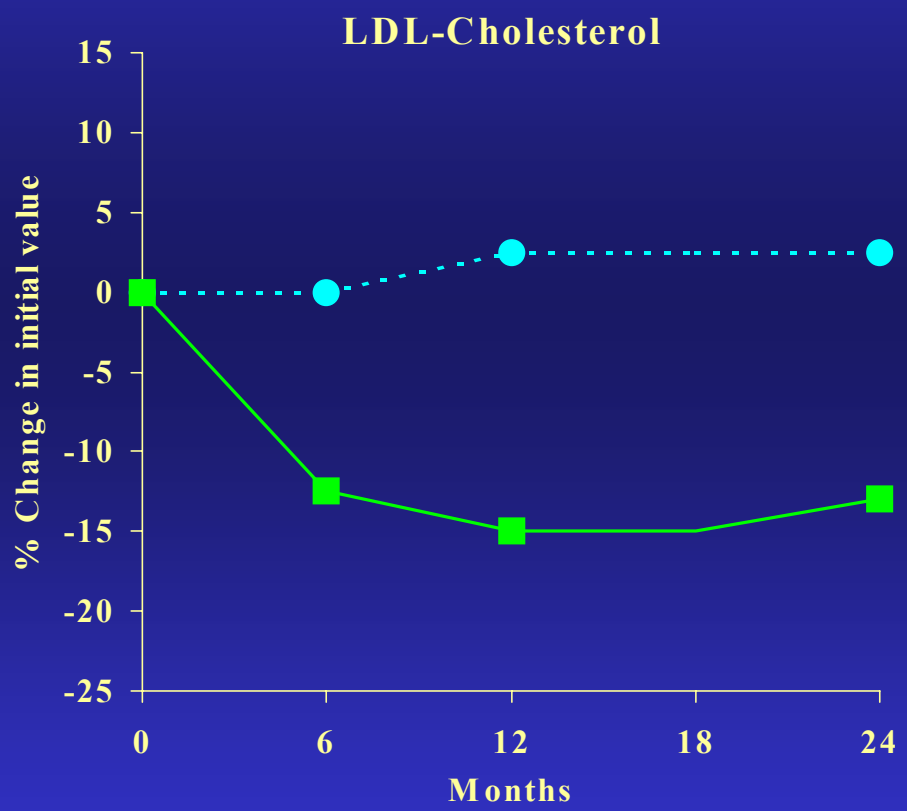
Changes in total cholesterol in post-menopausal women receiving either no treatment ■, trandermal oestradiol- 17β 0.05 mg daily with cyclical transdermal norethisterone acetate 0.25 mg daily ■, or oral conjugated equine oestrogens 0.625 mg daily with cyclical oral dl-norgestrel 0.15 mg daily ■.

