

# Risk factors, management and consequences of severe menopausal vasomotor symptoms

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## Abstract

Menopause, particularly the consequences of severe symptoms, has become the subject of intense media interest. Reducing the prevalent stigma around women's reproductive health has allowed more women to speak openly about their menopause experiences, the effects on their lives and the barriers they face. These effects are far-reaching and illustrate the importance of improving the understanding, management and awareness of severe menopausal symptoms. The cardinal symptoms are hot flushes (or flashes) and night sweats (vasomotor symptoms), although symptoms can vary by ethnicity. For example, some Asian women report other primary symptoms (such as bone and/or joint pain). Vasomotor symptoms affect around 70% of perimenopausal and postmenopausal women and are moderate or severe in around one-third of these women. The US Food and Drug Administration considers vasomotor symptoms to be severe if they cause the person to stop their current activity. Severe vasomotor symptoms drive treatment seeking and can affect quality of life, mental health and work ability. We review the incidence, management and potential long-term health consequences of severe vasomotor symptoms, including cardiovascular disease, diabetes mellitus, cognitive dysfunction, bone health and quality of life. We discuss potential underlying mechanisms and the efficacy of available treatments. Finally, we highlight the evidence gaps in this field and directions for future research.

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## Key points

- The experience of menopause varies dramatically between women, and for the same woman over time. Differences in the frequency and severity of vasomotor symptoms and uptake of treatment are evident between racial, ethnic and socio-economic groups.
- Emerging evidence suggests that severe vasomotor symptoms are associated with long-term adverse health outcomes, including cardiovascular disease and type 2 diabetes mellitus.
- It is not currently known whether treating severe vasomotor symptoms modifies the associations with long-term disease. Current evidence does not support use of menopause hormone therapy (MHT, also termed hormone replacement therapy) for the primary or secondary prevention of chronic disease.
- MHT appears to be the most effective therapy for severe vasomotor symptoms. Newer agents such as neurokinin receptor antagonists are also effective in reducing the frequency and severity of hot flushes and might also improve sleep and menopause-related quality of life.
- Future consistent implementation of validated measurement tools will better facilitate the development and evaluation of medical therapies for vasomotor symptoms through direct comparisons of treatment efficacy.

## Introduction

Menopause is the permanent cessation of menstruation and eventually affects all those born with functioning ovaries. Natural menopause is usually preceded by perimenopause (also termed the menopause transition), which starts with menstrual cycle changes and finishes at the final menstrual period<sup>1</sup> (Fig. 1). Vasomotor symptoms usually start during the perimenopause<sup>1</sup>. Other symptoms such as vaginal dryness usually start in the late perimenopause and postmenopause when circulating concentrations of oestradiol have fallen<sup>2</sup>.

Although the biology of natural menopause is ubiquitous, the experience varies dramatically<sup>3</sup>. An improved understanding of the mechanisms underlying vasomotor symptoms<sup>4</sup> has informed treatment options such as neurokinin receptor antagonists. However, the optimal choice of treatment, dose and duration of use remains uncertain<sup>5</sup>. Vasomotor symptoms are clearly attributable to the menopause, but whether other experiences at menopause such as mood, cognitive disturbance and sleep disturbance are secondary to vasomotor symptoms or are primary menopause symptoms is unclear<sup>6</sup>.

Menopause is usually a natural event that occurs at age 45–55 years, but premature (age <40 years) and early (age <45 years) menopause affects around 10–12% of women<sup>7</sup>. The cause of premature and early menopause can be spontaneous or iatrogenic. Iatrogenic causes include bilateral oophorectomy and gonadotoxic chemotherapy or radiation<sup>7</sup>. The cause and timing of menopause can directly influence symptom severity and health consequences<sup>8</sup>. For example, women undergoing breast cancer treatment appear to experience more severe vasomotor symptoms<sup>9,10</sup>. It is uncertain whether younger age at menopause and/or iatrogenic causes of menopause are more likely to cause severe vasomotor symptoms than natural menopause at the average age<sup>11</sup>. Menopause also affects some transgender men and

other gender-diverse people. As most published work refers to people experiencing menopause collectively as women, we have used the term ‘women’ to avoid inappropriate generalization. Small qualitative studies suggest that navigating menopause raises issues around embodied identity<sup>12</sup> and that transgender and gender-diverse people lack information and support in managing menopause<sup>13</sup>. More information is needed about menopause in this population.

## Severe vasomotor symptoms

Vasomotor symptoms are episodes of profuse heat accompanied by sweating and flushing, mainly in the upper body and head<sup>14</sup>. Vasomotor symptoms at night (‘night sweats’) can disturb sleep. Vasomotor symptoms are the leading reason women seek treatment for menopausal symptoms<sup>15,16</sup>. In the short term, vasomotor symptoms can be disruptive and cause embarrassment and anxiety. Vasomotor symptoms that disturb sleep can affect daytime function, including mood and concentration. An international Priority Setting Partnership across 51 countries and including over 4,000 women with lived experience of menopause concluded that managing vasomotor symptoms and sleep disturbance were leading priorities for future menopause research<sup>17,18</sup>.

In high-income countries, the perimenopause starts at the age of 47 years on average<sup>19</sup>. Vasomotor symptoms usually start in the early perimenopause (experienced by 40% of women in this stage) and peak at 60–80% of women in the 2 years after the final menstrual period<sup>1,20</sup>. These symptoms last for 4–7 years on average, usually with a gradual decrease in frequency and severity over time<sup>21</sup>. However, around 10% of women experience vasomotor symptoms for more than a decade<sup>21</sup>. Race and ethnicity might affect the duration of vasomotor symptoms.

