National Osteoporosis Society
Position Statement

# Hormone Replacement Therapy for the Treatment and Prevention of Osteoporosis

## Our Position

- In all cases, the decision to take Hormone Replacement Therapy (HRT) must only be made after full consultation between a woman and her clinician to ensure that she fully understands the risks and benefits involved with treatment. The use of HRT should be reviewed on a regular basis, taking into consideration any change in balance of benefits and risks.
- HRT is an effective treatment for menopausal symptoms that also offers protection against fractures at both hip and spine. For the large proportion of women affected by osteoporosis, who are over the age of 60, HRT is not considered a suitable treatment for osteoporosis. However in the under 60 age group HRT still has a role to play in the management of osteoporosis.
- In line with MHRA recommendations, women who have experienced an early menopause (whether natural or surgically induced) should be recommended HRT until at least the normal age of the menopause (around 50). This will help reduce bone loss and to avoid the symptoms and other complications of prolonged oestrogen deficiency.
- For postmenopausal women under the age of 60, who do not have risk factors for breast cancer, heart disease stroke or venous thromboembolism, the risks associated with HRT are low. For these women, HRT can be considered as a treatment for osteoporosis, providing that the beneficially effects on fracture risk reduction outweigh any adverse risks for that individual.
- In women up to the age of 60 who are using HRT for relief of menopausal symptoms it is accepted that the HRT benefit normally exceeds risk irrespective of the potential bone effect, which will be an additional benefit.

## The Issue

HRT has been at the centre of much controversy and debate. In the past it was thought to protect against a range of diseases including heart disease, colon cancer and dementia. It has been shown to increase bone density and reduce the risk of fracture and can successfully relieve menopausal symptoms such as hot flushes, vaginal dryness and loss of libido. Publication of two large high profile clinical studies, the Women's Health Initiative (WHI) and the Million Women Study (MWS), demonstrated that there are risks associated with taking HRT. The results and methods of these studies have been subject to much criticism and the role of HRT in the treatment of osteoporosis has become unclear. The purpose of this document is to clarify the Charity's position on the role of HRT in the management of osteoporosis.

## Definitions

**Hormone replacement therapy (HRT):**
in this document refers to combined (oestrogen and progestogen) and unopposed oestrogen (oestrogen alone) therapy. This does not include tibolone.

**Early Menopause:** permanent cessation of periods in a woman younger than 45yrs.

## Conclusions and Recommendations

HRT is an effective treatment for menopausal symptoms that also offers good protection for bone. However, the use of HRT is associated with increases in the risks of breast cancer, venous thromboembolism (particularly in the case of oral HRT) and stroke. The potential risks increase with age, being very low in women under the age of 60 who have no other risk factors. The risks of using HRT are also lower at all ages for women who have had a previous hysterectomy and who use oestrogen alone.

There is a range of treatments licensed for the prevention and treatment of osteoporosis all with their own benefits and risks. HRT should be considered for women younger than 60 in which the benefits outweigh the risks especially for those who cannot tolerate other osteoporosis treatments, or who have other reasons for wishing to take HRT; and recommended as a treatment option for osteoporosis in women who have undergone an early menopause

Women who are taking HRT for the treatment of menopausal symptoms also benefit from the protective effect against bone loss. The extent to which the protective effect on bone is maintained after HRT is stopped is controversial. However, for those women who are still at risk of fracture it is important that an alternative treatment for bone protection is provided once HRT use is discontinued.

The Medicines and Healthcare Regulatory Agency (MHRA) guidelines on the use of HRT for the relief of menopausal symptoms advises that 'For all women, the lowest effective dose should be used for the shortest time'. The National Osteoporosis Society would like to emphasise that this should be the lowest effective dose used for the shortest time appropriate to the purpose for which the HRT is given. More research is needed into the effects of lower doses and different preparations of HRT, since these potentially offer bone protection with lower risk.

