Hormone replacement therapy (HRT) for women and osteoporosis

What is osteoporosis?
Osteoporosis occurs when the struts which make up the mesh-like structure within bones become thin causing them to become fragile and break easily, often following a minor bump or fall. These broken bones are often referred to as ‘fragility fractures’. The terms ‘fracture’ and ‘broken bone’ mean the same thing. Although fractures can occur in different parts of the body, the wrists, hips and spine are most commonly affected. It is these broken bones or fractures which can lead to the pain associated with osteoporosis. Spinal fractures can also cause loss of height and curvature of the spine.

What is the menopause?
You are described as having completed your menopause (or being ‘post-menopausal’) when you have not had a period for at least one year. The average age for this to happen is 51 years. The whole process of going through the menopause is described as the ‘peri-menopause’ and this phase can last for two to five years.

At this time, the level of the sex hormone oestrogen fluctuates and then eventually decreases. This is one of the hormones needed for ovulating (egg producing) and pregnancy. Oestrogen also thickens the womb lining, so once levels drop considerably, menstrual periods no longer occur.

Sometimes, blood tests to monitor hormone levels are used, to confirm that this is happening.

During this time, you may experience some physical and emotional symptoms due to the decreasing levels of oestrogen. These will vary widely but can commonly include tiredness, hot flushes, changes to skin and hair, joint pains, night sweats, vaginal dryness, reduced libido and mood swings. However, about a third of women experience no symptoms at all, except that their periods stop.

What is hormone replacement therapy (HRT)?
HRT is a medical drug treatment that mimics the sex hormones, particularly oestrogen, which our bodies produce naturally. Oestrogen has many functions including helping to keep bones strong.

Along with oestrogen, HRT may also contain another hormone called progestogen. Progestogen is a synthetic version of a hormone called progesterone, which is also produced at lower levels after the menopause. Progestogen is prescribed to protect women from the increased risk of womb cancer associated with ‘oestrogen only’ HRT. ‘Oestrogen only’ HRT should only be given to women who have had their womb removed (hysterectomy).

Different HRT products use different types and amounts of oestrogen and progestogen.

Why do I need a drug treatment for osteoporosis and how does HRT help bones?
When women reach the menopause oestrogen levels drop, which causes a decrease in bone density. This contributes to reduced bone strength in later life. HRT is sometimes prescribed to prevent osteoporosis or to reduce the risk of fractures.

Drug treatments are prescribed if you have osteoporosis and are at a high risk of broken bones. These treatments help strengthen your bones and reduce your risk of having fractures. They do not help the pain that occurs when bones break.
Bone is constantly being broken down (resorption) and rebuilt (formation) by specialist bone cells. This is called bone remodelling. When this becomes out of balance and more bone is resorbed than rebuilt, osteoporosis may eventually develop.

When the levels of oestrogen decrease at the menopause this causes more bone to be removed than formed. An early menopause (before the age of 45) without HRT is known to be a risk factor for developing osteoporosis later in life, which can put you at a higher risk of breaking bones.

By taking HRT, your oestrogen levels increase and for many women this helps to prevent bone loss and reduce the risk of broken bones. Using HRT to increase oestrogen levels will also help to overcome the symptoms that are often associated with the menopause.

**What hormone replacement therapy products are there?**

There are currently more than 50 different HRT products available for prescription in the UK, although not all are licensed to be used as a drug treatment for osteoporosis.

HRT products include tablets, patches that you stick on your skin and gels you rub on your skin. There are also rings, creams and pessaries that can be inserted into the vagina, although these are only used for the relief of specific symptoms such as vaginal dryness.

HRT comes in three forms:

- **Sequential combined therapy:** The two hormones, oestrogen and progestogen, are taken separately during the month with oestrogen taken continuously and progestogen for around 12 days per month, causing you to have a bleed similar to a menstrual period.

- **Continuous combined therapy:** The two hormones are taken together continuously during the month and so no bleed occurs. This treatment is only prescribed if you are at least one year past the menopause, to reduce the risk of irregular bleeding.

- **Oestrogen only HRT:** This contains no progestogen and is only given if you have had your womb removed.

### Minimum doses of oestrogen licensed for bone protection

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol</td>
<td>1mg</td>
<td>Daily</td>
</tr>
<tr>
<td>Conjugated Equine</td>
<td>0.625mg</td>
<td>Daily</td>
</tr>
<tr>
<td>Oestrogen Transdermal Estradiol Patch</td>
<td>50μg</td>
<td>Twice weekly</td>
</tr>
<tr>
<td>Estradiol Gell</td>
<td>2.5g</td>
<td>Daily</td>
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</tbody>
</table>

A licensed drug has been checked for safety and effectiveness and can be prescribed by a doctor for a specific condition. Sometimes an unlicensed drug will be given at the discretion of your doctor.

