

Transforming Women's Long-term Health: A response to the government's call for evidence to inform their Major Conditions strategy.

The Department of Health and Social Care has called for evidence to inform a Major Conditions Strategy, that aims to improve the prevention, diagnosis, treatment, and management of six groups of major health conditions that affect people in the UK.

The six major conditions are: cancers, cardiovascular disease including stroke and diabetes, chronic respiratory diseases, dementia, mental ill health, and musculoskeletal disorders. It is hoped that better management of these major health conditions will improve the health of the nation and ease pressure on the healthcare system.

The Menopause Charity is keen to raise awareness about the long-term benefits of hormone replacement therapy (HRT) that could significantly improve women's health and longevity, with far reaching socio-economic benefits.

The Menopause Charity believes this call represents an exciting opportunity to transform women's long-term health. We believe that improved access to better menopause care and HRT is a cost-effective healthcare strategy that will improve the lives of women, their families, and society.

"Successful aging includes good health and low levels of disability. To that end, primary prevention is far better than managing subsequent organ damage" (1).

The Menopause Charity is keen to raise awareness about HRT's long term health benefits. There is mounting evidence that when initiated early, close to menopause, HRT can delay and prevent many major health conditions that affect women in their later years.

Before the menopause, oestrogen and testosterone are cardio-, bone- and neuro-protective. When hormone levels fall, the incidence of heart disease, dementia, osteoporosis, and many other long-term conditions rises. Consequently, after the menopause women are twice as likely to develop dementia compared with men (2). They are three times more likely to develop osteoporosis (3). Death rates from coronary heart disease (CHD) are considerably lower in premenopausal women than men but converge after the menopause, and CHD is the second most common cause of death in women (2, 4).

The menopause therefore represents a window of opportunity. Early recognition and improved access to hormone replacement therapy would improve quality of life for women with menopausal symptoms. 1 in 10 women leave work due to menopausal symptoms; effective

treatment would enable women to remain in work for longer (direct economic benefits). Enabling women to remain healthy for longer is likely to reduce pressure on the healthcare system, and ultimately save the NHS billions of pounds.

Talk menopause at the mandatory mid-life health check...

The mandatory health check at age 45 is an ideal opportunity for GPs to discuss the long-term health risks associated with hormone deficiency after the menopause.

Emphasising the importance of a healthy diet and regular exercise is also key to prevent chronic disease, but menopausal symptoms such as sugar cravings, joint pain, low mood, and insomnia can make it difficult for women to engage with healthy lifestyle behaviours. Hormone replacement therapy has both direct and indirect benefits because it effectively treats menopausal symptoms and reduces the risk of long-term conditions associated with hormone deficiency.

Body identical hormones are very safe. Unlike oral oestrogen, transdermal oestrogen (oestrogen patches, gels or sprays) does not increase the risk of blood clots (5). Unlike synthetic progestogens, body-identical progesterone doesn't increase the risk of breast cancer (6, 7). The benefits of HRT usually significantly outweigh the risks for most women.

HRT is inexpensive, and therefore likely to be an extremely cost-effective strategy to improve women's health and longevity without taking up valuable NHS resources.

Long-term health benefits of body-identical HRT

Cardiovascular diseases including stroke and diabetes

Diabetes currently affects around 4 million people in the UK, and the prevalence is expected to rise to 5.3 million by 2025 (8). It is a major cause of morbidity and mortality. For example, people with diabetes are more likely to suffer from cataracts and visual impairment, nerve damage and foot problems, skin ulcers, kidney disease, liver disease, and cardiovascular disease. It costs the NHS around £14 billion pounds each year, or £25,000 per minute – 10% of the NHS budget (9).

HRT has been shown to reduce the risk of diabetes in women by 30% (10).

Coronary heart disease is the second most common cause of death in women in the UK, and stroke is the third, accounting for around 9% and 8% of female deaths respectively (2).

Oestrogen and testosterone are cardioprotective (11). HRT using body-identical hormones reduces inflammation, blood pressure, blood cholesterol, and the risk of diabetes; factors that are all associated with an increased risk of coronary heart disease and stroke.