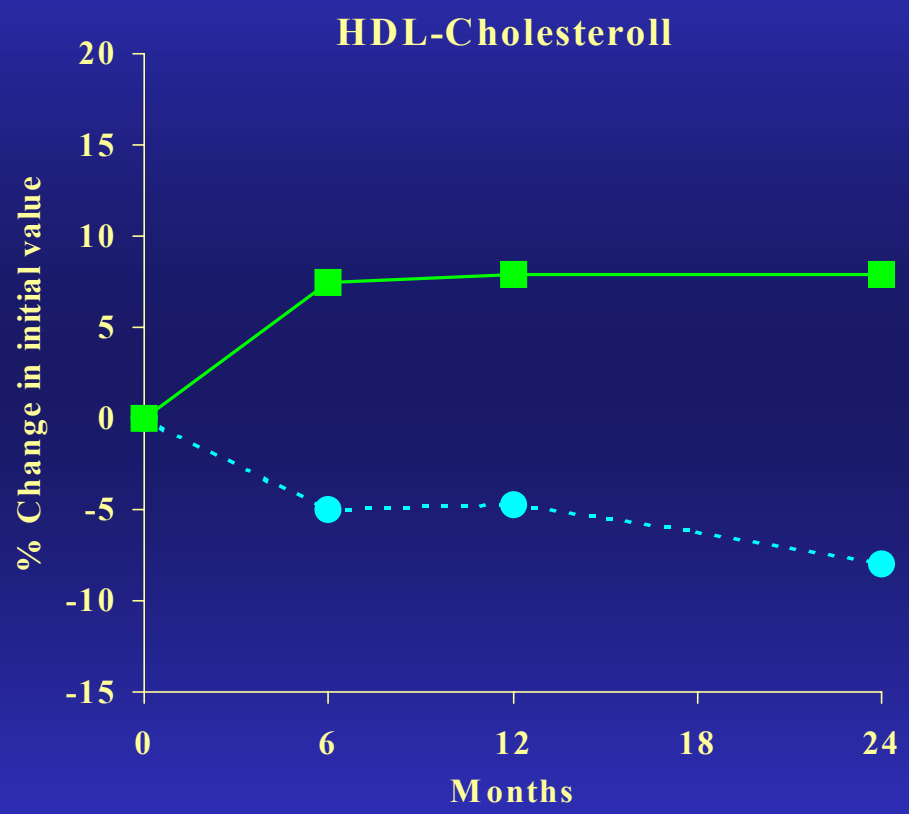


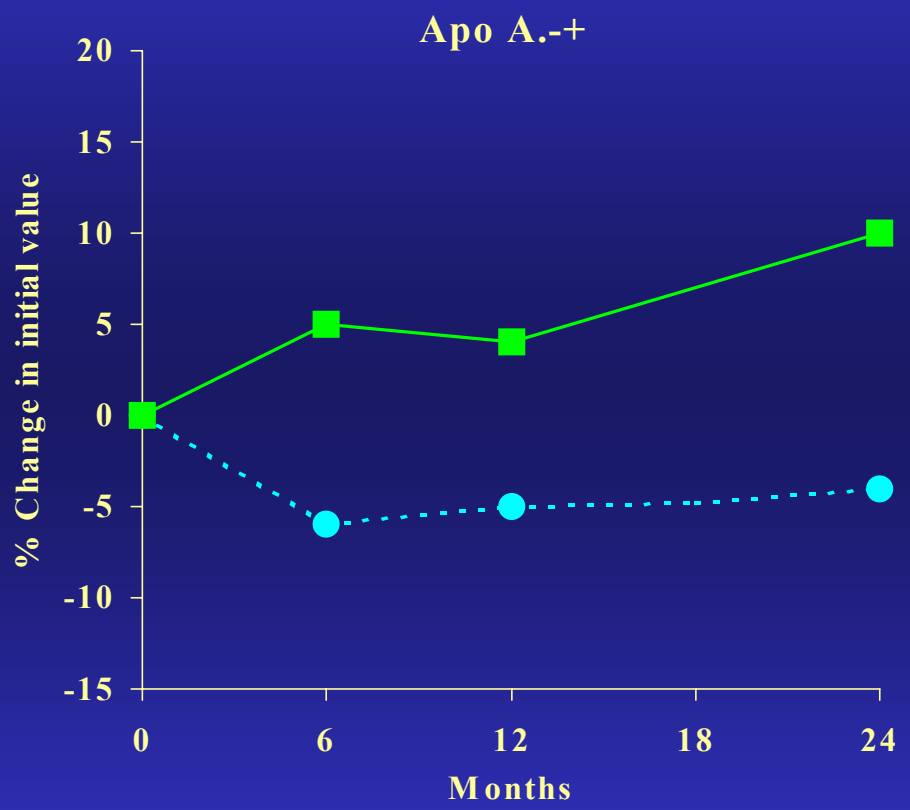
3A : oestrogen alone phase - 3B : combined phase - 6 : combined phases

