Menopause 1

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An empowerment model for managing menopause

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Menopause eventually happens to all people with typically functioning ovaries, and almost one billion women worldwide are postmenopausal. Although the biology of typical menopause is ubiquitous, the experience varies substantially. Factors contributing to the experience include not only individual factors, such as the nature and severity of symptoms, but also psychological, social, and contextual considerations, many of which are modifiable. In this first paper in the *Lancet* Series on menopause, we argue for a new approach that goes beyond the treatment of specific symptoms, to encompass a broad model to support women transitioning this life stage, using the model of empowerment. WHO defines empowerment as an active process of gaining knowledge, confidence, and self-determination to self-manage health and make informed decisions about care. Rather than focusing on menopause as an endocrine deficiency, we propose an empowerment model that recognises factors modifying the experience, in which the patient is an expert in their own condition and the health-care worker supports the patient to become an equal and active partner in managing their own care.

Background

Although menopause is biologically inevitable, experiences vary considerably and are shaped by factors including symptoms, race and ethnicity, social meanings, expectations, self-esteem, life adversity, and general health. In many high-income countries (HICs), menopause is commonly described as a medical problem and sometimes as a hormone deficiency disorder with typical symptoms and long-term health risks that are best managed by hormone replacement.1 However, this disease-based model is challenging in practice given the wide variation in experiences between women and their changing experiences over time. Also, the inevitability of menopause makes finding out whether long-term health outcomes are due to menopause or ageing difficult, particularly given the scarcity of adequate prospective data for long-term health consequences of premature or early menopause. Although management of symptoms is important, a medicalised view of menopause can be disempowering for women, leading to over-treatment and overlooking potential positive effects, such as better mental health with age and freedom from menstruation, menstrual disorders, and contraception.2

In this first paper in our *Lancet* Series, we consider a new approach to menopause that goes beyond the treatment of specific symptoms, based on the model of health empowerment. WHO defines empowerment as an active process of gaining knowledge, confidence, and self-determination to self-manage health and make informed decisions about care.³ Although the principles of health empowerment have not previously been applied to menopause, in 2005 the US National Institutes of Health (NIH) identified the need to develop and disseminate information emphasising menopause as an ordinary, healthy phase of women's lives and promoting its demedicalisation.⁴ Across several health domains there is growing evidence that empowerment is an effective tool to optimise

self-management of health, which can also reduce health-care costs.5

To be empowered, women must be informed and listened to. Women have clearly stated that they want their voices heard and their experiences of menopause acknowledged and validated. Unfortunately, some women report that their concerns are dismissed, particularly those from minority groups.6 We propose a more inclusive approach (figure 1). Key components of menopause empowerment include access to evidence-based and balanced information, preferably before the onset of menopause (panel), tools to support decision making around treatments for symptoms (eg, decision aids), and access to a supportive clinician who listens with empathy and offers treatment if needed by using a shared decisionmaking model (figure 1). More broadly, challenging widespread stigma about menopause as a period of decline and decay and creating a more menopause-friendly work environment might help to empower women.8

In this paper, we focus on empowerment in the context of typical menopause. In other papers in the Series, we consider other types of menopause which might affect the experience and we believe warrant more attention: early menopause, menopause after cancer, and mental health during the menopause transition.

Key messages

- Most women navigate menopause without the need for medical treatments
- Over-medicalisation of menopause can lead to disempowerment and over-treatment
- New tools are available to support the empowerment of women to navigate the menopause transition
- Empowerment is likely to confer benefits for women across socioeconomic and geographical locations, health services, and economies

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This is the first in a **Series** of four papers about menopause. All papers in the Series are available at www.thelancet.com/series/menopause-2024

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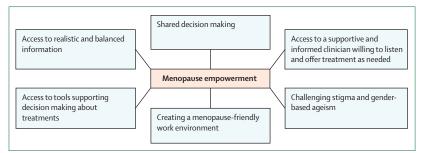


Figure 1: Empowering women to manage menopause

Panel: How clinicians can support empowerment in the management of menopause

Before menopause

- Provide evidence-based information about what to expect
- Challenge overly negative assumptions about menopause and ageing and encourage discussion with friends and family
- Encourage routines that might reduce stress and improve mood—eg, mindfulness and exercise

During the menopause transition

- Provide reassurance and offer effective treatments for symptoms as requested
- Provide realistic information about the likely effects of treatment, the potential for residual symptoms, and the possibility that symptoms could recur when treatment stops
- Offer reassurance that vasomotor symptoms are usually time limited and might be most frequent in the year around the final menstrual period⁷
- Offer behavioural strategies that might reduce the anxiety that can accompany hot flushes, and provide advice on sleep hydiene
- Offer advice about lifestyle factors, addressing sleep, alcohol, and smoking, which can exacerbate vasomotor symptoms
- Challenge self-critical beliefs, which can increase arousal and make flushes worse
- Offer advice about management of symptoms in the workplace⁸
- Encourage connections with other women for discussion and support

After menopause

- Offer effective treatments for persistent vasomotor or genitourinary symptoms
- Encourage good general health⁹
- Offer screening as indicated for primary and secondary prevention of chronic disease

Menopause as a hormone deficiency disease

Menopause became medicalised in the early 20th century, with the belief that women's identity (so-called femininity) and physical and mental health was predicated on the balance between oestrogen excess or deficiency.¹ A wide range of mental and physical disorders in women were (and still are) attributed to hormonal imbalance. Loss of oestrogen after menopause was thought to be individually and socially harmful, and to have consequences such as "untold misery of alcoholism, drug addiction, divorce and broken homes". 10 Oestrogen treatment emerged during the rejuvenation and antiageing movements of the early 1900s. Hormones extracted from animals were injected into humans to counter the perceived deficiencies of age.1 In women, oestrogens were widely prescribed for menstrual and reproductive disorders, pregnancy complications (eg, diethylstilbestrol), psychoses, and depression. 10 From the 1940s, purpose-designed hormone replacement therapy (HRT), extracted from pregnant mares' urine, was widely promoted for the "unstable, estrogen-starved postmenopausal woman".11

Access to HRT has directly benefited many women, bringing the first effective treatment for menopausal symptoms and potential long-term benefits for younger menopausal women. However, as predicted by *The Lancet* in 1975, "The prospect of universal treatment of a large section of the female population is clearly a glittering commercial prize for the pharmaceutical industry" and uptake was rapid. By the mid-1960s around a third of UK women aged 50–64 were taking HRT, making it the most commonly prescribed medication in this population. ¹² Uptake was low in low-income and middle-income countries (LMICs), where menopause is generally considered a part of the natural ageing process, bringing benefits, such as the cessation of menstruation. ¹³

The use of HRT (now called menopausal hormone therapy [MHT]) plummeted in 2002, when a large randomised placebo-controlled trial (RCT) terminated early due to its findings of an increased risk of breast cancer with combined MHT,14 inadequate benefit in the primary outcome (coronary heart disease), and increased risk of stroke with oestrogen-only MHT.15 This drop in MHT use was followed by a decreased incidence of breast cancer in some countries16 and an increased risk of fracture in others.¹⁷ Although longterm follow-up from this RCT has shown no increase in all-cause mortality after 5-7 years of MHT, uptake has never returned to previous levels in most countries. In the UK, use of MHT increased by around 60% between 2020 and 2022, particularly in women from the most affluent areas of the country.18 The reasons for this increased use are uncertain but might reflect the subtantial increase in media attention towards menopause. We argue that additional strategies beyond medication are needed to effectively support women as they transition menopause.

