

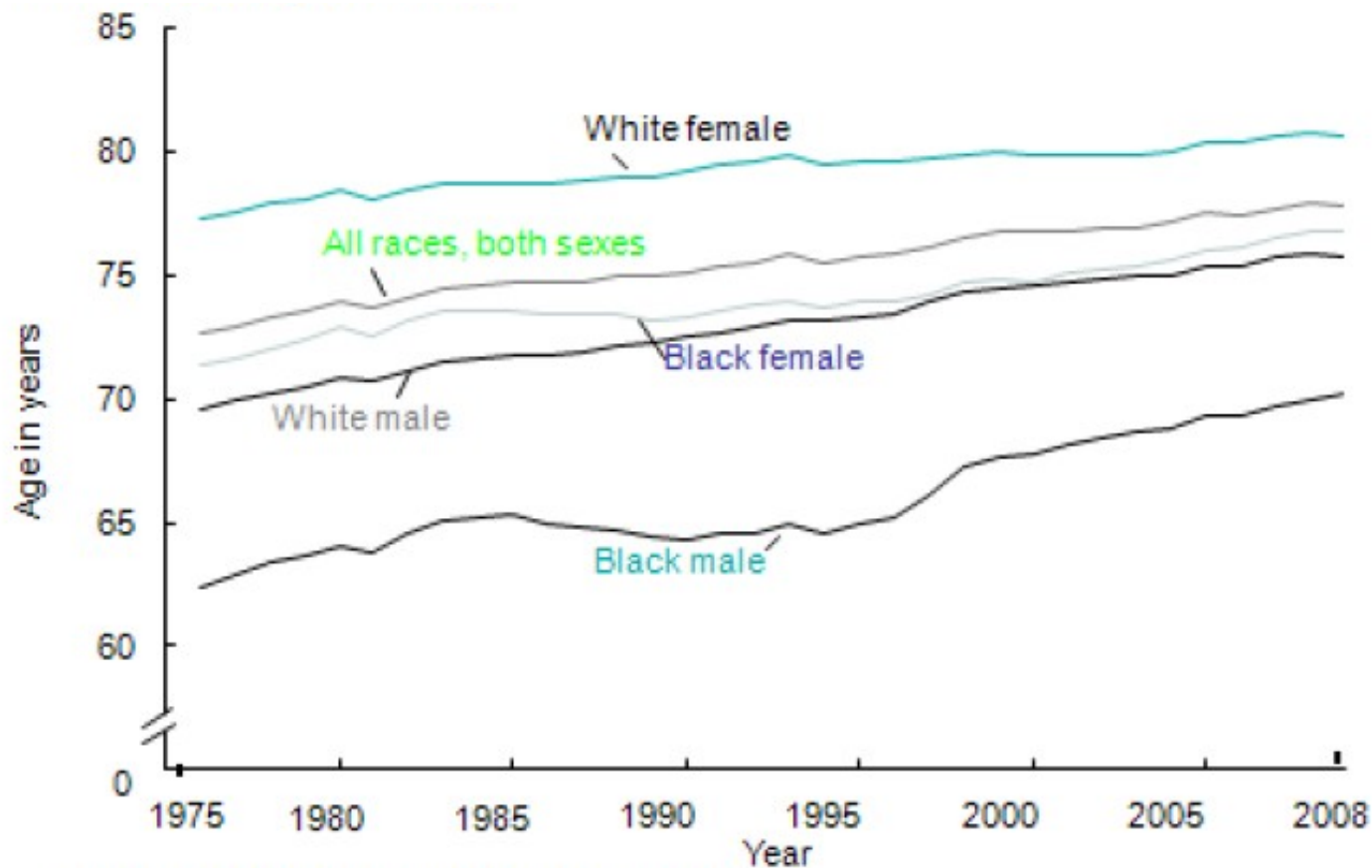


Cardiovascular Risk in Menopause

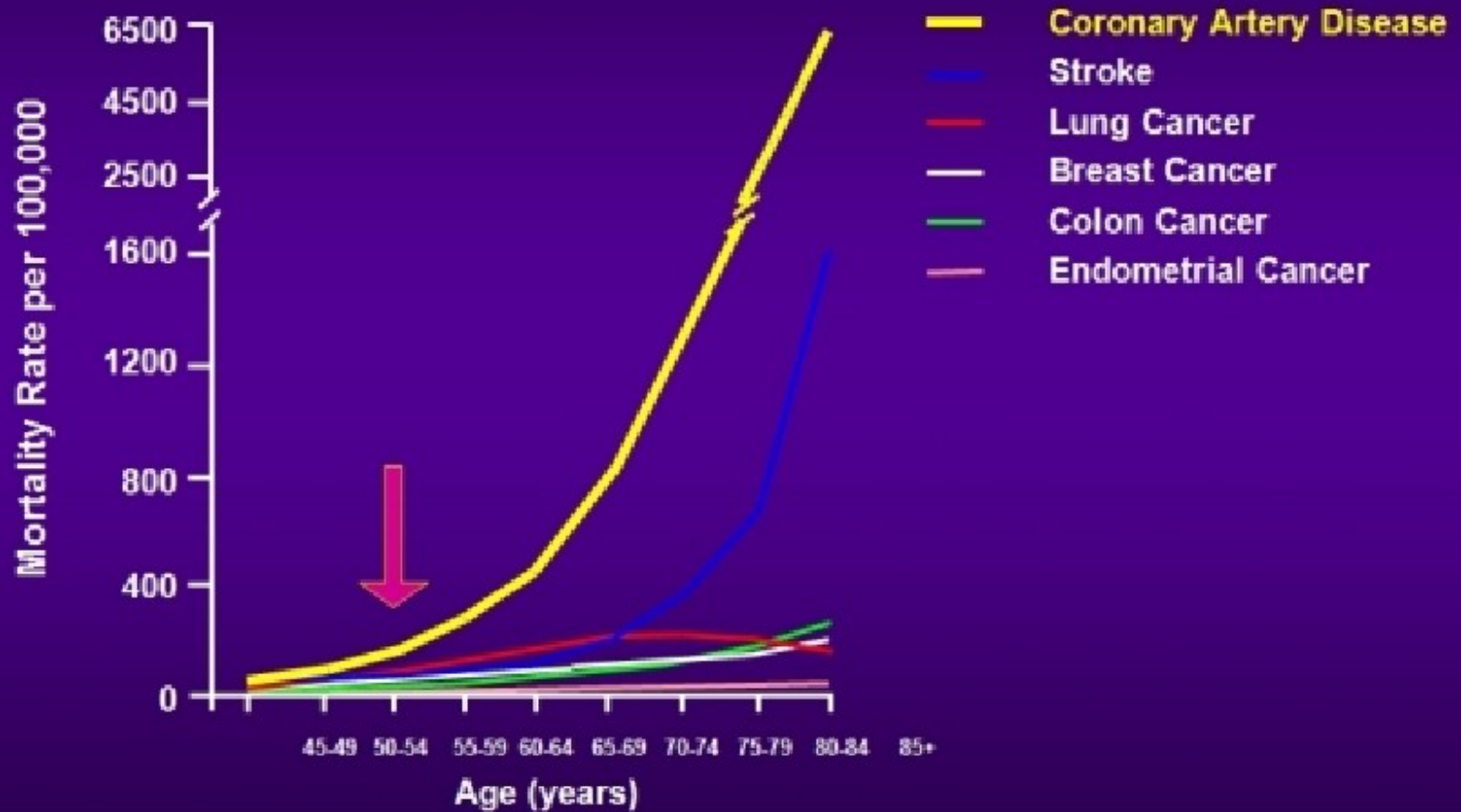
奇美醫院

蔡永杰

Life expectancy at birth, by race and sex: United States, 1975-2007 final and 2008 preliminary

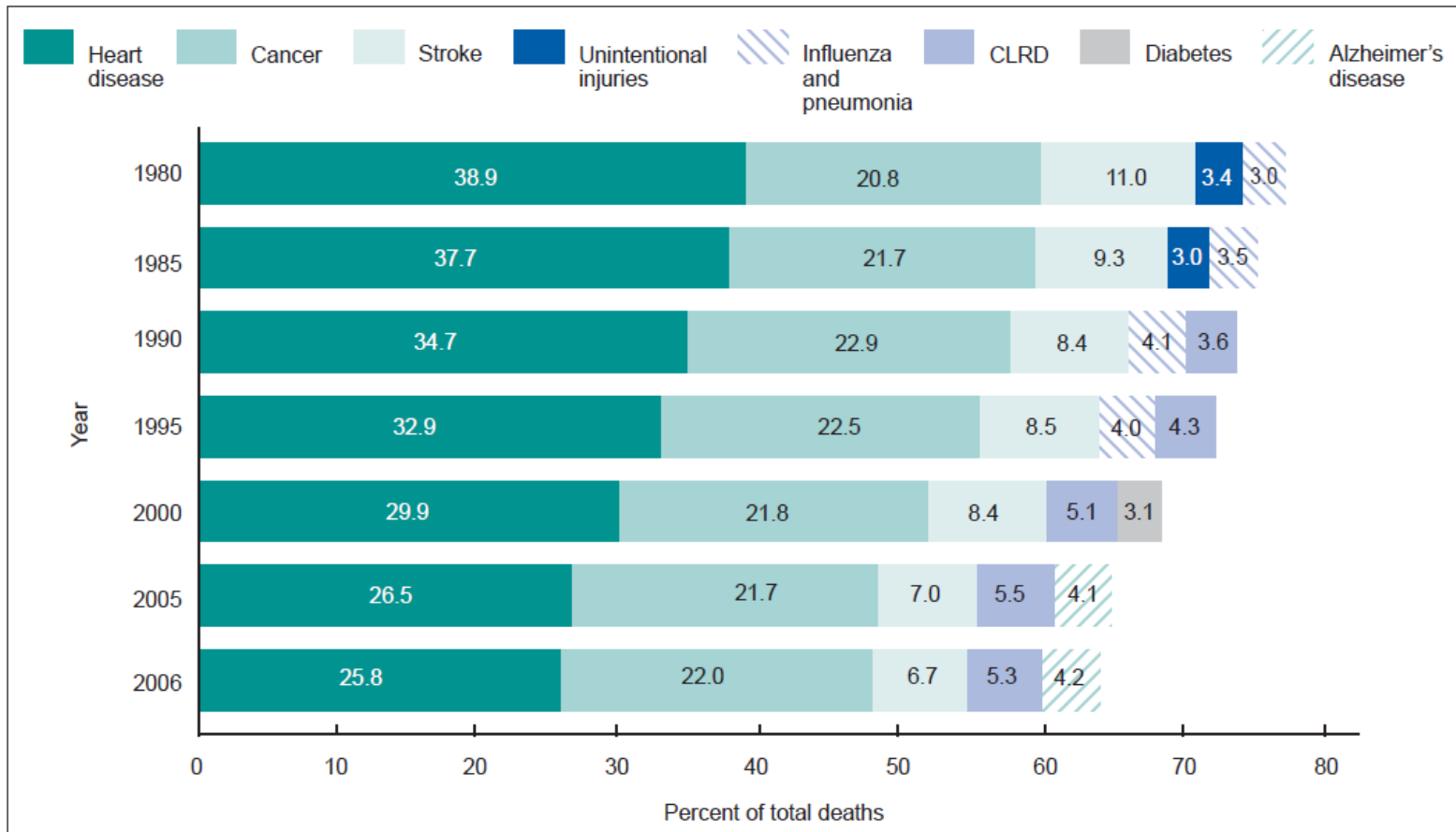


Mortality Rates in Women



Percentage of total death for the top 5 causes of death among female:United State 1980-2006