## Severity of vasomotor symptoms

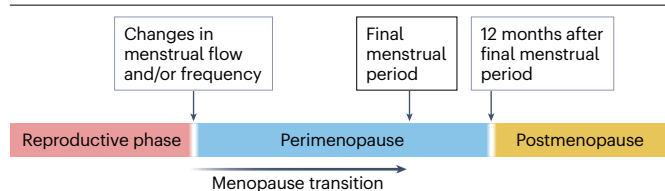
The US Food and Drug Administration (FDA) provides a classification of vasomotor symptom severity (Box 1).

Prospective studies report that most perimenopausal and postmenopausal women do not experience severe vasomotor symptoms. A pooled analysis of eight cohort studies ( $n = 21,460$ ) reported that only 14% of participants had severe vasomotor symptoms and 38% had moderate or severe vasomotor symptoms<sup>22</sup>.

The FDA recommends that participants in clinical trials of treatments for vasomotor symptoms should have at least 7–8 moderate-to-severe hot flushes per day, or 50–60 per week<sup>23</sup>. However, this frequency and severity of vasomotor symptoms is not common. A study of 4,402 women in the USA found that fewer than 10% have vasomotor symptoms of this frequency and severity<sup>24</sup>, creating uncertainty about the relevance of FDA recommendations for those seeking treatment for less frequent and/or severe symptoms. Also, inconsistencies in how clinical trials have classified and measured vasomotor symptoms limits comparisons between studies. In 2024, the global Core Outcomes in Menopause (COMMA) consortium developed a consensus set of measures and validated instruments to measure vasomotor symptoms in clinical trials<sup>17,25,26</sup> (Table 1). Implementation of this core outcome set in future trials will allow comparison between trial findings and data pooling, supporting the translation of evidence into practice<sup>17,25,27</sup>.

## Vasomotor symptoms, race and/or ethnicity and socio-economic position

Race, ethnicity and socio-economic position can be highly relevant to the frequency and severity of vasomotor symptoms. The longitudinal Study of Women’s Health Across the Nation (SWAN,  $n = 3,198$ ) found that Black women in the USA had a greater incidence and duration of



**Fig. 1 | Reproductive stages.** The reproductive lifespan is divided into premenopause, perimenopause and postmenopause. The perimenopause is characterized by changes in menstrual flow and/or frequency and ends with the final menstrual period. Postmenopause is defined as occurring 12 months after the final menstrual period.

vasomotor symptoms compared with white women, whereas Asian women report less frequent vasomotor symptoms than Hispanic and white women<sup>28</sup>. A 2022 survey ( $n = 3,460$ ) reported that more European women (40%) than American (34%) and Japanese (15%) women reported moderate-to-severe vasomotor symptoms<sup>29</sup>. The timing and experience of menopause also differs among racial and/or ethnic minorities and socio-economically disadvantaged groups<sup>30</sup>. Among eight racial and/or ethnic groups in the USA ( $n = 68,864$ ) Black women were almost twice as likely to report severe vasomotor symptoms than white women, followed by Hispanic and Indigenous and/or First Nations women (around 1.3 times more likely), even when accounting for socio-economic status<sup>28,30</sup>. Vasomotor symptoms also persisted longer in Black women in the USA than in white women: 10 years on average compared with 6.5 years for white women<sup>21,31</sup>. Asian women tended to report less severe vasomotor symptoms with a shorter duration compared with white women<sup>21,28,30</sup>. Longer duration of the perimenopause is associated with poorer health outcomes, including increased risk of depression<sup>32,33</sup>. Data from SWAN show that the duration of the perimenopause is longer in Black women than in white women<sup>34</sup>. Research addressing racial and/or ethnic differences in the experience of menopause was one of the Top Ten priorities for women with lived experience of perimenopause and/or menopause in the 2024 Priority Setting Partnership<sup>18</sup>.

Education level can also affect the experience of vasomotor symptoms. Women with a tertiary education were 30–40% less likely to experience frequent or severe symptoms than those with only primary education or no education<sup>35,36</sup>.

## Trajectories of vasomotor symptoms

An Australian longitudinal study identified four trajectories of vasomotor symptoms over the perimenopause: mild (42% of participants), moderate (18%), early severe (11%) and late severe (29%). The mild group reported little symptom change whereas in the moderate group, vasomotor symptoms peaked within 4 years of menopause. Women in the early severe group had the highest likelihood of vasomotor symptoms just at or before menopause. Conversely, the late severe group saw symptom probability increase through perimenopause and gradually peak well into postmenopause before a clear decline over 7 years postmenopause<sup>37</sup> (Fig. 2). These trajectories are similar to longitudinal data from SWAN and from the Medical Research Council National Survey of Health and Development<sup>3,20</sup>.

## Mechanisms of vasomotor symptoms

Withdrawal of oestrogen causes upregulation in the hypothalamic neuropeptide, neurokinin B (NKB) signalling and its receptor (neurokinin

3 receptor; NK3R)<sup>4</sup> (Fig. 3). This upregulation occurs via the median pre-optic nucleus in the hypothalamus, which is closely connected to the autonomic thermoregulatory pathway<sup>4</sup>. Genetic studies show that the *TACR3* gene locus is implicated in vasomotor symptoms<sup>38</sup>. This locus also encodes the NK3R, potentially explaining the mechanism of NK3R antagonists. A genome-wide association study from the UK Biobank identified specific patterns within genetic sequences near *TACR3* that were associated with a lower risk of vasomotor symptoms than in those who did not express these genetic signals<sup>39</sup>.

## Consequences of severe vasomotor symptoms

Severe vasomotor symptoms can be associated with adverse health outcomes. However, limitations include inconsistency in measurement and the lack of large-scale prospective studies with sufficient detail and duration to measure long-term health outcomes.