For **general health information** see https://www.nhs.uk/livewell/

Search strategy and selection criteria

We searched databases on MEDLINE, Embase, BioMed Central, Cochrane, and Google from December, 2020, to July, 2023, with key words tailored to each section of the manuscript combining "menopaus*", "psychotherapy*", "premature ovarian insufficiency", and "postmenopaus*" with "menopausal symptom*", "vasomotor symptom*", "genitourinary symptom*", "genitourinary syndrome of menopause", "hormone therap*", "hormone replacement therap*", "non-hormonal therapy*", "psychotherapy*", "empower*", "disempower*", "self confiden*", "self-determination", "self manag*", "care model", "model of care", "model of self care", "shared decision making", "menopause at work", "working", "employment", "ageism", "ageist", "age discrimination", and "age prejudice". We cross-referenced these terms with "systematic review*", "meta-analysis", "metaanalysis", "randomised/randomized controlled trial*", "clinical guideline*", "clinical practice guideline*", and "core outcomes" and websites and guidelines of menopause societies, including British Menopause Society, International Menopause Society, North American Menopause Society, Australasian Menopause Society, the United States Preventive Task Force (USPTF) recommendations on Menopause, and the National Institute of Clinical Excellence (NICE) guidelines. The Turning Research Into Practice and PubMed databases were searched for evidence-based guidelines and systematic reviews. We prioritised the most recent evidence from RCTs and recommendations from international guidelines based on systematic reviews of the evidence (eg, NICE and USPTF). Only publications in English were included.

What is menopause?

The menopause occurs with the final menstrual period; thus, the occurrence of menopause can only be determined in retrospect, and women are considered postmenopausal after 12 months with no periods. ¹⁹ The timing of menopause is thought to be predicated on the size of the primordial follicle pool (ie, ovarian reserve), which is fixed by the time of birth. When the follicle count drops below a critical threshold, ovulation becomes intermittent and eventually stops. The process of going through the menopause starts with menstrual cycle changes and ends 1 year after the final menstrual period (figure 2). ¹⁹ Women with irregular menstrual cycles, following endometrial ablation or hysterectomy, and users of hormonal contraception might be uncertain about the timing of menopause.

Menopause happens to all people with typically functioning ovaries who reach the relevant age. We recognise that this population includes some transgender men and other gender-diverse people; therefore, in some instances, we have referred to "people" rather than "women" to be as accurate and inclusive as possible. However, since much published work refers to people experiencing menopause collectively as women and does

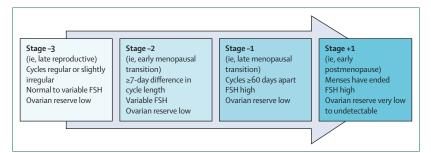


Figure 2: Reproductive stages over time spanning the menopausal transition²¹ FSH=follicle-stimulating hormone.

not clarify how findings might apply to the specific needs of gender-diverse people, we have also used "women" in some instances, to avoid inappropriate generalisation. Evidence on menopause in gender-diverse individuals is scarce and needs more attention.²⁰

Predicting the onset of menopause

Changes in the menstrual cycle are the most reliable indicator of the menopause transition.¹⁹ Blood tests, such as measurement of anti-mullerian hormone, are uninformative for women older than 45 years.²¹ The transition usually starts at around age 47 years in HICs and lasts for 4 years on average, with the average age at menopause being 51 years.²¹ Timing might be earlier in LMICs; for example, data from India indicate that the mean age at menopause is approximately 46 years.²² Globally, around 10% of women experience premature menopause (before age 40 years) or early menopause (at age 40–44 years),²³ which can be iatrogenic (eg, following chemotherapy or radiation for cancer or bilateral oophorectomy) or spontaneous.

What symptoms are caused by menopause?

In a large US longitudinal study, during the menopausal transition, prolonged menstrual bleeding affected more than 90% of women at least once and nearly 80% of women at least three times, and about a third of women had 3 or more days of heavy bleeding on at least three occasions. Heavy and irregular bleeding could affect many aspects of life, including work. Access to toilet facilities and breaks might help. The menopause transition is also when vasomotor symptoms are most likely to start. More information is needed about how best to manage bleeding problems and menopausal symptoms over this period.

Apart from menstrual cycle changes, there is uncertainty about what other symptoms menopause causes, with no universal menopause syndrome. In 2005, an NIH interdisciplinary expert consensus concluded that many women have few or no symptoms and that only vasomotor symptoms, vaginal dryness, and possibly sleep disturbance were clearly attributable to menopause. Subsequently, prospective studies reported that depressive symptoms and disturbances in sleep and

cognition can temporarily worsen for some women.^{27,28} Whether the menopause transition is associated with clinically significant increased anxiety is uncertain and prospective studies show inconsistent findings.²⁹

One US prospective study of 255 women reported an increase in aches, joint pain, and stiffness.³⁰ The 1946 British Birth Cohort reported that psychological symptoms and discomfort with sex increase in around 10–20% of women over the menopause transition.³¹ Less is known about menopausal symptoms in LMICs, but cross-cultural studies suggest that sleep disturbance and muscle and joint pain are more common than vasomotor symptoms,^{32,33} although findings are conflicting.³⁴

Vasomotor symptoms

In HICs, about 40% of women report vasomotor symptoms in the early menopause transition, peaking at 60–80% in the 2 years after the final menstrual period. ^{19,31} These can continue for 4–7 years on average but usually decrease over time. ⁷ Predicting individual symptoms is difficult but prospective studies show that vasomotor symptoms starting in the early menopause transition are more likely to be persistent. ³⁵ Symptom severity can contribute to women seeking treatment for vasomotor symptoms. A pooled analysis of eight cohort studies of more than 21000 women reported that 38% had moderate or severe vasomotor symptoms. ³⁶ A prospective US study (n=255) found that a third of women recruited before menopause had persistent moderate or severe symptoms for 10 years. ³⁷

Vasomotor symptoms seem to differ between ethnic and racial groups. For example, Black and Hispanic women report more severe vasomotor symptoms and Asian American women less severe vasomotor symptoms compared with White women,26 but less is known about minoritised racial and ethnic groups in other multicultural countries, such as the UK. Within the USA there might be sub-variations in the menopausal symptom experience of Asian women.38 As well as frequency and severity, other factors influence the experience of vasomotor symptoms, such as attitudes towards menopause and ageing, religion, socioeconomic status, lifestyle (eg. diet and exercise), and methodological limitations of individual studies.34 However, it is important not to make assumptions about women's experience of menopause based on ethnicity or race.

