

Cardiovascular disease in women

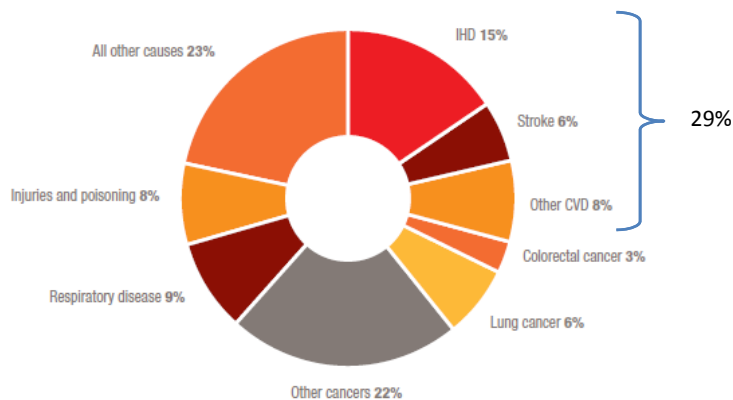
Dr Sonia Davison

MBBS FRACP PhD

Endocrinologist and Clinical Fellow, Jean Hailes for Women's Health
Women's Health Research Program, Monash University

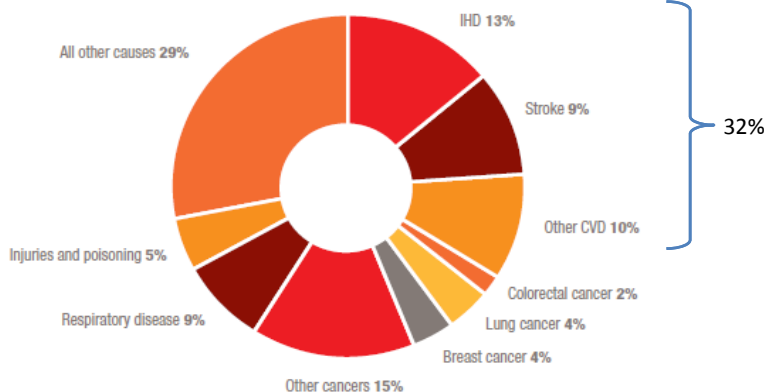


Deaths from major causes Australian males



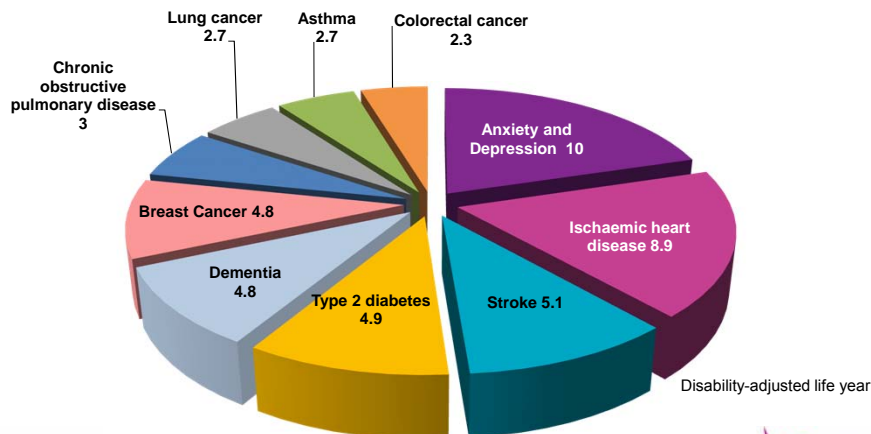
Australian Heart Disease statistics 2014 - National Heart Foundation of Australia

Deaths from major causes Australian females



Australian Heart Disease statistics 2014 - National Heart Foundation of Australia

Burden of disease – Australian women 10 most common diseases



Australian Government 2011

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Cardiovascular disease - cost

- 1992-3: **32%** of all PBS benefits (\$477 million) on CVS medications
vs. 2012-3: **21%** (\$1.8 billion)
- Most prescriptions for primary prevention