Heart disease is the # 1 killer in woman

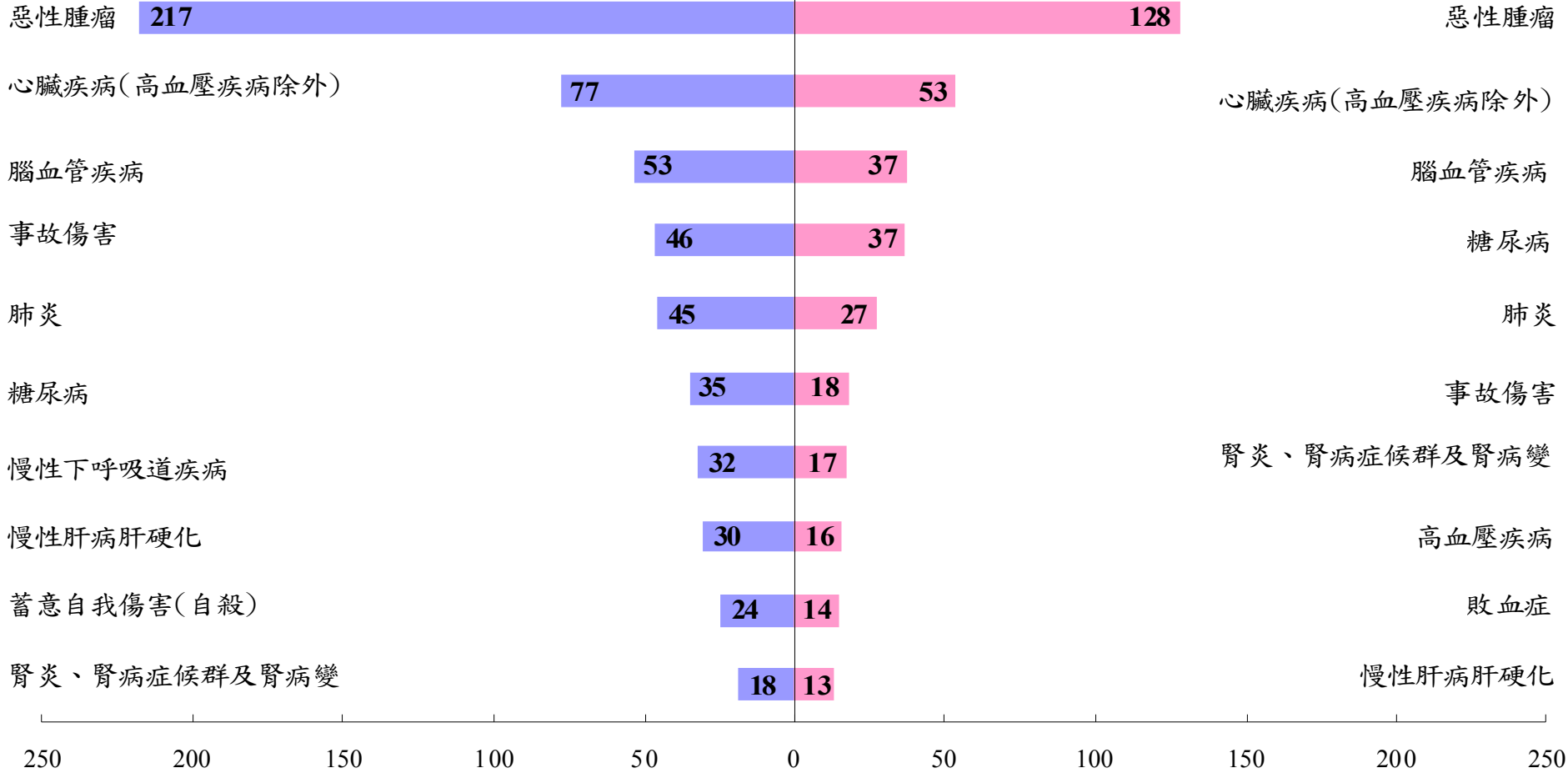


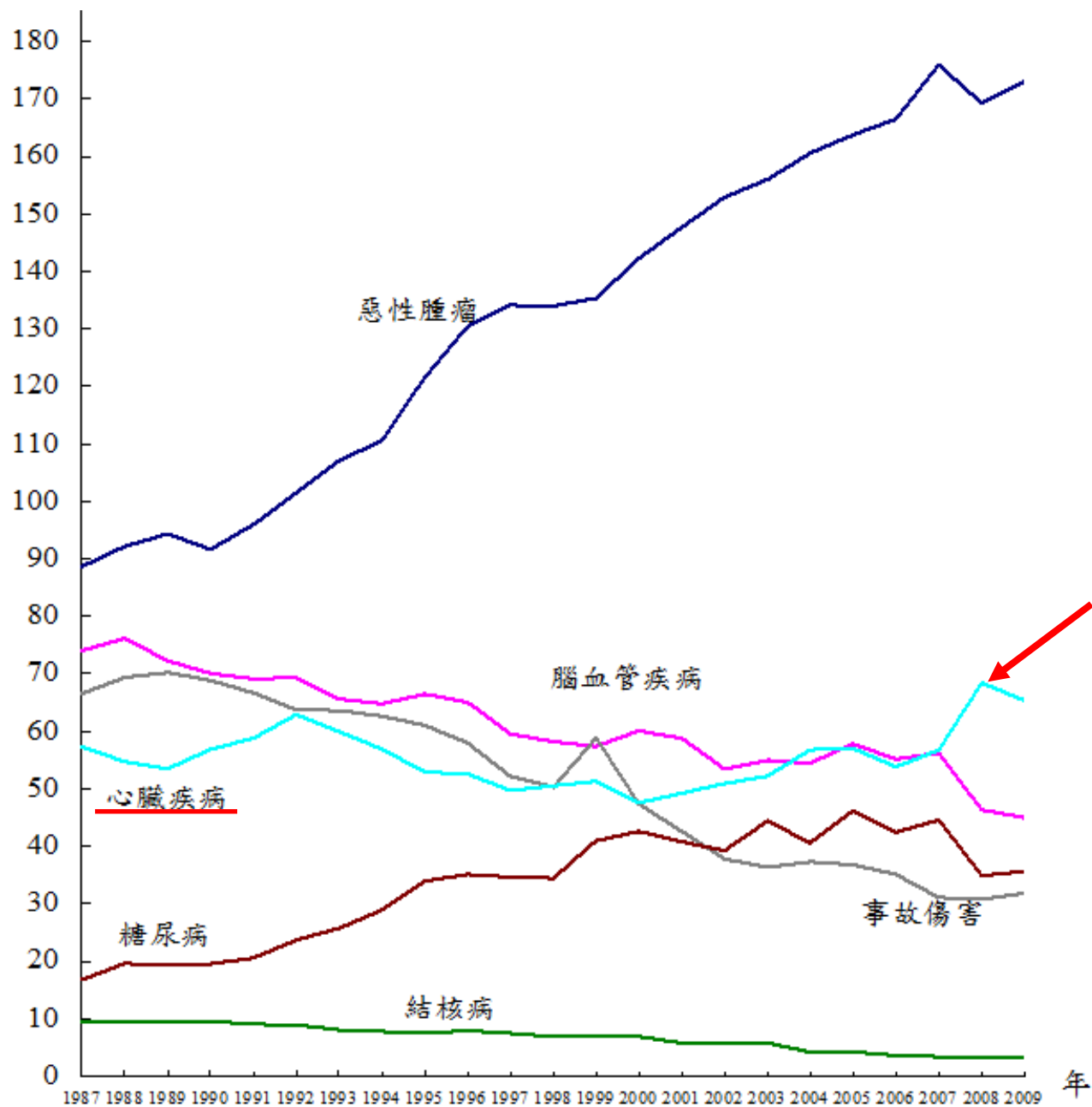
98年男女性十大死因比較

單位：0/0000

男性

女性



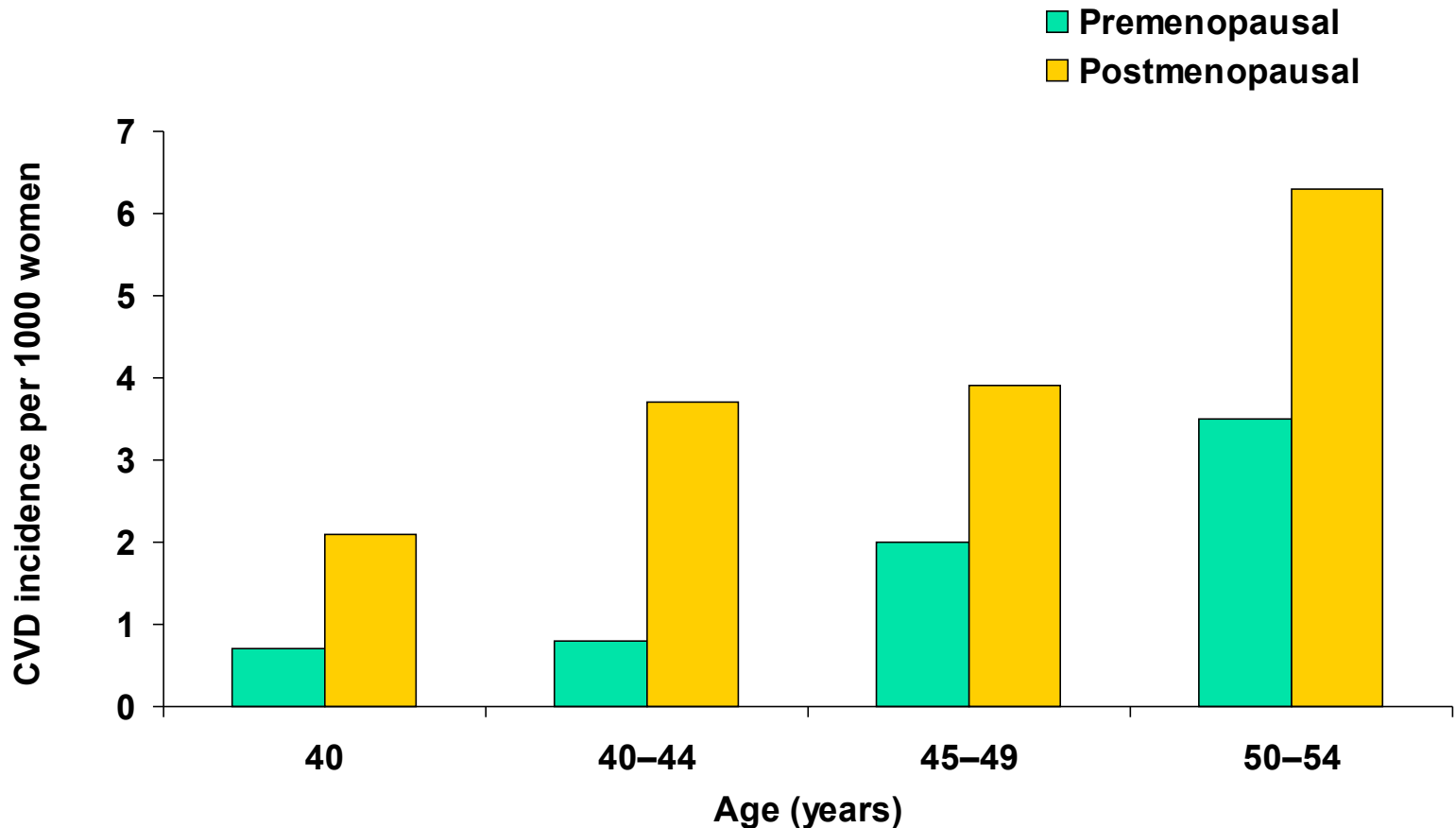




Risk factors for cardiovascular disease

- Age
- Genetic
 - Family history
 - Ethnic origin
- Metabolic
 - Diabetes mellitus
 - Dyslipidemia
 - Hypertension
 - Obesity
- Lifestyle
 - Diet
 - Exercise
 - Smoking
- Socioeconomic status
- **Menopause status**

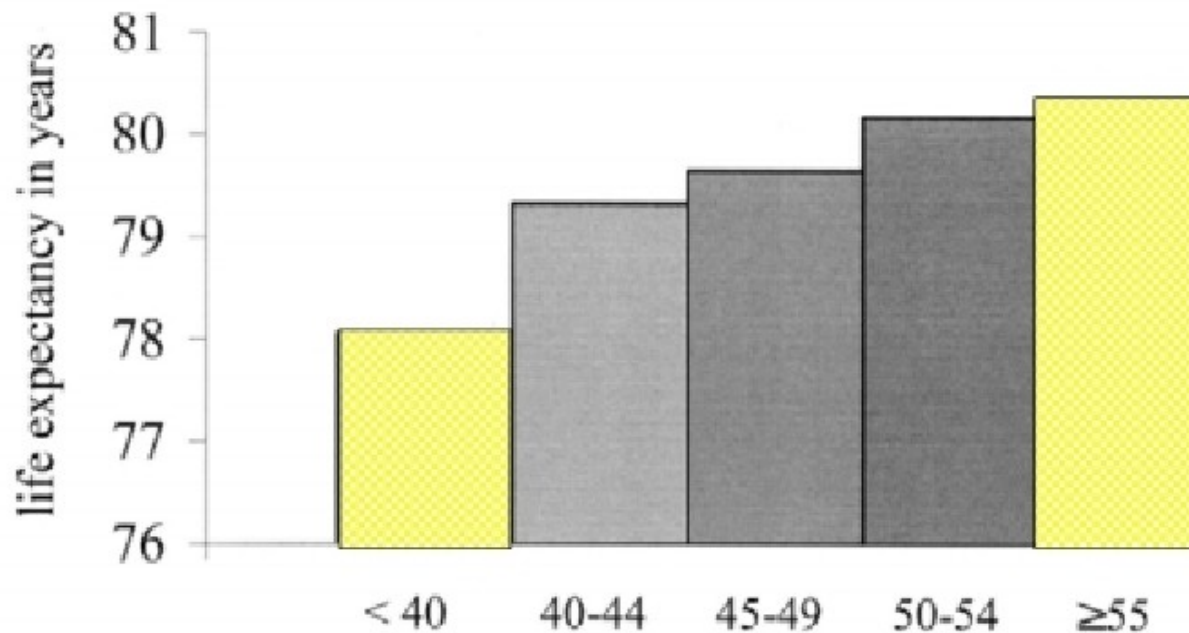
CVD and menopausal status



Adapted from the Framingham Study, DHEW No 74, 1974

Life expectancy by age at menopause

12134 Dutch PMW followed an average of 17 years
2607 deaths: CVD – 963; cancer – 812
Age adjusted mortality reduced by 2% with each
increasing year of age at menopause





CVD risk factors

- Lipids and lipoproteins
- Glucose and insulin metabolism
- Body fat distribution
- Coagulation and fibrinolysis
- Inflammatory markers
- Blood pressure
- Arterial function



CHD: metabolic changes

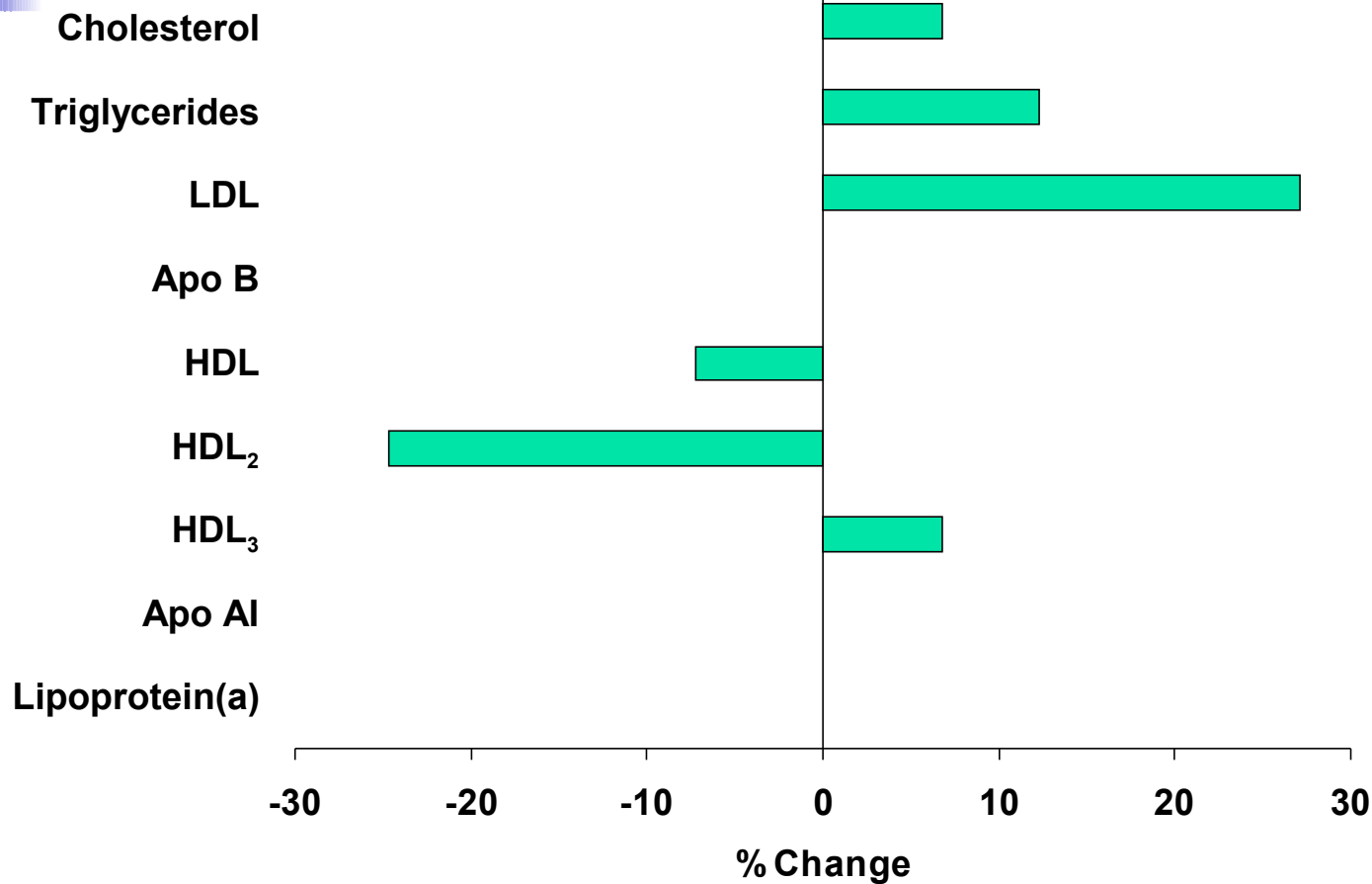
- Lower HDL and HDL₂
- Lower apolipoprotein AI
- Higher triglycerides
- Higher insulin response
- Lower insulin sensitivity
- Lower tissue plasminogen activator (tPA)
- Higher PAI-1
- Higher systolic blood pressure
- Greater android fat

A portrait of a man with a beard and mustache, wearing a dark, voluminous coat and a white ruff. He is seated and looking slightly to the right. The background is dark and indistinct.

