Effectiveness of transdermal oestradiol and natural micronised progesterone for menopausal symptoms

INTRODUCTION
This article discusses the role of hormone replacement therapy (HRT) in the management of menopausal symptoms, and specifically considers the advantages of different types and preparations of HRT, based on the current medical evidence.

The menopause is a normal life event for women, not an illness or a medical condition. However, the effects of the menopause often have a negative impact on women’s wellbeing and quality of life. Furthermore, the low oestrogen levels and other biological changes that occur in these women are also associated with an increased risk of cardiovascular disease, osteoporosis, diabetes, and dementia.

In addition to hot flushes and sweats, symptoms include mood changes, memory loss, urogenital atrophy, reduced libido, sleep disturbances, joint pains, and muscle stiffness. These symptoms can be non-existent, or can last for a few years or even decades.

HRT ‘SCARES’ ARE UNFOUNDED
Much of the negative publicity surrounding HRT stems from misinterpretation by the media of the findings from the Women’s Health Initiative (WHI) study, published more than a decade ago. Many women and healthcare professionals are still unnecessarily concerned about the perceived risks of HRT, resulting in a significant proportion of women currently being refused HRT and often being inappropriately offered antidepressants.

EVIDENCE TO SUPPORT HRT
There is clear evidence to support that, in addition to a benefit on symptoms, HRT can also play a role in quality of life improvement, prevention of coronary heart disease, osteoporosis and fracture risk, and reduction in mortality. No other treatments for menopausal symptoms have demonstrated a similar role. This is reflected in current guideline recommendations including from the National Institute for Health and Care Excellence [NICE]1,3,4

Reassuringly, during a cumulative 18-year follow-up of WHI trials, women taking HRT did not have a higher risk of all-cause, cardiovascular, or cancer mortality.

TYPE OF HORMONE REPLACEMENT THERAPY
The benefits and risks of HRT vary by origin of product (‘body identical’, which are hormones that are chemically the same as those that the body produces, or equine), dosage, route of administration, and timing of initiation.5 HRT is available mainly as oral or transdermal preparations, all of which contain oestrogen, either alone or combined with progesterone.

MODE OF OESTROGEN DELIVERY
A systematic review and meta-analysis of treatment effects from NICE guidelines has shown that transdermal oestradiol had the highest probability of being the most effective treatment for vasomotor symptoms compared with placebo.6

Risk of venous thromboembolism
The overall venous thromboembolism [VTE] risk increases about two-fold in women who take oral oestrogens. High levels of oral oestrogen concentrate in the liver, which results in activation of the coagulation and activation factors of the renin–angiotensin–aldosterone cascade. In addition, oral (but not transdermal) oestrogens induce resistance to activated protein C. In contrast, studies have shown no association between VTE risk and use of transdermal oestrogens. Guidelines recommend transdermal rather than oral HRT for menopausal women who are at increased risk of VTE, including those with a BMI >30 kg/m².1

Risk of stroke
Oral HRT containing oestrogen at either high or low doses is associated with an increased risk of ischaemic stroke, compared with non-
Micronised progesterone
Oral preparation given with oestrogen as part of HRT, does not increase VTE risk even in women who are at high risk, such as those with prothrombotic mutations (including factor V Leiden) and does not have this effect.

Costs around £4–£5 a month

More reliable absorption than oral oestrogen
Less likely than oral oestrogen to cause side effects such as nausea
Does not increase VTE risk even in women who are at high risk, such as those with prothrombotic mutations (including factor V Leiden)
Neutral effect on blood pressure
Neutral effect on CVD risk unlike other progestogens
Less likely to cause side effects such as fluid retention
Lower risk of breast cancer compared with progestogens
Costs around £4–£5 a month

CVD = cardiovascular disease. HRT = hormone replacement therapy. SHBG = sex hormone binding globulin
VTE = venous thromboembolism.

**REFERENCES**


**Box 1. The advantages of transdermal oestrogen and micronised progesterone**

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<thead>
<tr>
<th>Transdermal oestrogen</th>
<th>Micronised progesterone</th>
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<tr>
<td>More reliable absorption than oral oestrogen</td>
<td>Oral preparation given with oestrogen as part of HRT, either cyclically or continuously</td>
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<td>Does not increase VTE risk even in women who are at high risk, such as those with prothrombotic mutations (including factor V Leiden)</td>
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<td>Should be first line in women with obesity, diabetes, (or liver disease)</td>
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<td>Oral oestrogen can lower libido by increasing SHBG levels whereas transdermal oestrogen does not have this effect</td>
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**SUMMARY**

It is very important that broad, sweeping conclusions concerning HRT are not made. It is essential that healthcare professionals, women, and also the media are aware that there are important differences between various HRT products.

There is robust evidence demonstrating that transdermal oestrogen in association with natural MP could represent the optimal HRT regimen, particularly in women at risk of cardiovascular events (Box 1). This combination should ideally be initiated by healthcare professionals at a primary care level. The costs of these products are comparable with other types and formulations of HRT.

**Provenance**

Freely submitted; externally peer reviewed.

**Competing interests**

Louise Newson has had financial relationships (lecturer, writer, member of advisory boards, attendance at meetings, and/or consultant) with Pfizer, Meda, Mylan, Besins, Replens, Regelle, Syk, MonaLisa Touch, and La Roche-Posay. These companies have had no control of the content of any lectures, articles, or other work she has done for them. Amir Lass has been previously contracted to a company manufacturing HRT products.