Cardiovascular disease mortality

- Cardiovascular disease is the leading cause of death in women, accounting for one third of all deaths globally
- AMI kills 4 times as many women as breast cancer
Mozaffarian et al Circulation 2015;131(4):e29-322
- The mortality rate from coronary artery disease has declined over the last 3 decades, especially in men and women >65 yrs, but not in women <55 yrs
Wilmot et al Circulation 2015;132:997-1002
- Awareness of CVD as the primary cause of mortality in women is rising:
 - 55% of US women in 2012 vs. 30% in 1997
Mosca L et al Circ Cardiovasc Qual Outcomes 2010;3:120-7



Cardiovascular disease mortality - Australia

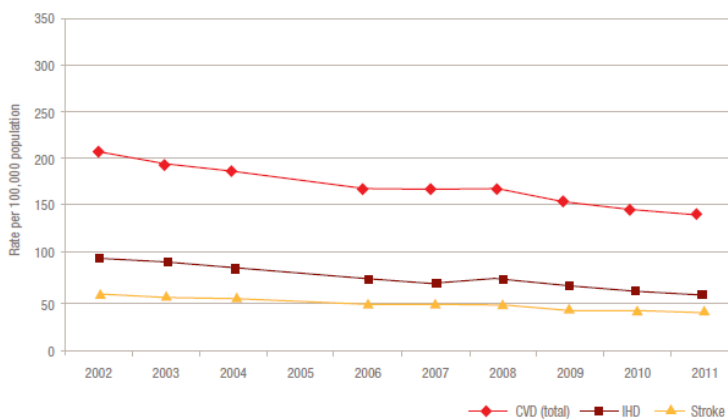
- Mortality rate from heart disease has decreased by 70% since the 1970s in Australia

O'Flaherty M et al Int J Cardiol 2012;158(2):193-8

- Death rates in indigenous Australians from heart disease are 1.5-3 times higher than non-indigenous Australians
- Heart disease death rates in Australia are lower than in Germany / UK / USA but higher than in Japan

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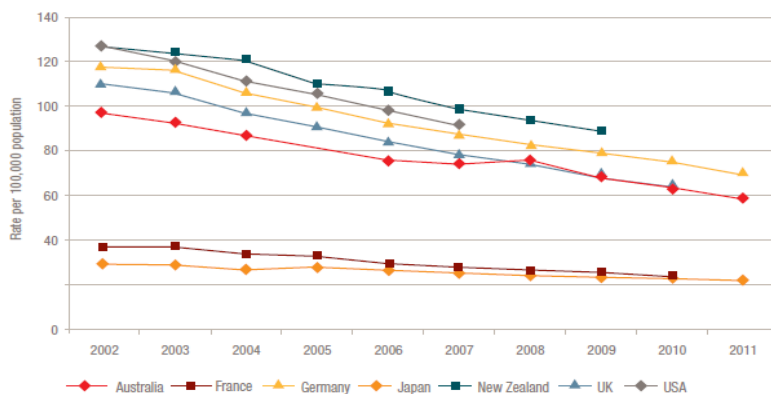
Trends in cardiovascular mortality – Australian women 2002-2011



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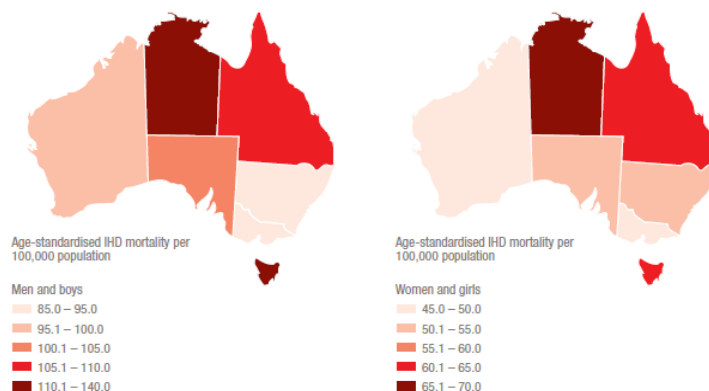
Mortality rates from IHD – global figures