The degree of interference from vasomotor symptoms, which is strongly influenced by psychological, social, and biological factors, is a priority for menopausal women.³⁹ There is a bi-directional association between vasomotor symptoms and stress, making stress a potentially modifiable factor. There is also a two-way association between vasomotor symptoms and depressed mood. Women with more severe vasomotor symptoms tend to report more depressive symptoms, and women who are depressed can find vasomotor symptoms hard to

manage. 40,41 Other potentially modifiable factors include smoking, high BMI, depressed mood, anxiety, and negative beliefs about menopause. Lifestyle and behavioural changes have shown some success in reducing troublesome symptoms, although findings are mixed (panel). 36,42,43

Muscle and joint pains

Most studies of menopausal symptoms were conducted in White women from HICs or in racial subgroups within these countries. Women in LMICs report substantial differences in the experience of menopause. Southeast Asian women in LMICs might be less troubled by vasomotor symptoms and more likely to report muscle and joint pains than women in HICs.⁴⁴ MHT can modestly improve joint pain but the effect on muscle aches is unknown.⁴⁵

Sleep disturbance

Sleep disturbances are more common in women than in men across the life course and can increase over the menopause transition. Hight-time awakenings due to vasomotor symptoms are common, but sleep can be disturbed for other reasons over this period, and conditions such as obstructive sleep apnoea or depression can contribute. Menopausal symptoms that disturb sleep can affect daytime function, including mood and concentration. An international, consumer-driven process to find out what outcomes should be measured in menopause clinical trials concluded that the effect of treatments on sleep was a priority area.

Genitourinary symptoms

Between 10% and 40% of postmenopausal women report symptoms such as vaginal dryness, vulvovaginal irritation or itching, and dyspareunia. Unlike vasomotor symptoms, these genitourinary symptoms tend to start after menopause and can persist into older age. Genitourinary changes, such as vaginal dryness, can also be secondary to ageing.

Other symptoms

The effects of hormone changes can be difficult to differentiate from concurrent life events such as caring for children at home, managing paid and unpaid employment, taking responsibility for ageing parents, and balancing conflicting life roles.⁴⁹ In particular, changes in mood and cognition and sexual difficulties commonly ascribed to menopause can be caused or exacerbated by these life stressors.⁵⁰ Similarly, although subjective changes in concentration and memory are common over the menopause transition, these have not been clearly linked to long-term cognitive decline. Prospective studies of objective measures of cognition over the menopause transition show only small and mostly temporary memory changes in a minority of women, an observation that many find reassuring.^{51,52}

Subjective changes in memory and concentration can be more common, but whether these changes are secondary to factors such as sleep disturbance is uncertain.⁵³

Menopause and long-term health

Natural menopause at the average age is associated with an increased incidence of some health problems and a reduced incidence of others. Although bone density is known to decline after menopause, whether menopause at the average age increases other chronic conditions such as diabetes, dementia, or cardiovascular disease is uncertain. Prospective studies of body composition and weight have shown mixed findings, but the Study of Women's Health Across the Nation showed a small increase in weight gain of $0.25~{\rm kg}$ per year over the menopause transition, which stabilised postmenopause. The average absolute weight gain associated with menopause was $1.6~{\rm kg}.^{54}$

Managing menopausal symptoms

Although there is uncertainty about the symptoms menopause causes, vasomotor symptoms are consistently reported and are the leading patient priority for treatment, followed by sleep, concentration, and fatigue.⁵⁵

Psychological therapies

The most troublesome aspects of vasomotor symptoms are frequency, severity, bother, and impact on sleep.55 Effective non-pharmacological treatments for vasomotor symptoms include purpose-designed cognitive behaviour therapy (CBT) and hypnosis.⁵⁶ In 2022, a systematic review and meta-analysis including 14 RCTs reported that CBT was superior to control groups in reducing hot flushes, night sweats, sleep disturbance, depression, anxiety, and fatigue and significantly improved quality of life, although effects were generally small to moderate.57 CBT also reduces problematic vasomotor symptoms at work and after breast cancer.58 CBT can be delivered in groups by health professionals, with the use of self-help books, online, or by telephone.⁵⁸ Clinicians should advise patients that RCTs of acupuncture, plant-based therapies, and exercise have largely not shown benefit over placebo or sham procedure for vasomotor symptoms. 59 Clinicans should offer advice about lifestyle factors, addressing sleep, alcohol, and smoking, which can exacerbate vasomotor symptoms (panel).

The North American Menopause Society recommends clinical hypnosis for vasomotor symptoms. This recommendation is based on two RCTs showing a statistically significant improvement in the frequency and severity of vasomotor symptoms. At 12 weeks the reduction in subjective hot flushes with hypnosis was 74·2% versus 17·1% in controls. Clinical hypnosis also reduced interference due to vasomotor symptoms and improved sleep quality. Hypnosis can be delivered by a trained provider or accessed on a smartphone app.

Medical therapies

The North American Menopause Society recommends specific MHT, gabapentin, and oxybutynin, which have mild to moderate efficacy and reduce hot flushes by 1-2 per day with no clinically significant improvement in menopause-related quality of life. 60 Targeted therapy with the neurokinin B receptor antagonist fezolinetant is available in the USA and some European countries. Two large RCTs have compared the efficacy of fezolinetant versus placebo for vasomotor symptoms over 12 weeks, with a 40-week open label extension. 62,63 With 45 mg per day (the dose now marketed), there was a statistically significant reduction in hot flush frequency and severity up to 1 year and serious adverse events were infrequent. Fezolinetant also improved menopause-related quality of life.64 Although clinical trials of neurokinin B receptor antagonists in patients with cancer have not yet been published, breast cancer is not a contraindication to fezolinetant use in the USA. However, improvements in vasomotor symptoms with fezolinetant are modest and do not meet the minimally important clinical difference⁶⁵ for hot flush frequency or menopause-related quality of life. A meta-analysis published in 2024,66 which included 2168 patients from five RCTs, reported a 22.5% mean improvement in frequency of vasomotor symptoms, with small improvements in menopause-related quality of life. In 2023, the independent US Institute for Clinical and Economic Review concluded that fezolinetant was less effective than MHT for vasomotor symptoms, and that MHT might provide additional benefits for sleep, vaginal dryness, and fracture prevention.67

Help-seeking for menopausal symptoms is highly contextual, but 13% of women in HICs are given MHT.36 In the UK, NICE recommends MHT after discussion of the short-term and long-term risks and benefits, which are likely to differ according to patient's age and type of MHT.68 For those with problematic symptoms, MHT generally leads to statistically and clinically significant reductions in vasomotor symptom frequency and severity, along with improvements in menopause-related quality of life.⁶⁷ For standard (1 mg) and low (0.5 mg) dose estradiol, this improvement equates to around 2-4 fewer hot flushes per day versus placebo, which might not be clinically meaningful for those with very frequent symptoms.67 Vasomotor symptoms can co-occur with sleep and mood disturbance^{69,70} and a 2022 systematic review reported that MHT led to small improvements in sleep.⁷¹ However, the primary indication for MHT is the treatment of problematic vasomotor symptoms.72 MHT might improve sleep, memory, and concentration in women taking it for vasomotor symptoms but it is unlikely to have any effect in women without vasomotor symptoms.73 For symptom clusters such as hot flushes, disturbed sleep, and depressed mood, RCTs show that CBT is effective.55

Systemic MHT improves vaginal dryness, but a 2023 systematic review of ten RCTs reported that MHT can worsen or cause urinary incontinence.⁷⁴ Hence, vaginal

For more on CBT delivered in groups by health professions see https://thebms.org.uk

dryness is best managaed with vaginal oestrogen. Patients' priorities for symptom control should inform shared decision making around treatment.