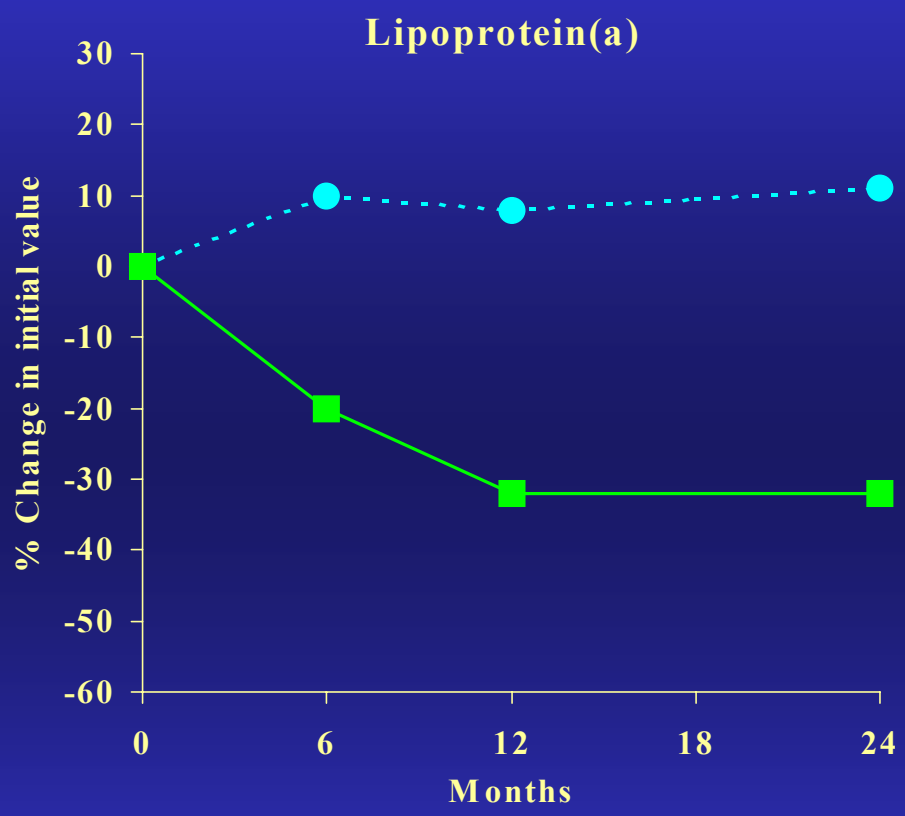
*** $p < 0.001$

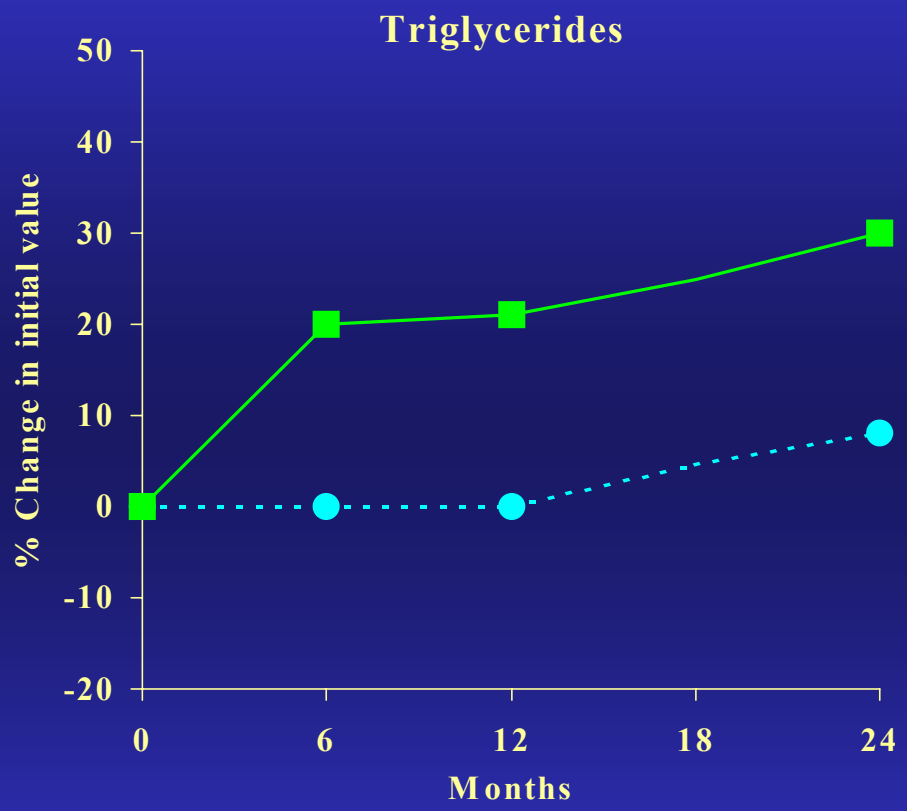

Cholesterol
% Change in initial value
10
5
0
-5
-10
0
6
12
18
24
Months


LDL-Cholesterol
% Change in initial value
15
10
5
0
-5
-10
-15
-20
-25
0
6
12
18
24
Months