Lipoproteins



Menopause and lipids





The Epidemiology of Cholesterol Levels and Subfractions

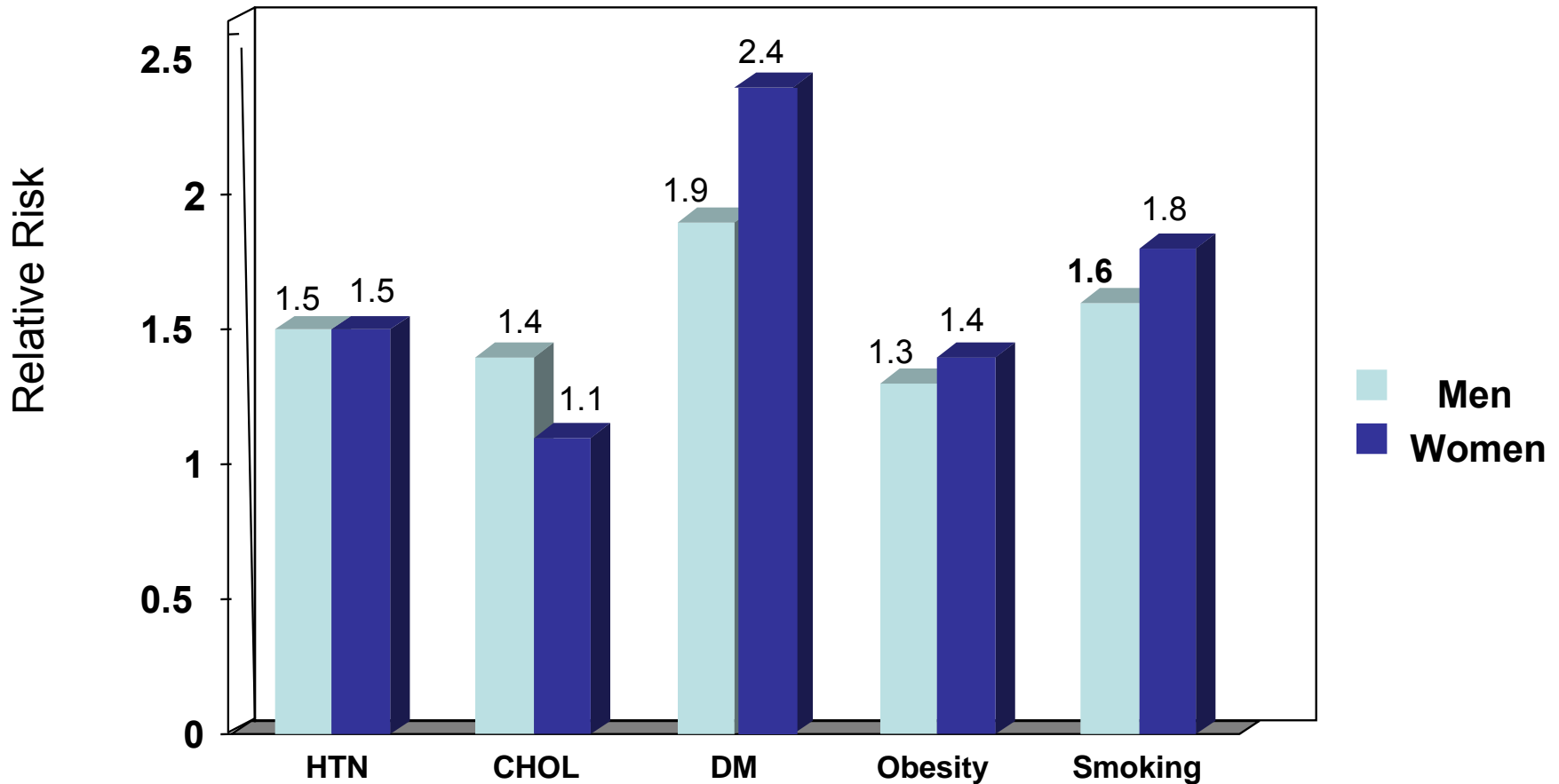
- Low HDL more important in women than men
 - For every 1 mg/dL increase in HDL
 - 3% decrease in CHD risk for women
 - 2% decrease in CHD risk for men
- Total cholesterol/HDL ratio very predictive of CHD risk in women
- Triglyceride elevation associated with greater atherogenic significance in women than in men



Cholesterol Levels and Subfractions

- LDL > 160 mg/dL associated with 3.3-fold elevation in risk for women less than 65 years old
- LDL pattern of small, dense particles (more atherogenic) present in 25% of population, but less frequently seen in women
- Menopausal transition associated with increasing proportion of this subfraction

Relative Risk of Various Factors for CHD for Women and Men





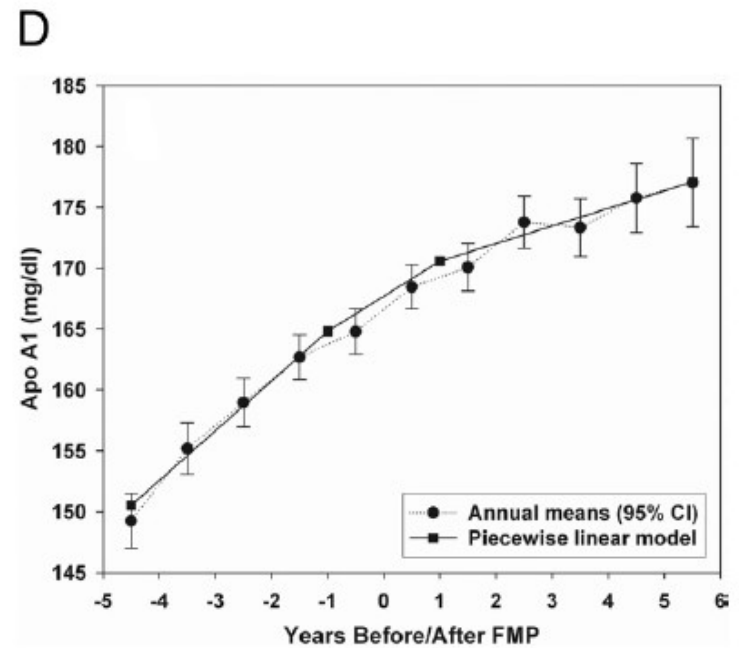
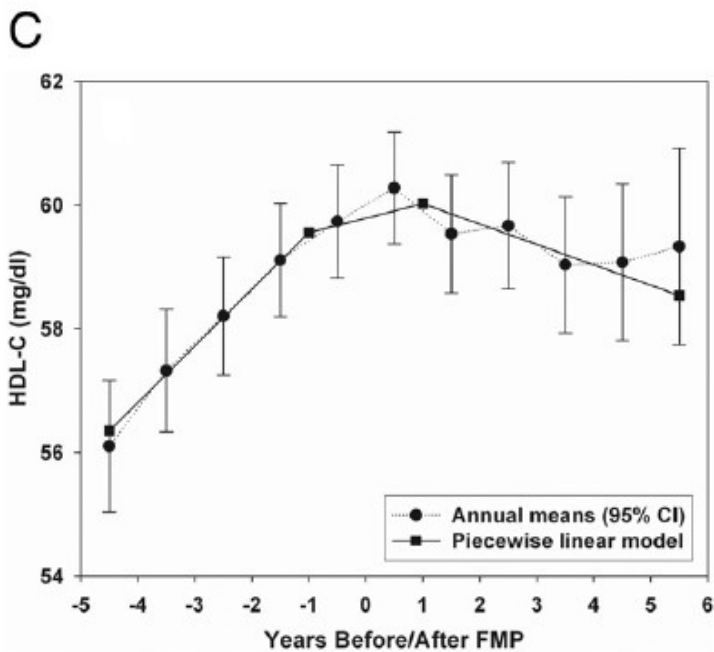
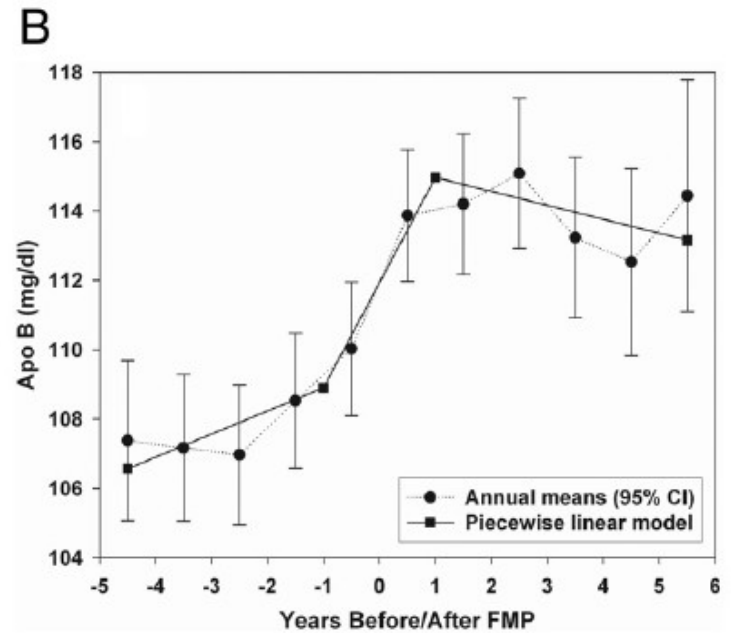
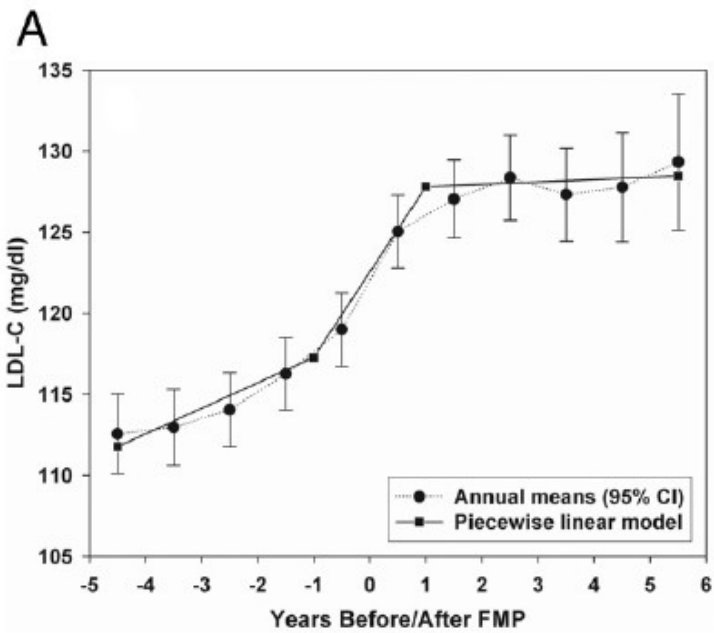
Are Changes in Cardiovascular Disease Risk
Factors in Midlife Women Due to Chronological
Aging or to the Menopausal Transition?

SWAN (Study of Women's Health Across the Nation)

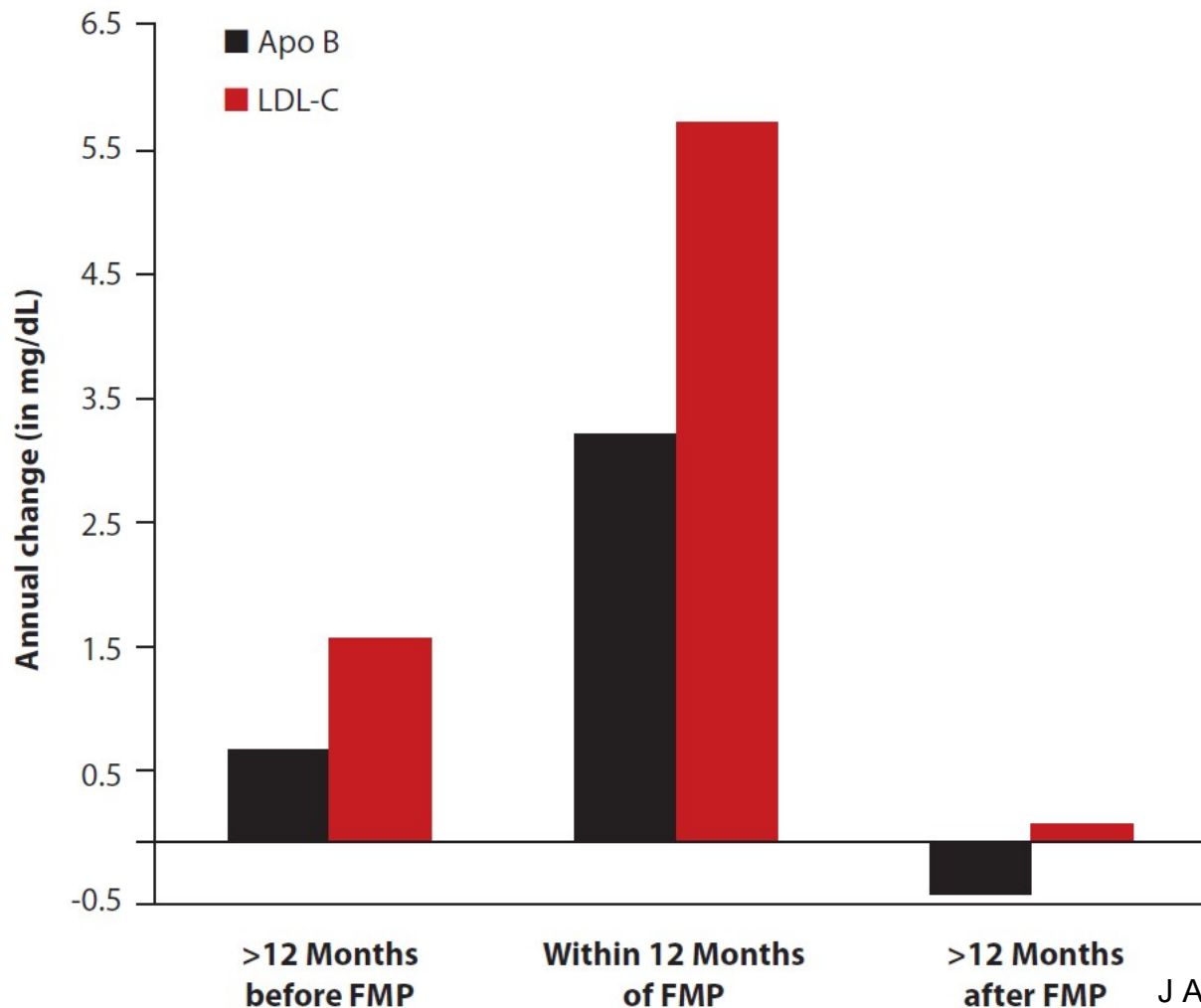


Methods

SWAN (Study of Women's Health Across the Nation) is a prospective study of the menopausal transition in 3,302 minority (African American, Hispanic, Japanese, or Chinese) and Caucasian women. After 10 annual examinations, 1,054 women had achieved an FMP not due to surgery and without hormone therapy use before FMP. Measured CHD risk factors included lipids and lipoproteins, glucose, insulin, blood pressure, fibrinogen, And C-reactive protein.