**Tibolone (Livial)**

Tibolone is a synthetic steroid medicine that mimics the activity of oestrogen and progesterone and the androgen testosterone in the body. Tibolone can be used in the same way as ordinary HRT products.

**How can I get the most out of my hormone replacement therapy?**

1. **Be informed**

   Find out about your HRT so that you can be involved in decisions being made and you will know what to expect. Read the Patient Information Leaflet (which comes in the box with your HRT product). This describes how the drug is taken and the possible side effects. Talk to your doctor and/or contact the Royal Osteoporosis Society's Helpline if you have any questions or concerns about taking HRT for osteoporosis. It is useful to gather information and discuss any worries you may have before you start taking HRT.

2. **Make sure HRT is the right treatment for you.**

   There are some conditions or situations which may mean HRT is not suitable for you. These are:

   - If you have ever had a stroke, or blood clot (such as in the leg or lungs)
   - If you have had cancer of the breast, womb or ovary
   - If you have heart disease or untreated high blood pressure
   - If you have liver disease
Longer term risks associated with HRT

Until the early 1990s, HRT was the only treatment for osteoporosis. Since then other drug treatments for osteoporosis such as the bisphosphonates and denosumab have been developed and licenced. The publication of two large clinical studies on HRT in 2002 and 2003 raised concerns about the potential risks associated with HRT, resulting in a significant reduction in its use. These studies were the Women's Health Initiative (WHI) in the USA, and the Million Women study (MWS) in the UK.

After more than a decade, there is still much discussion among specialists about the conclusions of these studies as both provided evidence for the benefits and risks associated with HRT. The initial reluctance to use HRT is now more balanced, with HRT being used in early menopause and in younger women with conditions affecting hormone levels up to the age of 50. It is also sometimes used in women between 50 and 60 with a high fracture risk, particularly if they also have menopausal symptoms that need treatment.

Breast cancer

Your risk of developing breast cancer is increased by using combined (oestrogen and progestogen) HRT. Research suggests that there will be around five extra cases of breast cancer in every 1,000 women using combined HRT.

However, this risk will drop and be the same as a woman not taking HRT within five years of stopping. HRT with oestrogen alone is associated with little or no change in the risk of breast cancer.

Endometrial cancer (cancer of the womb lining)

If you have not had your womb removed (hysterectomy) you need to take progesterone as well as oestrogen, as oestrogen on its own will significantly increase your risk of endometrial cancer. This increase in risk (between 5 and 55 extra cases per 1,000 women) varies depending on the dose of oestrogen used, and how long it is used for. If you take progesterone as directed, this risk is eliminated.

Ovarian cancer

One study showed that HRT causes a slight increase in your risk of ovarian cancer even if you are taking it for less than five years. If 1,000 women aged 50 use HRT for five years it is estimated that there will be one extra case of ovarian cancer. Again, when you stop taking HRT your risk gradually goes back down over time.

Cardiovascular (heart) disease

Oestrogen only HRT is not associated with an increase in the risk of cardiovascular disease.

Combined HRT is associated with little or no increase in the risk of coronary heart disease, particularly if started before the age of 60.

Blood Clots (venous thromboembolism – VTE)

Your risk of a blood clot is increased by oral oestrogen-only or combined HRT (tablets), but not by HRT given via skin patches (transdermal). It's estimated that if 1,000 women take HRT tablets for 7.5 years, less than two will develop a blood clot.

Stroke

Oestrogen-only and combined HRT tablets are associated with a small increase in the risk of stroke, causing an extra 3-6 strokes in 1,000 women over 7.5 years. HRT patches are not thought to increase this risk.

Dementia

The WHI study suggested a link between HRT and dementia in women over 65, however other studies have showed a potential decrease in the risk of dementia. As there are no conclusive clinical trial data, the effect of HRT on a woman's risk of dementia is unknown.

Tibolone (Livial)

In younger women, the risk profile of tibolone is broadly similar to that for conventional combined hormone-replacement therapy (HRT). For women over 60 the risks associated with tibolone start to outweigh the benefits because of an increased risk of stroke, with an additional 13 cases per 1,000 women over 5 years.

It is important to remember that your natural ‘background’ risk of any of these longer term risks will rise with your age.

Therefore whilst HRT might cause minimal health risks for a woman of 50, it may pose more of a risk for a woman ten years older whose chance of problems such as breast cancer, stroke or heart disease is naturally higher.
2. Continue to take your medication regularly for the correct length of time.

