Myth: One size does fit all

Onset of menopause and symptoms vary

Average age of menopause is 51 y in the UK

Over the age of 45

• Perimenopause: Irregular periods and *symptoms that can start 5-8 years before periods stop*
• Menopause: No periods for 12 months
• No need for laboratory confirmation

• Bloods will not predict menopause
• Women should seek treatment if symptomatic
Premature Ovarian Insufficiency (POI)

- <40 years with no periods or less frequent periods (1%)
- Blood test can be helpful: High FSH hormone x2 will be helpful
- Exclude other medical conditions
Treatment of POI with HRT

• **Regardless of symptoms** treatment should be offered
• Increased risk of mortality (80% risk of heart attack and 50% of fractures - 65% osteopenia)
• Treatment with contraceptive pill or HRT
• **No greater risk** of breast cancer until the average age of menopause
• Benefits outweigh any risks until the average age of menopause
Myth: It is just hot flushes

Other Menopausal Symptoms - Only 1 in 2 women seek treatment

- Hot flushes: 62%
- Sleeplessness: 20%
- Mood swings: 17%
- Irritability: 13%
- Depression: 13%
- Headaches/migraines: 9%
- Dyspareunia: 8%
- Reduced sex drive: 6%
- Urine incontinence: 4%
- Osteoporosis: 3%
- Other: 17%
- None (of this): 7%

Genanazzani et al, Gyn Endocrinology 2006
Myth: Hot flushes will go away soon
Hot flushes affect 70% of women and can last for over 11 years

Prevalence of Hot flushes

Duration of Hot flushes

Hunter et al, BJOG 2012
Avis et al, JAMA Intern Med 2015
HRT: the most effective treatment against hot flushes and night sweats

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number of trials</th>
<th>Number of hot flashes per day (mean difference 95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oestrogen</td>
<td>6</td>
<td>-3.2 (-5.1 to -1.5)</td>
</tr>
<tr>
<td>Transdermal oestradiol</td>
<td>6</td>
<td>-2.6 (-3.3 to -1.9)</td>
</tr>
<tr>
<td>Oral oestrogen</td>
<td>9</td>
<td>-2.8 (-3.8 to -1.8)</td>
</tr>
<tr>
<td>Oestrogen + progestagen</td>
<td>3</td>
<td>-2.1 (-2.9 to -1.2)</td>
</tr>
<tr>
<td>Oestrogen alone</td>
<td>6</td>
<td>-2.05 (-2.80 to -1.30)</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>2</td>
<td>-1.13 (-1.70 to -0.57)</td>
</tr>
<tr>
<td>SSRI/SNRI antidepressants</td>
<td>7</td>
<td>-1.66 (-2.43 to -0.89)</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>2</td>
<td>-1.37 (-3.03 to 0.29)</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>2</td>
<td>-0.49 (-2.40 to 1.41)</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>2</td>
<td>-0.20 (-1.45 to 1.05)</td>
</tr>
<tr>
<td>Citalopram</td>
<td>1</td>
<td>-0.95 (-1.44 to 0.47)</td>
</tr>
<tr>
<td>Clonidine</td>
<td>4</td>
<td>-1.15 (-2.33 to 0.03)</td>
</tr>
<tr>
<td>Soy-extract isoflavones</td>
<td>5</td>
<td>-0.44 (-1.47 to 0.58)</td>
</tr>
<tr>
<td>Red-clover isoflavones</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

Takahashi et al, Medical Clinics 2015
What is Hormone Replacement Therapy (HRT)

- Oestrogen
- Progestogen – either a synthetic version of the hormone progesterone, or a version called micronised progesterone (sometimes called body identical, or natural)

- Combined HRT- cyclical (peri-menopause/ within a year) or continuous
- Oestrogen only- when womb has been removed (hysterectomy)
Types of HRT

- Individualized approach
- Transdermal lower risk of blood clots
HRT CAN DOUBLE RISK OF BREAST CANCER

WOMEN today face a stark warning over links between HRT and breast cancer.

A massive British study of a million women found the risk of cancer can be twice as high for those taking the most common form of HRT for ten years. Government experts are now issuing an alert to GPs and hospital consultants over the treatment, which is being blamed for 20,000 cancer cases in the past ten years. HRT taken by 1.5 million women in Britain to relieve symptoms of the menopause was already at the centre of growing concern over cancer, heart disease and stroke.

By Beezy Marsh
Health Correspondent

Lancet today provides conclusive evidence.

Turn to Page 4, Col. 1
HRT: does not increase breast cancer mortality

- No risk when Oestrogen only or combined with micro-ionized progesterone
- Possible small risk of Breast Cancer over the age of 50 years when combined and when over 5 years
- No greater risk of Breast cancer mortality
- Risk is regressed to background after 5 years of discontinuation