Annual changes in low-density lipoprotein cholesterol and apolipoprotein B





Conclusions

- Women experience a unique increase in lipids at the time of the FMP.
- The menopause-associated changes in total cholesterol, LDL-C, and Apo B observed here may play an important role in women's increased risk of CHD in the post-menopausal years.



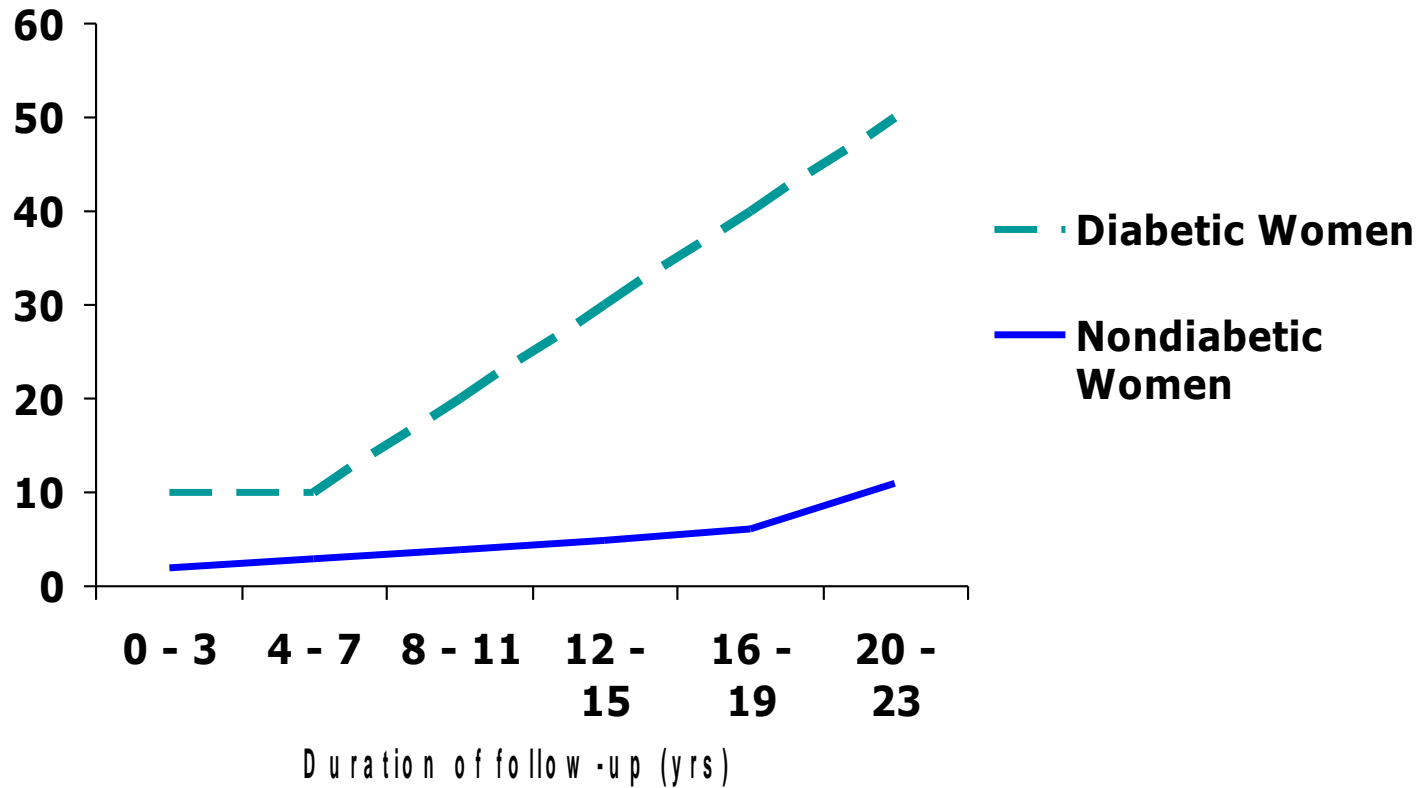
Diabetes



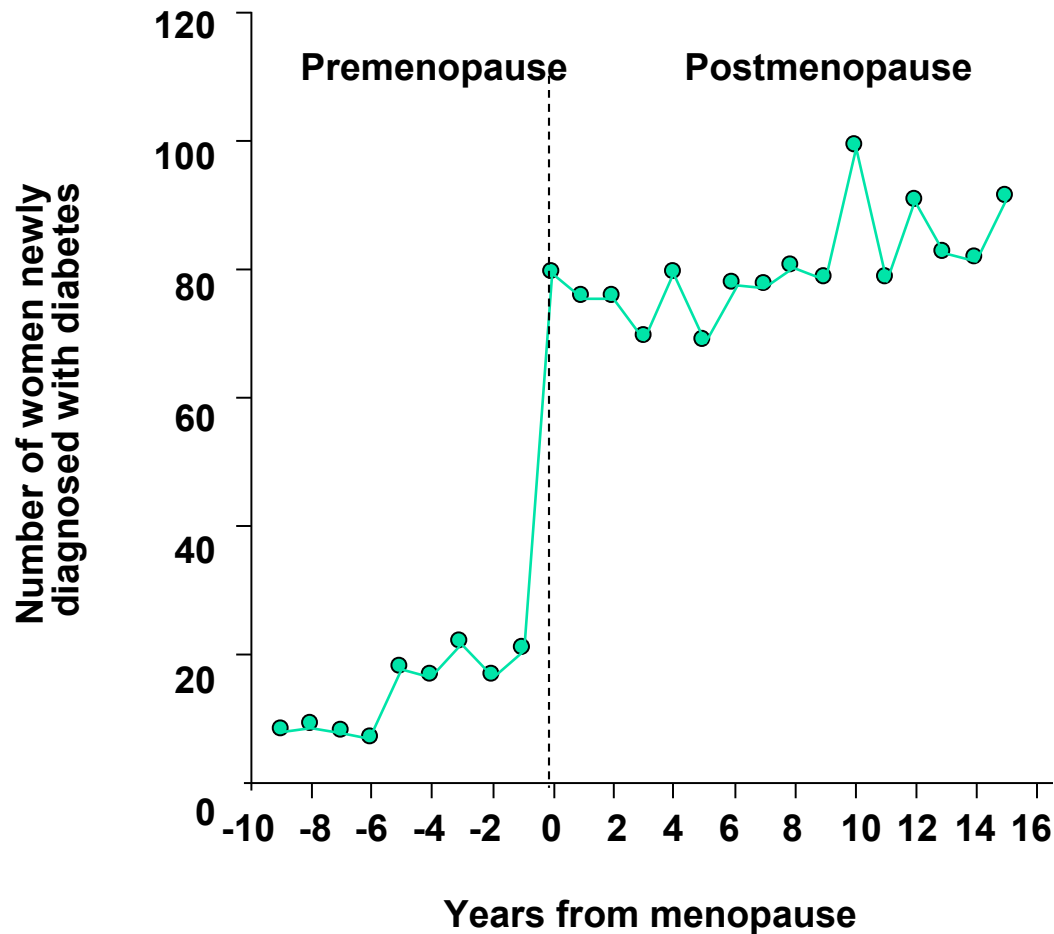
Diabetes

- 65% of diabetics die of cardiovascular disease
- Diabetics have death rates from heart disease that are 2 to 4 times higher than non-diabetics

Coronary Disease Mortality and Diabetes in Women

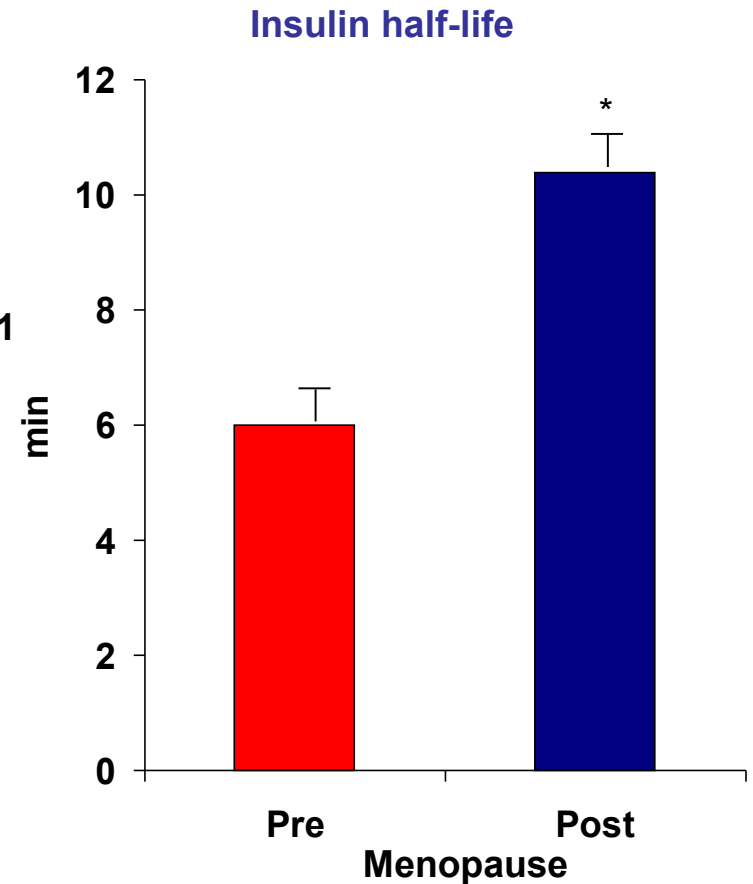
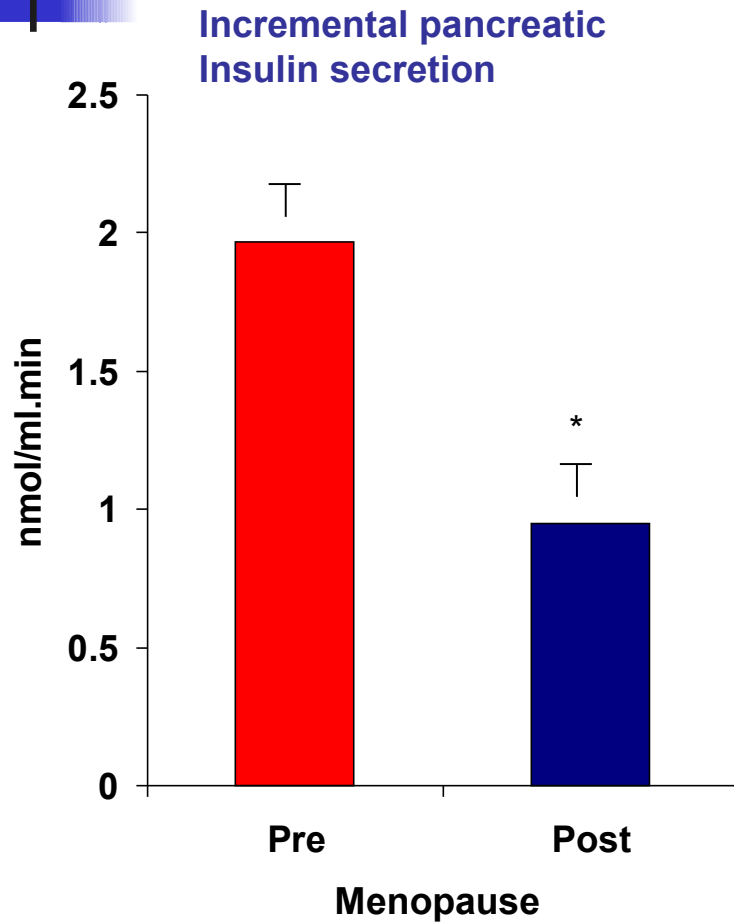


Menopause and diabetes

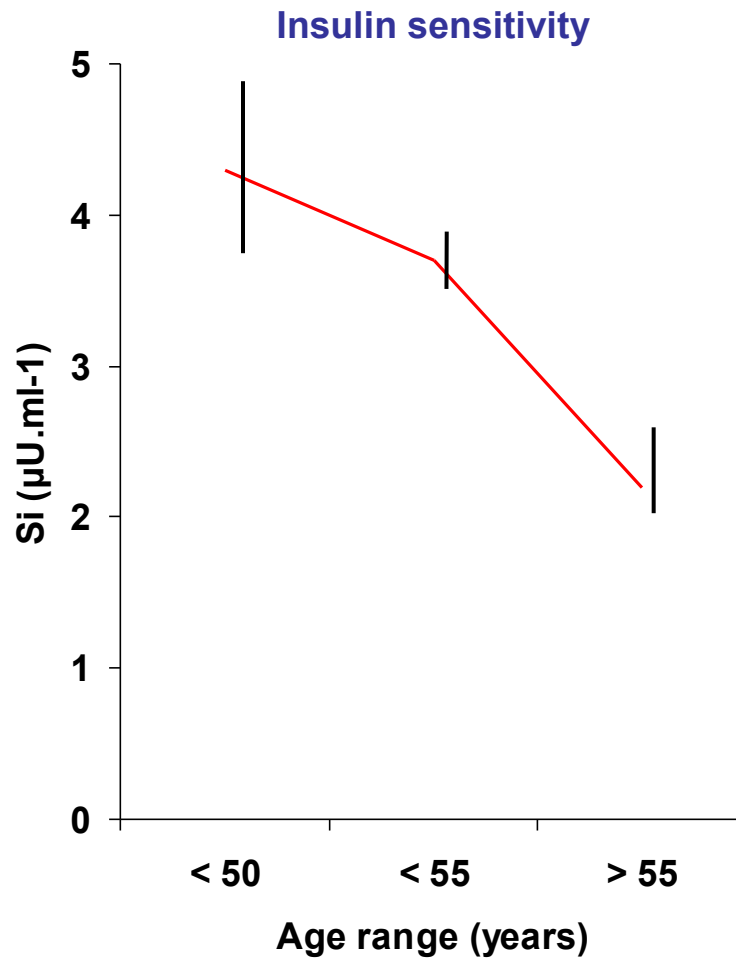


Seige K, *et al.* 6th Symposium of the German Endocrinological Society: Modern Developments in Progestagenic Hormones in Veterinary Medicine; 1959, 1960; Kiel: Springer Verlag; 1959. p. 274–9

