Hormone replacement therapy

Menopausal symptoms are extremely common but are likely to be under-recognised and under-treated. Vasomotor symptoms (hot flushes and night sweats) are the most commonly reported symptoms, occurring in about 80% of postmenopausal women, with 25% of these women reporting a severe impact on quality of life.[1]

Symptoms of the menopause often last far longer than most women anticipate. Frequent menopausal vasomotor symptoms persist in more than half of women for more than seven years.[2]

See also the articles on Menopause and its Management, Hot Flushes and Atrophic Vaginitis.

What is hormone replacement therapy?

Hormone replacement therapy (HRT) is an effective treatment for typical menopause-related symptoms. There are also other long-term health problems associated with the menopause for which HRT can be beneficial, particularly reducing the increased risk of osteoporosis.

However HRT is also associated with some increased risks of health problems. Therefore the Medicines and Healthcare products Regulatory Agency (MHRA) recommends that HRT should only be initiated for relief of postmenopausal symptoms that adversely affect quality of life. HRT should be continued only as long as the benefit in alleviating menopause symptoms outweighs the risks associated with HRT use.[3]

See also the separate HRT - Initial Consultation, HRT - Follow-up Assessments and HRT - Topical Vaginal articles, including information on contra-indications, side-effects and indications for stopping HRT.

Indications for hormone replacement therapy[4]

HRT with small doses of an oestrogen (together with a progestogen in women with a uterus) is appropriate for alleviating menopausal symptoms such as vaginal atrophy or vasomotor symptoms. Menopausal atrophic vaginitis may respond to a short course of a topical vaginal oestrogen preparation used for a few weeks and repeated if necessary.

HRT may be used in women with early natural or surgical menopause (before age 45 years), since they are at particularly high risk of osteoporosis. For early menopause, HRT can be given until the approximate age of natural menopause (until age 50 years).

Oestrogen given systemically in the perimenopausal and postmenopausal period or tibolone given in the postmenopausal period also diminish postmenopausal osteoporosis. Tibolone combines oestrogenic and progestogenic activity with weak androgenic activity. However, alternatives to HRT should be considered if osteoporosis is the only concern.

Raloxifene hydrochloride is licensed for the treatment and prevention of postmenopausal osteoporosis. Raloxifene does not reduce menopausal vasomotor symptoms.

HRT does not prevent coronary heart disease or protect against a decline in cognitive function and it should not be prescribed for these purposes.

Experience of treating women who are over 65 years of age with HRT is limited. Starting HRT in women over the age of 60 years is generally not recommended.

Benefits and risks of hormone replacement therapy[1] [5]

For more detail about the benefits and risks of HRT, use the reference links for:

- Summary of HRT risks and benefits during current use and current use plus post-treatment from age of menopause up to age 69 years, per 1,000 women with five years or 10 years of HRT use.[6]

- Summary of relative and absolute risks and benefits during current HRT use per 1,000 women with five years or 10 years of HRT use.[7]

Benefits of hormone replacement therapy

The benefits of HRT outweigh the risks for many women aged under 60 years.[5] [8] The potential benefits of HRT include:

Fragility fractures

- The baseline risk of fragility fracture for women around menopausal age varies from one woman to another.
- The risk of fragility fracture is decreased while taking HRT, and this benefit is maintained during treatment but decreases once treatment stops; this benefit may continue for longer in women who take HRT for longer.
- Although HRT is considered effective for the prevention of postmenopausal osteoporosis, it is generally recommended as an option only for women at significant risk for whom non-oestrogen therapies are unsuitable.[9]

Muscle mass and strength: there is limited evidence that HRT may improve muscle mass and strength.

Reduction in vasomotor symptoms

- HRT is the most effective treatment for reducing vasomotor symptoms.
- Vasomotor symptoms are usually improved within four weeks of starting treatment and maximal benefit is gained by three months.

See also the article on Hot Flushes.

Improvement in quality of life

HRT can also improve sleep, muscle aches and pains and quality of life in symptomatic women.

Improvement in mood changes

- HRT can improve mood and also depressive symptoms.[10]

- HRT should be considered to alleviate low mood that arises as a result of the menopause. Cognitive behavioural therapy may be beneficial too.[5]

Improvement of urogenital symptoms

- HRT is effective in improving the symptoms related to vaginal atrophy.
- Topical oestrogen is effective in improving urinary symptoms in menopausal women.[11]
- Vaginal symptoms are improved, vaginal atrophy and pH decrease and there is improved epithelial maturation with topical oestrogen preparations compared to placebo or non-hormonal gels.[12]

See also the article on Atrophic Vaginitis.

Premature menopause/premature ovarian insufficiency

- Starting hormonal treatment (either with HRT or a combined hormonal contraceptive) and continuing treatment until at least the age of natural menopause (unless contra-indicated) reduces the risk of chronic diseases, including cardiovascular disease and osteoporosis.
- HRT may have a beneficial effect on blood pressure when compared with a combined hormonal contraceptive.
- Both HRT and combined hormonal contraceptives offer bone protection.

Risks associated with hormone replacement therapy

HRT increases the risk of venous thromboembolism, stroke, endometrial cancer (reduced by a progestogen), breast cancer, and ovarian cancer.