In the short term, severe vasomotor symptoms can adversely affect quality of life<sup>40–42</sup> and daily activities<sup>29</sup>. Data are mixed, but some studies report that severe vasomotor symptoms can negatively affect productivity, absenteeism, presenteeism and wellbeing at work<sup>43,44</sup>. In a USA survey of 5,219 women aged 40–60 years, around 13% reported at least one adverse work outcome from menopausal symptoms and 10.8% reported missing work in the previous year for 3 days on average due to menopausal symptoms<sup>45</sup>. Greater severity of symptoms increased adverse work outcomes, calculated at an annual productivity loss of US\$1.8 billion<sup>45</sup>.

Mental health can also be affected. A cross-sectional survey of 2,020 Australian women reported that moderate-to-severe vasomotor symptoms were associated with a threefold increased risk of moderate-to-severe depressive symptoms when compared to no-or-mild vasomotor symptoms<sup>46</sup>. A pooled analysis of 21,312 women from eight studies (InterLACE), showed a strong dose-dependent association between vasomotor symptoms and depressed mood, which was largely explained by sleep difficulties<sup>47</sup>. Moderate-to-severe vasomotor symptoms are independently associated with poor concentration and impaired wellbeing<sup>40,46,48</sup>.

## Severe vasomotor symptoms and cognition

The association between menopause and cognition is of growing interest. Cross-sectional studies report that around two-thirds of perimenopausal and/or postmenopausal women experience cognitive concerns such as poor memory, mental fatigue and difficulties with planning, decision-making and multitasking<sup>49,50</sup>. The term 'brain fog' is increasingly used to describe this constellation of subjective cognitive symptoms<sup>49</sup>.

## Box 1 | FDA classification of vasomotor symptom severity

- Mild: sensation of heat without sweating
- Moderate: sensation of heat with sweating, but able to continue activity
- Severe: sensation of heat with sweating, causing cessation of activity

Vasomotor symptoms have been classified according to the US Food and Drug Administration (FDA) criteria as mild, moderate and severe, based on the presence of sweating and whether symptoms resulted in cessation of usual activity<sup>23</sup>.

**Table 1 | A core outcome set for vasomotor symptoms: the Core Outcomes in Menopause (COMMA) consortium**

Outcome	Construct	Measurement instrument
Frequency	Number of self-reported hot flushes and/or night sweats within a stated time frame	Daily hot flush diary (manual or electronic)
Severity	The intensity or severity of vasomotor symptoms <sup>a</sup> in terms of the degree to which the following are experienced: sensations of heat, sweating, ability to continue activity	Daily hot flush diary (manual or electronic)
Distress and/or bother and/or interference	A measure of the degree to which vasomotor symptoms cause distress, bother or interference to normal life, as reported by the woman	Hot Flash Related Daily Interference Scale <sup>151</sup>
Effect on sleep	Overall effect of vasomotor symptoms on ability to fall and stay asleep, and on sleep quality	Hot Flash Related Daily Interference Scale <sup>151</sup>
Satisfaction with treatment	Overall satisfaction with treatment for vasomotor symptoms, considering any advantages and disadvantages of treatment, as reported by the woman	Not yet determined
Adverse effects of treatment	Any adverse outcome that might have resulted from treatment	As per good clinical practice

<sup>a</sup>Vasomotor symptoms are defined as a sudden feeling of warmth and/or heat that then resolves and can be accompanied by sweating or a cold chill; vasomotor symptoms can occur during the day or night.

Although prospective data are very limited, an Australian cross-sectional study ( $n = 5,509$ ) reported that cognitive complaints peaked in early perimenopause and were less prevalent in postmenopause<sup>51</sup>.

Menopausal cognitive complaints are a priority for perimenopausal and postmenopausal women and clinicians. The global Menopause Priority Setting Partnership, guided by the James Lind Alliance methodology, brought together people with lived experience of menopause and healthcare professionals to identify the most important unanswered research questions<sup>52</sup>. In 2024 they reported that cognitive problems was the number three priority for future menopause research<sup>18</sup>. Similarly<sup>18</sup>, in 2025, the UK Royal College of Obstetricians and Gynaecologists published their identified priorities in women's health across the life course and investigating the diagnosis, causes, management and prevention of the cognitive effects of perimenopause and postmenopause was in the top ten<sup>53</sup>.

Although subjective cognitive complaints are common, the evidence for objective cognitive changes is mixed<sup>54</sup>. A 2025 systematic review ( $n = 5,629$ ) reported only one small statistically significant correlation between subject and objective cognition<sup>55</sup>. Multiple factors could contribute to the onset or exacerbation of subjective cognitive symptoms over the perimenopause, including a sensitivity to endogenous hormonal changes and their associated neuroendocrine effects, sleep disturbances, vasomotor symptoms, mood changes (depression, anxiety) as well as factors including chronological ageing and psychosocial stress<sup>49,56</sup>.

Vasomotor, sleep and mood symptoms might have direct and indirect effects on cognition<sup>56</sup>. A small cross-sectional study ( $n = 14$ ) reported that experiencing a higher number of physiologically measured vasomotor symptoms was associated with worse verbal memory in postmenopausal women compared with postmenopausal women

experiencing fewer or no such symptoms, as well as with altered brain activation in frontal and hippocampal brain regions during an encoding task<sup>57</sup>. A cross-sectional study of 226 women aged 45–67 years reported increased white matter hyperintensities, a marker of cerebral small vessel damage, in those with physiologically measured vasomotor symptoms, particularly those occurring during sleep<sup>58</sup>. Hence, vasomotor symptoms might contribute to the cognitive symptoms of menopause either directly or indirectly<sup>59</sup>. Preliminary findings suggest that objectively measured vasomotor symptoms are associated with differences in measures of cognitive function<sup>57,60</sup>. However, a US longitudinal study ( $n = 5,326$ ) reported that self-reported vasomotor symptoms did not predict cognition at age 65 or 72 years<sup>61</sup>. A small cross-sectional study ( $n = 68$ ) reported that moderate-to-severe vasomotor symptoms were associated with reduced objective memory assessment<sup>60</sup>. It is uncertain whether cognitive changes at menopause are dependent or independent of other symptoms such as sleep, mood or vasomotor symptoms.

