

Newson Clinic Knowledge Factsheet

Why are women prescribed different doses of HRT?

Why some women may be prescribed lower or higher doses of hormone replacement therapy (HRT)

Many women come to Newson Clinic because they are unable to get help on the NHS and/or because the type of hormone replacement therapy (HRT) they are receiving is insufficient to alleviate their symptoms.

At Newson Clinic, our patients are central to all treatment decisions. We start our patients with the minimal effective doses of hormones, then assess scope for any changes based on clinical response and patients' views.

We follow NICE menopause guidelines, adhere to the General Medical Council's decision making and consent guidelines, and NICE shared decision-making guidelines¹⁻³.

In this article, we share our background to this approach.

If you are wondering if HRT is right for you, you can book an appointment to speak to a Newson Clinic clinician.

Background on HRT prescribing and doses

The decision as to whether to prescribe HRT, the dose of HRT given, and the duration of its use is made on an individualised basis after discussing the benefits and risks with each patient.

The optimum dose and duration of HRT treatment is decided according to the severity of a woman's symptoms, her response to treatment and how the HRT is absorbed and metabolised in her body.

Every woman is different, so a 'one size fits all' approach to HRT is not the best for women. Medicine is both a science which uses scientific evidence, and an art in responding to individual patients.

There are many benefits of taking HRT as it usually improves symptoms and can also improve future health by reducing future risk of important diseases including heart disease, osteoporosis, type 2 diabetes, bowel cancer, clinical depression and dementia. Many women choose to take HRT for ever and there is no maximum time for taking HRT.

The dose of hormones – oestradiol (the beneficial type of oestrogen), progesterone and testosterone – can vary between women, and often women find that their doses need to change (either increase or decrease) with time.

For example, a woman may start on a low dose during the perimenopause and then increase as her own hormones decline with time.

Some women need higher doses of oestradiol than other women to achieve the same benefits, especially as oestradiol can often be absorbed differently through the skin.

Is there a 'highest dose' of HRT, or maximum dose? And how do I know if I need a higher dose?

UK manufacturers have set a recommended maximum dose for each HRT medication. These maximum doses are based on studies

involving very small numbers of women (fewer than 40) over a very short amount of time – with some studies taking place only over four days. In addition, these studies only include women who are menopausal, and don't include women who are perimenopausal.

Monitoring average oestradiol levels over such a short period of time can be misleading because there is substantial individual variation in how patients respond to oestradiol; research has shown there can be up to ten-fold differences in oestradiol levels between women using the same dose gel or patch⁴.

Some women have suboptimal oestradiol levels even when using the highest licensed dose: studies have shown between 5 and 20% of women are so-called 'poor absorbers', which means that they do not absorb the oestradiol gel or patch well through their skin⁵. These women are likely to require higher off-label doses or a change in formulation – for example change from a patch to a gel to achieve physiological levels of oestradiol⁶.

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However, this does not mean that higher doses are not safe. The British National Formulary (BNF), a medical and pharmaceutical publication that contains information and advice on prescribing and pharmacology, states that doses of oestradiol should be adjusted according to response⁷. In addition, a consensus statement by the British Menopause Society states that HRT dosage, regimen and duration should be individualised, with annual evaluation of advantages and disadvantages⁸.

There is no evidence that higher doses or higher blood levels of oestradiol are associated with risks in women.

Newson Clinic's position on evidence-based medicine

Evidence-based medicine is based not only on clinical trial data, but also a clinician's experience and expertise individualised to a patient's values and preferences. This approach is particularly important in menopause care and women's health because they are undervalued, underfunded and under-researched.

Newson Clinic clinicians use both individual clinical expertise and the best available external evidence, and neither alone is enough.

Absence of evidence does not mean proof of harm.

Off-label is not the same as unlicensed

Many medicines, including HRT, are prescribed 'off-label' – meaning it is used in a different way described in the license, for example using a medicine at a higher dose than stated in the license. There are many medicines that are prescribed off-label: for example some medication for children, some medication for migraines and mental health conditions. Note: this is not the same as 'unlicensed', which is a medicine that has no license, either in the UK or elsewhere. Oestradiol in HRT is a licensed treatment.

Newson Health clinicians refer to Medicines and Healthcare products Regulatory Agency (MHRA) guidance on off-label or unlicensed use of medicines and best practice for patient communication⁹.

Maximum doses explained

Manufacturers usually state a recommended maximum dose for a medication. However, this does not mean prescribing over that level is dangerous nor that clinicians cannot or should not do so – higher doses may be essential for an individual patient's needs.

In the case of HRT, it is well documented there is a wide variation in the efficiency of transdermal drug (oestradiol as a patch, gel or spray) delivery across individuals.

Absorption can be affected by both modifiable and non-modifiable factors such as sex, age, ethnicity hydration, skin temperature, metabolism, and site of application¹⁰⁻¹³.