Insulin metabolism



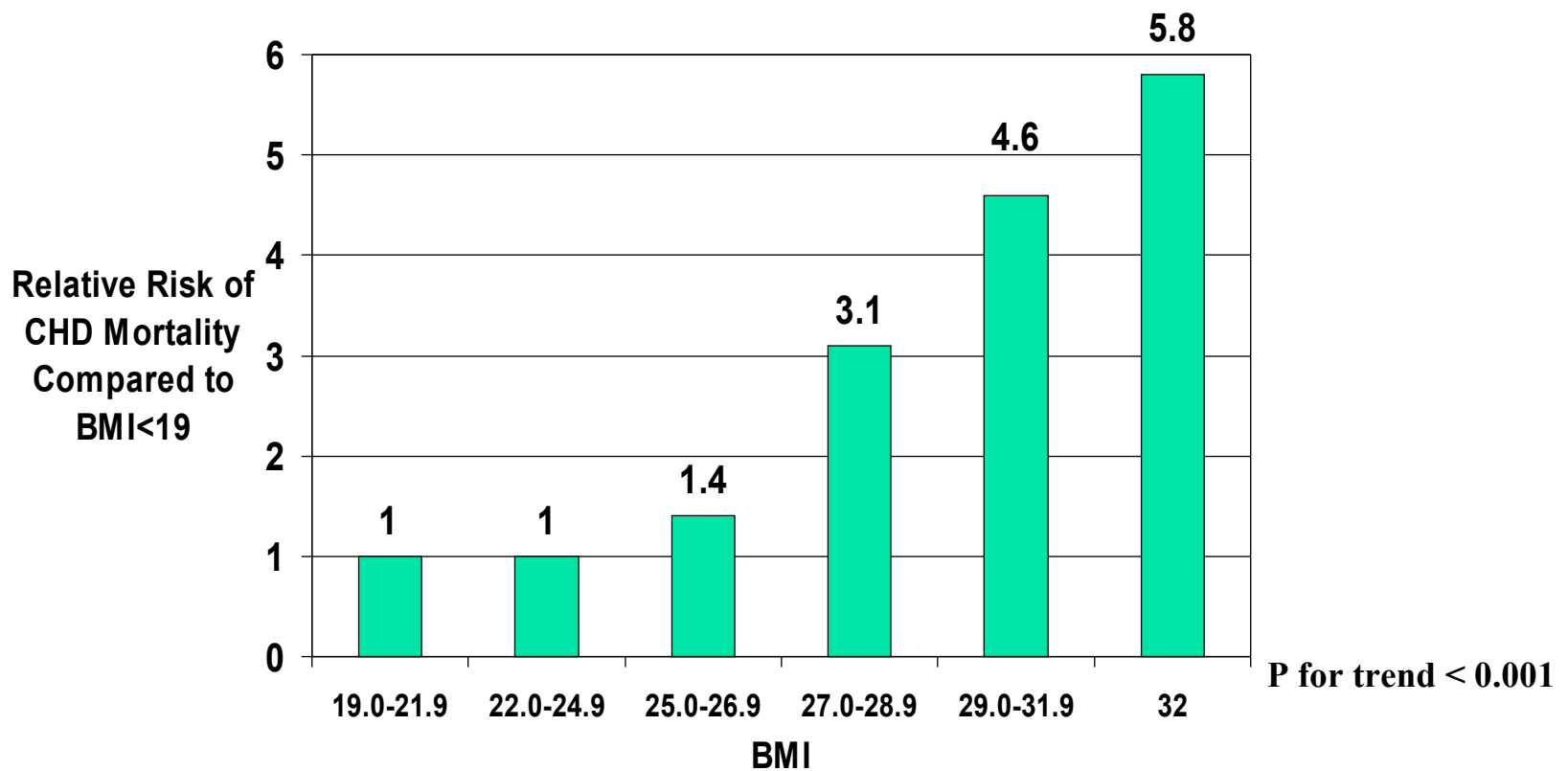
Insulin metabolism



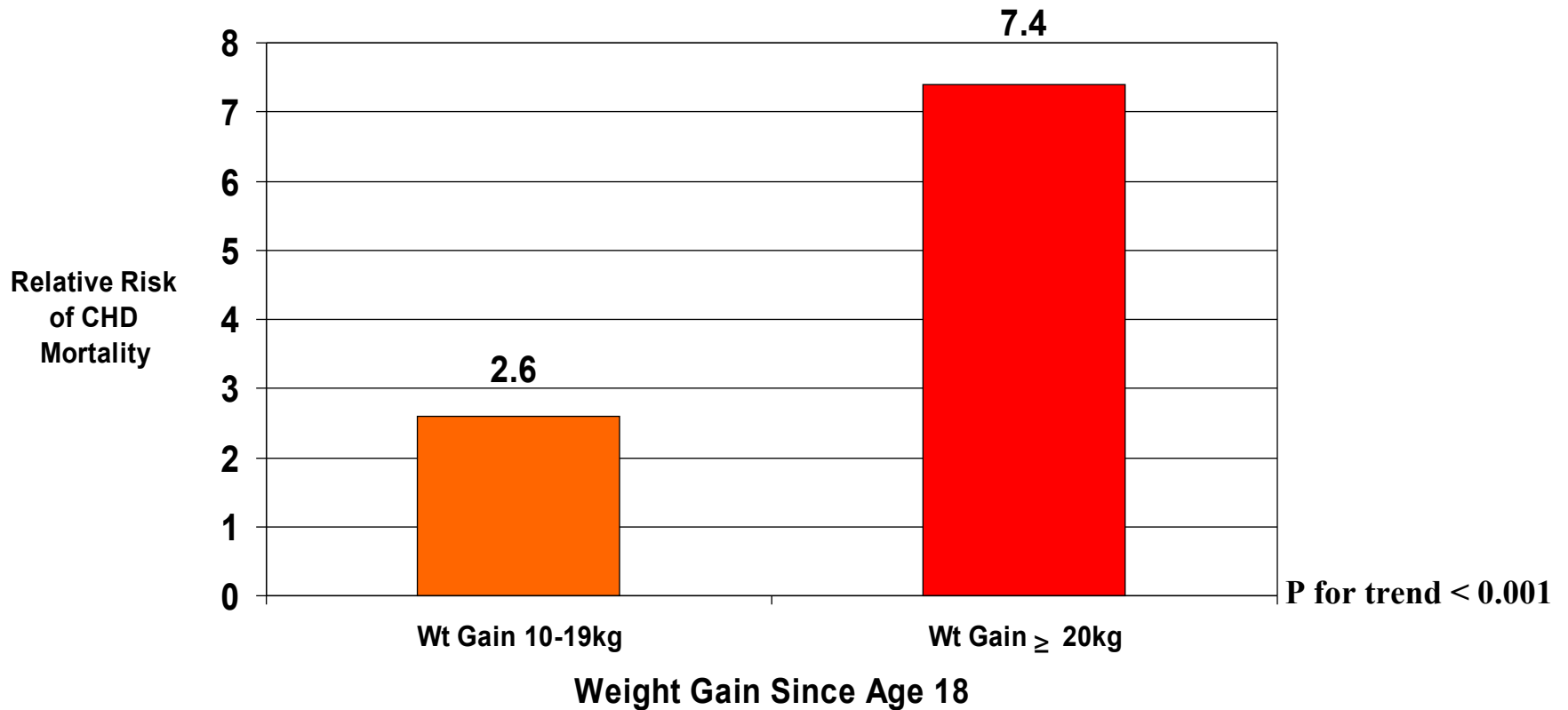


Obesity

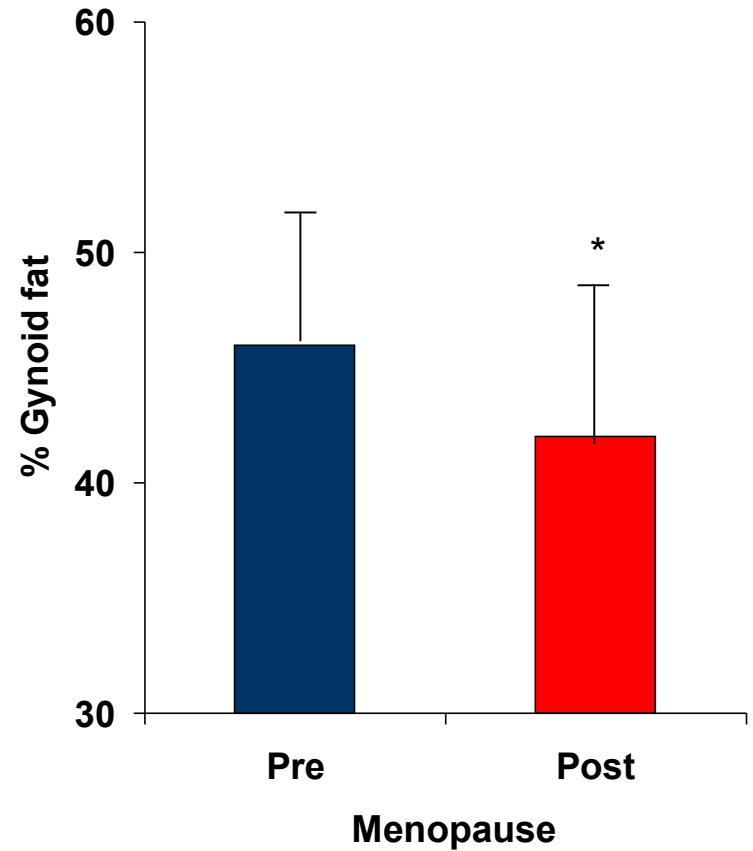
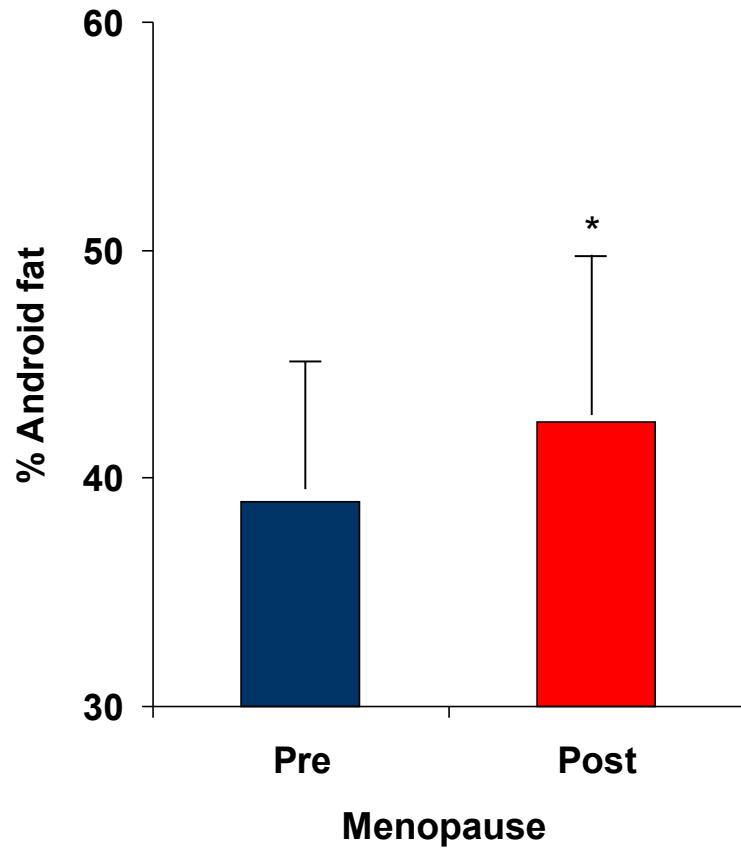
Body Weight and CHD Mortality Among Women



Body Weight and CHD Mortality Among Women



Body Composition



* $p < 0.001$

A portrait of a man with long, wavy white hair, looking slightly to the left. He is wearing a dark, heavy robe over a dark garment with a white collar. His right hand is visible, wearing two rings. The background is dark and indistinct.

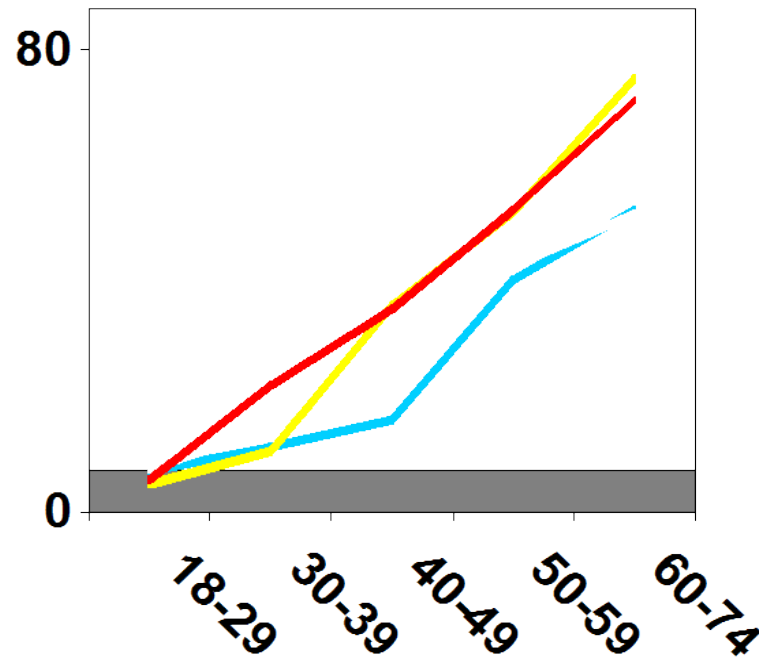
Hypertension




Menopause and Hypertension

- Hypertension is more prevalent among older women than older men
- Death from CHD progresses increasingly and linearly as blood pressure increases
- For every 20 mmHg systolic or 10 mmHg diastolic increase in blood pressure, risk of death from CHD doubles

Prevalence of High Blood Pressure by Age and Race



■ African American men ■ African American women ■ Caucasian men ■ Caucasian women