Cross-sectional data from the Japan Nurses' Health Study ( $n = 12,500$ ) reported 'poor memory or forgetfulness' in 27.9% of women aged 50–54 years, associated with poor sleep, shift work and severe vasomotor symptoms<sup>62</sup>. However, prospective data from SWAN showed that objective changes in cognition across the menopausal transition were not accounted for by vasomotor symptoms, depression or sleep disturbance but that increased anxiety and depressive symptoms affected objective cognition<sup>63</sup>.

It is uncertain whether treating severe vasomotor symptoms improves cognition. A 2024 systematic review found that taking MHT in general was associated with cognitive decline (Mini Mental State Examination) versus placebo, but oestrogen-only MHT slightly improved cognition after surgical menopause<sup>64</sup>, with marked variability. In the Kronos Early Oestrogen Prevention Study (KEEPS) randomized controlled trial (RCT) cognition study, MHT started within 3 years of menopause did not benefit or harm cognitive function at 48 months<sup>65</sup>.

## Severe vasomotor symptoms and cardiovascular disease

Growing evidence suggests that severe vasomotor symptoms could increase the later risk of cardiovascular disease (CVD)<sup>66</sup>. Vasomotor symptoms have been linked to a range of subclinical biomarkers for CVD events including measures of endothelial dysfunction, atherosclerosis and arterial stiffness<sup>67</sup>. Specifically, more frequent and severe vasomotor symptoms are associated with lower flow-mediated dilation, a measure of endothelial dysfunction<sup>68</sup>. Carotid intima-media thickness (cIMT) can be a marker for future atherosclerosis. Earlier onset and more frequent and severe vasomotor symptoms are consistently associated with greater cIMT across several patient populations<sup>69–72</sup>. These studies have reported associations between vasomotor symptoms and other CVD markers including hypertension, insulin resistance, poorer lipid profiles, greater subclinical CVD, poorer endothelial function and greater carotid atherosclerosis<sup>66</sup>. Prospective measures of vasomotor symptoms and CVD in SWAN ( $n = 3,000$ ) over 22 years reported that frequent and persistent vasomotor symptoms are associated with an increased risk of later CVD events<sup>73</sup>. The prospective Australian Longitudinal Study on Women's Health (ALSWH) ( $n = 11,725$ ) reported that more frequent vasomotor symptoms predicted an increased risk of coronary heart disease over a 14-year follow-up period<sup>74</sup>. However, at 20-year follow-up ( $n = 8,881$ ), no association between vasomotor symptoms and coronary heart disease or cerebrovascular disease was observed<sup>75</sup>.

The potential mechanisms linking severe vasomotor symptoms with CVD are uncertain. Specifically, it is not known whether severe vasomotor symptoms are a marker of underlying vascular disturbance

(manifesting as CVD) or whether they cause CVD. Endothelial dysfunction could be an underlying mechanism. Women with vasomotor symptoms have lower flow-mediated dilation<sup>70</sup>, increased cIMT, increased hypertension and vascular plaques<sup>66,68,70,76</sup>. The Women's Health Initiative observational study reported that severe and persistent vasomotor symptoms were associated with accelerated epigenetic ageing that could manifest in worse cardiovascular health<sup>77</sup>. Palpitations often co-occur with vasomotor symptoms but appear to be unrelated to CVD biomarkers<sup>78</sup>.

The 2020 InterLACE study ( $n = 23,365$ ), an international women's health consortium pooling individual-level data from multiple cohort studies, found that the severity, rather than frequency, of vasomotor symptoms was associated with risk of CVD and stroke<sup>79</sup>. Women with severe vasomotor symptoms had more than double the risk of CVD compared to those with no symptoms<sup>79</sup>. A 2023 meta-analysis of 11 studies found that only women reporting vasomotor symptoms while under age 60 years were at increased risk of later CVD<sup>80</sup>.

### Severe vasomotor symptoms and type 2 diabetes mellitus

Severe vasomotor symptoms are associated with later type 2 diabetes mellitus. The Women's Health Initiative ( $n = 150,007$ , mean follow-up of 13.1 years) reported an association between severe vasomotor symptoms and risk of type 2 diabetes mellitus adjusting for obesity (hazard ratio 1.48; 95% confidence interval (CI), 1.34–1.62)<sup>81</sup>. Data from ALSWH ( $n = 4,895$ ) over 15 years found that early severe vasomotor symptoms conferred an elevated likelihood of type 2 diabetes mellitus, after adjusting for BMI (odds ratio 1.55; 95% CI, 1.11–2.17)<sup>82</sup>. SWAN ( $n = 3,075$ , 8 years follow-up) found that vasomotor symptoms were associated with increased insulin resistance (measured via homeostasis model assessment), particularly for women reporting  $\geq 6$  hot flushes in the past 4 weeks<sup>83</sup>.