When initiated within 10 years of the menopause, HRT has been shown to halve the risk of coronary heart disease in women (12). Limited data suggests that transdermal oestrogen in the form of a patch, gel or spray may lower stroke risk by up to 40%, which is equivalent to 7 fewer stroke deaths per 1000 women over 10 years (13).

Dementia

Alzheimer's disease is the most common cause of death in women in the UK, accounting for 15% of all female deaths (2). Alzheimer's disease is twice as common in women compared with men. The drop in sex hormones (oestrogen and testosterone) during the menopause transition triggers changes in brain structure and function that progress to Alzheimer's disease in 1 in 5 women. Because the changes start earlier in women, women are more likely to present at a younger age and with more severe disease compared with men.

In 2020 the Lancet published a report listing 12 modifiable risk factors for dementia and estimated that around 40% of dementia cases could be prevented or delayed with lifestyle modification (14). The list includes 5 risk factors that are independently associated with the menopause: high blood pressure, obesity, diabetes, physical inactivity, and depression. Thus, menopause also increases dementia risk indirectly, by increasing the risk of conditions linked with dementia. It can be much harder for menopausal women to adopt healthy lifestyle behaviours that lower dementia risk, because menopause symptoms including sugar cravings, weight gain, joint pains, low motivation, low mood, and insomnia, make it harder for women to exercise, eat healthily, and get adequate sleep.

In a large randomised controlled trial, women who had undergone a hysterectomy and subsequently used oestrogen-only HRT had a reduced risk of dementia death after 18 years (15). There was no beneficial or harmful effect on the risk of dying from dementia in women using combined 'old-fashioned' HRT – oral oestrogen with a synthetic progestogen. Benefit may have been underestimated because the researchers were unable to stratify the data by age, and the benefits of HRT are greater when used by younger women. Mounting experimental evidence and limited observational study data suggests that women who start using body-identical hormone replacement within 10 years of the menopause may have a lower risk of dementia (16, 17).

The incidence of Alzheimer's Disease is predicted to triple by 2050 (18). There is currently no effective therapeutic preventive strategy or cure. Body-identical HRT started within 10 years of the menopause is safe and may mitigate adverse neurological changes that increase dementia risk in some women, especially those with non-modifiable risk factors for dementia such as the APOE4 genotype. Body-identical hormone replacement will also facilitate lifestyle modification strategies that will further reduce dementia risk.

Mental ill-health

Oestrogen and testosterone are neuro- and psycho-protective (19). Hormone fluctuations in the perimenopause and early menopause are associated with psychological symptoms in one third of women. Pre-existing mental illness often gets worse, and the risk of developing new-onset depression doubles in women aged 40-50 (20). Suicidal thoughts are up to 8 times

more prevalent in perimenopausal women (0.6–1.0% of men vs 1% of pre- and postmenopausal women vs 7.8% of perimenopausal women report suicidal ideation) (21), and female suicide rates peak in middle age (22). Schizophrenia is more likely to present in young adulthood, but there is a second smaller peak in first admission rates in women during the perimenopause (23).

The most effective treatment for perimenopausal depression is body-identical hormone replacement. NICE guidance tells us that there is no clear evidence supporting the efficacy of conventional antidepressants in this patient group, yet in a recent on-line survey of over 5000 perimenopausal women, 40% of those with negative mood symptoms who consulted their GP were offered antidepressants rather than HRT (24, 25).

Mental health problems represent the largest single cause of disability in the UK. The cost to the economy is estimated at £105 billion a year, and mental health support and services cost the NHS around £14 billion per year (26, 27). Better training and education of health care professionals working in primary care and mental health services is needed to raise awareness about the link between hormone imbalance and poor mental health. Improved access to menopause care and HRT is likely to significantly reduce the risk of mental ill health in the menopause transition and improve quality of life for many perimenopausal women and their families. Reduced demand for NHS services and increased productivity will benefit the workplace, society, and the UK economy.

