

Safe HRT prescribing

Dr Louise Newson and Dr Alice Scott with all you need to know on safe HRT prescribing

What you should already know

There are numerous potential benefits to be gained by women taking HRT in improving their menopausal symptoms, such as hot flushes, mood swings, memory problems, low mood and reduced libido.

Many women and healthcare professionals are worried about the perceived risks of HRT. Much of the negativity regarding HRT, however, stems from the misinterpretation of the Women's Health Initiative (WHI) study in 2002, which led to a worldwide reduction in HRT use.¹ The subsequent sub-analysis of this study showed some really reassuring and positive results to support the use of HRT, which is reiterated in current national and international menopause guidelines.^{2,3}

The NICE guidelines are clear that for the majority of women who take HRT, the benefits outweigh any risks. In particular, women with an early menopause (below 45 years of age) or premature ovarian insufficiency (below 40 years of age) should be given HRT provided there are no contraindications, at least until the average age of the menopause, which is 51 years old.

Numerous studies have shown that when HRT is started in women who are within 10 years of their menopause onset, it can reduce their future risk of developing osteoporosis, type 2 diabetes, osteoarthritis and all-cause mortality.⁴⁻⁶

Women with a uterus need a progestogen in addition to oestrogen:

- Give cyclical HRT if the LMP was less than one year previously, otherwise a continuous combined preparation is usually indicated.
- Continuous progestogens are better for endometrial protection and should confer no bleeding.
- A woman can take continuous HRT at any age but it may cause erratic bleeding if given too early. Usually women can switch from cyclical to continuous after one year of use or at least by the age of 54.
- Micronised progesterone (Utrogestan) has fewer side effects than other progestogens.
- Micronised progesterone is associated with a lower risk of breast cancer, cardiovascular disease and thromboembolic events compared with androgenic progestogens.
- A Mirena coil can be used for five years as endometrial protection.

HRT should be prescribed alongside advice on optimising lifestyle in terms of diet, exercise, weight, smoking cessation and ensuring safe levels of alcohol consumption.

Vaginal oestrogen to treat genitourinary syndrome of menopause can be prescribed alone or in addition to systemic HRT and does not require a progestogen for endometrial protection to be prescribed simultaneously. In addition, vaginal oestrogen can be (and should be) given in the long term so can be put on a repeat prescription.

What isn't as widely known, but that you should think about

Most women and healthcare professionals are concerned about the possible risks of breast cancer in women taking HRT. However, the risk of breast cancer is far lower than many realise.

Here are the facts regarding breast cancer risk with HRT:

- Women who take oestrogen only HRT (women who have had a hysterectomy) do not have a greater risk of breast cancer. Studies have shown they actually have a lower risk of breast cancer.¹
- Women who take oestrogen and a progestogen may have a small increased risk of breast cancer. However, this increased risk is a similar magnitude to the risk of breast cancer for women who are overweight or drinking a glass or two of wine each night. Telling women this often really helps to put this risk into perspective.
- Studies have shown that women who take micronised progesterone have an even lower risk of breast cancer than other women who take other progestogens.⁷
- Other risks of HRT, especially risk of venous thromboembolic disease and also contraindications to taking HRT, vary dependent on the route of administration.

Transdermal 'body identical' 17 beta oestradiol (i.e. in the form of patch or gel) is the safest as:

- It avoids the increased risks of venous thromboembolism^{8,9}, ischaemic stroke and gallbladder problems that are associated with oral oestradiol.¹⁰
- Oral oestrogen also increases sex hormone binding globulin, which reduces free androgen index and lowers libido.
- Absorption is more reliable compared to oral oestrogen.¹¹
- It is not contraindicated in women who have migraine with aura, whereas oral oestrogen should not be given to these women.
- It is preferable to give to women who are overweight or obese.
- It contains body identical oestrogen. Synthetic conjugated equine oestrogens contain a mixture of different hormones, including equine-specific steroids, which have unknown properties in humans and should not be prescribed first line.

Women can continue to take HRT as long as the benefits outweigh any risks. Women taking HRT should have an annual review to ensure they are still getting benefit, but it is no longer about taking the lowest dose for the shortest time. Many women decide to continue taking HRT in the long term in view of the health benefits it affords.

HRT is far safer than many women and also many healthcare professionals realise.¹³

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References

1. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial. *JAMA* 2002;288:321-33
2. Baber R, Panay N, Fenton A, for the IMS Writing Group. 2016 IMS recommendations on women's midlife health and menopause hormone therapy. *Climacteric* 2016; 19 (2): 109–150.
3. NICE. *Menopause: diagnosis and management*. NICE Guideline 23. NICE, 2015. Available at: www.nice.org.uk/ng23
4. Stevenson, J. C. (2018). Prevention and treatment of osteoporosis in women. *Post Reproductive Health*, 24(4), 167–170
5. Lobo R, Pickar J, Stevenson J et al. Back to the future: hormone replacement therapy as part of prevention strategy for women at the onset of menopause. *Atherosclerosis* 2016; 254: 282–290
6. Boardman HM, Hartley L, Eisinga A, Main C, Roque i Figuls M, Bonfill Cosp X, et al. Hormone therapy for preventing cardiovascular disease in post-menopausal women. *Cochrane Database Syst Rev* 2015:CD002229
7. Stute P, Wildt L, Neulen J. The impact of micronized progesterone on breast cancer risk: a systematic review. *Climacteric* 2018; 21 (2): 111–122
8. Mueck A. Postmenopausal hormone replacement therapy and cardiovascular disease: the value of transdermal estradiol and micronized progesterone. *Climacteric* 2012; 15 (Suppl 1): 11–17
9. Canonico M, Plu-Bureau G, Lowe G, Scarabin P. Hormone replacement therapy and risk of venous thromboembolism in postmenopausal women: systematic review and meta-analysis. *BMJ* 2008; 336: 1227
10. L'Hermite M. HRT optimization, using transdermal estradiol plus micronized progesterone, a safer HRT. *Climacteric* 2013; 16: 44–53
11. Goodman MP Are all estrogens created equal? A review of oral vs. transdermal therapy. *J Womens Health (Larchmt)* 2012 Feb;21(2):161-9
12. Davey DA Menopausal hormone therapy: a better and safer future, *Climacteric* 2018 21:5, 454-461
13. Newson L, Lass A. Effectiveness of transdermal oestradiol and natural micronised progesterone for menopausal symptoms. *BJGP* 2018; 68: 499-500