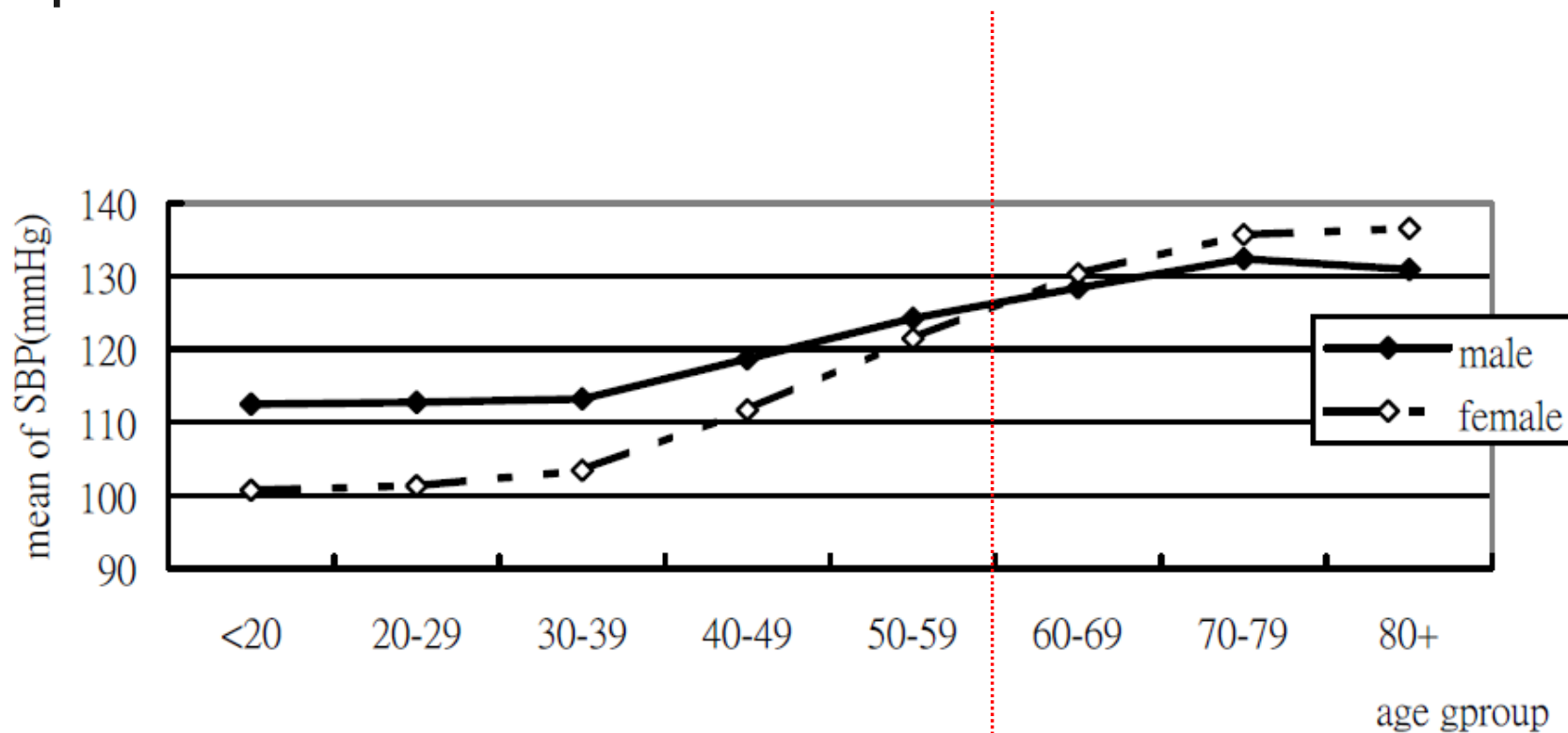


台灣地區高血壓、高血糖、高血脂盛行率調查

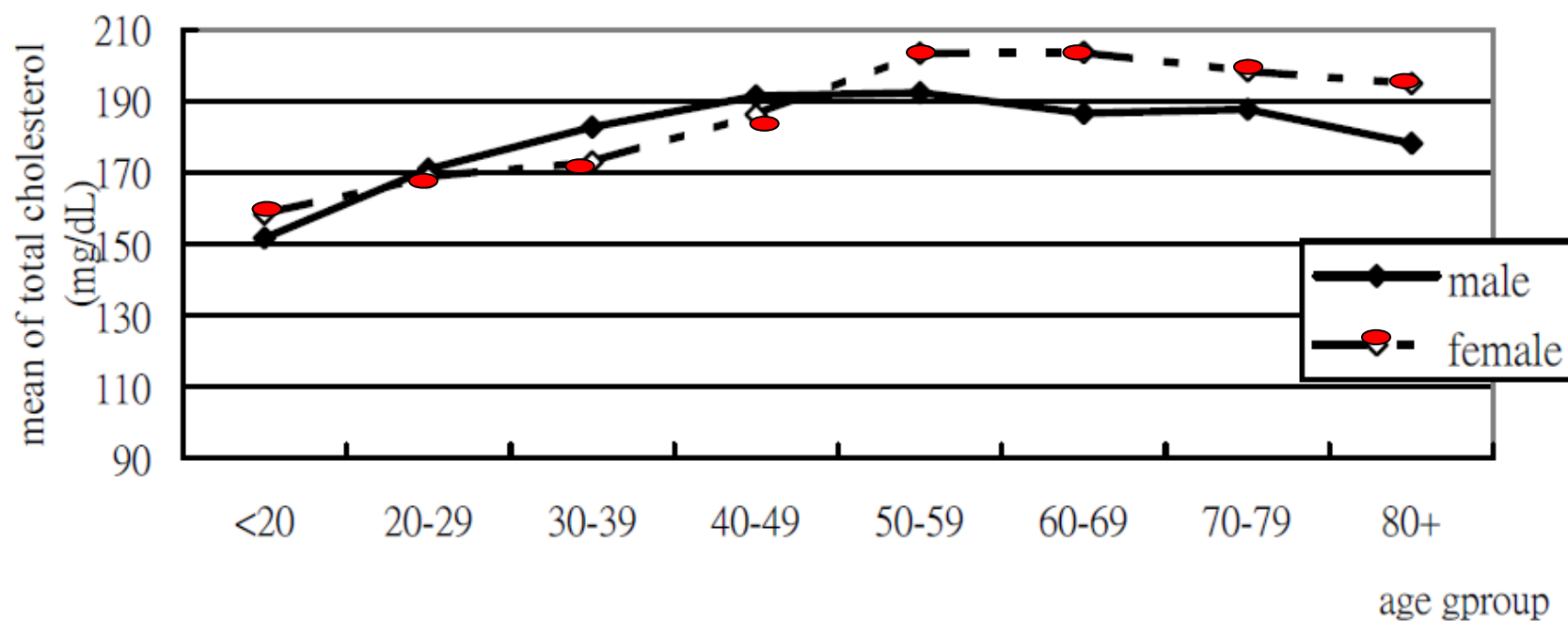
計畫主持人：陳建仁教授

協同主持人：游山林博士、白其卉博士、蘇大成醫師、曾慶孝醫師、簡國龍醫師、黃麗卿醫師

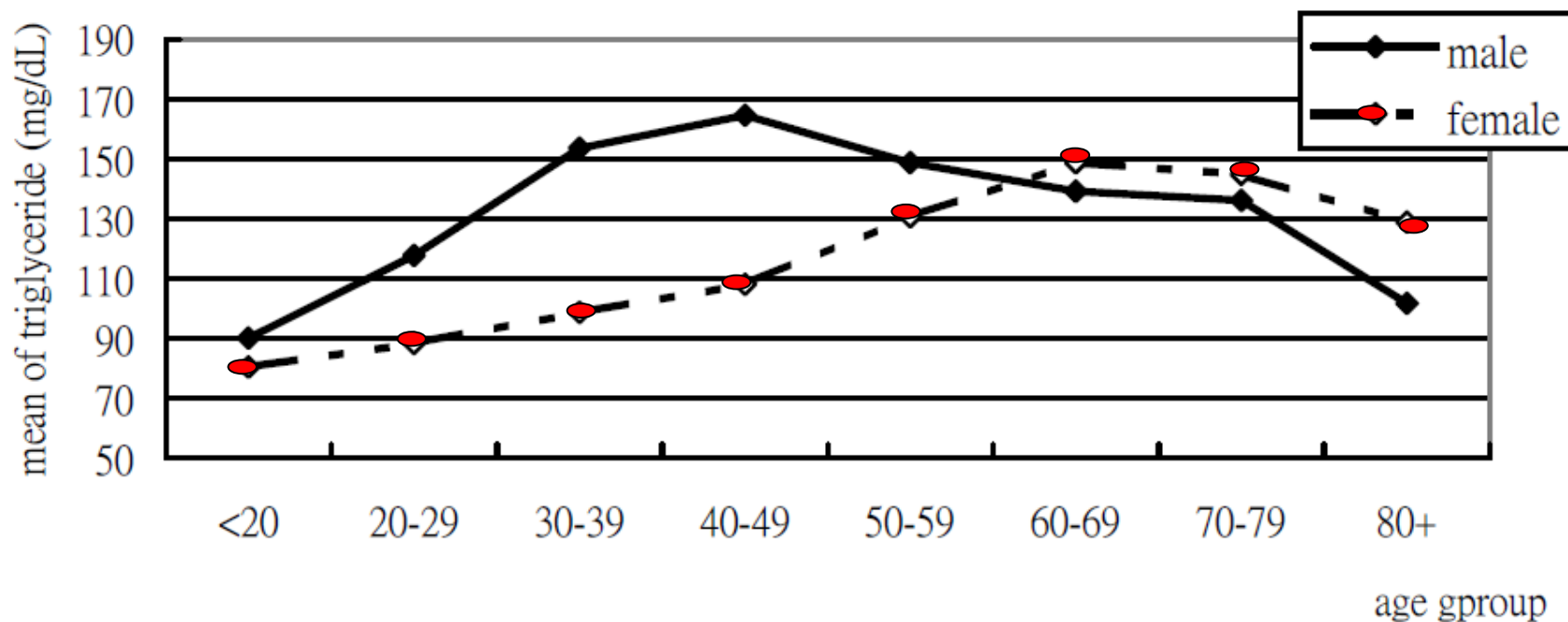
15 歲以上國人收縮壓之年齡趨勢



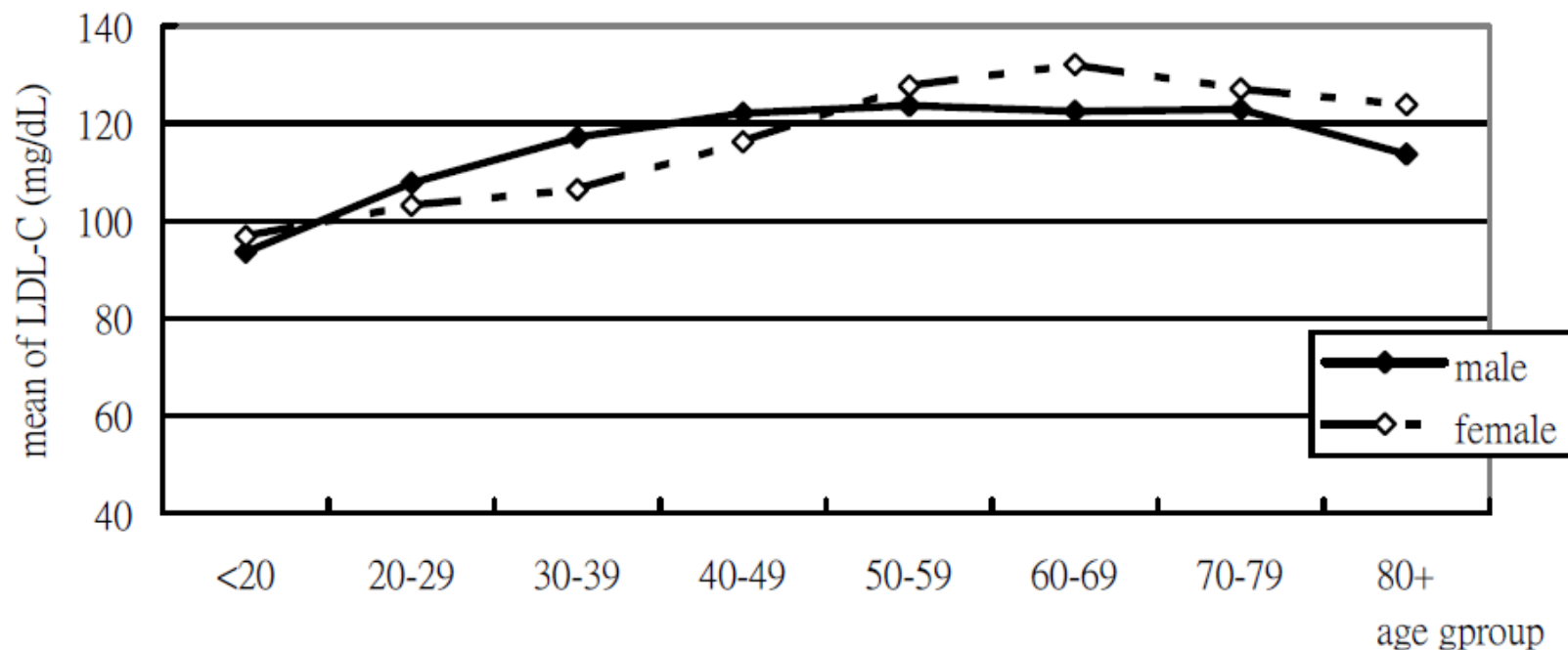
15 歲以上國人總膽固醇平均值之年齡趨勢



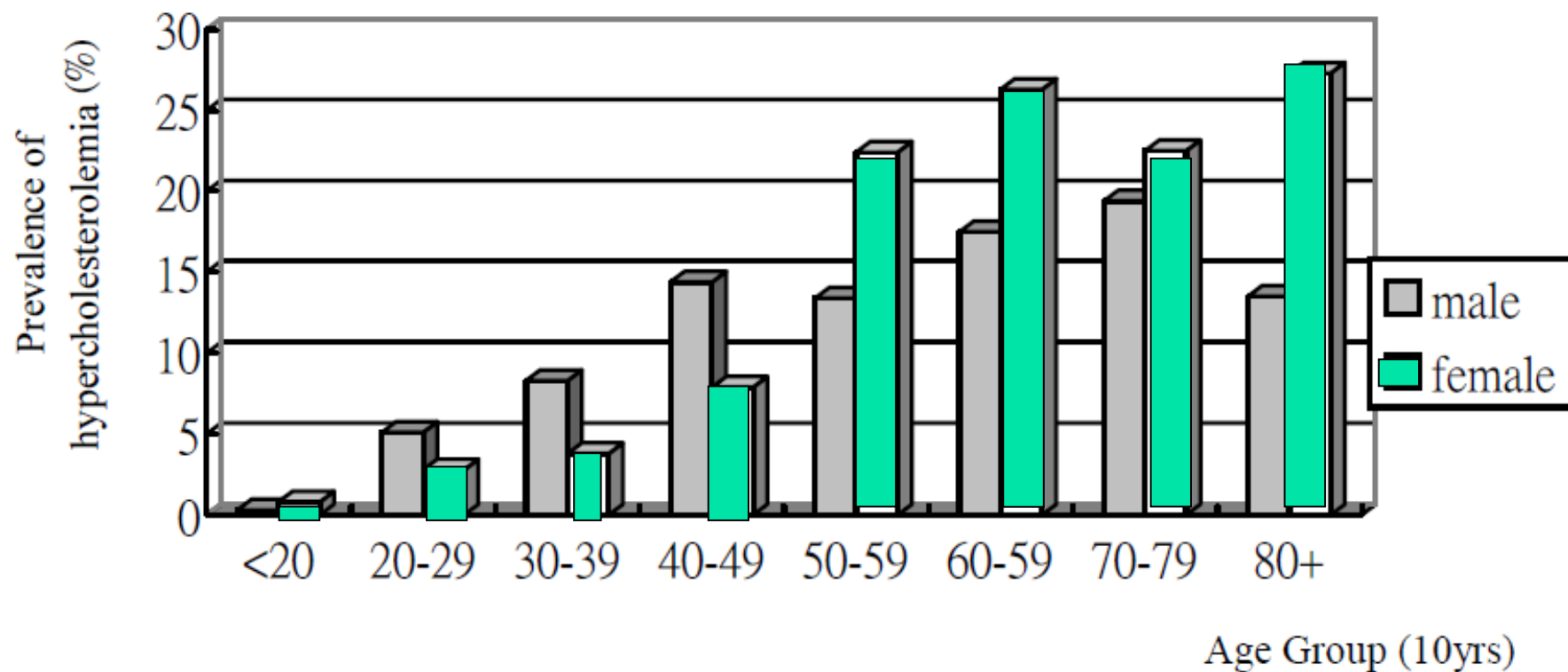
15 歲以上國人三酸甘油脂平均值之年齡趨勢



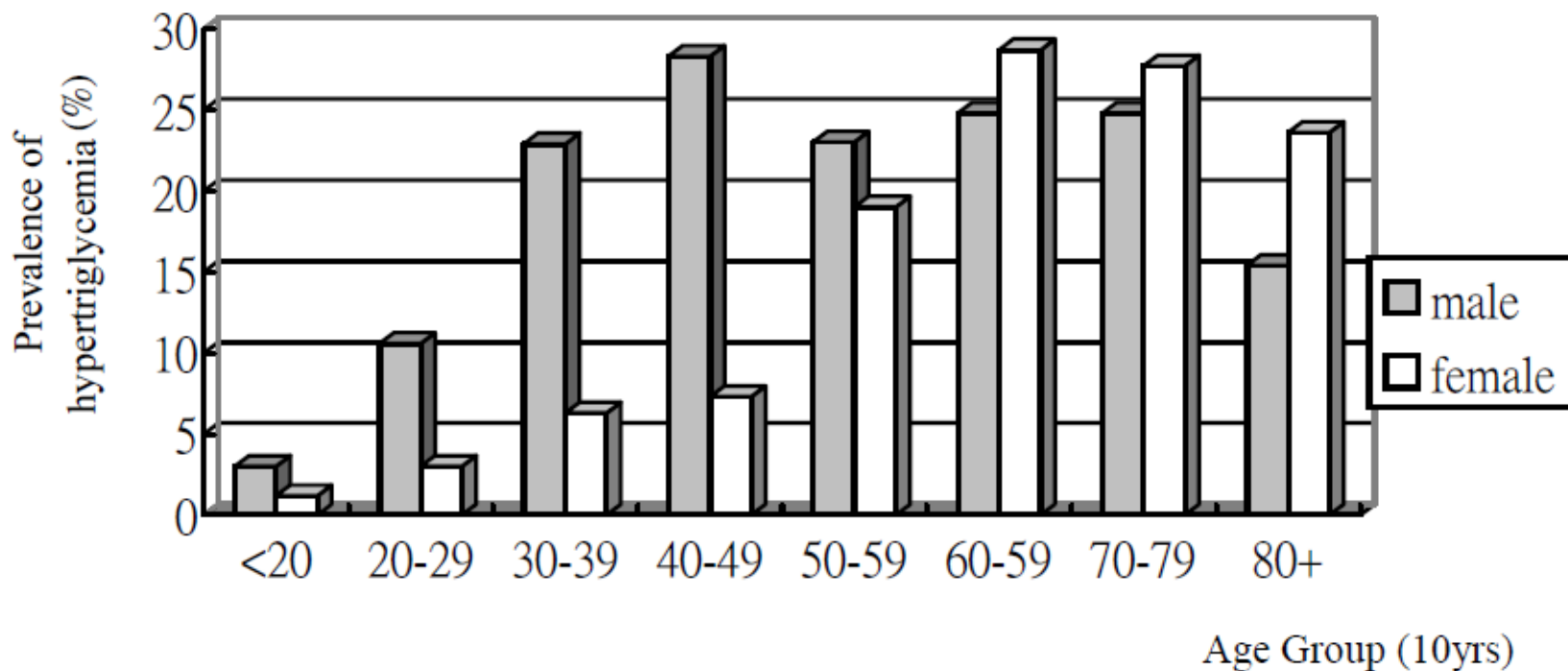
15 歲以上國人低密度膽固醇平均之年齡趨勢



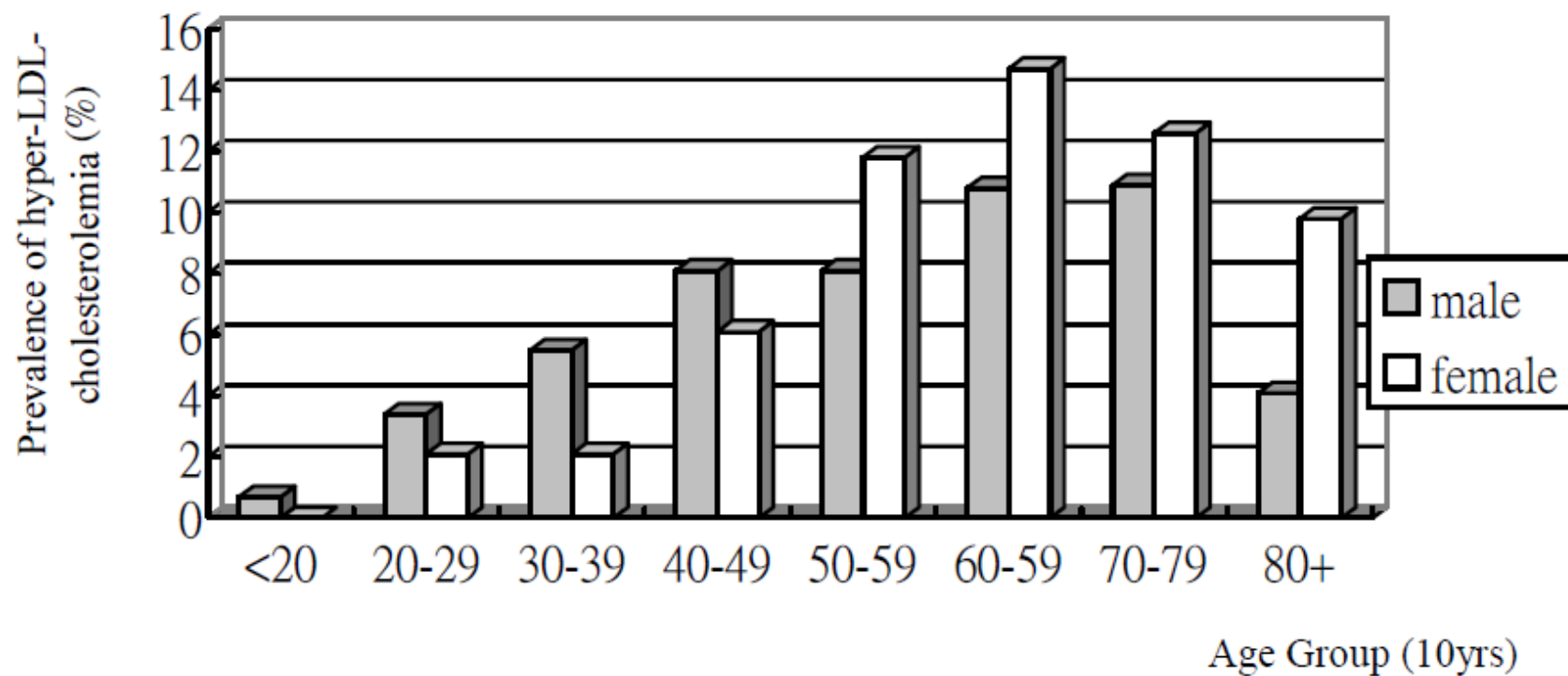
15 歲以上國人之高總膽固醇盛行率年齡分佈



15 歲以上國人之高總三酸甘油脂盛行率年齡分佈



15 歲以上國人之過高之 LDL 盛行率年齡分佈

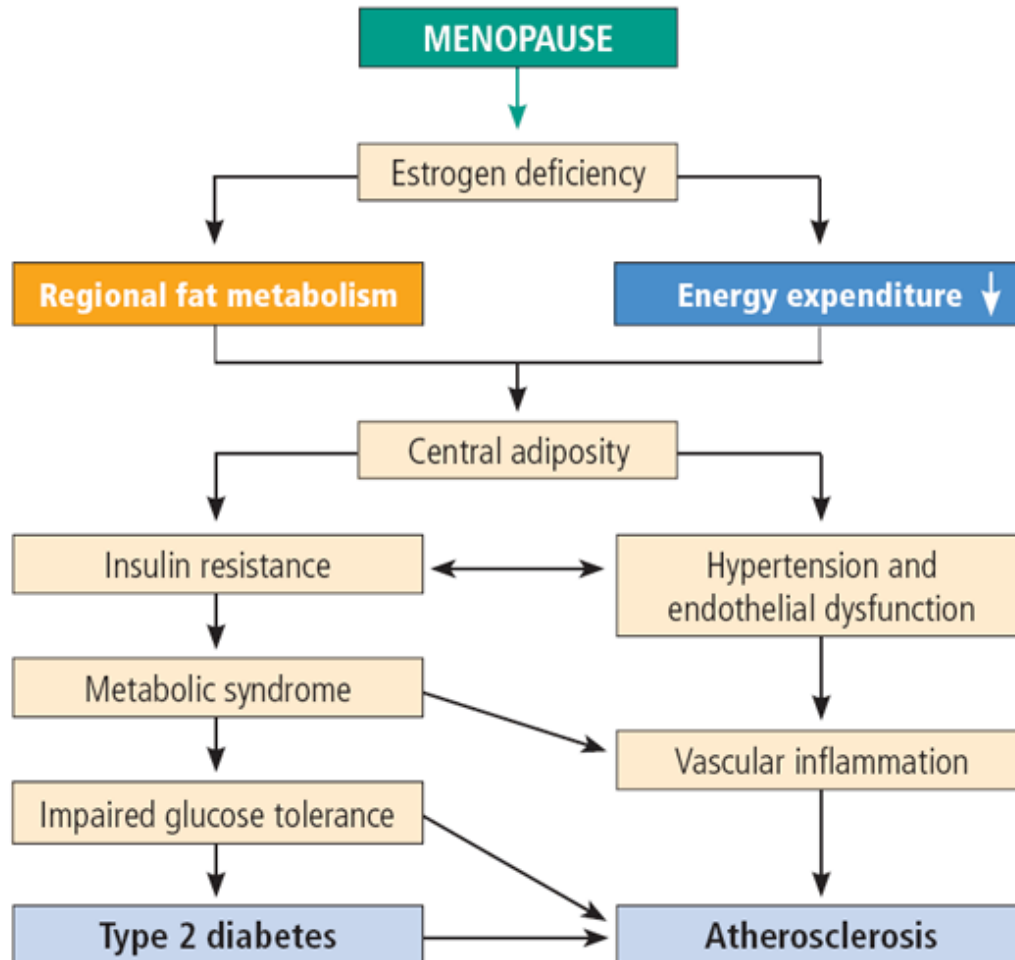




Metabolic Syndrome in Women

- Abdominal obesity - waist circumference > 35 in.