Musculoskeletal disorders

Osteoporosis

3.5 million people in the UK are currently living with osteoporosis (28). The rapid fall in oestrogen during the menopause transition causes accelerated bone loss, and bone density may decrease by up to 20% (29). Consequently, women are three times more likely to develop osteoporosis and 1 in 2 women will sustain a fragility fracture, compared with 1 in 5 men (28). Fragility fractures cause chronic pain, disability, loss of independence, and the one-year mortality after a hip fracture is 25%. Osteoporosis costs more than £4.5 billion pounds each year, a figure that is predicted to rise to £6 billion by 2030 as the population ages (30).

HRT is the most effective and appropriate treatment to mitigate bone loss and prevent osteoporosis resulting from hormone deficiency in postmenopausal women (31). When initiated more than 10 years after the menopause, HRT reduces fracture risk by 24% (32). The benefits are greater if HRT is started earlier before bone loss occurs. In a large meta-analysis fracture risk was reduced by 45% in younger women who started HRT within 10 years of the menopause (33).

Despite evidence that HRT is the optimal strategy to prevent osteoporosis and fragility fractures in postmenopausal women, bisphosphonates are more commonly prescribed, and doctors are only advised to 'consider' HRT for younger postmenopausal women with menopausal symptoms (34). HRT is not recommended as first-line treatment due to safety concerns. However, we now know that the 'older' HRT formulations do not increase risk of death from cardiovascular disease (coronary heart disease and stroke), cancer (including breast), or dementia (15). Initiating HRT within 10 years of the menopause, especially 'newer'

body-identical HRT, is associated with a reduced risk of coronary heart disease and a 30% reduction in all-cause mortality (12).

Bisphosphonates prevent fragility fractures in women with established disease (secondary prevention) but, unlike HRT, evidence suggests that they don't prevent osteoporosis from developing in healthy postmenopausal women (primary prevention) (35, 36). Side effects are common and up to 80% of patients discontinue treatment within a year (37). HRT costs the NHS around £120 per person per year, whereas Fosamax (alendronate) – the most commonly prescribed bisphosphonate – costs the NHS around £300 per person per year (38).

Osteoarthritis, fibromyalgia, and other musculoskeletal conditions

Approximately 20 million people in the UK live with pain and disability caused by musculoskeletal (MSK) conditions such as back pain, fibromyalgia, and osteoarthritis. People with arthritis are 20% less likely to be in work than people without arthritis, and 23.3 million working days were lost in 2021 due to MSK conditions (39).

Musculoskeletal ill health accounts for around 1 in 7 GP consultations, 8.3% of hospital admissions, 30 million prescriptions, and more than 100,000 hip and knee replacements each year (mainly for osteoarthritis). MSK conditions account for the third largest area of NHS spending, approximately £6 billion in 2022 (39).

MSK conditions are more prevalent in women (19.5% women vs 14.2% of men). The sex-specific difference in the risk of developing an MSK condition becomes apparent after the menopause. During the perimenopause up to two thirds of women report muscle and/or joint pain, and from age 45 upwards the prevalence of long term MSK conditions increases more steeply in females than males. Consequently, almost a half of women over the age of 75 suffer from an MSK condition, compared with just under a third of elderly men. 6 million women in the UK have osteoarthritis compared with 4 million men (40, 41).

Oestrogen and testosterone have anti-inflammatory effects. Oestrogen and testosterone receptors are present in muscle, bone, and cartilage. It is likely that hormone deficiency after the menopause is a major contributory factor to the higher prevalence of MSK conditions in women, although a causal relationship has yet to be established. Very little research has been done in this field, but the available evidence suggests that HRT reduces joint pain and inflammation, osteoarthritis pain and disability, and joint arthroplasty rates (42). Testosterone therapy has been shown to reduce symptoms (pain, stiffness, fatigue) and improve the quality of life of patients with fibromyalgia (43, 44). More research is urgently needed into the potential benefits of HRT in the prevention and treatment of long term MSK conditions.

Minority ethnic groups and women living in deprived areas

The prevalence of chronic disease varies in different ethnic groups. For example, people from South Asian and Black ethnic groups are more likely to be obese and suffer from type 2 diabetes. The prevalence of cardiovascular disease is highest in people from South Asian and Pakistani groups (45). 29.1% of Pakistani women suffer from a MSK condition, compared with 16.4% of people from other ethnic groups (39). Women from Black Asian and minority ethnic

groups are more likely to suffer from mental ill-health, but less likely to receive support and treatment compared with White women (46).

