

# Effects of gender, age and menopausal status on serum apolipoprotein concentrations

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**Introduction:** Inconsistent data exist as to whether menopause is associated with increased cardiovascular disease (CVD) risk. However, few studies have evaluated differences in apolipoprotein metabolism according to menopausal status and gender. The **aim of this study** was to investigate the effects of gender and menopause on serum apolipoprotein B (apoB), A-I (apoA-I) and A-II (apoA-II) concentrations.

**Methods:** A cross-sectional analysis was undertaken of age and gender-related differences in apparently healthy Caucasian premenopausal and postmenopausal women not taking oral contraceptives or hormone replacement, and Caucasian men. Measurements included serum apoA-I, apoA-II, apoB, total cholesterol, low-density and high-density lipoprotein cholesterol (LDL-C and HDL-C respectively), triglycerides, cholesterol in HDL subfractions 2 and 3 and the apoB/apoA-I, LDL-C/apoB, HDL-C/apoA-I and HDL-C/apoA-II ratios. Analyses were undertaken with and without standardization for confounding characteristics and in 5 year age ranges.

**Results:** 109 pre-menopausal women (aged  $32.9 \pm 5.4$  years), 253 post-menopausal women (aged  $57 \pm 6.5$  years) and 307 men (aged  $52.4 \pm 10.5$  years) were included in the analysis.

- Overall, apoB concentrations were highest in men but rose with age and menopause in women to converge with concentrations in men in the age range 50-55 years.
- The LDL-C/apoB ratio was generally higher in women than men, especially postmenopausally.
- Both apoA-I and apoA-II concentrations were highest in postmenopausal women and lowest in men.
- Men generally had the lowest ratios of HDL-C to apoA-I and to apoA-II, but the highest ratios were apparent in premenopausal women. I
- In multivariable analyses, incorporating age, BMI, smoking, alcohol, exercise and number of pregnancies, the above differences were sustained.

