

  
**Premature menopause**

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**Menopause**

- = the last natural menstrual period
  - depletion of oocyte (egg) reserve
- Median 51-52 years
- Normal 45-55 years
- Early menopause
  - <45 years (5% of women)
- Premature menopause
  - <40 years




**Premature menopause**

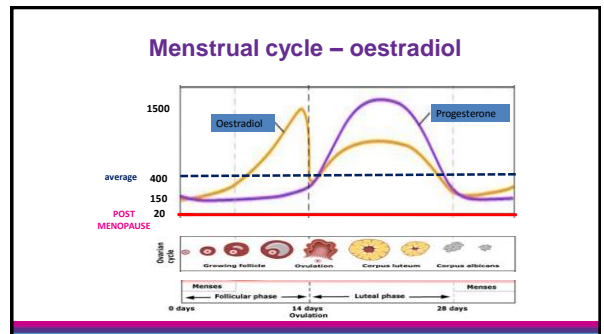
- Prevalence ~1%

Higher incidence:

- Smoking
- Nulliparity
- Hysterectomy
- HIV infection
- Illicit drug use
- Adverse life events

Davis S et al. Nature Reviews Disease Primers 2015;1-19






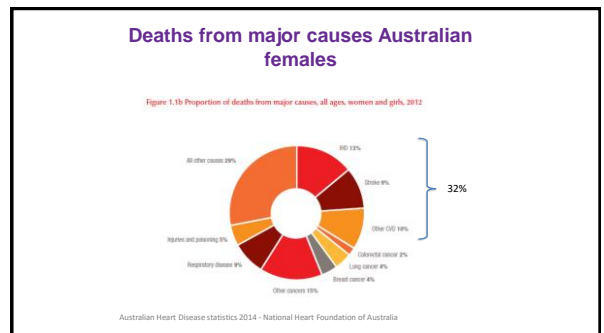
**Premature menopause**

Increased risks of:

- Cardiovascular disease
  - 40% increase in risk
- Osteoporosis and fracture
  - 2-3 fold increase in risk
- Cognitive decline / dementia
  - 2 fold increase in risk
- Type 2 DM
- Parkinson's disease
- Glaucoma

Shuster L et al. Menopause Int. 2008;14:111-6  
Parker W et al. Obstet Gynaecol 2013;121:709-16





## Premature menopause

### CAUSES:

- **Genetic/cytogenetic**
  - Fragile X
  - Turner syndrome
- **Enzymatic defects**
- **Immune disturbances**
- **Defects in gonadotropin structure or actions**
- **Physical insults**
  - Ionizing radiation - pelvic
  - Chemotherapy
    - older age / greater cumulative dose / cyclophosphamide
  - Viral infection
  - Cigarette smoking
  - Bilateral oophorectomy / gynaecological surgery
- **Idiopathic**

## Primary ovarian insufficiency - POI

- Previously called Premature Ovarian Failure (POF)
- 90% - no cause
- Genetic and autoimmune links
  - Fragile X carriers
  - Turner syndrome
- At higher risk of developing autoimmune conditions:
  - Hypothyroidism (1 in 4 women)
  - Adrenal insufficiency or type 1 DM (3%)
  - Pernicious anaemia
  - Myasthenia gravis
  - Connective tissue disorders
  - Hypoparathyroidism

## Primary ovarian insufficiency - POI

- Intermittent ovarian function may occur in ~50%
  - Erratic menstrual cycles
  - Spontaneous conception in 5-10% of women
- Higher incidence of anxiety and depression, low self-esteem, isolation

Schmitt P et al JCEM 2011;96:E275-87  
Schmitt P et al JAMA 2006;295:1374-6

## Premature menopause – key issues

- Diagnosis
- Education
- Symptom management
- Fertility management
- Psychological support
- Prevention
  - Cardiovascular disease
  - Osteoporosis
  - Cognitive decline