### Severe vasomotor symptoms and bone health

The evidence is mixed about whether vasomotor symptoms are associated with bone health, and some studies report lower bone mineral density in those with severe vasomotor symptoms<sup>84</sup>. A systematic review in 2024 reported that the presence of vasomotor symptoms was associated with low bone mineral density but not increased fracture risk, and there was no association between the severity of vasomotor symptoms and fracture risk<sup>85</sup>. In a cross-sectional study ( $n = 5,600$ ), more frequent vasomotor symptoms were associated with lower bone mineral density<sup>86</sup>. In a prospective study ( $n = 23,573$ , age 50–79 years) moderate and/or severe vasomotor symptoms were associated with statistically significantly lower bone mineral density at the femoral neck and lumbar spine compared to those without moderate and/or severe vasomotor symptoms<sup>87</sup>.

### Risk factors for severe or frequent vasomotor symptoms

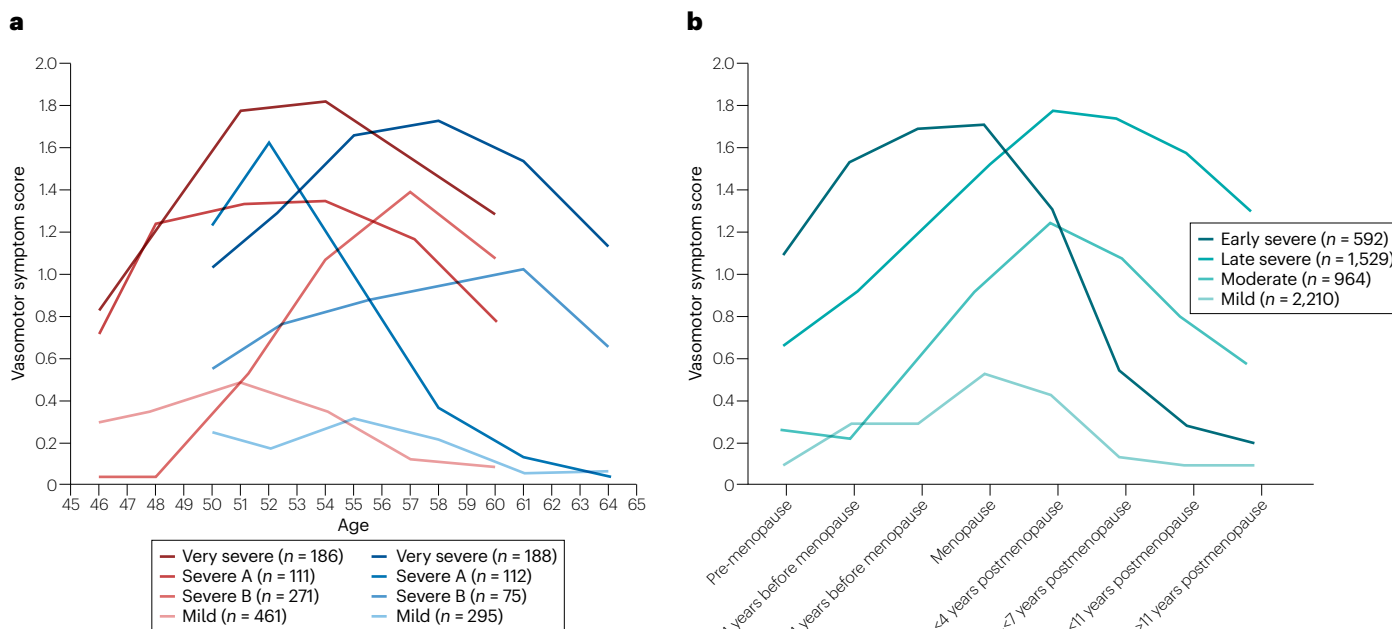
The severity and frequency of vasomotor symptoms can be affected by a large variety of risk factors, both modifiable and unmodifiable (Box 2).

#### Early life factors

Two large studies report that adverse childhood experiences, including childhood abuse or neglect, are associated with severe vasomotor symptoms<sup>88,89</sup>. Similarly, childhood sexual and physical abuse are associated with more frequent night sweats compared with those without a history of childhood abuse ( $n = 295$ )<sup>90</sup>.

#### Reproductive factors

InterLACE ( $n = 18,555$ ; pooled analysis of six cohort studies) demonstrated that earlier age of menarche (age  $\leq 11$  years) was associated



**Fig. 2 | Trajectories of vasomotor symptoms across midlife. a**, Age-specific trajectories of vasomotor symptom scores during midlife ( $n = 5,296$ ), identifying four symptom profiles. Age at baseline is indicated by red-shaded lines (age 46 years) and blue-shaded lines (age 50 years). **b**, Trajectories of

vasomotor symptom scores according to age at menopause ( $n = 5,296$ ), showing four corresponding symptom profiles that differ in severity and temporal pattern, including early and late onset severe profiles. Reprinted with permission from ref. 37.



There is a gap in clinical care for managing severe vasomotor symptoms after breast cancer<sup>9</sup>.

## Psychological factors

Severity of vasomotor symptoms is subjective, and psychological stress and environmental factors such as workplace stress can contribute to perceived severity. Those women reporting high stress, depression and anxiety also report more severe vasomotor symptoms, but the direction of association is uncertain<sup>99</sup>. Interventions to reduce stress such as mindfulness might reduce vasomotor symptom severity<sup>100</sup>. Furthermore, those with more positive attitudes towards menopause might experience less severe vasomotor symptoms<sup>99</sup>. Depressed mood also contributes to the perception of symptom severity. A pooled analysis of eight cohort studies ( $n = 21,312$ ) showed that those with frequent and/or severe depressed mood at baseline were 1.9 times (95% CI, 1.47–2.44) more likely to subsequently report moderate or severe vasomotor symptoms compared with those without depressed mood<sup>47</sup>. A multi-ethnic study ( $n = 2,016$  women, mean age 60 years) found that those experiencing stress and/or intimate partner violence were more likely to report vasomotor symptoms<sup>101</sup>. Together, these findings suggest that expectations and psychological factors modify perceived symptom severity, raising the possibility of interventions to address these factors.