Table 2: Lipid-related variables - standardized analysis

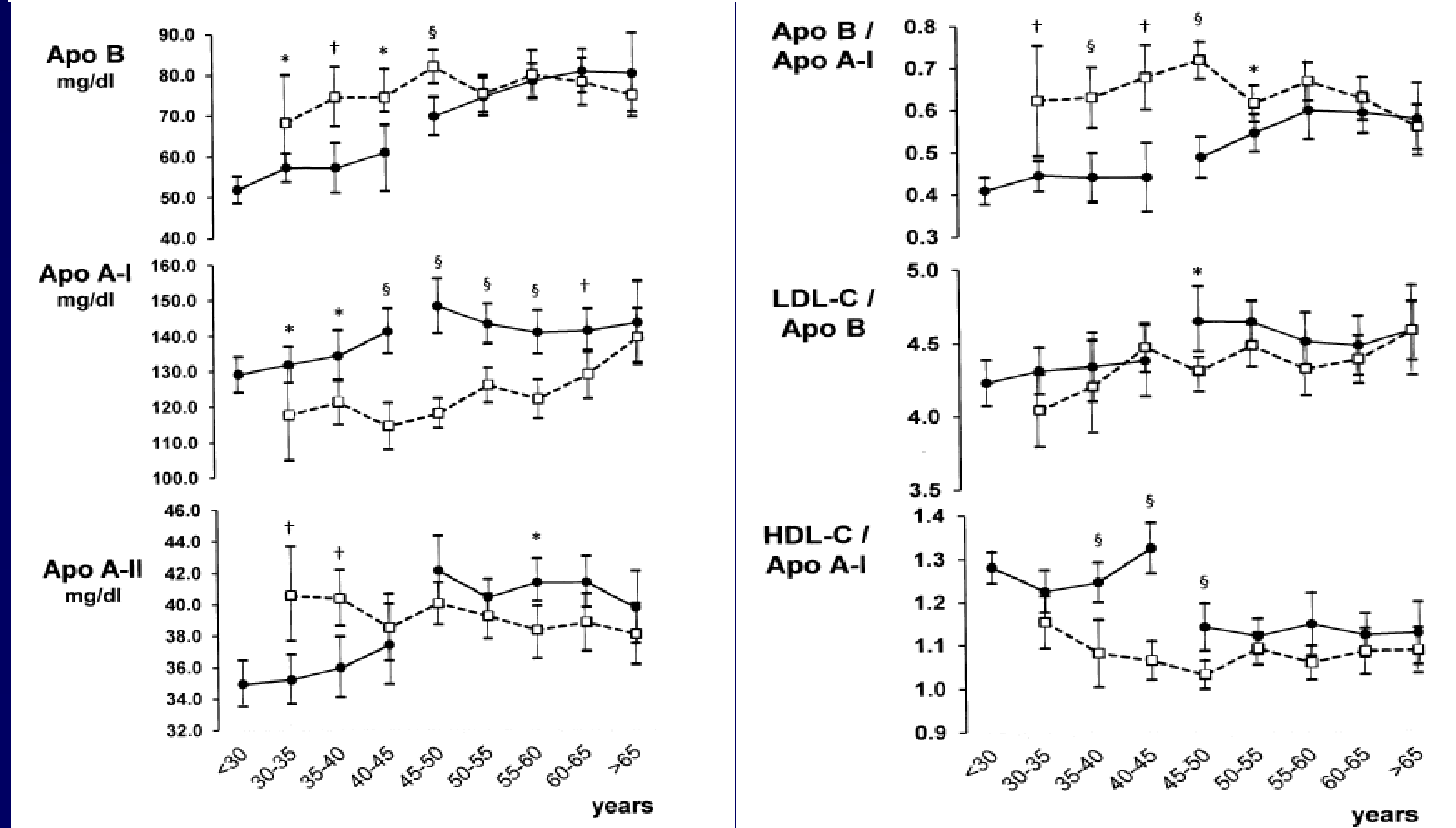
	Group 1 1987-1991 Premenopausal women (n=109)	Group 2 1994-1998 Postmenopausal women (n=252)	Group 3 1992-1998 Men (n=307)	p Group 2 v Group 1	p Group 3 v Group 1	p Group 3 v Group 2
apolipoprotein B (mg/dL)	67.0 (62.1, 74.2)	72.4 (63.2, 83.9)	74.6 (63.8, 87.0)	0.002	<0.001	0.1
apolipoprotein A-I (mg/dL)	134 (124, 144)	144 (130, 158)	119 (108, 132)	<0.001	<0.001	<0.001
apolipoprotein A-II (mg/dL)	32.9 (30.5, 35.7)	40.3 (37.5, 44.5)	36.5 (33.0, 40.1)	<0.001	<0.001	<0.001
apoB / apoA-I	0.50 (0.45, 0.56)	0.50 (0.41, 0.61)	0.64 (0.53, 0.76)	0.9	<0.001	<0.001
LDL-C / apoB $\times 10^2$	4.88 (4.61, 5.13)	4.78 (4.40, 5.18)	4.46 (4.06, 4.79)	0.1	<0.001	<0.001
HDL-C / apoA-I $\times 10^2$	1.26 (1.20, 1.34)	1.11 (1.02, 1.23)	1.12 (1.04, 1.22)	<0.001	<0.001	0.7
HDL-C / apoA-II $\times 10^2$	5.37 (4.78, 5.80)	4.03 (3.43, 4.59)	3.63 (3.27, 4.13)	<0.001	<0.001	<0.001
total cholesterol (mmol/L)	5.16 (4.74, 5.46)	5.63 (5.11, 6.29)	5.29 (4.69, 5.94)	<0.001	0.1	<0.001
triglycerides (mmol/L)	0.41 (0.28, 0.56)	0.92 (0.72, 1.28)	1.12 (0.75, 1.67)	<0.001	<0.001	<0.001
calculated LDL cholesterol (mmol/L)	3.15 (2.93, 3.50)	3.51 (2.98, 4.07)	3.32 (2.74, 3.86)	<0.001	0.1	0.006
HDL cholesterol (mmol/L)	1.71 (1.53, 1.88)	1.61 (1.39, 1.88)	1.33 (1.17, 1.56)	0.01	<0.001	<0.001
HDL <sub>2</sub> cholesterol (mmol/L)	0.76 (0.64, 0.96)	0.73 (0.58, 0.96)	0.57 (0.45, 0.72)	0.3	<0.001	<0.001
HDL <sub>3</sub> cholesterol (mmol/L)	0.93 (0.85, 0.99)	0.87 (0.77, 0.99)	0.77 (0.67, 0.86)	0.001	<0.001	<0.001
cholesterol/HDL cholesterol	3.01 (2.77, 3.29)	3.48 (3.01, 4.15)	3.92 (3.31, 4.79)	<0.001	<0.001	<0.001
non-HDL cholesterol (mmol/L)	3.40 (3.15, 3.69)	3.95 (3.45, 4.57)	3.91 (3.31, 4.57)	<0.001	<0.001	0.3

Standardisation was to age 50 years, BMI 25 kg/m<sup>2</sup> and zero smoking, alcohol, exercise and pregnancies: median (IQ range). Sampling periods are shown for each

group. Significances: Kruskal-Wallis ANOVA all returned p<0.001 for significant variation between the three groups. Post-hoc, between-group comparisons were made using Mann-Whitney U test.