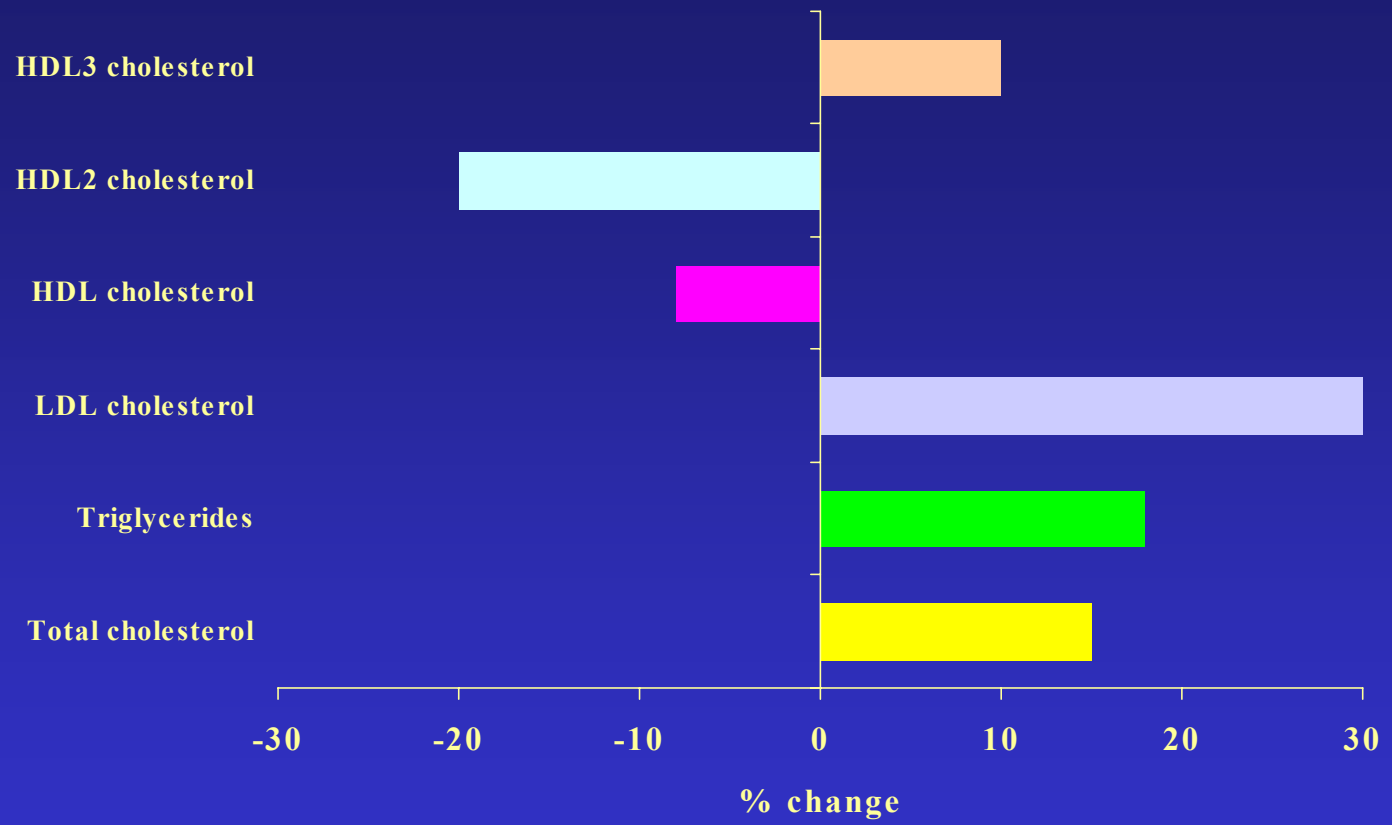

HDL-Cholesteroll
% Change in initial value
20
15
10
5
0
-5
-10
-15
0
6
12
18
24
Months


Apo A.-+
% Change in initial value
20
15
10
5
0
-5
-10
-15
0
6
12
18
24
Months


Lipoprotein(a)
% Change in initial value