Guidance in the UK from organisations such as the National Institute for Health and Care Excellence (NICE), and the Medicines and Healthcare products Regulatory Agency (MHRA) helps to ensure that HRT is prescribed following an assessment of your needs and risks. In general it is felt that if HRT is used appropriately on a short-term basis (no more than five years), the benefits outweigh the risks.

It is likely your doctor will want to review your HRT use annually. Your doctor will be able to advise you on what is best for you based on your individual circumstances. If you stop taking HRT but still have an increased risk of fracture, your doctor may recommend a non-hormonal osteoporosis treatment as the beneficial effects of HRT on bones decrease once you stop taking it.

3. Lead a healthy lifestyle to keep your bones strong

Factors that can help to maintain healthy bones are a well-balanced diet with adequate calcium rich foods, safe exposure to sunlight to obtain vitamin D, regular weight bearing exercise, avoiding smoking and keeping alcohol consumption within the recommended limits.

If you are taking a drug treatment for osteoporosis, you may need to boost your calcium intake up to around 1000mg a day. Your doctor can prescribe supplements of calcium and/or vitamin D if you need them.

4. Understand the risk of side effects and what can be done to reduce them

As with any drug, there are potential side effects with HRT. It is important to remember that:

- Most people will not experience side effects, or if they do they are generally short lived.
- Not all the side effects you may read about on-line or see listed on your patient information leaflet are necessarily caused by the drug.

Symptoms that have been reported by patients taking part in the research trials may be included as possible side effects even if they were seen in as many people who took the placebo (dummy treatment) as those taking HRT. The potential side effects listed above are thought to be associated with the use of HRT.

<table>
<thead>
<tr>
<th>Potential side effects</th>
<th>How common is it?</th>
<th>What can I do to reduce the risk of this occurring and what should I do if I experience this problem?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast enlargement and tenderness</td>
<td>1 in 10 to 1 in 100</td>
<td>Eating a low-fat, high carbohydrate diet may reduce breast tenderness</td>
</tr>
<tr>
<td>Breakthrough bleeding</td>
<td>1 in 10 to 1 in 100</td>
<td>Discuss changing to a different HRT preparation</td>
</tr>
<tr>
<td>Leg cramps</td>
<td>1 in 10 to 1 in 100</td>
<td>Regular stretches and exercise may help</td>
</tr>
<tr>
<td>Stomach upset, feeling sick (nausea) and bloating</td>
<td>1 in 10 to 1 in 1,000</td>
<td>Take your tablet with food, which may help to reduce nausea and indigestion</td>
</tr>
</tbody>
</table>

*Note – the likelihood of potential side effects varies slightly with the different HRT preparations.

If you are taking medications for other conditions it is important to establish that it is not these that are causing your side effects. Talk to your doctor who may be able to suggest ways of investigating this further.

If you experience these or any other symptoms which you think may be due to your HRT, speak with your doctor or pharmacist about other types of HRT which may suit you better.
Useful contacts

For urgent medical help or advice for something that is not life threatening.

Contact:

NHS 111 in England and Scotland
Tel: 111

NHS Direct Wales (Galw Iechyd Cymru)
Tel: 0845 4647

NHS Choices
NHS Choices is the UK’s biggest health website. It provides comprehensive health information helping you to make the best choices about your health and lifestyle, but also about making the most of NHS and social care services in England.

nhs.uk

Women’s Health Concern

WHC provides an independent service to advise, reassure and educate women of all ages about their health, wellbeing and lifestyle concerns.

WHC also runs a helpline and email service which can be arranged via their website for a fee.

womens-health-concern.org

Breast Cancer Care
5-13 Great Suffolk Street
London SE1 ONS
Tel: 0808 800 6000
breastcancercare.org.uk

Macmillan Cancer Support
89 Albert Embankment
London SE1 7UQ
Tel: 0808 808 00 00
macmillan.org.uk

British Heart Foundation
Greater London House
180 Hampstead Road
London NW1 7AW
Tel: 0300 330 3311
bhf.org.uk

This information reflects current evidence and best practice but is not intended to replace the medical advice provided by your own doctor or other healthcare professional.

This is one of many information resources available about osteoporosis and bone health. View the range at theros.org.uk and order more by calling us on 01761 471 771 or emailing info@theros.org.uk

For osteoporosis information and support contact our free specialist nurse Helpline:

nurses@theros.org.uk
0808 800 0035

This information is provided free of charge. If you would like to become a member or support the charity with a donation, please go online or call us:

theros.org.uk
01761 473 287

@RoyalOsteoSoc

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