Australian Heart Disease statistics 2014
National Heart Foundation of Australia



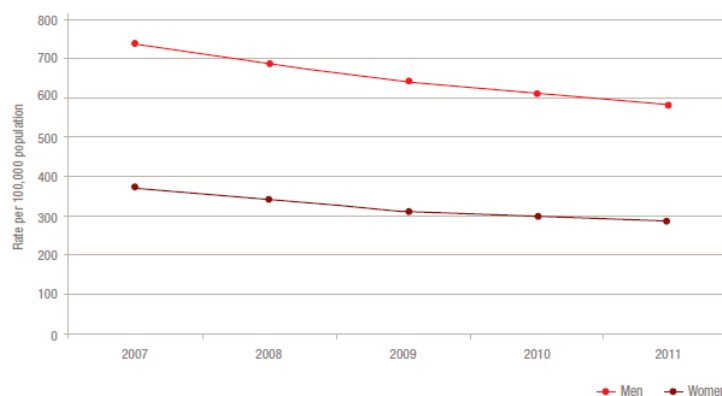
Age-standardised mortality rates for Australians - IHD



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Incidence of AMI - Australia



Australian Heart Disease statistics 2014
National Heart Foundation of Australia

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CVD in women

- Cardiovascular disease develops 7-10 yrs later in women compared to men
- Women have smaller and stiffer hearts and stiffer vasculature

Jacobs AK Circ Cardiovasc Interv 2009;2:69-78

- NHANES: rate of AMI has increased over the last 20 years in women aged 35-54 years compared to a fall in men of the same age
- The pathophysiology of heart disease differs in women and men

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CVD in women

- Women are less likely to receive preventive Rx (aspirin / lipid-lowering Rx / lifestyle advice) compared to men of similar CVD risk

Mosca L et al Circulation 2005;111:499-510

- When medications are prescribed treatment is less likely to achieve optimal results
- Women are 55% less likely to attend cardiac rehabilitation compared to men
- Women have a higher incidence of heart failure after AMI (46% vs. 22% in men)
- Women have less LV systolic dysfunction but more CCF

Jacobs AK Circ Cardiovasc Interv 2009;2:69-78

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Symptoms

- Women with coronary artery disease are more likely to present with atypical symptoms:
 - Shortness of breath, back, neck and abdominal pain, indigestion, nausea or vomiting, palpitations and fatigue

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Presentation with CHD - women

- delay health-care seeking behaviour
 - one study 155.1 minutes from onset of pain to emergency department in women vs. 134.6 minutes in men
- usually older with higher incidence of diabetes / HT / other co-morbidities
- longer time to diagnosis vs. men

Bairey Merz CN et al J Am Coll Cardiol. 2006;7;47(3 Suppl):S21-9



Women – differences in treatment

- Less likely to receive intensive treatment for acute coronary presentations
 - Lawesson SS et al BMJ Open 2012;2:e000726
- Higher prevalence of adverse outcomes after reperfusion treatment (bleeding etc)
 - Jacobs AK Circ Cardiovasc Interv 2009;2:69-78
- Higher rates of cough on ACE inhibitors
- Higher rates of oedema on calcium channel blockers but better systolic BP reduction in women
 - Zanchetti A et al J Hypertens 2006 Nov;24(11):2163-8
- Bleeding more frequent on anticoagulants / antiplatelet agents
- Aspirin more effective for CVA prevention in women vs. men
- In those who discontinue medications after AMI, lower one year survival rates
 - Older women more at risk of discontinuing Rx
 - Ho P et al Arch Intern Med 2006 Sep 25;166(17):1842-7



CVD Pathophysiology - women

- Less obstructive CAD
- Preservation of systolic function
- More cardiac failure
- Functional tests do not always match coronary anatomy
- Twice as likely as men to have 'normal' coronary arteries, but IV US – more intramural plaque vs. men
- More vasospastic disease
- Higher rates of coronary artery dissection



Risk factors in women – Hypertension (HT)

- 1 in 5 Australians has HT (1 in 4 indigenous Australians)
- >50% of Australians >75 yrs have HT
- Higher rates of CCF / CVA in women with HT vs. men
- Link with hot flushes and HT in postmenopausal women Gerber LM et al Menopause 2007;14:308-15
- Women with the same degree of HT have higher CVD mortality vs. men
- 3-fold higher mortality with HT
- HT less well-controlled in women vs. men

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Risk factors in women – treating HT

- Much higher reduction in coronary events by optimal control of BP in women with metabolic syndrome vs. men