- High triglycerides \geq 150mg/dL
- Low HDL cholesterol < 50mg/dL
- Elevated BP \geq 130/85mm Hg
- Fasting glucose \geq 100mg/dL

Menopause Metabolic Syndrome



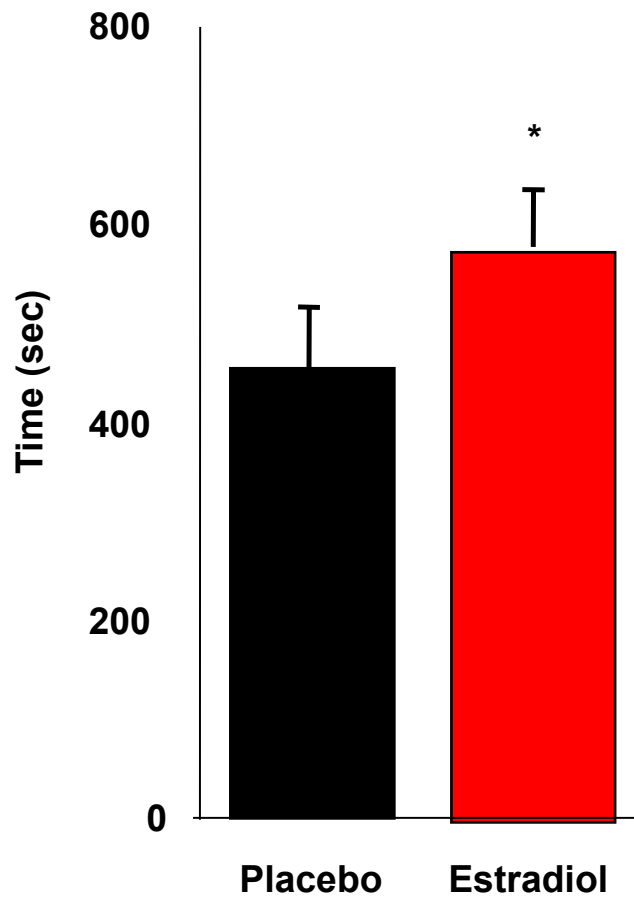


Vascular Effects of Estrogen

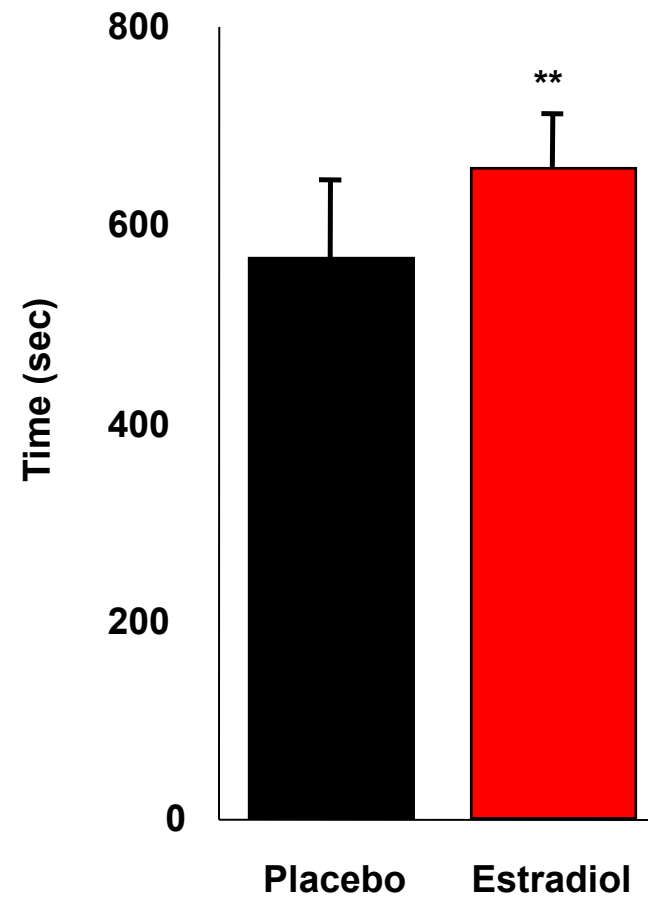
- Estrogens are natural vasoprotective agents.
- Estrogens cause shortterm vasodilation by increasing the formation and release of nitric oxide and prostacyclin in endothelial cells.
- Estrogens reduce vascular smooth-muscle tone by opening specific calcium channels through a mechanism that is dependent on cyclic guanosine monophosphate.