Although combined and oestrogen-only preparations have similar efficacy, their risk profile differs. For example, a 2004 RCT of more than 27000 women showed that combined MHT increased breast cancer risk, but oestrogen-only MHT did not.15 More recently, large observational studies including individual participant meta-analyses from 108 000 patients with breast cancer found that all types of systemic MHT increased risk of breast cancer: risk was substantially greater with combined MHT compared with oestrogen alone. The authors estimated that about one in 50 users of combined MHT will develop breast cancer after 5 years of continued use.75 Combined MHT is the most frequently prescribed form of MHT. In the UK, an estimated 80% of MHT users take a combined preparation because adequate dose and duration of progestogen is needed to prevent endometrial hyperplasia.68

The mode of delivery of MHT also affects the risk to benefit ratio. Transdermal MHT is as effective as oral MHT for vasomotor symptoms⁷⁶ but a systematic review in 2018 found that transdermal MHT did not increase venous thromboembolic disease, although evidence quality was low to moderate. Decisions about how to take MHT should be shared, although patients should be made aware that transdermal preparations appear safer regarding venous thromboembolic risk.

The Monthly Index of Medical Specialities lists contraindications to MHT including oestrogen-sensitive cancer, history of venous thromboembolism or pulmonary embolism, active or recent arterial thromboembolic disease (eg, angina and myocardial infarction), acute liver disease, unexplained genital bleeding, pregnancy, elevated triglycerides, untreated hypertension, porphyria, and previous stroke or transient ischaemic attack. Recommendations on the duration of MHT use vary, but in their 2022 guidelines, the North American Menopause Society cautions against starting MHT after age 60 years or beyond 10 years since menopause.⁵⁶ However, the relative risks versus benefits of continuing MHT beyond age 60 years are uncertain and require a shared decisionmaking approach. Stopping MHT commonly leads to resurgent vasomotor symptoms in up to 50% of patients, and whether this resurgence reflects ongoing menopausal symptoms or a withdrawal effect from MHT is uncertain.79 Neither stopping MHT slowly nor stopping gradually have been shown to prevent resurgent symptoms.80 Shared decision making about treatment should consider the degree of symptom bother, personal preferences, cardiovascular disease and breast cancer risk, and uterine status (ie, having had a hysterectomy or not).72

Fracture risk increases after menopause and NICE indicates that 5 years of MHT reduces risk by 25 fractures per 1000 women on average (range nine to 37 fewer fractures per 1000 women). However, benefits dissipate

by 5 years after MHT is discontinued. 68,81 Therefore, 10 years of MHT from age 50 years to 60 years will not appreciably reduce fracture risk because fractures are uncommon at this age. Although MHT is approved in some countries for the prevention of osteoporosis, the US Preventive Services Task Force recommended in 2022 that MHT should not be used for the primary prevention of any chronic conditions solely because of the unfavourable risk versus benefit balance. 82 In 2023, the Endocrine Society recommended that MHT only be used to prevent osteoporosis in those at substantial risk for whom other therapies are not tolerated or appropriate. 72

For women with predominantly genitourinary symptoms, a 2021 meta-analysis reported that vaginal (topical) oestrogens can reduce dryness and prevent recurrent urinary tract infection.83 An RCT of daily intravaginal dehydroepiandrosterone showed significantly reduced dyspareunia and vaginal dryness at 12 weeks.84 Placebo-controlled RCTs have shown that ospemifene, a selective oestrogen receptor modulator, improves vaginal dryness and dyspareunia.85 However, there are no clinical trials directly comparing ospemifene with vaginal oestrogen, and published trials have focused on objective outcomes such as vaginal pH and the appearance of vaginal cells on microscopy, which are not priorities for symptomatic women or clinicians.⁷¹ Information about vaginal laser is still emerging, but RCTs in participants with and without breast cancer have shown no benefit over sham procedure for genitourinary symptom severity, 86,87 stress incontinence, 88 or sexual function.89 Shared decision making for genitourinary symptoms should include discussion of over-the-counter moisturisers and lubricants, vaginal oestrogen or dehydroepiandrosterone, and oral ospemifene.72

Interventions to support empowerment

Many women navigate menopause without the need for medical intervention, but some experience symptoms that affect function and quality of life. Those seeking medical care are often looking for information rather than drug treatment unless their symptoms are severe.90 Women need easy access to unbiased, accurate information in a form they can understand, created without industry influence and without any hidden agendas to sell a drug or service.⁹¹ Accessing credible information can be challenging, particularly for women in LMICs where home remedies, ayurvedic, and homoeopathic therapies are often preferred to medical treatments for menopausal symptoms.³³ Clinicians caring for patients with menopausal symptoms can empower and support them by listening with empathy, validating experiences, and being aware of social and cultural differences that can underlie those experiences (figure 1). Normalising menopause and providing realistic and balanced information about the likely nature, severity, and duration of symptoms can be empowering for women and help them to make decisions about management (panel).

For those seeking treatment, clinicians should offer evidence-based information about the range of effective interventions for problematic symptoms, including nonpharmacological and non-hormonal methods, with a model of shared decision making (figure 1).92 However, MHT is the only treatment that benefits both vasomotor and genitourinary symptoms and reduces fracture risk. Menopausal symptoms commonly cluster, and patients experiencing clusters of hot flushes, disturbed sleep, and depressed mood might benefit from interventions that improve multiple symptoms, such as CBT, or nonhormonal treatments that benefit both vasomotor symptoms and depressed mood.^{58,93} A qualitative study of CBT for vasomotor symptoms reported that women felt empowered by learning to self-manage their symptoms, including greater knowledge about menopause, acceptance of their symptoms, and new coping strategies leading to greater confidence and a sense of control.94 Empowerment can directly improve the experience of menopause. A UK qualitative study reported the complex narrative of menopause as a normal event, a struggle, a loss of identity, and as a time of liberation and transformation.95 Unfortunately, many women seeking treatment for menopausal symptoms report feeling dismissed and receiving inaccurate information and ineffective treatments.96

Provision of realistic and impartial information is essential. For example, My Meno Plan was funded by the US NIH and developed without commercial input. It provides evidence-based information about typical changes over the menopause transition and postmenopause and options for self-management and treatment. No treatments are 100% effective, and counselling should be realistic about what improvements to expect and what side-effects can occur (for example, improvement of sleep, memory, and concentration with MHT only for those with problematic vasomotor symptoms⁷³). Also, postmenopausal women considering combined MHT should be aware that up to 50% develop bleeding in the initial months, which might require investigation to rule out endometrial hyperplasia or cancer with ultrasound and potentially lead to hysteroscopy and biopsy. 97 The effect of MHT on bleeding patterns in the perimenopause are not well understood, but intrauterine progestogen might offer better control of heavy bleeding compared with combined MHT.98