The National Institute for Health and Care Excellence (NICE) reviewed the evidence on the risks associated with hormone replacement therapy (HRT) in 2019.[5]

Venous thromboembolism (VTE)

The risk of VTE associated with HRT is greater for oral than transdermal preparations. The risk associated with transdermal HRT given at standard therapeutic doses is no greater than baseline risk.

Coronary heart disease (CHD) and stroke

The baseline risk of coronary heart disease (CHD) and stroke for women around menopausal age varies from one woman to another, depending on the presence of cardiovascular risk factors.

- HRT with oestrogen alone is associated with no, or reduced, risk of CHD. Combined HRT with oestrogen and progestogen is associated with little or no increase in the risk of CHD.
- However, there is an increased risk of coronary heart disease in women who start combined HRT more than 10 years after menopause.
- The baseline risk of stroke in women younger than 60 years is very low. Oral (but not transdermal) oestrogen is associated with a small increase in the risk of stroke.
- HRT does not increase cardiovascular disease (CVD) risk when started in women younger than 60 years. HRT does not affect the risk of dying from CVD.

The presence of cardiovascular risk factors is not a contra-indication to HRT, as long as any risk factors are optimally managed.

Type 2 diabetes

HRT (either orally or transdermally) is not associated with an increased risk of developing type 2 diabetes.

Dementia

The likelihood of HRT affecting the risk of dementia is unknown.

Breast cancer

The baseline risk of breast cancer for women around menopausal age in the UK varies from one woman to another.

- HRT with oestrogen alone is associated with little or no increase in the risk of breast cancer.

- Combined HRT with oestrogen and progestogen is associated with an increased risk of breast cancer that is dependent on duration of treatment, which reduces after stopping HRT.
- HRT does not affect the risk of dying from breast cancer.

In 2019, additional evidence was published by the Collaborative Group on Hormonal Factors in Breast Cancer.[13]

- A meta-analysis of 108,647 women with breast cancer in prospective studies has shown that some excess risk of breast cancer with systemic HRT persists for more than 10 years after stopping, compared with never-users.
- There is an increased risk with HRT use duration for longer than one year.
- There is an increased risk irrespective of type of oestrogen or progestogen, or route of delivery, with slightly lower risks with cyclical compared with continuous combined HRT.
- For women using combined oestrogen-progestogen HRT and oestrogen-only HRT, after stopping HRT the increased risk of breast cancer decreases, and the time needed to return to baseline depends on duration of prior HRT use.
- For women using low-dose vaginal oestrogens, the evidence has not shown an increase in breast cancer in women with no history of breast cancer in the past.

Ovarian cancer
The Collaborative Group on Epidemiological Studies of Ovarian Cancer published a meta-analysis of 52 epidemiological studies in 2015.[14]

- During prospective follow-up, 12,110 postmenopausal women, 55% (6,601) of whom had used HRT, developed ovarian cancer.
- Among women last recorded as current users of HRT, the risk was increased even with fewer than five years of use (relative risk (RR) 1.43).

- Combining current or recent use (any duration but stopped less than five years before diagnosis) resulted in an RR of 1.37. This risk was similar for oestrogen-only and combined oestrogen-progestogen HRT and was increased for the two most common types of ovarian cancer (serous and endometrioid). The risk declined the longer ago use had stopped, although about 10 years after stopping long-term HRT there was still an excess of serous or endometrioid tumours (RR 1.25).
- The authors of the meta-analysis concluded that women who use hormone therapy for five years from around the age of 50 years have about one extra ovarian cancer per 1,000 users and, if its prognosis is typical, about one extra ovarian cancer death per 1,700 users.

Endometrial cancer

- Oestrogen-only HRT substantially increases the risk of endometrial cancer in women with a uterus.
- The use of cyclical progestogen for at least ten days per 28-day cycle lowers this risk. Switching to continuous combined HRT after one year removes the risk.

Hormone replacement therapy and contraception

- Contraception is needed along with HRT. HRT is not a contraceptive and a woman is considered potentially fertile for two years after her last menstrual period if she is aged under 50 years and for one year if she is aged over 50 years.
- For many women oestrogen HRT and an intrauterine system (IUS) are an optimal combination.
- Alternatively, the progestogen-only contraceptive pill can be given to women who are taking cyclical combined HRT.
- Women aged 50 years and over should not be prescribed the combined oral contraceptive pill.

See also the separate Contraception from 40 to the Menopause article.

Starting hormone replacement therapy

See the separate HRT - Initial Consultation article.

Follow-up of a woman taking hormone replacement therapy

The separate HRT - Follow-up Assessments article gives advice about following up women taking HRT and when to stop HRT.

Initial follow-up after starting HRT should occur at about 3 months if HRT has been started or changed, then at least annually thereafter, unless there are clinical indications for an earlier review (such as treatment ineffectiveness or adverse effects).[1] Most symptoms are likely to have responded to oestrogen in this time period and any residual problems may require alternative management.

Further reading

- Cobin RH, Goodman NF; American Association of Clinical Endocrinologists and American College of Endocrinology Position Statement on Menopause - 2017 Update. Endocr Pract. 2017 Jul;23(7):869-880. doi: 10.4158/EP171828.PS.

Last updated by: Dr Colin Tidy, MRCGP 27/02/2023	
Peer reviewed by: Dr Rachel Hudson, MRCGP 27/02/2023	**Next review date:** 26/02/2028

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