## Obesity and weight gain

High BMI and adiposity are associated with more frequent and/or severe vasomotor symptoms<sup>22,102,103</sup>. A pooled analysis of eight studies ( $n = 21,460$ ) found that women with obesity had a 1.6-fold greater risk of frequent and/or severe symptoms<sup>22</sup>. SWAN ( $n = 1,659$ ) found that both BMI and waist circumference predicted vasomotor symptom frequency<sup>104</sup>. The Women's Health Initiative Dietary Modification trial ( $n = 17,473$ ) reported that weight loss of  $\geq 10$  pounds (4.5 kg) or  $\geq 10\%$  of baseline weight was associated with reduced vasomotor symptoms<sup>105</sup>. The effect of weight loss medications on vasomotor symptoms is not yet known.

## Smoking

A meta-analysis ( $n = 27,054$ ) reported more vasomotor symptoms in women who smoked than in those who did not<sup>106</sup>. InterLACE ( $n = 21,460$ ) demonstrated that current smokers had a 1.8-fold (95% CI, 1.45–2.30) increased risk of frequent and/or severe symptoms versus those who never smoked<sup>22</sup>. There was a clear dose–response relationship between smoking and vasomotor symptoms, with greater number of cigarettes smoked, longer duration, higher cumulative dose and earlier age at initiation of smoking all associated with more frequent and/or severe vasomotor symptoms<sup>22</sup>. This association was not detectable 5 years after cessation of smoking.

## Physical activity

A 2023 review of RCTs concluded that regular, moderate-intensity exercise might reduce vasomotor symptoms, but recognized many gaps in the evidence<sup>107</sup>. A systematic review and meta-analysis of 21 RCTs ( $n = 2,884$ ) reported that physical exercise might reduce vasomotor symptom severity (but not frequency), with very low certainty<sup>108</sup>.

## Diet

A prospective study of 6,040 women reported that a high-fat and high-sugar diet were associated with more frequent vasomotor symptoms versus a high-fruit or Mediterranean diet<sup>35</sup>. The Women's Health

Initiative Dietary trial ( $n = 17,473$ ) reported no effect of a low-fat diet on the frequency of moderate-to-severe vasomotor symptoms<sup>105</sup>. A cross-sectional analysis of five studies ( $n = 19,351$ ) found that frequent soy consumption was associated with less frequent vasomotor symptoms<sup>109</sup>. A cross-sectional survey of 754 perimenopausal or postmenopausal women in the USA reported that severe vasomotor symptoms were less common in women on a vegan diet versus those on an omnivorous diet<sup>110</sup>.

## Treatment of severe vasomotor symptoms

### Pharmacological treatments

Severe vasomotor symptoms drive treatment-seeking for perimenopausal and postmenopausal women and several effective treatments are available<sup>111</sup>. Oestrogen-containing MHT appears to be the most effective<sup>112</sup>. Use of MHT varies globally and within populations in the same country<sup>113</sup>. Combined data from eight studies ( $n = 21,460$ , median age 50 years) in high-income countries reported that 19% of participants were using MHT<sup>22</sup>. As around one-third of perimenopausal and postmenopausal women have moderate-to-severe symptoms, this suggests that many symptomatic women are not seeking or receiving treatment. Socio-economic factors could be contributing to this. For example, data from the UK show that social deprivation is associated with a 30% reduction in MHT prescribing in deprived areas compared with affluent areas<sup>113</sup>.

The combined oral contraceptive pill might also treat severe vasomotor symptoms and control bleeding in perimenopause<sup>114</sup>. Only two small studies have investigated this possibility. In one prospective study ( $n = 100$ ), vasomotor symptoms resolved in 90% of participants within 2 months of starting the combined oral contraceptive pill<sup>115</sup>. One double-blinded RCT of 132 perimenopausal women showed a reduction of  $\geq 50\%$  in frequency and severity of vasomotor symptoms when taking the combined oral contraceptive pill versus a placebo<sup>116</sup>. The relative efficacy of MHT versus combined oral contraceptive pill for severe vasomotor symptoms is uncertain.

Mode of delivery might affect the efficacy of MHT. In 2017, a systematic review and network meta-analysis of RCTs ( $n = 8,326$ ) reported that transdermal oestrogen was more effective than oral MHT for vasomotor symptoms<sup>112</sup>. Efficacy is also dose related. A systematic review of RCT ( $n = 3,069$ ) with participants with  $\geq 7$  vasomotor symptoms per day reported that higher oestrogen doses were more effective: participants reported a mean decrease from baseline of  $-7$  to  $-9.38$  symptoms per day with increasing oestrogen dose (versus a decrease of

## Box 2 | Factors associated with increased risk of severe or frequent vasomotor symptoms

### Unmodifiable risk factors

- Adverse childhood experience
- Early menarche
- Black race and/or ethnicity
- Hypertension during pregnancy
- Breast cancer treatment

### Modifiable risk factors

- Unhealthy diet
- Obesity
- Smoking

5.07 symptoms per day with placebo)<sup>117</sup>. Similarly, a 2016 Cochrane review of oestradiol products ( $n = 5,779$ ) reported that higher oestrogen doses were more effective but had more adverse effects<sup>118</sup>. A 2020 RCT of oral MHT also found that higher oestrogen doses were more effective for severe vasomotor symptoms<sup>119</sup>. Dose-related adverse effects of MHT include endometrial hyperplasia<sup>120</sup>, stroke and venous thromboembolic events<sup>121</sup>. Adverse effects such as venous thromboembolic events might be less likely to occur with transdermal versus oral oestrogen products, although the evidence quality is low to moderate<sup>122,123</sup>.

