HRT: Unpicking the evidence
Do the benefits outweigh the risks?

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Case history – Mrs Smith
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- 49-year-old woman
- Irregular periods
- Flushes and night sweats
- History of migraine which is worsening
- DVT after long flight 10 years ago
- Obese
- FSH 9/12 ago was normal

What would you do?

A. Advise her to lose weight
B. Repeat her FSH blood test
C. Inform her that she can not take HRT due to her weight
D. Inform her that she can not take HRT due to her VTE risk
E. Prescribe HRT to her with confidence
What is the menopause?

- Meno – pause
  - Natural / Induced
- Perimenopause
- Average age 51 years
- Range 45-55 years
- Early menopause
- Premature ovarian insufficiency (POI)
Effect of oestrogen on body

- Physical shape
- Breasts
- Uterus / vagina / urethra
- Collagen
- Cardiovascular system
- Emotions
- Brain
- Bones

History of the menopause

- 1900
  - Age menopause 57 years
  - Life expectancy 59 years
History of the menopause

2017
- Age menopause 51 years
- Life expectancy 82 years
- 30% of life postmenopausal

Symptoms of the menopause

- Hot flushes
- Night sweats
- Mood swings
- Tiredness
- Lack of libido
- Poor sleep
- Poor concentration
- Weight / body “shape”
Symptoms of the menopause

- Heavy periods
- Worsening PMS
- Joint pains
- Hair and skin changes
- Depression, anxiety and irritability
- Poor memory
- Headaches / worsening migraine
- Palpitations
- “Brain fog”

Local symptoms

- Vaginal irritation
- Vaginal dryness
- Soreness

- Increased frequency
- Increased urgency
- Symptoms of urine infections
Risks to health with menopause

- Bone loss
- Osteoporosis
- Raised cholesterol
- Central obesity
- Cardiovascular disease
- Diabetes mellitus
- ?Dementia

Menopause as “an opportunity”

- Medical intervention at this point of life offers women years of benefits from preventive health care
Hormone replacement therapy (HRT)

HRT and younger women

- Women under 45 years need HRT
- Especially those with POI
- NO increased risk
- Benefits
Who takes HRT?

- 75% women say they don’t know enough about HRT to make an informed choice
- Around a third of women think their symptoms are not bad enough for HRT
- Doctors and women have been worried
- 2000 around 26% took HRT
- 2016 around 10% women take HRT

Benefits of HRT

- Improves symptoms!
HRT and osteoporosis

- HRT:
  - Increases bone density
  - Prevents bone loss after the menopause
  - Reduces fractures
  - More effective than other treatments
- Maximum prevention of fractures start HRT within 5 years
- Even low dose HRT is bone protective

HRT and osteoporosis

- Oestrogens are the most effective way of increasing BMD and preventing osteoporotic fractures
- Risk of any fragility fracture is significantly lower for women taking HRT
- NICE recommends women should be informed that their risk of fragility fracture is decreased while taking HRT and that this benefit:
  - Is maintained during treatment but decreases once treatment stops
  - May continue for longer in women who take HRT for longer
HRT and heart disease

- Risk of heart disease reduced in those under 60 years
- HRT does not increase CVD in women under 60 years
- HRT does not increase risk of dying from CVD
- Reduction of cholesterol
- Arteries
- Timing of HRT very important
- Having CVD risk factors is not a contraindication

HRT: Impact on cardiovascular disease in post-menopausal women

- 19 trials
- 40,410 women
- HRT all age cohorts
  - no protection for CVD / mortality
- HRT <10yrs postmenopause
  - lower mortality RR 0.70
  - lower CHD RR 0.52

Boardman et al Cochrane Database Syst Rev 2015
Women’s Health Initiative (WHI) Study

- Assess long term risks and benefits of HRT
- Average age 63 years
- High dose HRT
- Older progestogen (MPA)
- Results leaked to press early
Absolute risk of events by age

