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Understanding the long-term benefits and risks of HRT

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Understanding the major long-term benefits of HRT

All-cause mortality

Women aged 50–59

7 deaths per 1000 women aged 50–59 each year in the UK[1]

2 fewer deaths in women who initiate oral oestrogen and a synthetic progestogen within 10 years of the menopause[2]

2.5 fewer deaths in women who initiate body-identical oestradiol (oral or transdermal) and a progestogen within 10 years of the menopause*[3]

Women aged 60–69

16.5 deaths per 1000 women aged 60–69 each year in the UK[1]

No reduction in all-cause mortality is seen when older women start oral oestrogen and a synthetic progestogen more than 10 years after menopause[2]

6.5 fewer deaths in older women who start body-identical oestrogen (oral or transdermal) with a progestogen more than 10 years after menopause*[3]

*Very few studies have assessed all-cause mortality in women using transdermal oestrogen. To our knowledge, this is the only study that has stratified all-cause mortality in women using transdermal oestrogen by age. No studies, including this one, have evaluated all-cause mortality in women using transdermal oestrogen with body-identical progesterone, which has greater cardiovascular benefits. Randomised clinical trials are needed to quantify the effects of body-identical hormones on all-cause mortality in women.

Coronary heart disease (CHD)

Women aged 50–59

9 cases of CHD per 1000 women aged 50–59 over 5 years[4]

4 fewer cases of CHD (cardiovascular death or non-fatal MI) in women who start HRT within 10 years of the menopause[2]

Transdermal oestradiol and body-identical progesterone have a superior cardiovascular safety profile and may further reduce cardiovascular mortality in women aged 50–59[5]

Statins have not been shown to prevent CHD or reduce all-cause mortality when used for primary prevention in women[6]

Coronary heart disease (CHD)

Women aged 60–69

18 cases per 1000 women aged 60–69 over 5 years [4]

No change in CHD incidence in women who start HRT more than 10 years after the menopause [2]

9 fewer deaths in women who start body-identical oestrogen (oestradiol) +/– a progestogen more than 10 years after menopause* [3]

*Very few studies have assessed CHD risk in women using transdermal oestrogen. To our knowledge, this is the only study that has stratified CHD risk in women using transdermal oestrogen by age. No studies, including this one, have evaluated CHD risk in women using transdermal oestrogen with body-identical progesterone, which has greater cardiovascular benefits. Randomised clinical trials are needed to quantify the effects of body-identical hormones on CHD risk in women.

Diabetes

Women aged 50–59

Globally, 15% of women aged 50–59 are estimated to have diabetes [7]

4.5 fewer cases in women aged 50–59 who take HRT [8]

Women aged 60–69

Globally, 20% of women aged 60–69 are estimated to have diabetes [7]

6 fewer cases in women aged 60–69 who take HRT [7]

HRT also has beneficial effects on glycaemic control in women with established diabetes (reduced insulin resistance, reduced HbA1c) [9]

**Pooled data from 107 clinical trials with 33,315 participants followed for a mean duration of 1.5 years. Limited data suggests that benefits are greater in women who use HRT for more than 1.5 years; in a prospective observational study the risk of new onset diabetes was reduced by 69% in women aged 52 to 62 years who used HRT for between 2.5 and 5 years. [10]

Osteoporosis

Women aged 50–59

There are 15 fractures per 1000 women aged 50–59 each year [11]

7 fewer fractures in women aged 50–59 who use HRT [12]

Women aged 60–69

There are 21 fractures per 1000 women aged 60–69 each year [11]

5 fewer fractures in women aged 60–69 who take HRT [12]

Dementia

46 cases per 1000 women aged > 65 years [13]

14.5 fewer cases in women who start oestrogen only HRT within 10 years of menopause [14]

10 fewer cases in women who start oestrogen and progestogen HRT within 10 years of menopause* [14]