5 year HRT is safer than drinking 2 units/ day or being obese

<table>
<thead>
<tr>
<th>Case Type</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 cases of breast cancer diagnosed in the UK general population</td>
<td></td>
</tr>
<tr>
<td>An additional four cases in women on combined hormone replacement therapy (HRT)</td>
<td></td>
</tr>
<tr>
<td>Four fewer cases in women on oestrogen only Hormone Replacement Therapy (HRT)</td>
<td></td>
</tr>
<tr>
<td>An additional four cases in women on combined hormonal contraceptives (the pill)</td>
<td></td>
</tr>
<tr>
<td>An additional five cases in women who drink 2 or more units of alcohol per day</td>
<td></td>
</tr>
<tr>
<td>Three additional cases in women who are current smokers</td>
<td></td>
</tr>
<tr>
<td>An additional 24 cases in women who are overweight or obese (BMI equal or greater than 30)</td>
<td></td>
</tr>
<tr>
<td>Seven fewer cases in women who take at least 2½ hours moderate exercise per week</td>
<td></td>
</tr>
</tbody>
</table>
Transdermal HRT does not increase the risk of clots
This is irrespective the the dose

<table>
<thead>
<tr>
<th>Different types of HRT</th>
<th>Odds ratio (95% CI)</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oestrogen only oral HRT</td>
<td>1.49 (1.39 to 1.60)*</td>
<td>1.27 (1.16 to 1.39)*</td>
</tr>
<tr>
<td>Conjugated equine oestrogen</td>
<td>2.10 (1.92 to 2.31)*</td>
<td>1.73 (1.57 to 1.91)*</td>
</tr>
<tr>
<td>Norprogesterone</td>
<td>1.44 (1.09 to 1.89)*</td>
<td>1.18 (0.98 to 1.42)</td>
</tr>
<tr>
<td>Estradiol</td>
<td>1.68 (1.57 to 1.80)*</td>
<td>1.42 (1.00 to 2.03)</td>
</tr>
<tr>
<td>Combined oral HRT</td>
<td>0.96 (0.88 to 1.04)</td>
<td>0.86 (0.73 to 1.01)</td>
</tr>
<tr>
<td>Transdermal HRT</td>
<td>Estradiol</td>
<td>1.02 (0.90 to 1.15)</td>
</tr>
<tr>
<td>Combined estradiol</td>
<td>1.49 (1.24 to 1.79)*</td>
<td></td>
</tr>
</tbody>
</table>

Vinogradova et al, BMJ 2019
HRT does not increase the risk of heart attack or stroke up to the age of 60 years

<table>
<thead>
<tr>
<th>Primary Endpoints</th>
<th>CEE+MPA Trial</th>
<th>CEE Alone Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary heart disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>Active N(%)</td>
<td>38(0.33)</td>
</tr>
<tr>
<td>60-69</td>
<td>Active N(%)</td>
<td>79(0.37)</td>
</tr>
<tr>
<td>70-79</td>
<td>Active N(%)</td>
<td>79(0.82)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stroke</th>
<th>CEE+MPA Trial</th>
<th>CEE Alone Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-59</td>
<td>Active N(%)</td>
<td>26(0.15)</td>
</tr>
<tr>
<td>60-69</td>
<td>Active N(%)</td>
<td>72(0.34)</td>
</tr>
<tr>
<td>70-79</td>
<td>Active N(%)</td>
<td>61(0.63)</td>
</tr>
</tbody>
</table>
HRT is not contraindicated in dyslipidaemia or hypertension

- No evidence that HRT affects lipid profile – prefer transdermal
- Hypertension is not a contraindication for HRT - optimize and monitor - prefer transdermal
- Obesity is not a contraindication for HRT - opportunity for lifestyle modification advice - prefer transdermal

Gregersen et al, Thrombosis Research 2019
HRT delays type 2 diabetes and improves insulin resistance
Oral may be better

Diabetes incidence by treatment arm (Oestrogen Plus Progestin [O+P] versus Placebo). Hazard ratio (95% CI), 0.79 (0.67–0.93). Blue line: Oestrogen Plus Progestin; red line: Placebo
Myth: Natural alternatives or bio-identical are safer

- Less research on natural alternatives/ bio-identical
- Interaction with other medications eg anticoagulants which is less known
- Not appropriate absorption
- Individualized approach with healthier lifestyle, weight loss, exercising (strength) and less alcohol and processed food diet
Myth: Menopause means less sex

- Low oestrogen can be associated with low libido
- But less sleep/ relationship challenges/ vaginal atrophy due to menopausal symptoms exaggerate this
- HRT can contribute to improving low libido
- Testosterone can be considered
Myth: Pregnancy cannot happen while on HRT

- Small chance of pregnancy while on HRT
- Menopause and no chance of pregnancy after > 1 year of no periods without the impact of hormones/ treatment
- Contraception till 55 if on HRT (and not clear when menopause happened)
Key Facts

- Always treatment if periods stop before 40 years
- Menopausal symptoms onset can vary
- Hot flashes are the commonest symptoms can last ~7-8 years for over 50%
- Other menopausal symptoms are common too
- HRT especially oestrogen only or combined with micro-ionised progesterone does not increase the risk of breast cancer mortality
- Transdermal HRT does not increase the risk of clots
- HRT does not increase risk of stroke or heart attack up to the age of 60 years
- HRT is not contraindicated in hypertension or dyslipidaemia
- T2DM is not a contraindication for HRT
- Seek advise if symptoms- discuss with your manager too
- In most cases, HRT benefits outweigh risks when for symptom relief
THANK YOU

Ask for advice if symptoms
In most cases, HRT benefits outweigh risks when for symptom relief

s.iliodromiti@qmul.ac.uk