Women aged 45–55 years represent a highly productive group making an essential contribution to society and social structures. Women older than 40 years are the fastest growing sector of the paid workforce in HICs, and most essential and voluntary workers are women. ⁹⁹ Many are working during the menopause transition, and symptoms at work can be particularly problematic due to embarrassment and concerns about the reactions of other people. This situation can be particularly

challenging for those working in informal economies and in LMICs. According to the UK Health and Safety Executive, women aged 45-54 years report more workrelated stress than men or women of any other age group, associated with high job demands and inadequate control and support at work. 100 These women have clearly indicated how things could improve. A qualitative study with 137 participants reported that women want their managers to be informed and empathetic about menopause and how symptoms might be exacerbated by the work environment.101 They also wanted their workplace to offer open and supportive communication and helpful work policies including flexible work hours. Many health and social care workers are women. Uniforms that are heavy or made of non-breathable fabric are an avoidable source of discomfort for menopausal women.¹⁰² Practical adjustments to support and empower menopausal women at work include informed and empathetic managers, fans, control of ambient air temperature, and uniforms made from breathable fabrics. 8,100

Evidence from the UN (in 2023) and WHO (in 2021) reports that around 90% of people hold gender biases103 and more than 50% hold ageist attitudes. 104 For older women experiencing menopause, these biases can intersect to reinforce negative attitudes and experiences. Clinicians can help by recognising these biases in themselves and avoiding framing menopause as a period of decay and decline (panel). Negative attitudes towards menopause can directly affect personal experiences. In 2010, a systematic review reported that women with neutral or positive attitudes towards menopause tended to have a greater sense of control than women with more negative attitudes. 105 On the basis of a systematic review of qualitative studies, clinicians can offer reassurance that many women experience growing confidence and assertiveness, freedom from some responsibilities, shifts in family relationships, and accepting and embracing age.95,105

Future developments

There is considerable variation between women in their experience of menopause and few ways to predict who might have symptoms and for how long. Predictive models using genetic and environmental data can inform tools for individual use. Similarly, future studies might be able to identify personalised treatments for those with specific clusters of symptoms or those identified by digital health measures. There is clearly a need for more evidence-based strategies to relieve menopausal symptoms, which requires a skilled workforce to provide clinical care.

Ageism is a powerful social determinant of health, and in countries where menopause is equated with physical and mental decline, it is not surprising that many find this transition daunting. Actively challenging ageism and encouraging a more positive discourse can help reduce

For more on **My Meno Plan** see https://mymenoplan.org/

For Menopause Cafe see https:// www.menopausecafe.net/ For Flesh after Fifty see https:// www.fleshafterfifty.com/

For **Henpicked** see https:// henpicked.net/

For **Women Living Better** see https://womenlivingbetter.org

For the **Global Coalition on Aging** see https://globalcoalitiononaging.com/

For more on the **National Library of Medicine tool** see
https://medlineplus.gov/
webeval/webeval.html

For **Menopause at Work** see https://www.menopauseatwork.

anxiety for women approaching menopause.92 The social value of older women can affect this experience. In contexts in which women's value is predicated on reproduction, menopause tends to reduce social status. By contrast, in societies in which ageing confers respect, such as in Indigenous communities in Australia, menopause is considered less problematic. 106 Growing public discourse about menopause in some settings (eg, the UK) is raising awareness and could help change the culture by reducing stigma and shame and encouraging open discussion. Women have indicated that they want this topic to come out of the shadows and be more openly discussed, particularly in the workplace. They want their experiences heard by each other and their health-care providers.91 Public initiatives aiming to empower women by dispelling myths, sharing realistic experiences, and promoting positive images include Menopause Café, and arts initiatives such as Flesh after Fifty directly challenge negative beliefs and create new positive role models.

Digital health, including use of mobile health apps, telemedicine, and data analytics to improve health systems, surged during the COVID-19 pandemic. New tools are emerging that are designed to empower women to recognise, understand, and manage their own menopausal symptoms through digital technology. For example, Henpicked menopause hub and Women Living Better provide evidence-based, realistic, and clear information about the menopause transition and its symptoms, including stories from women with lived experience and information about treatment options. Women can use the My Meno Plan tool to compare treatments and develop their own management approach in consultation with their health-care provider. Much information about menopause available online is driven by commercial interests. The National Library of Medicine tool can be used for evaluating the quality of online health information. People in LMICs can benefit from proactive information from health-care providers about what to expect at menopause.

In 2021, a European consensus recommended that workplaces should create an open, inclusive, and supportive culture around menopause, with occupational health professionals and human resource managers working together.⁸ To enable employers to make these changes, online resources such as Menopause at Work provide evidence-based and practical information for employers to support their employees, including education, communication, and flexible work policies. However, more information is needed about what workplace interventions are effective.

Despite substantial gaps in knowledge about menopause, research has largely focused on developing new drugs for vasomotor symptoms, although most women do not choose to take medication. Interpretation of these clinical trials has been hindered by inadequate agreed patient-reported outcome measures and inconsistent measures for the same symptom, 107 which

limits comparisons between treatments and precludes data pooling. To standardise these measures, the Core Outcomes in Menopause initiative reached global consensus among clinicians, researchers, and women with lived experience of menopause across 28 countries to find out which outcomes should be measured in future clinical trials for menopausal symptoms.^{47,108}

Most research in menopause is from HICs. Little is known about the diversity of experience across LMICs, and what is known suggests that the differences are greater than the similarities.¹⁰⁹ In addition, women have not been widely consulted about their priorities for menopause research. A Menopause Priority Setting Partnership is underway with the James Lind Alliance¹¹⁰ to find out the research priorities of affected women and their health-care providers for menopause research.

In her 2023 book Period, Kate Clancy described how menstruation is routinely stigmatised as an unruly pathology requiring medical management and as a lamentable curse of womanhood.111 Perceptions of menopause are similar and contribute to disempowerment and negative experiences. Women are shamed for menstruating, and then shamed for not menstruating. 2020 was the start of the WHO and UN decade of healthy ageing. Priority areas of the Global Coalition on Aging include women's lifelong health needs and risks and how best to deliver integrated, person-centred care across the life course. Health literacy, access to quality health care, and economic participation are inextricably linked. By connecting healthy ageing with women's rights, global and national policy leaders can help to empower women to live long, healthy lives.

Contributors

MH conceived and designed the paper, wrote the initial draft, and was responsible for revising this draft on the basis of comments from the other authors. AZL, JD, GDM, MS, DG, and MSH made substantial contributions to the conception or design of the work, or to the acquisition, analysis, or interpretation of data for the work. AZL, JD, GDM, MS, DG, and MSH contributed towards drafting the work or revising it critically for important intellectual content, approved the final version to be published, and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. MH is responsible for the final approval of this manuscript and agrees to be accountable.