NHANES III Am J Cardiol 2003;91:1421

- Less regression of LV hypertrophy in women vs. men

Gerdtz E Hypertension 2008;51(4):1109



Risk factors in women – Type 2 diabetes

- increasing in prevalence
- >5% of Australians have T2DM (and 5% at risk of developing it)
- T2DM is a stronger risk for CVA in women
- In combination with HT:
 - RR for death: **4.57** in women vs. 2.32 in men
 - vs. HT alone: RR for death: **1.89** in women

Hu G et al Diabetologia 2003;46(5):608-17



Risk factors in women – Hyperlipidemia

- 1/3rd of Australians have high cholesterol levels
 - Confers greater risk for coronary artery death in women

Barrett-Connor EL et al JAMA 1991;265:627-31

- Around 4 in 5 Australians with high cholesterol or triglyceride levels are not receiving Rx
- Differential effect on response to statin Rx has been debated (men vs. women)
- Meta-analysis of statin Rx:
for each 1mmol/L reduction in LDL:
 - 21% lower risk for major cardiovascular events
 - 9% reduction in risk of death
 - 12 CVD events avoided in men; 9 events avoided in women for every 1000 Rx over 5yrs

Lancet 2015;385(9976);1397



Risk factors in women – weight excess

- 55% of Australian women are overweight or obese (vs. >66% men)
- Indigenous Australians have more than double these rates
- The impact of obesity on the development of CAD appears to be greater in women vs. men
 - Framingham study ↑ risk CAD 64% in women vs. 46% in men

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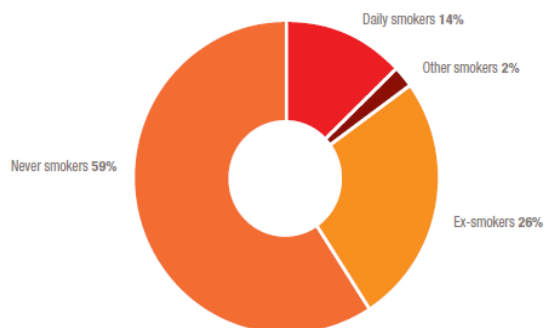
Risk factors in women – cigarette smoking

- 14% of women (vs. 18% of men) in Australia are daily smokers
- Indigenous Australians have more than double these rates
- In women >45 yrs cigarette smoking confers a 25% increased risk for CAD vs. men

Huxley RR et al Lancet 2011 Oct 8;378(9799):1297-305

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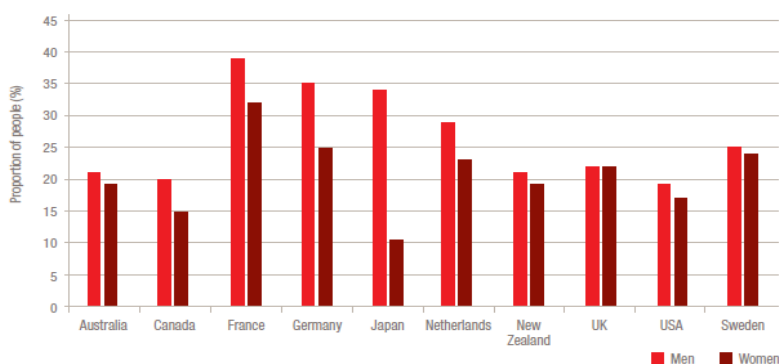
Prevalence of smoking in Australian women



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Prevalence of smoking - Global



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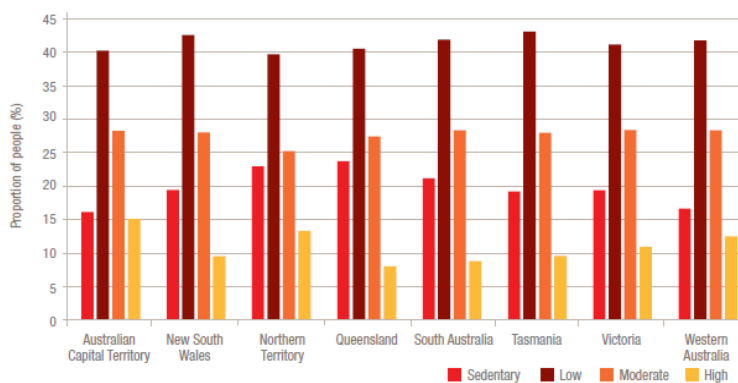
Risk factors in women – exercise