30
20
10
0
-10
-20
-30
-40
-50
-60
0
6
12
18
24
Months


Triglycerides
% Change in initial value
50
40
30
20
10
0
-10
-20
0
6
12
18
24
Months

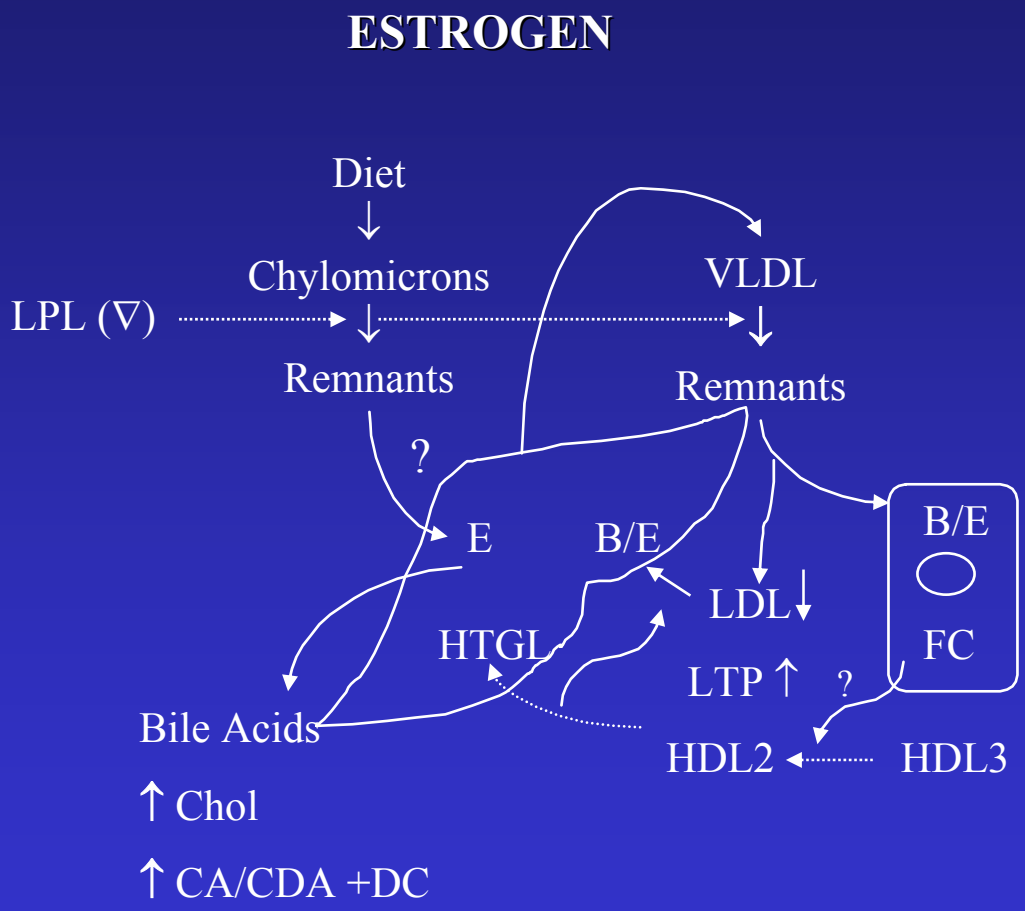
Effect of menopause on lipids and lipoproteins.