Declaration of interests

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References

- Banks E. From dogs' testicles to mares' urine: the origins and contemporary use of hormonal therapy for the menopause. Feminst Review 2002; 72: 2–25.
- Steptoe A, Deaton A, Stone AA. Subjective wellbeing, health, and ageing. *Lancet* 2015; 385: 640–48.
- 3 WHO. Health promotion glossary. Geneva: World Health Organisation, 1998.
- 4 National Institutes of Health. National Institutes of Health Stateof-the-Science Conference statement: management of menopauserelated symptoms. Ann Intern Med 2005; 142: 1003–13.
- 5 Scambler S, Newton P, Asimakopoulou K. The context of empowerment and self-care within the field of diabetes. Health (London) 2014; 18: 545–60.
- 6 Williams RE, Kalilani L, DiBenedetti DB, Zhou X, Fehnel SE, Clark RV. Healthcare seeking and treatment for menopausal symptoms in the United States. *Maturitas* 2007; 58: 348–58.
- 7 Avis NE, Crawford SL, Greendale G, et al. Duration of menopausal vasomotor symptoms over the menopause transition. *JAMA Intern Med* 2015; 175: 531–39.
- 8 Rees M, Bitzer J, Cano A, et al. Global consensus recommendations on menopause in the workplace: a European Menopause and Andropause Society (EMAS) position statement. *Maturitas* 2021; 151: 55–62.
- 9 NHS, Age UK. A practical guide to healthy ageing. https://www. nhs.uk/Livewell/men60-plus/Documents/Age%20UK%20and%20 NHS%20A%20Guide%20To%20Healthy%20Ageing.pdf (accessed Feb 9, 2024).
- 10 Winston RA. Feminine forever. London: W H Allen and Virgin Books, 1966.
- Wilson RA, Wilson TA. The fate of the nontreated postmenopausal woman: a plea for the maintenance of adequate estrogen from puberty to the grave. J Am Geriatr Soc 1963; 11: 347–62.
- 12 Townsend J. Hormone replacement therapy: assessment of present use, costs, and trends. *Br J Gen Pract* 1998; **48**: 955–58.
- 13 Aaron R, Muliyil J, Abraham S. Medico-social dimensions of menopause: a cross-sectional study from rural south India. Natl Med J India 2002; 15: 14–17.
- 14 Rossouw JE, Anderson GL, Prentice RL, 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.
- 15 Anderson GL, Limacher M, Assaf AR, et al. Effects of conjugated equine estrogen in postmenopausal women with hysterectomy: the Women's Health Initiative randomized controlled trial. *JAMA* 2004; 291: 1701–12.
- Banks E, Canfell K. Recent declines in breast cancer incidence: mounting evidence that reduced use of menopausal hormones is largely responsible. *Breast Cancer Res* 2010; 12: 103.
- 17 Karim R, Dell RM, Greene DF, Mack WJ, Gallagher JC, Hodis HN. Hip fracture in postmenopausal women after cessation of hormone therapy: results from a prospective study in a large health management organization. *Menopause* 2011; 18: 1172–77.
- NHS Business Services Authority. NHS publishes new HRT official statistics. Oct 6, 2022. https://media.nhsbsa.nhs.uk/news/nhspublishes-new-hrt-official-statistics (accessed Feb 9, 2024).
- 19 Harlow SD, Gass M, Hall JE, et al. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. *Menopause* 2012; 19: 387–95.
- 20 Glyde T. LGBTQIA+ menopause: room for improvement. Lancet 2022; 400: 1578–79.
- 21 Santoro N, Roeca C, Peters BA, Neal-Perry G. The menopause transition: signs, symptoms, and management options. J Clin Endocrinol Metab 2021; 106: 1–15.
- 22 Prasad JB, Tyagi NK, Verma P. Age at menopause in India: a systematic review. *Diabetes Metab Syndr* 2021; 15: 373–77.
- 23 Zhu D, Chung HF, Dobson AJ, et al. Type of menopause, age of menopause and variations in the risk of incident cardiovascular disease: pooled analysis of individual data from 10 international studies. Hum Reprod 2020; 35: 1933–43.
- 24 Paramsothy P, Harlow SD, Greendale GA, et al. Bleeding patterns during the menopausal transition in the multi-ethnic Study of Women's Health Across the Nation (SWAN): a prospective cohort study. BJOG 2014; 121: 1564–73.

- 25 Santoro N, Roeca C, Peters BA, Neal-Perry G. The menopause transition: signs, symptoms, and management options. J Clin Endocrinol Metab 2021; 106: 1–15.
- 26 Avis NE, Crawford SL, Green R. Vasomotor symptoms across the menopause transition: differences among women. Obstet Gynecol Clin North Am 2018; 45: 629–40.
- 27 Woods NF, Mitchell ES. The Seattle Midlife Women's Health Study: a longitudinal prospective study of women during the menopausal transition and early postmenopause. Womens Midlife Health 2016; 2.6
- 28 El Khoudary SR, Greendale G, Crawford SL, et al. The menopause transition and women's health at midlife: a progress report from the Study of Women's Health Across the Nation (SWAN). *Menopause* 2019; 26: 1213–27.
- Bryant C, Judd FK, Hickey M. Anxiety during the menopausal transition: a systematic review. J Affect Disord 2012; 139: 141–48.
- 30 Freeman EW, Sammel MD, Lin H, et al. Symptoms associated with menopausal transition and reproductive hormones in midlife women. Obstet Gynecol 2007; 110: 230–40.
- 31 Mishra GD, Kuh D. Health symptoms during midlife in relation to menopausal transition: British prospective cohort study. BMJ 2012; 344: e402.
- 32 Obermeyer CM. Menopause across cultures: a review of the evidence. *Menopause* 2000; 7: 184–92.
- 33 Singh V, Sivakami M. Normality, freedom, and distress: listening to the menopausal experiences of Indian women of Haryana. In: Bobel C, Winkler IT, Fahs B, Hasson KA, Kissling EA, Roberts T-A, eds. The Palgrave handbook of critical menstruation studies. Singapore: Springer Singapore, 2020: 985–99.
- 34 Islam RM, Bell RJ, Rizvi F, Davis SR. Vasomotor symptoms in women in Asia appear comparable with women in Western countries: a systematic review. *Menopause* 2017; 24: 1313–22.
- 35 Paramsothy P, Harlow SD, Nan B, et al. Duration of the menopausal transition is longer in women with young age at onset: the multiethnic Study of Women's Health Across the Nation. *Menopause* 2017; 24: 142–49.
- 36 Anderson DJ, Chung HF, Seib CA, et al. Obesity, smoking, and risk of vasomotor menopausal symptoms: a pooled analysis of eight cohort studies. Am J Obstet Gynecol 2020; 222: 478.e1–17.
- 37 Freeman EW, Sammel MD, Sanders RJ. Risk of long-term hot flashes after natural menopause: evidence from the Penn Ovarian Aging Study cohort. *Menopause* 2014; 21: 924–32.
- 38 Im EO, Lee SH, Chee W. Subethnic differences in the menopausal symptom experience of Asian American midlife women. J Transcult Nurs 2010; 21: 123–33.
- 39 Hunter MS, Chilcot J. Testing a cognitive model of menopausal hot flushes and night sweats. J Psychosom Res 2013; 74: 307–12.
- 40 Woods NF, Mitchell ES, Percival DB, Smith-DiJulio K. Is the menopausal transition stressful? Observations of perceived stress from the Seattle Midlife Women's Health Study. Menopause 2009; 16: 90–97.
- 41 Arnot M, Emmott EH, Mace R. The relationship between social support, stressful events, and menopause symptoms. *PLoS One* 2021; 16: e0245444.
- 42 Freeman EW, Sherif K. Prevalence of hot flushes and night sweats around the world: a systematic review. Climacteric 2007; 10: 197–214.
- 43 Freeman EW, Sammel MD, Gross SA, Pien GW. Poor sleep in relation to natural menopause: a population-based 14-year follow-up of midlife women. *Menopause* 2015; 22: 719–26.
- 44 Islam MR, Gartoulla P, Bell RJ, Fradkin P, Davis SR. Prevalence of menopausal symptoms in Asian midlife women: a systematic review. Climacteric 2015; 18: 157–76.
- 45 Chlebowski RT, Cirillo DJ, Eaton CB, et al. Estrogen alone and joint symptoms in the Women's Health Initiative randomized trial. *Menopause* 2013; 20: 600–08.
- 46 Baker FC, Lampio L, Saaresranta T, Polo-Kantola P. Sleep and sleep disorders in the menopausal transition. Sleep Med Clin 2018; 13: 443–56.
- 47 Lensen S, Bell RJ, Carpenter JS, et al. A core outcome set for genitourinary symptoms associated with menopause: the COMMA (Core Outcomes in Menopause) global initiative. *Menopause* 2021; 28: 859–66.
- 48 Lethaby A, Ayeleke RO, Roberts H. Local oestrogen for vaginal atrophy in postmenopausal women. Cochrane Database Syst Rev 2016: 2016; CD001500.