## Background Information

At the menopause there is a significant fall in the levels of the hormone oestrogen. Oestrogen has been shown to protect against osteoporosis and therefore postmenopausal women who are oestrogen deficient are at a higher risk of bone loss and fractures. HRT can be used to treat a range of menopausal symptoms which are caused by declining oestrogen levels (including hot flushes, difficulty sleeping and vaginal dryness). It works by providing oestrogen, with or without added progestogen, to replace those hormones that the body no longer produces after the menopause. However, a number of studies have shown that there are risks associated with using HRT beyond the age of natural menopause.

## Benefits of HRT:

**Osteoporosis:** HRT has been shown to significantly decrease the number of fractures at hip and spine compared to placebo[1;2]. Recent research has shown that even very low doses of HRT are effective in increasing bone density[3], although data on fracture reduction are unavailable for these lower doses. The effect of HRT on BMD after treatment has ended is controversial. There is some evidence to show that HRT can offer a protective effect on BMD for several years after treatment is stopped[4;5], while other evidence shows that HRT only offers a protective effect on BMD while it is being taken[6;7]. Taking HRT for the treatment of osteoporosis therefore may imply relatively long-term use. Women who have experienced an early menopause (either naturally or surgically induced) should be recommended to take HRT up to the age of normal menopause (49-53 years), as advised by the MHRA. In these women HRT maintains oestrogen at normal levels up to the age of natural menopause, and it is thought that at this age the risks associated with HRT are negligible.

**Relief from menopausal symptoms:** HRT is the most effective treatment to relieve symptoms associated with the menopause.
It has also been shown that a lower dose than previously thought is effective[8].

**Decreased risk of colorectal cancer:** Results from the WHI showed that combined HRT can reduce the risk of colorectal cancer[9]. Results from the oestrogen only arm of the study were inconclusive.

## Risks of HRT:

**Breast cancer:** Many studies have linked combined HRT with a slight but significant increase in the risk of breast cancer, and have shown that there is an increase in risk which corresponds with age and length of use[10]. 5 years after HRT use is discontinued, the risks associated with breast cancer returns to the level of those who have never used HRT[10]. It should be noted that HRT is just one of many factors (e.g. early menarche or late menopause, a positive family history11 or high alcohol consumption) which can increase risk of breast cancer.

**Venous thromboembolism:** Both combined and oestrogen only oral HRT increase the risk of venous thromboembolism[12;13]. This does not appear to be the case with transdermal HRT[14].

**Stroke:** Both oestrogen only and combined HRT have been shown to increase the risk of stroke[15;16]. Risk of stroke increases with age and therefore older women have a greater absolute risk.

**Ovarian Cancer:** Observational studies suggest oestrogen only and combined HRT very slightly increase the risk of ovarian cancer when used long term[17]. This risk appears to return to normal when HRT is discontinued.

**Endometrial cancer:** Oestrogen only HRT treatments are known to cause an increased risk of endometrial cancer, and are thus given only to women who have undergone a hysterectomy[18]. However this increase in risk is not seen with combined continuous HRT. [19 20]

## Unknown:

**Coronary Heart Disease (CHD):** Some studies have shown that HRT can increase the risk of CHD, while others have shown no effect[21;22]. There is evidence that the age at which HRT is started and the time since menopause could be critical in determining the effect of HRT on CHD[23]. There may be a beneficial effect for women who start HRT within 10 years of menopause[24]. Other studies have demonstrated no effect at all[25].

**Dementia:** The WHI memory study showed a detrimental effect of HRT on cognition and dementia for women over the age of 65[26;27]. Similarly, oestrogen only HRT has been shown to be ineffective in treating Alzheimer's disease and may cause the disease to progress more rapidly[28]. However several observational studies have suggested that HRT can decrease the risk of dementia. It has been suggested that a window of opportunity may exist around the time of the menopause when HRT treatment may offer a beneficial and preventative effect[29], although no clinical trial data yet exists. Regrettably there are no clear data one way or another.

## Licensed Indications for HRT

Hormone Replacement Therapy (HRT) for oestrogen deficiency symptoms in postmenopausal women.

Prevention of osteoporosis in postmenopausal women at high risk of future fractures who are intolerant of, or contraindicated for, other medicinal products approved for the prevention of osteoporosis.

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