## Premature menopause - diagnosis

- FSH >40 IU/L on 2 occasions at least 1 month apart following 4-6 months of amenorrhoea (not on hormone therapy / OCP)
- Exclude secondary causes of amenorrhoea
  - Hypothalamic amenorrhoea
    - High levels of exercise / low body weight or BMI / low calorie or fat-restricted diet / Type A personality / low FSH and LH levels / low oestradiol levels
  - Hypothyroidism
  - Pregnancy
  - Polycystic ovary syndrome

## Investigations

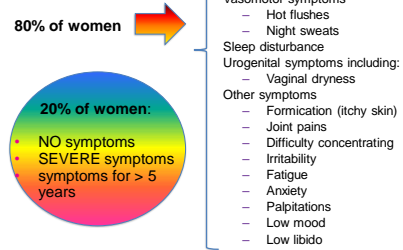
- Oestradiol / FSH / LH
- Prolactin
- TSH
- Testosterone / SHBG / calculated free testosterone
- DHEAS
- Cortisol
- Thyroid antibodies
- FBG
- Vitamin B12
- +/- β-hCG
- Gynaecological ultrasound

### Premature menopause - diagnosis

- AMH – issues with assay sensitivity; not necessary for diagnosis
- Diagnosis can take time and may be associated with considerable patient anxiety
- Referral to specialist / tertiary referral centre with expertise – Endocrinologist / Gynaecologist / Menopause Clinic
  - Fragile X / chromosomal analysis
  - DXA
  - Adrenal antibodies



### Menopause symptoms



### Treatment – Premature menopause

- Depends on the cause
  - Unless contraindicated, some form of oestrogen and progestogen replacement until around the age of natural menopause
    - 45-50yrs
  - Either combined oral contraceptive pill (COCP) or MHT (HRT)
    - COCP may be more acceptable; in line with peers and offer contraception if pregnancy not desired (in POI)
    - Oestrogen and progestogen if intact uterus
    - Oestrogen only after hysterectomy
  - If MHT higher doses recommended
    - Symptom relief
    - Bone protection
- <https://www.menopause.org.au/for-women/information-sheets/426-ams-guide-to-equivalent-hrt-mht-doses>
- Vaginal oestrogen / moisturisers / lubricants
  - ?Testosterone?



### Benefits of hormone treatment

- Symptom relief
- Reduced risk of cognitive decline
- Reduction in fracture risk
- Reduction in CVD risk
  - presumed from studies of natural menopause



### Hormone Replacement Therapy Versus the Combined Oral Contraceptive Pill in Premature Ovarian Failure: A Randomized Controlled Trial of the Effects on Bone Mineral Density.

- 30 ♀ spontaneous POF, 18-44 yrs
- Oestradiol 2mg + NETA 1mg (oral) vs. Microgynon 30 OCP vs. no Rx
  - 2yrs

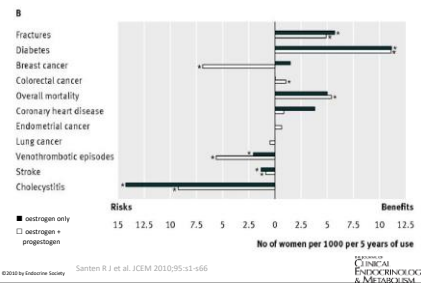
Groups	Lumbar spine BMD	Femoral neck BMD	Bone turnover markers: CTx / PINP
HRT	↑	↔	↓
OCP	↔	↔	↓
No Rx	↓	↓	↑