- 49 Tooth L, Mishra G. Socioeconomic factors associated with trajectories of caring by young and mid-aged women: a cohort study. BMC Public Health 2014; 14: 74.
- 50 Nelson HD. Menopause. Lancet 2008; 371: 760-70.
- 51 Greendale GA, Huang MH, Wight RG, et al. Effects of the menopause transition and hormone use on cognitive performance in midlife women. *Neurology* 2009; 72: 1850–57.
- 52 Maki PM. Verbal memory and menopause. *Maturitas* 2015; 82: 288–90.
- 53 Woods NF, Coslov N, Richardson MK. Effects of bothersome symptoms during the late reproductive stage and menopausal transition: observations from the Women Living Better Survey. *Menopause* 2023; 30: 45–55.
- 54 Greendale GA, Sternfeld B, Huang M, et al. Changes in body composition and weight during the menopause transition. JCI Insight 2019; 4: e124865.
- 55 Carpenter JS, Woods NF, Otte JL, et al. MsFLASH participants' priorities for alleviating menopausal symptoms. *Climacteric* 2015; 18: 859–66.
- 56 The 2022 Hormone Therapy Position Statement of The North American Menopause Society Advisory Panel. The 2022 hormone therapy position statement of The North American Menopause Society. *Menopause* 2022; 29: 767–94.
- 57 Ye M, Shou M, Zhang J, et al. Efficacy of cognitive therapy and behavior therapy for menopausal symptoms: a systematic review and meta-analysis. *Psychol Med* 2022; 52: 433–45.
- 58 Hunter MS. Cognitive behavioral therapy for menopausal symptoms. Climacteric 2021; 24: 51–56.
- 59 Franco OH, Chowdhury R, Troup J, et al. Use of plant-based therapies and menopausal symptoms: a systematic review and meta-analysis. JAMA 2016; 315: 2554–63.
- 60 The 2023 Nonhormone Therapy Position Statement of The North American Menopause Society Advisory Panel. The 2023 nonhormone therapy position statement of The North American Menopause Society. *Menopause* 2023; 30: 573–90.
- 61 Elkins GR, Fisher WI, Johnson AK, Carpenter JS, Keith TZ. Clinical hypnosis in the treatment of postmenopausal hot flashes: a randomized controlled trial. *Menopause* 2013; 20: 291–98.
- 62 Lederman S, Ottery FD, Cano A, et al. Fezolinetant for treatment of moderate-to-severe vasomotor symptoms associated with menopause (SKYLIGHT 1): a phase 3 randomised controlled study. *Lancet* 2023; 401: 1091–102.
- 63 Johnson KA, Martin N, Nappi RE, et al. Efficacy and safety of fezolinetant in moderate to severe vasomotor symptoms associated with menopause: a phase 3 RCT. J Clin Endocrinol Metab 2023; 108: 1981–97.
- 64 Santoro N, Waldbaum A, Lederman S, et al. Effect of the neurokinin 3 receptor antagonist fezolinetant on patient-reported outcomes in postmenopausal women with vasomotor symptoms: results of a randomized, placebo-controlled, double-blind, doseranging study (VESTA). Menopause 2020; 27: 1350–56.
- 65 Constantine GD, Simon JA, Kaunitz AM, et al. TX-001HR is associated with a clinically meaningful effect on severity of moderate to severe vasomotor symptoms in the REPLENISH trial. *Menopause* 2020; 27: 1236–41.
- 66 Bonga KN, Mishra A, Maiti R, Padhy BM, Meher BR, Srinivasan A. Efficacy and safety of fezolinetant for the treatment of menopause associated vasomotor symptoms: a meta-analysis. Obstet Gynecol 2024, published online Jan 16. doi:10.1097/AOG.000000000000005508.
- 67 Beaudoin FL, McQueen RB, Wright A, et al. Fezolinetant for moderate to severe vasomotor symptoms associated with menopause: effectiveness and value; final evidence report. Jan 23, 2023. https://icer.org/wp-content/uploads/2022/06/ICER_ Menopause_FinalReport_01232023.pdf (accessed Feb 9, 2024).
- 68 Lumsden MA, Davies M, Sarri G. Diagnosis and management of menopause: the National Institute of Health and Care Excellence (NICE) guideline. JAMA Intern Med 2016; 176: 1205–06.
- 69 Cray LA, Woods NF, Herting JR, Mitchell ES. Symptom clusters during the late reproductive stage through the early postmenopause: observations from the Seattle Midlife Women's Health Study. Menopause 2012; 19: 864–69.
- 70 Woods NF, Hohensee C, Carpenter JS, et al. Symptom clusters among MsFLASH clinical trial participants. *Menopause* 2016; 23: 158–65.