***Dementia is the leading cause of female death in the UK. The reduction in risk in women using combined HRT (oestrogen plus progestogen) is not statistically significant. However, in clinical studies benefit is likely to have been underestimated because most women received oral oestrogen, typically conjugated equine oestrogen, with or without a synthetic progestin. In the only study that has assessed dementia risk in women treated with body-identical hormones, formulations containing 17β-oestradiol +/- progesterone were associated with greater reductions in the risk of combined neurodegenerative diseases including Alzheimer's disease.[15] Evidence suggests that the risk of dementia is lower in women who use HRT for more than 10 years.[14-15]**

Menopause symptom relief is a key benefit of HRT that is not included here. There is also mounting evidence that HRT may prevent or reduce the risk of other long-term health conditions such as Parkinson's disease, arthritis, lung cancer, and colorectal cancer. The long-term conditions listed above are those for which there is the strongest evidence of benefit. This information is based upon the best currently available evidence.

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Understanding the risks of HRT

Breast cancer

23 cases of breast cancer in women aged 50–59 per 1,000 women over five years [1]

An additional 4 cases in women who use combined HRT consisting of oral oestrogen with a synthetic progestogen [1]

4 fewer cases in women who use oral oestrogen alone [1]

No additional cases in women who use oestrogen with body-identical progesterone for up to 5 years [2,3*]

*It is not currently possible to quantify breast cancer risk in women who use body-identical progesterone for more than 5 years due to a lack of long-term safety data.

Venous thrombo-embolism (VTE) Women aged 50–59

5 cases of VTE per 1000 women aged 50–59 over 5 years [4]

An additional 1.5 cases in women who use oral oestrogen only for 5 years [4]

An additional 7 cases who use combined HRT consisting of an oral oestrogen with a synthetic progestogen for 5 years [4]

No evidence of increased risk in women aged 50–59 who use transdermal oestrogen with or without body-identical progesterone or dydrogesterone [5–7]

Venous thrombo-embolism (VTE) Women aged 60–69

8 cases of VTE per 1000 women aged 60–69 over 5 years [4]

An additional 2.5 cases in women who use oral oestrogen only for 5 years [4]

An additional 10 cases who use combined HRT consisting of an oral oestrogen with a synthetic progestogen for 5 years [4]

No evidence of increased risk in women aged 60–69 who use transdermal oestrogen with or without body-identical progesterone or dydrogesterone [5–7]

Stroke

Women aged 50–59

4 cases of stroke per 1000 women aged 50–59 each year [4]

No additional cases in women aged 50–59 who initiate HRT within 10 years of the menopause [8-10*]

*This is true for all types and combinations of HRT. In the Women's Health Initiative (WHI) study there was no increased risk of stroke in women aged 50–59 who used an oral oestrogen combined with a synthetic progestogen.[8] Observational studies have reported no increased risk of stroke in women aged 50–59 using transdermal oestrogen with or without a progestogen.[9-10] The event rate in women aged 50–59 in clinical studies is low. Stroke risk in younger women is linked to thromboembolic risk.[11] Transdermal oestrogen and body-identical progesterone are not associated with an increased risk of thrombosis and are the safest options.[7]

Stroke

Women aged 60–69

9 cases of stroke per 1000 women aged 60–69 each year [4]

4.5 additional cases per 1000 women aged 60–69 who start HRT more than 10 years after the menopause and use an oral oestrogen alongside a progestogen [8]

No additional cases in women aged 60–69 using transdermal oestrogen +/– progestogen [10, 12*]

*A single observational study has reported a small increased risk of stroke in older women who used higher doses of transdermal oestrogen (> 50mcg patch twice weekly; +2 additional cases per 1000 women per year) 12 . The event rate was very low – just 103 of 15,710 cases of stroke occurred in women using transdermal oestrogen, and the authors did not report the duration of use, age of initiation or type of progestogen. More research is needed to explore stroke risk associated with body-identical hormones in older women.

These figures are based on the best currently available evidence. Mounting observational study data suggests that body- identical hormones are safer and associated with fewer risks, but randomised clinical trials are needed to confirm and quantify these findings. For more information and evidence-based support for your perimenopause and menopause, download the free balance app available on the App Store or Google Play.

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Confidence in Menopause

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