Despite differences in chronic disease risk, a recent survey revealed that only 8% of menopausal women from Black and minority ethnic groups are currently using HRT, compared with 15% of White menopausal women (40). Women from different ethnic groups experience menopause differently and have different cultural beliefs and attitudes about HRT. Research is needed to identify barriers to seeking help for menopause symptoms and explore ways of engaging with women from different cultural backgrounds, to ensure equitable access to HRT for all women who are likely to benefit from it (47).

HRT use also varies according to area deprivation. Prescribing rates are 29% lower in GP practices in deprived areas, and women in deprived areas are more likely to be prescribed older, oral HRT that has an inferior safety profile compared with newer HRT formulations (48).

There are strong associations between ethnicity and deprivation, and between deprivation and most health outcomes. Women living in the most deprived areas have a shorter life expectancy. People in Bangladeshi, Pakistani and Black ethnic groups are more likely to live in deprived neighbourhoods, and chronic conditions present at an earlier age in people from ethnic minority groups. Consequently, the gap between the least and most deprived is even wider for 'healthy life expectancy' – women living in more affluent areas remain healthy for on average 20 years longer than women from the most deprived areas (45). Improving access to HRT for all women is likely to reduce morbidity, increase longevity, and narrow the gap in healthy life expectancy between women living in the most and least deprived areas.

Raising awareness about menopause-related health inequalities and improving menopause care for women in high-risk ethnic minority groups and women living in deprived areas, is likely to significantly improve the health and quality of life of thousands of women and may save the NHS billions of pounds.

In summary...

HRT was standard care for the management of menopausal symptoms until the early 2000s, when prescription rates plummeted following the publication of the Women's Health Initiative (WHI) study in 2002. The WHI reported a small increased risk of coronary heart disease, stroke, thrombosis, and breast cancer in HRT-users, equivalent to around 1 event per 1200 women. The risk was very small, and 70% of the women in the WHI were over 60 years old.

We now know that HRT is much safer when used by younger women and has significant long-term health benefits. When initiated within 10 years of the menopause, HRT reduces the risk of diabetes by 30%, halves the risk of coronary heart disease, halves the risk of osteoporosis, and reduces all-cause mortality by 30%. More modern formulations don't increase the risk of blood clots, stroke, or breast cancer. Effective relief of menopausal symptoms enables women to engage with healthy life-style behaviours that further reduce their risk of chronic disease.

Sadly, despite the favourable benefit risk profile, HRT prescribing rates have never fully recovered. Today, only 14% of eligible women use HRT. Women from ethnic minority groups and deprived areas are more likely to benefit, but less likely to use HRT.

The Menopause Charity believes that encouraging more widespread use of body-identical hormone therapy in the menopause transition would result in significant health benefits for many women. Including menopause in the Quality and Outcomes Framework (QOF) would incentivise GPs to provide better menopause care, leading to improved health outcomes and significant cost savings for the NHS.

The Menopause Charity hopes this submission will be a “lightbulb moment” for women’s health. We have experts on hand who are passionate about raising awareness and supporting women to improve their menopause-related and long-term health. It is essential that the importance of high-quality menopause care is recognised, as there is no other single therapeutic intervention that would have a greater positive impact on women’s future health. We look forward to working with women, clinicians, and policy makers in this vital area.

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The Menopause Charity aims

The Menopause Charity is committed to educating everybody so that perimenopause and menopause are properly understood.

We want women, and other individuals experiencing menopause, to understand the changes that are happening to them and know what to do next.

We want to make sure that family, friends, co-workers, employers and health care professionals have the information and resources to provide appropriate support.

What does this look like?

Eliminate needless suffering by providing trusted information in a way that everyone understands.

Everyone has equal access to appropriate treatment and support. So they have the tools they need to manage the mental and physical changes of perimenopause and menopause.

Replace existing stigma and social taboo with the view that menopause is part of our health journey. And, handled well, it can be the beginning of a positive new chapter in our lives.

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