Table 1: Group characteristics

	Group 1 1987-1991 Premenopausal women (n=109)	Group 2 1994-1998 Postmenopausal women (n=252)	Group 3 1992-1998 Men (n=307)	p Group 2 v Group 1	p Group 3 v Group 1	p Group 3 v Group 2
age (years)	32.9 (5.4)	57.0 (6.5)	52.4 (10.5)	<0.001	<0.001	<0.001
BMI (kg/m <sup>2</sup> )	21.6 (1.9)	24.3 (3.0)	26.2 (2.9)	<0.001	<0.001	<0.001
number of pregnancies	0.5 (1.0)	1.7 (1.6)	-	<0.001	-	-
smoking				<0.001	0.01	0.04
None	83 (76)	166 (93)	267 (88)			
<15/day	18 (17)	10 (6)	26 (8)			
≥15/day	8 (7)	1 (1)	12 (4)			
alcohol				<0.001	<0.001	<0.001
None	4 (4)	138 (55)	26 (8)			
<28 units/week	101 (92)	115 (45)	226 (74)			
≥28 units/week	4 (4)	0 (0)	55 (18)			
exercise				<0.001	<0.001	0.001
None	50 (46)	146 (58)	136 (44)			
non-aerobic	49 (45)	41 (16)	47 (16)			
Aerobic	10 (9)	66 (26)	124 (40)			
apolipoprotein B (mg/dL)	55 (47, 62)	77 (65, 88)	76 (66, 90)	<0.001	<0.001	0.5
apolipoprotein A-I (mg/dL)	133 (119, 142)	144 (126, 158)	121 (110, 139)	<0.001	<0.001	<0.001
apolipoprotein A-II (mg/dL)	36 (33, 38)	41 (37, 45)	39 (36, 43)	<0.001	<0.001	<0.001
apoB / apoA-I	0.41 (0.35, 0.49)	0.53 (0.43, 0.64)	0.63 (0.52, 0.75)	<0.001	<0.001	<0.001
LDL-C / apoB $\times 10^2$	4.31 (4.00, 4.62)	4.59 (4.13, 4.99)	4.36 (4.00, 4.79)	<0.001	0.1	<0.001
HDL-C / apoA-I $\times 10^2$	1.25 (1.17, 1.33)	1.10 (1.01, 1.24)	1.06 (0.97, 1.16)	<0.001	<0.001	<0.001
HDL-C / apoA-II $\times 10^2$	4.78 (4.11, 5.31)	3.80 (3.29, 4.56)	3.24 (2.83, 3.82)	<0.001	<0.001	<0.001
total cholesterol (mmol/L)	4.35 (4.01, 4.77)	5.64 (5.07, 6.29)	5.41 (4.77, 6.07)	<0.001	<0.001	0.002
triglycerides (mmol/L)	0.57 (0.43, 0.75)	1.06 (0.83, 1.41)	1.27 (0.86, 1.94)	<0.001	<0.001	<0.001
calculated LDL cholesterol (mmol/L)	2.35 (1.95, 2.69)	3.47 (2.94, 4.11)	3.34 (2.80, 3.94)	<0.001	<0.001	0.1
HDL cholesterol (mmol/L)	1.66 (1.53, 1.84)	1.60 (1.33, 1.87)	1.30 (1.11, 1.53)	0.07	<0.001	<0.001
HDL <sub>2</sub> cholesterol (mmol/L)	0.73 (0.57, 0.91)	0.64 (0.48, 0.89)	0.45 (0.31, 0.64)	0.1	<0.001	<0.001
HDL <sub>3</sub> cholesterol (mmol/L)	0.93 (0.88, 1.01)	0.91 (0.79, 1.03)	0.83 (0.72, 0.92)	<0.001	<0.001	<0.001
cholesterol/HDL cholesterol	2.56 (2.28, 2.97)	3.50 (2.91, 4.24)	4.13 (3.31, 5.06)	<0.001	<0.001	<0.001
non-HDL cholesterol (mmol/L)	2.64 (2.25, 3.06)	4.01 (3.40, 4.61)	3.99 (3.37, 4.79)	<0.001	<0.001	0.7



**Conclusions:** Adverse effects of ageing in women, male gender and menopause on apoB concentrations and of menopause and, in particular, male gender on the cholesterol content of HDL particles were consistent with adverse effects on CVD risk, with male gender having the greatest effect.

## References:

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