- 71 Pan Z, Wen S, Qiao X, Yang M, Shen X, Xu L. Different regimens of menopausal hormone therapy for improving sleep quality: a systematic review and meta-analysis. *Menopause* 2022; 29: 627–35.
- 72 Cappola AR, Auchus RJ, El-Hajj Fuleihan G, et al. Hormones and aging: an Endocrine Society Scientific statement. J Clin Endocrinol Metab 2023; 108: 1835–74.
- 73 Savolainen-Peltonen H, Hautamäki H, Tuomikoski P, Ylikorkala O, Mikkola TS. Health-related quality of life in women with or without hot flashes: a randomized placebo-controlled trial with hormone therapy. *Menopause* 2014; 21: 732–39.
- 74 Christmas MM, Iyer S, Daisy C, Maristany S, Letko J, Hickey M. Menopause hormone therapy and urinary symptoms: a systematic review. *Menopause* 2023; 30: 672–85.
- 75 Collaborative Group on Hormonal Factors in Breast Cancer. Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence. *Lancet* 2019; 394: 1159–68.
- 76 Santoro N, Allshouse A, Neal-Perry G, et al. Longitudinal changes in menopausal symptoms comparing women randomized to lowdose oral conjugated estrogens or transdermal estradiol plus micronized progesterone versus placebo: the Kronos Early Estrogen Prevention Study. Menopause 2017; 24: 238–46.
- 77 Canonico M, Plu-Bureau G, Lowe GD, Scarabin PY. Hormone replacement therapy and risk of venous thromboembolism in postmenopausal women: systematic review and meta-analysis. *BMJ* 2008; 336: 1227–31.
- 78 Rovinski D, Ramos RB, Fighera TM, Casanova GK, Spritzer PM. Risk of venous thromboembolism events in postmenopausal women using oral versus non-oral hormone therapy: a systematic review and meta-analysis. *Thromb Res* 2018; 168: 83–95.
- 79 Brunner RL, Aragaki A, Barnabei V, et al. Menopausal symptom experience before and after stopping estrogen therapy in the Women's Health Initiative randomized, placebo-controlled trial. Menopause 2010; 17: 946–54.
- 80 Lindh-Astrand L, Bixo M, Hirschberg AL, Sundström-Poromaa I, Hammar M. A randomized controlled study of taper-down or abrupt discontinuation of hormone therapy in women treated for vasomotor symptoms. *Menopause* 2010; 17: 72–79.
- 81 Stuenkel CA, Davis SR, Gompel A, et al. Treatment of symptoms of the menopause: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2015; 100: 3975–4011.
- 82 Mangione CM, Barry MJ, Nicholson WK, et al. Hormone therapy for the primary prevention of chronic conditions in postmenopausal persons: US Preventive Services Task Force recommendation statement. JAMA 2022; 328: 1740–46.
- 83 Chen YY, Su TH, Lau HH. Estrogen for the prevention of recurrent urinary tract infections in postmenopausal women: a meta-analysis of randomized controlled trials. *Int Urogynecol J* 2021; 32: 17–25.
- 84 Labrie F, Archer DF, Koltun W, et al. Efficacy of intravaginal dehydroepiandrosterone (DHEA) on moderate to severe dyspareunia and vaginal dryness, symptoms of vulvovaginal atrophy, and of the genitourinary syndrome of menopause. Menopause 2018; 25: 1339–53.
- 85 Archer DF, Goldstein SR, Simon JA, et al. Efficacy and safety of ospemifene in postmenopausal women with moderate-to-severe vaginal dryness: a phase 3, randomized, double-blind, placebocontrolled, multicenter trial. *Menopause* 2019; 26: 611–21.
- 86 Li FG, Maheux-Lacroix S, Deans R, et al. Effect of fractional carbon dioxide laser vs sham treatment on symptom severity in women with postmenopausal vaginal symptoms: a randomized clinical trial. JAMA 2021; 326: 1381–89.
- 87 Page AS, Verbakel JY, Verhaeghe J, Latul YP, Housmans S, Deprest J. Laser versus sham for genitourinary syndrome of menopause: a randomised controlled trial. *BJOG* 2023; 130: 312–19.
- 88 Alexander JW, Karjalainen P, Ow LL, et al. CO(2) surgical laser for treatment of stress urinary incontinence in women: a randomized controlled trial. Am J Obstet Gynecol 2022; 227: 473.
- 89 Mension E, Alonso I, Anglès-Acedo S, et al. Effect of fractional carbon dioxide vs sham laser on sexual function in survivors of breast cancer receiving aromatase inhibitors for genitourinary syndrome of menopause: the LIGHT randomized clinical trial. JAMA Netw Open 2023; 6: e2255697.

- 90 Constantine GD, Graham S, Clerinx C, et al. Behaviours and attitudes influencing treatment decisions for menopausal symptoms in five European countries. Post Reprod Health 2016; 22: 112–22.
- 91 LaCroix A, Ensrud K. The flash dance of midlife: the Skylight 1 trial. Nat Med 2023; 29: 1324–25.
- Hickey M, Hunter MS, Santoro N, Ussher J. Normalising menopause. BMJ 2022; 377: e069369.
- 93 Hickey M, Szabo RA, Hunter MS. Non-hormonal treatments for menopausal symptoms. BMJ 2017; 359: j5101.
- 94 Balabanovic J, Ayers B, Hunter MS. Cognitive behaviour therapy for menopausal hot flushes and night sweats: a qualitative analysis of women's experiences of group and self-help CBT. Behav Cogn Psychother 2013; 41: 441–57.
- 95 de Salis I, Owen-Smith A, Donovan JL, Lawlor DA. Experiencing menopause in the UK: the interrelated narratives of normality, distress, and transformation. J Women Aging 2018; 30: 520–40.
- 96 Williams RE, Levine KB, Kalilani L, Lewis J, Clark RV. Menopause-specific questionnaire assessment in US population-based study shows negative impact on health-related quality of life. *Maturitas* 2009; 62: 153–59.
- 97 Abdullahi Idle S, Panay N, Hamoda H. A cross-sectional national questionnaire survey assessing the views of members of the British Menopause Society on the management of patients with unscheduled bleeding on hormone replacement therapy. Post Reprod Health 2021; 27: 159–65.
- 98 Somboonporn W, Panna S, Temtanakitpaisan T, Kaewrudee S, Soontrapa S. Effects of the levonorgestrel-releasing intrauterine system plus estrogen therapy in perimenopausal and postmenopausal women: systematic review and meta-analysis. Menopause 2011; 18: 1060–66.
- 99 Hammarberg K, Holton S, Michelmore J, Fisher J, Hickey M. Thriving in older age: a national survey of women in Australia. *Maturitas* 2019; 122: 60–65.
- 100 Hardy C, Thorne E, Griffiths A, Hunter MS. Work outcomes in midlife women: the impact of menopause, work stress and working environment. Womens Midlife Health 2018; 4: 3.

- 101 Hardy C, Griffiths A, Hunter MS. What do working menopausal women want? A qualitative investigation into women's perspectives on employer and line manager support. *Maturitas* 2017; 101: 37–41.
- 102 Jack G, Riach K, Bariola E, Pitts M, Schapper J, Sarrel P. Menopause in the workplace: what employers should be doing. Maturitas 2016; 85: 88–95.
- 103 Zarocostas J. UNDP reports that 90% of people hold gender-based biases. Lancet 2023; 401: 2026.
- 104 Mikton C, de la Fuente-Núñez V, Officer A, Krug E. Ageism: a social determinant of health that has come of age. *Lancet* 2021; 397: 1333–34.
- 105 Ayers B, Forshaw M, Hunter MS. The impact of attitudes towards the menopause on women's symptom experience: a systematic review. *Maturitas* 2010; 65: 28–36.
- 106 Jurgenson JR, Jones EK, Haynes E, Green C, Thompson SC. Exploring Australian Aboriginal women's experiences of menopause: a descriptive study. BMC Womens Health 2014; 14: 47.
- 107 Iliodromiti S, Wang W, Lumsden MA, et al. Variation in menopausal vasomotor symptoms outcomes in clinical trials: a systematic review. BJOG 2020; 127: 320–33.
- 108 Lensen S, Archer D, Bell RJ, et al. A core outcome set for vasomotor symptoms associated with menopause: the COMMA (Core Outcomes in Menopause) global initiative. *Menopause* 2021; 28: 852–58.
- 109 Avis NE, Brockwell S, Colvin A. A universal menopausal syndrome? Am J Med 2005; 118 (suppl 12B): 37–46.
- 110 The University of Chicago Obstetrics & Gynecology. Menopause priority setting partnership. https://obgyn.uchicago.edu/research/ menopause-priority-setting-partnership (accessed Feb 15, 2024).
- 111 Clancy K. Period: the real story of menstruation. Princeton, NJ: Princeton University Press, 2023.

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