In clinical practice, managing severe vasomotor symptoms is challenging<sup>124</sup>. Oestrogen-containing MHT reduces the frequency and severity of vasomotor symptoms, but it often does not completely resolve these symptoms<sup>124</sup>. MHT has been shown to work well for vasomotor symptoms but there is little evidence that MHT improves the other symptoms often reported. The evidence for MHT efficacy is almost exclusively based on studies of vasomotor symptoms, and on whether MHT improves other frequently reported symptoms in the perimenopause and menopause such as brain fog, anxiety or depression<sup>5,49</sup>. Oestrogen-only MHT might improve depressive symptoms that arise with vasomotor symptoms, particularly those that disturb sleep<sup>125</sup>. Most clinical guidelines advise titration of MHT to symptoms, but there is no consensus about what level of residual symptoms are acceptable and the maximum dose to use. Severe symptoms might require higher MHT doses, but whether treatment duration should be longer for patients with severe symptoms is uncertain. In general, the risks of MHT increase with dose and duration of use and with older age<sup>126</sup>. Furthermore, on stopping MHT, up to 50% of women experience resurgent vasomotor symptoms<sup>127,128</sup>, and there are no reliable tools to predict the severity of these resurgent symptoms or how long they will last. Shared decision-making that empowers women to make informed and individualized decisions around treatment of vasomotor symptoms should be prioritized<sup>5</sup>.

Severity of vasomotor symptoms is a strong driver for MHT use. However, it is uncertain whether treating severe vasomotor symptoms confers any long-term health benefits. Current evidence does not support the use of MHT solely for primary or secondary prevention of CVD, cognitive function or dementia<sup>126,129</sup>.

## Non-hormonal treatments for severe vasomotor symptoms

Identifying effective non-hormonal treatments for severe vasomotor symptoms is critical because patients who should avoid MHT (such as breast cancer survivors) tend to have more severe vasomotor symptoms<sup>96,130,131</sup>. In addition to the distress and effect on quality of life of experiencing severe symptoms, these patients are at risk of stopping breast cancer treatments (such as endocrine therapy) because of vasomotor symptoms, which directly increases morbidity and mortality from breast cancer<sup>132</sup>.

Non-hormonal pharmacological treatments for vasomotor symptoms that have been shown to be superior to placebo include oxybutynin, neurokinin B receptor antagonists (NKBa, fezolinetant and elinzanetant), gabapentin, oxybutynin, selective serotonin reuptake inhibitors (SSRIs) and selective noradrenaline reuptake inhibitors (SNRIs) and clonidine<sup>133</sup>. Comparison of the relative efficacy and tolerability of these agents is limited by differences in how vasomotor symptoms were measured across studies.

Guidance on the selection and use of non-hormonal treatments is available<sup>133</sup>. A core outcome set has been developed, surveying people with lived experience of menopause across 41 countries and garnering

support from leading international menopause societies and journals to standardize measurement of vasomotor symptoms in clinical trials<sup>17,25</sup>. Neurokinin receptor antagonists are a newer treatment for vasomotor symptoms that target the hypothalamic receptors modulating vasomotor symptoms<sup>4</sup> (Fig. 3). A phase III double blind RCT trial of the NK3 receptor agonist fezolinetant in  $n = 307$  postmenopausal women with moderate-to-severe vasomotor symptoms demonstrated a statistically significant reduction in the frequency of moderate-to-severe vasomotor symptoms at 12 weeks when taking 30 mg or 45 mg per day, from 11.23 and 11.79 to 4.80 and 4.49 per day, respectively, which was maintained over a further 40 weeks of treatment<sup>134</sup>. Symptom severity was also reduced. However, a similar study in Asia with 30 mg of fezolinetant per day did not show a statistically significant change in the frequency of moderate-to-severe vasomotor symptom at 12 weeks (primary outcome)<sup>135</sup>. Two RCTs of the dual NK1 and NK3 receptor agonist elinzanetant (120 mg) in  $n = 396$  postmenopausal women with moderate-to-severe vasomotor symptoms versus placebo demonstrated a statistically significant reduction in frequency and severity of vasomotor symptoms and also improved sleep-related and menopause-related quality of life at 12 weeks<sup>136</sup>. At 52 weeks, descriptive analysis showed ongoing improvement in vasomotor symptoms, sleep-related and menopause-related quality of life<sup>137</sup>. Around one-third of elinzanetant users (versus 14.6% placebo) reported adverse events. The safety profile was largely favourable for both products, but post-marketing surveillance has subsequently demonstrated rare but serious liver injury for fezolinetant leading to FDA advice to measure liver function after 3, 6 and 9 months of use<sup>138</sup>. No signals for liver injury are reported after 52 weeks of elinzanetant<sup>137</sup>.

## Non-pharmacological treatments for vasomotor symptoms

For those who do not wish to use pharmacological treatment for vasomotor symptoms, growing evidence supports cognitive behaviour therapy<sup>139</sup> and clinical hypnosis<sup>140</sup>. Cognitive behaviour therapy delivered individually, in groups, via a self-help booklet or online reduces bother and/or interference from vasomotor symptoms and might also improve mood and sleep<sup>139</sup>. Clinical hypnosis reduces the frequency and severity of vasomotor symptoms. A 2025 RCT demonstrated that self-administered hypnosis was superior to sham hypnosis for vasomotor symptoms, reducing both frequency and severity<sup>141</sup>.