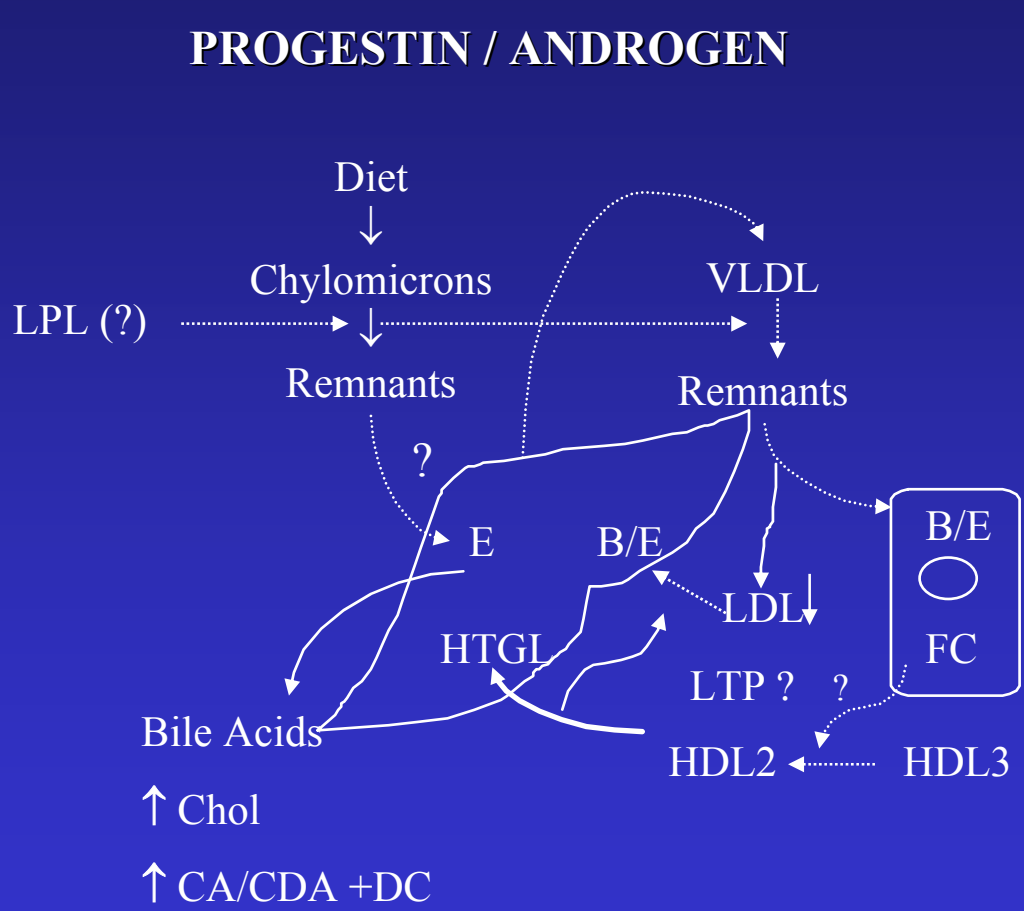


542 healthy, non obese caucasian females 18-70 yrs

LDL, low density lipoproteins; HDL, high density lipoproteins

Effects of sex steroids on lipid metabolism. Width of lines indicate the rate of cholesterol traffic under influence of estrogen (L) or progestin/androgen (R). Question marks indicate effects for which documentation is uncertain or unclear





Effect of treatment with Placebo or 17β -Estradiol on concentrations of plasma lipids, lipoproteins, plasma nonesterified Fas, C Peptide, and HbA1c (6 weeks)