(a) conjugated equine estrogens (CEE) + medroxyprogesterone (MPA) (b) unopposed CEE

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Breast Cancer Now Generations Study

- 39,000 women
- Oestrogen only HRT makes no difference
- Current use of **combined** HRT increases risk of breast cancer
- Longer use increases risk further
- 6 years use 2.7 x risk
- 15 years use 3.3 x risk
- Risk returns to normal levels within 2 years of discontinuation

Breast cancer

- Breast cancer is common
- Increased risk of breast cancer with:
  - Increasing age
  - Family history
  - Obesity
  - Alcohol
  - Reduced exercise
HRT and breast cancer

- Baseline risk of breast cancer for women around menopausal age varies from one woman to another according to the presence of underlying risk factors
- Risk depends on preparation of HRT taken
- HRT with oestrogen alone is associated with little or no change in risk of breast cancer
HRT and breast cancer

- **No** increased risk of death from breast cancer
- HRT with oestrogen and progestogen can be associated with an increase in risk of breast cancer
- Less advanced cancers
- Any increased risk is related to treatment duration and is reversed after stopping HRT

Breast cancer risk: The type of progestogen matters

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<thead>
<tr>
<th>E3N French Cohort Study</th>
<th>Finnish Cohort Study</th>
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<tbody>
<tr>
<td>Baseline risk without HRT</td>
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<tr>
<td>Estrogen/progestosterone</td>
<td>Estradiol/dydrogesterone</td>
</tr>
<tr>
<td>(0.83–1.22)</td>
<td>(0.49–2.22)</td>
</tr>
<tr>
<td>Estradiol/dydrogesterone</td>
<td>Estradiol/MPA</td>
</tr>
<tr>
<td>(0.94–1.43)</td>
<td>(1.49–1.79)</td>
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<tr>
<td>Estradiol/other progestogens</td>
<td>Estradiol/NETA</td>
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<tr>
<td>1.16 (1.50–1.91)</td>
<td>1.64 (1.88–2.18)</td>
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<tr>
<td>Estradiol/other progestogens</td>
<td>Estradiol/other progestogens</td>
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<tr>
<td>1.00</td>
<td>2.03 (1.76–2.04)</td>
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<tr>
<td>1.13 (1.49–1.79)</td>
<td>2.07 (1.76–2.04)</td>
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Breast cancer risk was lower with natural progesterone / dydrogesterone

Hormone replacement therapy - HRT

- Women need to know about the available options and their risks and benefits, and be empowered to become part of the decision making process
- When discussing menopause with women, it is paramount that they receive individualised care

Hormone replacement therapy - HRT

- Cyclical HRT
- Continuous combined HRT
  - Not had a period for a year
  - Taken cyclical HRT for one year
- The benefits of HRT outweigh the risks for the majority of women who start HRT under the age of 60 years
Type of HRT

- Transdermal oestrogen is not associated with VTE risk
- Use for patients:
  - Who are obese
  - With diabetes
  - With history of migraine
  - With history of gallbladder / liver problems
  - With history of DVT

Prescribing HRT

- HRT benefits and risks vary by dosage, regimen and timing of initiation
- Explain vaginal bleeding may occur in first 3 -6/12
- The initiating dose should be judged according to the severity of symptoms, the age of the woman and also her individual circumstances
- Younger women are more likely to require higher levels of oestrogen compared with older women
Case history – Mrs Smith

Robert Langer, WHI Investigator

"Let’s get past the misinformation and hysteria of the WHI and stop denying the benefits of hormone replacement therapy"
“Take Home” Messages

- Diagnosis of menopause is clinical
- Symptoms can be very debilitating
- HRT is safe for most women under 60 years
- No maximum length of time for HRT
- Transdermal HRT lowest risk of VTE / stroke
- No increased breast cancer risk with oestrogen only
- Women under 45 need to have HRT