- 58% of women of Australians are sedentary or have low levels of activity
- Indigenous Australians have more than double these rates
- The prevalence of no exercise / low levels of exercise is higher in women vs. men
- Recommended levels for women = 150mins / week of moderate exercise

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Physical activity in women 2011-12



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Risk factors in women – diet

- Fewer than 10% of Australians meet NH&MRC targets for vegetable consumption
- Rates of risky alcohol intake highest in 55-64 yr age group
- 10% of women consume alcohol above safe range

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Risk factors in women - menopause

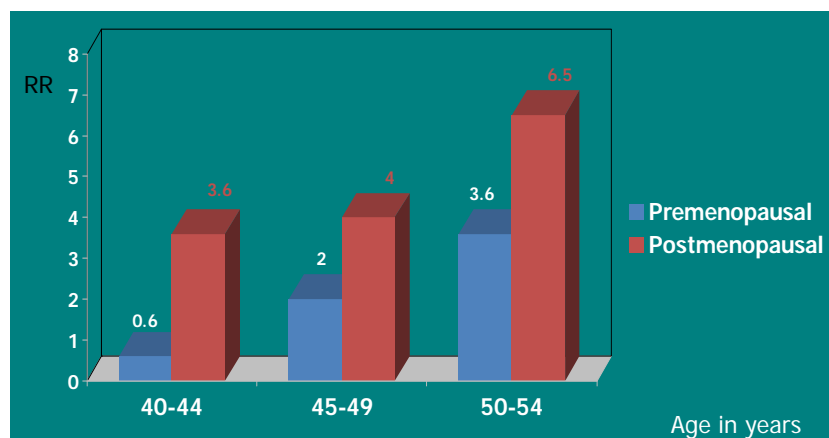
- Increased risk of cardiovascular disease after menopause
- Research has focused on the role of oestrogen in CVD
- Potential effects of lowered oestradiol:
 - endothelial dysfunction
 - loss of arterial compliance
 - microvasculature dysfunction

Burke AP et al Circulation 2003;108



Incidence of cardiovascular disease by age, sex and menopausal status

Rate 1000 per year



Kannel W et al Ann Int Med 1976;85:447



MHT and cardiovascular disease

- Observational studies suggested that MHT conferred a cardiovascular benefit
 - selection bias (healthier women may opt to take MHT)

Grady D et al Ann Intern Med. 1992; 117: 1016–1037

Grodstein F et al. Ann Intern Med. 2000; 133: 933–941

- Subsequent studies designed to explore the relationship between MHT and CVD
 - Placebo-controlled design



HERS study

- 2763 PM women with heart disease
- Average 67 yrs
- CEE +/- MPA vs. placebo
- Favourable effects on LDL and HDL cholesterol
- 52% increase in CVD events in the first year
- No difference between groups at study completion (4 years)
- Increase in VTE

Hulley S et al JAMA 1998;280(7):605-13



WHI study

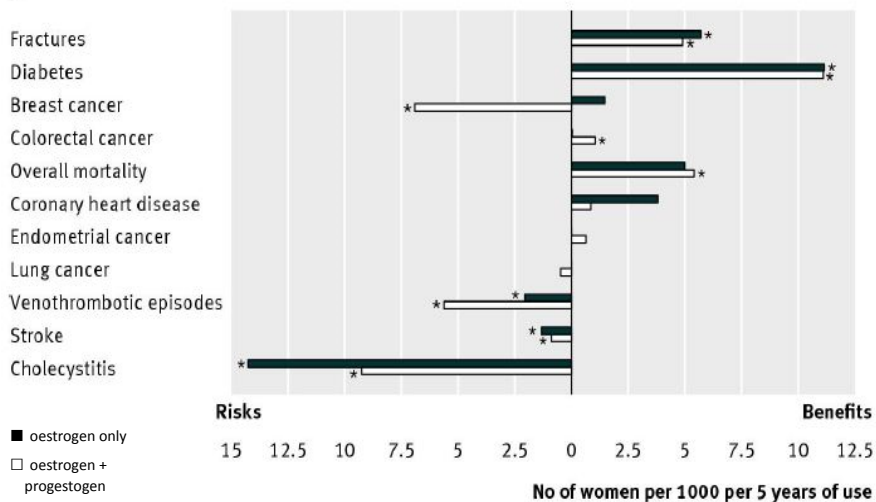
- 27,000 PM women without heart disease
- Average 63 yrs
- CEE +/- MPA vs. placebo
- MHT group:
 - 29% increase in CHD events soon after randomisation (increase of 7 events per 10,000 women yrs)
 - 41% increase in CVA in 1st 2 yrs (increase of 8 events per 10,000 women yrs)
 - increase in VTE