Newson Health audit data has shown that there is usually no strong correlation between dose of oestradiol prescribed and blood levels of oestradiol in the body. There are many women who use lower doses and have higher levels of oestradiol in their bodies than other women who are using higher doses.

Furthermore, a Newson Clinic analysis of clinic data of 1,508 perimenopausal and menopausal patients found a wide variation in oestradiol absorption when using transdermal preparations. Around a quarter of women required higher doses of oestradiol to absorb adequate amounts through the skin, while almost one in three women using standard doses of oestradiol were found to have low levels of oestradiol in their blood¹⁴.

It follows that two patients on the same dosage of oestradiol may therefore absorb quite different amounts, meaning that the patient who absorbs less will often need to be prescribed a higher dose simply to ensure her serum levels are equivalent to a patient who has better absorption. References to 'high' or 'low' doses cannot be made about the general population because patients will often benefit from different doses of oestradiol in the HRT they are prescribed.

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Response to any hormone treatment is unique to each woman: some women may respond well to a low dose of one preparation but not respond well to a high dose of another.

In practical terms, the dose of oestradiol needs to be individualised to each woman, and many women need to have their dose altered – either increased or decreased – with time.

There is no robust evidence that higher doses of oestradiol are associated with any risks or an increased incidence of side effects, such as bleeding, to a patient, and there have been no randomised controlled trials undertaken in this area.

How often does Newson Clinic prescribe above the manufacturer's maximum dose?

Many women come to Newson Clinic because they are unable to access help on the NHS and/or because the prescription they are receiving is insufficient to alleviate their symptoms.

About a third of women who come to Newson Clinic are already taking HRT, but they are still experiencing symptoms and their dose and/or type of HRT needs altering.

A minority of Newson Clinic's follow up patients are receiving a dose of oestradiol higher than the maximum stated dose. However, these women will have already been prescribed lower doses, with inadequate results in terms of either symptom control, blood levels, or both. Newson Clinic does not start women who have never taken HRT before on a 'high' dose.

The aims of our prescribing pathways

Newson Clinic has developed and produced various treatment pathways which our clinicians use.

Our prescribing pathways aim to:

- Standardise the treatment of women receiving higher doses of oestradiol
- Maintain patients' wellbeing and safety
- Support individualised care
- Adhere to the MHRA guidance about prescribing off-label
- Uphold the integrity of Newson Clinic and its clinicians.

Oestradiol blood tests

Many of our patients using oestrogen (oestradiol) as a patch or gel are recommended to have their oestradiol blood test undertaken.

However, oestradiol blood level results should be interpreted with caution as they can be unreliable.

The usual range of oestradiol is similar to the range for women who are still having periods. Fluctuations in oestradiol levels usually occur during perimenopause, and so levels of oestradiol can be very high as well as very low in perimenopausal women regardless of whether or not they take HRT.

In addition, levels can sometimes be raised in some women taking HRT, so repeating the test is usually recommended as levels can vary in women taking HRT. Repeat tests are often normal so dose and type of HRT do not usually need changing after one blood test showing raised oestradiol levels.

Our recent research showed that around one in three women using licensed doses of oestradiol had low levels of oestradiol in their blood tests, so were unlikely to be absorbing adequately¹⁴.

Women are usually advised not to apply their oestradiol gel to their arms on the morning before their blood test and to apply it to their legs on the day of the blood test if they usually apply the gel on their arms. Using gel on their arms on their day of blood test can lead to falsely raised levels¹⁵.

In addition, there can be cross reactivity with other substances (such as biotin) so a high level may not be accurate for oestradiol.

We do not interpret oestradiol results in isolation as the clinical situation is always taken into consideration.

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Note about progesterone doses

The Newson Clinic treatment pathways for women who bleed while taking HRT state that the dose of progesterone should usually be increased, regardless of the dose of HRT, in addition to these women having appropriate investigations when clinically indicated. There is no good quality evidence from studies demonstrating that a higher dose of progesterone (which would be an off-label dose) should routinely be given for women who are prescribed different doses of oestradiol and do not have any bleeding or have low oestradiol blood levels despite a higher dose.

Benefits and risks of HRT

Oestradiol, progesterone and testosterone as natural (body identical) hormones have never been shown to be associated with an increased risk of any cancer unlike synthetic hormones. Newson Health has created two visual aids summarising the evidence to help you understand the long-term risks and benefits of HRT.

You can access the visual aids at www.balance-menopause.com/menopause-library/understanding-the-benefits-and-risks-of-hrt-downloadable-visual-aids/

In summary, women are individuals, and all treatment should involve joint decision making between clinicians and patients¹⁶.

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Please note that content of this website is not intended in any way to be a substitute for professional medical advice, diagnosis, or treatment. Always seek the advice of your doctor or other qualified health provider with any questions you may have regarding a medical condition. You should not disregard professional medical advice or delay in seeking it because of something you have read within our content. If you think you may have a medical emergency, speak to your doctor or contact the emergency services immediately.

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