## Future directions

Despite the inevitability of menopause, there are considerable knowledge gaps that undermine the provision of evidence-based care for those with severe vasomotor symptoms. Most studies have focused on pharmacological treatments. However, symptomatic women do not always seek medical therapies<sup>18</sup>. Also, determining which treatments are most effective for severe symptoms has been impeded by use of inconsistent and unvalidated outcome measures. Future implementation of the COMMA core outcome sets and validated measurement tools will help to address this<sup>17,25,27,142–144</sup>. The ability to compare treatment efficacy is particularly important because pharmaceutical companies fund most vasomotor symptom trials and are unlikely to fund direct comparisons with other treatments.

For women approaching natural menopause there is no reliable way of predicting who will experience severe vasomotor symptoms, or for how long, and who might have mild or no symptoms. This fact could cause anxiety for women approaching menopause<sup>145</sup>, who report that their concerns are often dismissed<sup>146</sup>. Providing high-quality

## Box 3 | Empowerment model for managing menopause

- Shared decision-making
- Access to a supportive and informed clinician willing to listen and offer treatment as needed
- Challenging stigma and gender-based ageism
- Creating a menopause-friendly work environment
- Access to tools supporting decision-making about treatments
- Access to realistic and balanced information

This empowerment model considers individual, workplace and societal factors to bring a holistic approach to supporting symptomatic women. Women seeking advice for managing severe vasomotor symptoms need access to a supportive and informed clinician, willing to offer effective treatment using a model of shared decision-making. These women might also benefit from workplace adjustments and supports. Ageism and sexism are highly prevalent in many societies and might worsen the expectations and experience of menopause, including vasomotor symptoms.

information and support could help women to prepare for menopause better, know what to expect and know where to seek help when needed<sup>145</sup>.

Better predictive models of menopause symptom severity using genetic and environmental data could identify those at risk and facilitate preparation and access to effective treatment<sup>38</sup>. Collaborative research with women experiencing menopause is needed to identify optimal strategies to raise awareness. The Top Ten research priorities for those with lived experience of menopause could act as guidance for future initiatives to ensure that research focuses on questions of importance to patients<sup>18</sup>.

Clinical trials of treatments for vasomotor symptoms have largely excluded perimenopausal women<sup>147,148</sup>. This is a substantial research gap, as perimenopause is the time when vasomotor symptoms are most likely to emerge and when women might also be managing heavy and/or irregular bleeding<sup>19</sup>. Although MHT is generally safe for healthy women within 10 years of menopause, less is known about continuing MHT beyond age 60 years. However, starting MHT at older ages (60+ years) might confer additional risks such as increased risk of stroke and dementia<sup>149</sup>. Prospective studies following MHT users from around age 50 years into older age are needed.

## Conclusions

Moderate or severe vasomotor symptoms affect around one-third of women during perimenopause and menopause and can be persistent. Factors over the life course associated with an increased risk of severe vasomotor symptoms include Black race and/or ethnicity, adverse childhood experiences, early menarche, high-fat and high-sugar diets, obesity, smoking and breast cancer treatment. Severe vasomotor symptoms can cause disruption and distress in the short term and are associated with adverse health outcomes, including effects on quality of life and mental health, cognitive function, CVD, diabetes mellitus and bone loss. Current understanding of these effects is limited by inconsistencies in measurement and a lack of large-scale prospective studies with sufficient detail and duration to measure long-term health outcomes. Critically, although effective treatments are available, it is not known

whether treating severe vasomotor symptoms reduces the long-term disease risks associated with severe vasomotor symptoms.

Women seeking advice for managing severe vasomotor symptoms need access to a supportive and informed clinician, willing to offer effective treatment using a model of shared decision-making<sup>5</sup>. These women might also benefit from workplace adjustments and support<sup>44</sup>. Ageism and sexism are highly prevalent in many societies and can worsen the experience of vasomotor symptoms<sup>5</sup>. In addition, socio-demographic, socio-economic and gendered disparities can increase the risk of severe vasomotor symptoms and reduce access to effective treatment<sup>150</sup>. The empowerment model for managing menopause (Box 2) considers these individual, workplace and societal factors to bring a holistic approach to supporting symptomatic women (Box 3).

Published online: 25 March 2026

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## Author contributions

The authors contributed equally to all aspects of the article.

## Competing interests

M.H. was topic expert for the 2024 NICE UK menopause guidelines and is an unpaid board member of BreastScreen Victoria, and editor for the Cochrane Collaboration. All other authors declare no competing interests.

## Additional information

**Peer review information** *Nature Reviews Endocrinology* thanks Joann V. Pinkerton and the other, anonymous, reviewer(s) for their contribution to the peer review of this work.

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**Review criteria** We searched PubMed for all articles published up to 19 February 2026. The search terms included the following keywords in the title and/or abstract: (“vasomotor symptoms” or “VMS” or “hot flashes/flushes” or “night/cold sweats”) AND (“severity/severe” or “frequency/frequent” or “intensity/intense” or “duration” or “bothersome”) AND (“cardiovascular disease” or “diabetes” or “metabolic syndrome” or “osteoporosis” or “quality of life” or “chronic health” or “non-communicable disease” or “breast cancer” or “cancer” or “genitourinary symptoms” or “risk factors” or “demographic” or “socioeconomic” or “race” or “ethnicity” or “stress” or “physiological” or “lifestyle” or “reproductive” or “obesity” or “body mass index” or “weight gain” or “smoking” or “diet” or “exercise” or “physical activity” or “sedentary behaviour” or “type of menopause” or “age at menopause” or “surgical menopause” or “oophorectomy” or “hysterectomy”). This returned 2,011 results. Titles and abstracts were screened, and 298 articles were included for full-text review. We summarized evidence from systematic reviews, meta-analyses and large population-based studies ( $n > 500$ ) where possible.

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