	Baseline			Absolute and percentage changes after treatment		
	Placebo (n=20)	Estradiol (n=20)	*p*	Placebo (n=20)	Estradiol (n=20)=	*p*
TC, mmol/L	5.28 ± 0.66 (4.07-6.52)	5.25 ± 0.60 (3.96-7.02)	.81	0.04 ± 0.46 (1%±9%)	-0.28 ± 0.44 (-5%±8%)	.02 (.04)
LDL-C, mmol/L	3.36 ± 0.68 (2.32-4.72)	3.30 ± 0.74 (2.11-4.68)	.68	0.06 ± 0.38 (2 %±11%)	-048 ± 0.44 (-14 %±12 %)	.0001 (.0001)
HDL-C, mmol/L	1.20 ± 0.30 (0.77-1.95)	1.20 ± 0.47 (0.47-2.24)	.88	0.03 ± 0.16 (3 %± 13 %)	0.26 ± 0.18 (23 %±14 %)	.0002 (.0001)
HDL_2-C, mmol/L	0.36 ± 0.19 (0.13-0.85)	0.41 ± 0.29 (0.06-1.18)	.89	0.02 ± 0.12 (11% ± 35 %)	0.20 ± 0.17 (60%±44%)	.0007 (.0007)
HDL_3-C, mmol/L	0.84 ± 0.14 (0.62-1.10)	0.79± 0.21 (0.38-1.12)	.47	0.02 ± 0.08 (3 % ± 9 %)	0.07 ± 0.11 (11 % ± 15 %)	.14 (.10)
VLDL-C, mmol/L	0.64 ± 0.35 (0.20-1.48)	0.69± 0.43 (0.22-1.76)	.86	-0.04 ± 0.20 (-11 % ±29 %)	-0.06 ± 0.25 (-11 % ± 37 %)	.61 (.70)

Effect of treatment with Placebo or 17β -Estradiol on concentrations of plasma lipids, lipoproteins, plasma nonesterified Fas, C Peptide, and HbA1c (6 weeks)

	Baseline			Absolute and percentage changes after treatment		
	Placebo (n=20)	Estradiol (n=20)	*p*	Placebo (n=20)	Estradiol (n=20)=	*p*
TGs, mmol/L	1.53 ± 0.83 (0.39-3.83)	1.74 ± 0.95 (0.28-3.72)	.48	0.08 ± 0.48 (4 % ± 24 %)	0.05 ± 0.62 (13 % ± 59 %)	.65 (.66)
VLDL TGs, mmol/L	1.06 ± 0.63 (0.11-2.44)	1.09 ± 0.83 (0.22-3.13)	.7	0.02 ± 0.32 (2 % ± 31 %)	0 ± 0.32 (4 % ± 41 %)	.85 (.67)
ApoA-1, g/L	1.44 ± 0.18 (1.16-1.81)	1.39 ± 0.28 (0.81-1.85)	.68	0.05 ± 0.10 (3 % ± 7 %)	0.22 ± 0.13 (17 %± 10 %)	.0001 (.0001)
ApoB, g/L	1.27 ± 0.28 (0.87-1.88)	1.26 ± 0.36 (0.72-2.09)	.89	0.03 ± 0.14 (2 % ± 11 %)	-013± 0.13 (-9 % ± 9 %)	.0004 (.001)
Nonesterified Fas, mmol/L	0.36 ± 0.21 (0.12-0.81)	0.47 ± 0.32 (0.06-1.13)	.30	0.05 ± 0.29 (29 % ±113 %)	-0.02 ± 0.37 (37 % ± 105%)	.79 (.62)
C peptide, nmol/L	0.54 ± 0.38 (0-1.41)	0.38 ± 0.39 (0-1.68)	.11	-0.02 ± 0.42 (8 %± 90 %)	-0.14± 0.33 (-16 % ± 89 %)	.26 (.10)
HbA1c, %	8.1 ± 1.6 (5.6-11.2)	8.7 ± 1.5 (6.3-11.2)	.24	-0.34± 0.45 (-4% ± 5 %)	-0.66 ± 0.67 (-7 %± 7 %)	.02 (.03)