Estradiol and myocardial ischemia

Time to 1 mm ST depression

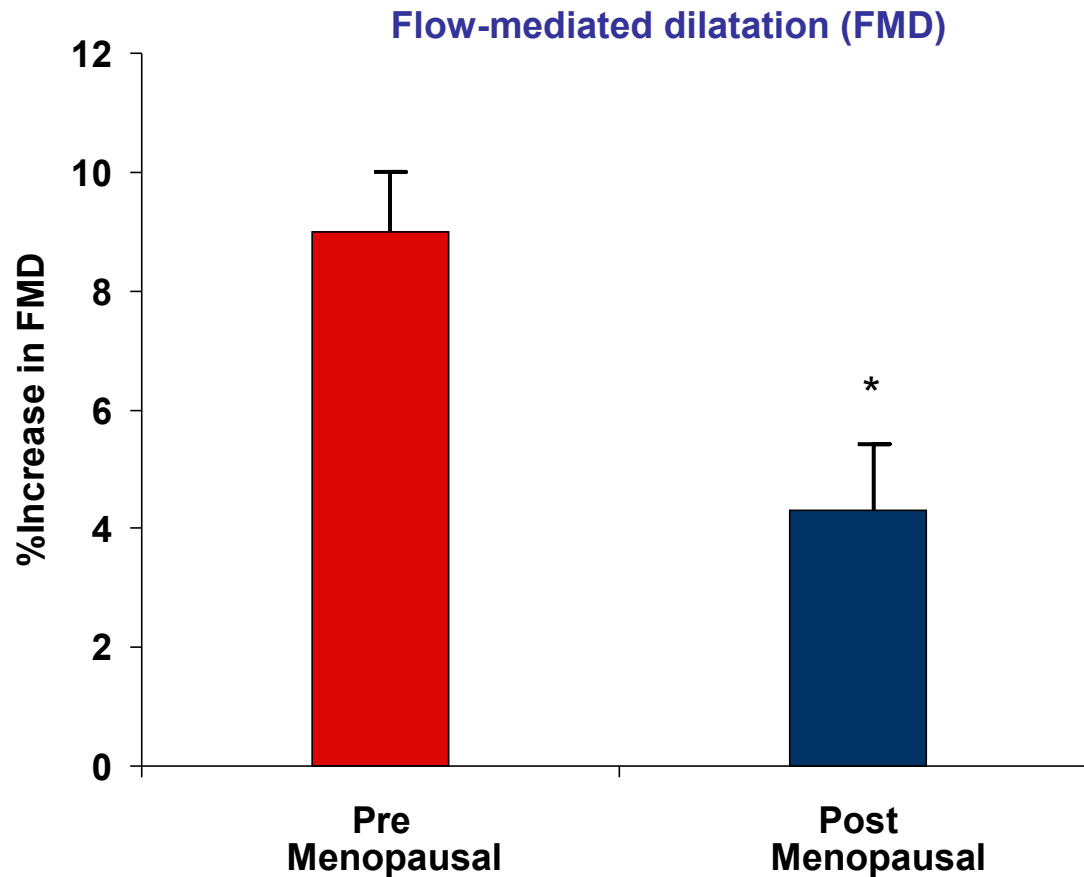


Total exercise time



* $p = 0.01$; ** $p < 0.01$

Endothelial Function



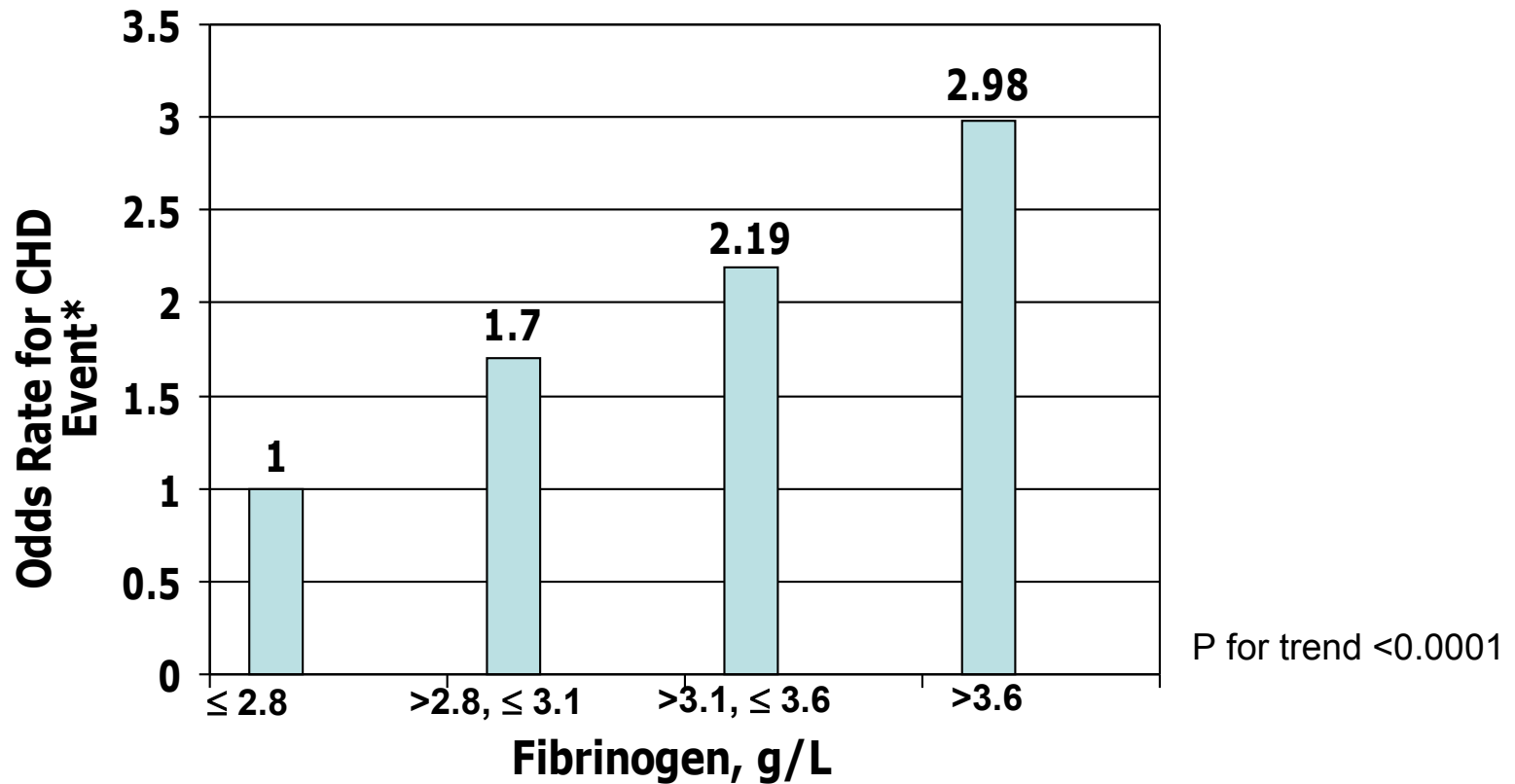
* $p < 0.01$



Menopause and Hemostasis

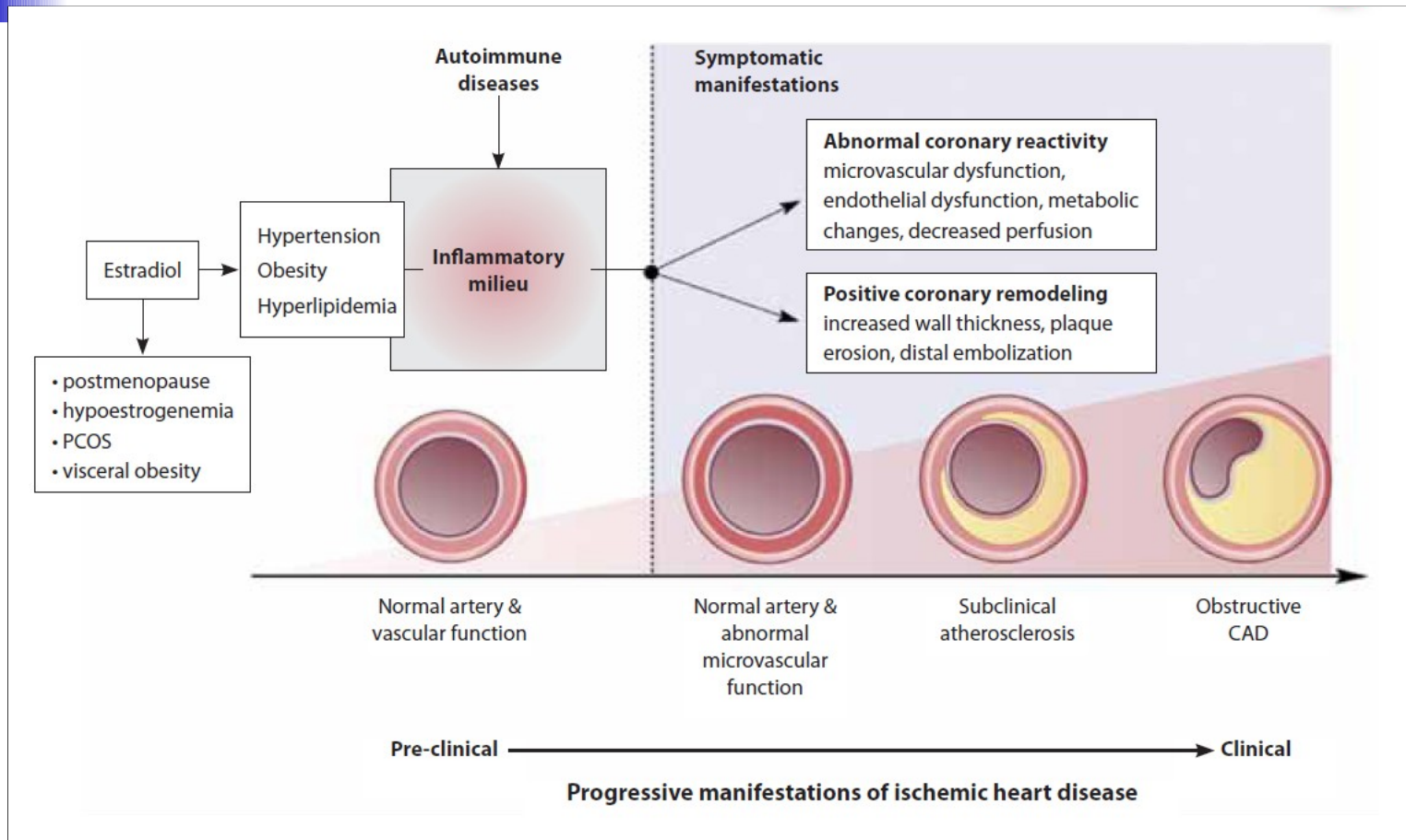
- Increased fibrinogen
- Increased factor VII
- Increased plasminogen activator inhibitor-1 (PAI-1)
- Increased antithrombin
- Increased tissue plasminogen activator (tPA)

Fibrinogen Levels and CHD Risk in Women



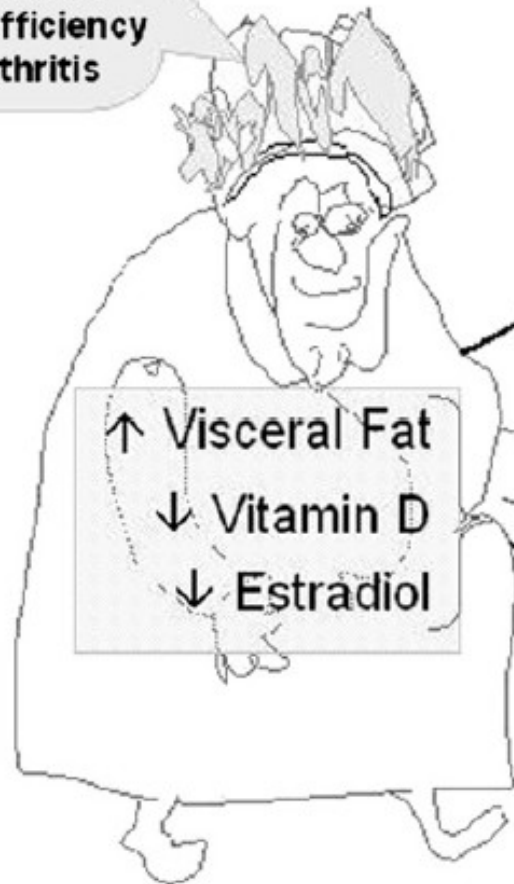
*Adjusted for age, smoking, BMI, systolic blood pressure, total cholesterol, HDL, triglycerides, and educational level

Model of development of ischemic heart disease



Co-morbidity

- Sleep disorders
- Depression
- Stress
- Psychosocial factors
- Vitamin D insufficiency
- Rheumatoid arthritis



↑ Visceral Fat
↓ Vitamin D
↓ Estradiol

↑ FFA
↑ TNF α , IL-6, Leptin, Resistin
↓ Adiponectin

Insulin resistance
Metabolic syndrome
Hypertension
Atherosclerosis

↑ Endothelial dysfunction
↑ Inflammation
↑ Oxidative stress
↑ LDL-C and triglyceride



Conclusions

- During the menopausal transition there is an emergence of the characteristics of the metabolic syndrome (METS) which increase CVR.
- Estrogenic deficiency , lifestyle factors and other prevalent health conditions or co-morbidities might further increase the risk of CVD in menopausal women..