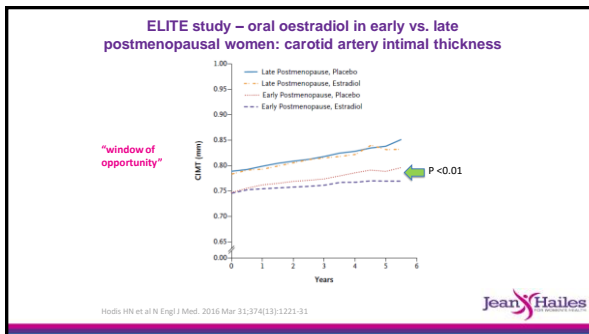
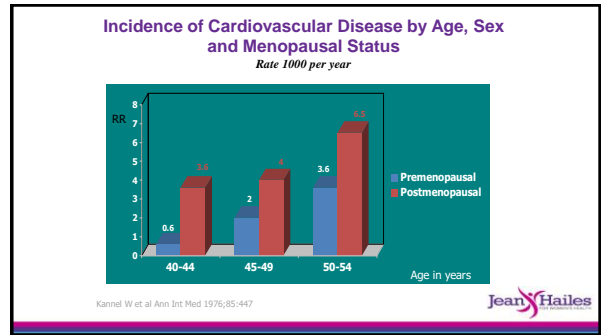
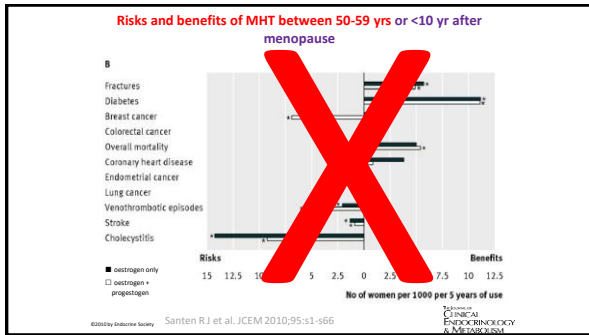
\*All P<0.05 for differences

Cartwright B et al. JCEM 2016;101(9):3497-505



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





- ### Management - other
- Psychological support
  - Fertility counselling
  - Sexual counselling
  - CVD and osteoporosis risk reduction:
    - Avoid smoking and alcohol excess / encourage weight bearing exercise / adequate calcium in diet / vitamin D
  - General screening
    - Lipids / BP / FBG / Pap smear / breast exam
  - Osteoporosis medications
    - If osteoporosis / fracture and hormone therapy contraindicated
  - Non-hormonal treatments for flushes / sweats
    - If hormone therapy contraindicated
    - Venlafaxine / SSRIs / Clonidine / Gabapentin
    - <https://www.menopause.org.au/for-women/information-sheets/35-nonhormonal-treatments-for-menopausal-symptoms>

- ### Take home messages
- Premature menopause is not common but is associated with increased risks for cardiovascular disease, osteoporosis and cognitive decline.
  - Unless contraindicated women should be offered some form of oestrogen +/- progestogen (MHT/HRT or COCP) until at least the average age of menopause; ~50yrs.
  - Women with premature menopause should be assessed by someone with expertise in this area.
  - Psychological support and fertility management are important considerations in addition to the usual management of the postmenopausal woman.

<https://jeanhailes.org.au/health-a-z/menopause/premature-early-menopause>

Source: [http://jeanhailes.org.au/contents/documents/Resources/Tools/Menopause\\_tool.pdf](http://jeanhailes.org.au/contents/documents/Resources/Tools/Menopause_tool.pdf)

<https://www.menopause.org.au/for-women/information-sheets/1030-spontaneous-premature-ovarian-insufficiency>

The screenshot shows the website's navigation menu with options like Home, About Us, For Women, For Men, For Health Professionals, and For Researchers. The main content area is titled 'Spontaneous Premature Ovarian Insufficiency' and includes a sub-section for 'Definitions and Epidemiology'. The text explains that menopause occurring spontaneously is more common than 40 years of age, affecting approximately 1% of women. It also notes that the condition is associated with an increased risk of osteoporosis, cardiovascular disease, and cognitive decline. The page includes a search bar, social media links for Facebook, Twitter, and LinkedIn, and a 'Members Login' button.

The poster features a night view of the Sydney Opera House and the Sydney Harbour Bridge. The text on the poster reads: 'Menopause: Exploring the evidence', '21st Annual Congress', 'Australasian Menopause Society', and 'Softel Sydney Wentworth • 13 - 15 October 2017'. There is a small 'Find an AMS doctor near you' button in the top right corner.

**Jean Hailes**  
FOR WOMEN'S HEALTH

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