Roussow J et al JAMA 2002 Jul 17;288(3):321-33

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Risks and benefits of MHT between 50-59 yrs or <10 yr after menopause

B

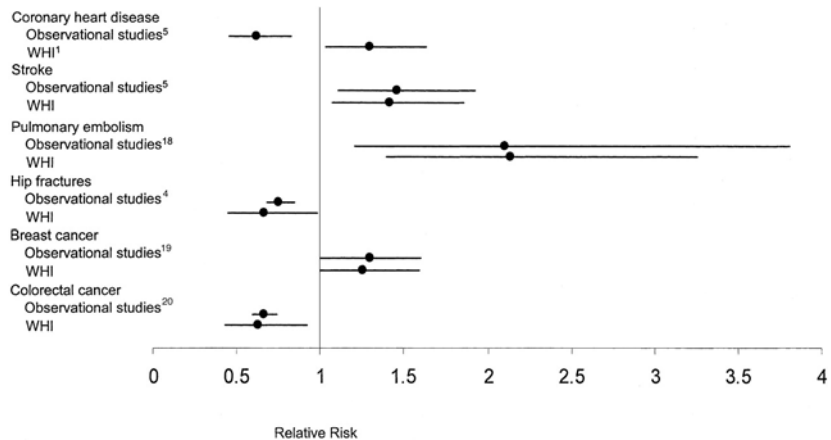


©2010 by Endocrine Society

Santen R J et al. JCEM 2010;95:s1-s66

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Relation between MHT and various clinical end points in observational studies and in the WHI.

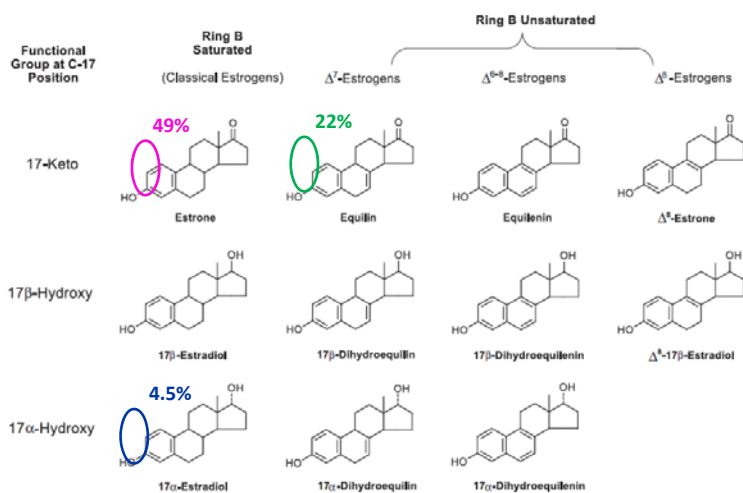


Karin B. Michels, and JoAnn E. Manson *Circulation*. 2003;107:1830-1833



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Conjugated equine oestrogens = CEE



Bhavnani V, Stanczyk F J *Steroid Molec Biol* 2014

Progestogens in MHT

A. Related to progesterone

– Progesterone

- Micronised progesterone –oral / vaginal
- Vaginal - gel

– Pregnane derivatives

- Acetylated
- Medroxy progesterone acetate - oral
- Cyproterone acetate - oral
- Non-acetylated
- Dydrogesterone - oral

B. Related to testosterone

– 19-nortestosterone derivatives

- Norethindrone / Norethisterone acetate
- Oral / transdermal

- Levonorgestrel
- Intrauterine system

– Spironolactone derivatives

- Drospirenone
- Oral

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ELITE

- Early (<6yrs) vs. late (≥ 10 yrs) PM \ddagger ; 5 yr study

Primary outcome measure:

- rate of change of carotid intimal medial thickness

Treatment:

Oral 17B-oestradiol 1mg vs. Placebo

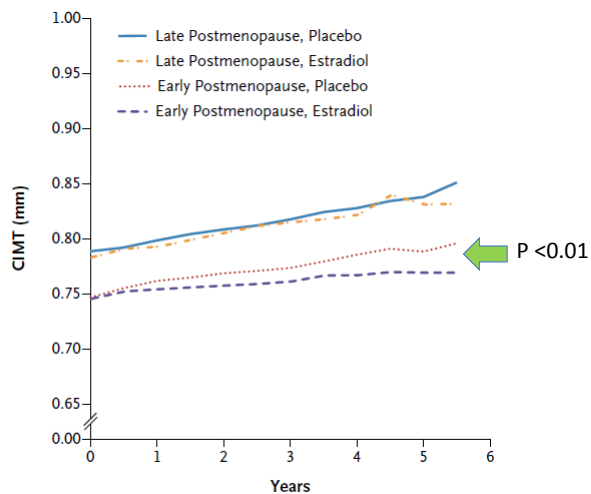
(+/-vaginal micronised progesterone gel 4% (45mg) (or a placebo gel) ten days per month)

- 643 women

Hodis HN et al N Engl J Med. 2016 Mar 31;374(13):1221-31

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ELITE - Carotid artery intimal thickness



Hodis HN et al N Engl J Med. 2016 Mar 31;374(13):1221-31



CLIMACTERIC 2015;18:437-438

Editorial

Hormone therapy and cardiovascular disease – are we back to the beginning?

Anna Fenton and Nick Panay

EDITORS-IN-CHIEF



CVD in women: Health practitioner role

- Awareness of ↑ CVD risk around mid-life
- Family history
- Smoking
- Alcohol use
- Diet
- Exercise
- Menopausal symptoms



CVD in women: Health practitioner role

- Weight / waist circumference
- Screening
 - BP / blood glucose / lipids / ECG
- Australian Absolute Cardiovascular Risk Calculator <http://www.cvdcheck.org.au/>
- Education
- Optimise BP / lipids / blood glucose
 - Lifestyle / medication
- Referral
 - Functional testing (IHD)
 - Resources
 - Cardiological review



Australian absolute cardiovascular disease risk calculator

Enter patient information below:

PRINT

Sex Male Female
 Age years
 Systolic blood pressure mmHg
 Smoking status Yes No
 Total cholesterol mmol/L
 HDL cholesterol mmol/L
 Diabetes Yes No
 ECG LVH Yes No Unknown



Your heart and stroke risk score is **19%**

This means you are at high risk of getting cardiovascular disease in the next 5 years.

[Click here](#) if you would like to have a look at the information on this website that explains what your risk score means.

The next step is to talk to your doctor about what steps you can take to lower your chance of getting cardiovascular disease.

Please note: the absolute risk calculator score is only a guide to your heart and stroke risk score. Print out this page and take it to your doctor for further information on your personal risk.

[View guidelines and resources](#)



strokefoundation

Resources for consumers – Jean Hailes

[Home](#) / [Health A-Z](#) / [Cardiovascular health](#)

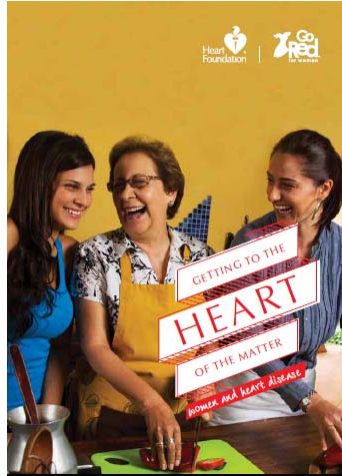
CARDIOVASCULAR HEALTH
 Overview
[About cardiovascular disease](#)
[Risks & causes](#)
[Symptoms of heart attack & stroke in women](#)
[Management & treatment](#)
[Mental health & emotions](#)
[Healthy living](#)

Cardiovascular health
 What is cardiovascular disease?

<http://jeanhailes.org.au/health-a-z/cardiovascular-health>



Resources for consumers – Heart Foundation



https://www.heartfoundation.org.au/images/uploads/main/Programs/nsw/Heart_of_the_Matter_2015.pdf

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