THE 2023 NONHORMONE THERAPY POSITION STATEMENT OF THE NORTH AMERICAN MENOPAUSE SOCIETY

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OBJECTIVE

To update the evidence-based 2015 Nonhormonal Management of Menopause-Associated Vasomotor Symptoms Position Statement of The North American Menopause Society.

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METHODS

An advisory panel of clinicians and research experts in women's health was selected to review and evaluate the literature published since the 2015 Position Statement on the Nonhormonal Management of Menopause-Associated Vasomotor Symptoms. Topics were divided into five sections for ease of review: lifestyle; mind-body techniques; prescription therapies; dietary supplements; and acupuncture, other treatments, and technologies. The panel assessed the most current and available literature to determine whether to recommend or not recommend use based on these levels of evidence:

- Level I Good and consistent scientific evidence
- Level II Limited or inconsistent scientific evidence
- Level III Consensus and expert opinion

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LIFESTYLE

- **Cooling techniques**
  - Hot flashes can be triggered by small, core-body-temperature elevations; therefore, it is feasible that changing lifestyle practices that control core body temperature may decrease vasomotor symptom (VMS) frequency. (Level II; not recommended)
- **Avoiding triggers**
  - There are no clinical trials assessing the effects of avoiding triggers for the alleviation of VMS. Not recommended. (Level II; not recommended)
- **Exercise and yoga**
  - Although there are other health benefits associated with exercise or yoga, the evidence of those interventions for the treatment of VMS is sparse. (Level II; not recommended)
- **Dietary modification**
  - There is limited evidence from strong clinical trials to support the use of dietary modification for improving VMS. (Level III); not recommended)
- **Weight loss**
  - The limited available evidence suggests that weight loss may be used to improve VMS for some women. (Levels II-III; recommended)

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LIFESTYLE KEY POINTS

- There is no strong evidence that lifestyle changes such as cooling techniques and avoiding triggers improve VMS.
- There is insufficient or poor evidence to consider exercise or yoga as a treatment for VMS.
- A healthy diet is important for health promotion and chronic disease prevention. Limited evidence supports dietary modifications as a tool for improving VMS.
- Weight loss may be considered for improving VMS.

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MIND-BODY TECHNIQUES

- **Cognitive-behavioral therapy (CBT)**
  - The body of literature as a whole supports that CBT alleviates bothersome VMS for both survivors of breast cancer and menopausal women. (Level I; recommended)
- **Clinical hypnosis**
  - Hypnosis has been studied for the treatment of hot flashes in two trials. In both trials, clinical hypnosis was significantly better at reducing hot flashes than no treatment. (Level I; recommended)
- **Mindfulness-based interventions (MBI)**
  - Common features of MBI include instruction in meditation practices and how to approach thoughts, feelings, and bodily sensations in an accepting, nonjudgmental manner. Future trials are needed to test the efficacy of MBI for VMS. (Level II; not recommended)
- **Paced respiration**
  - Several studies did not show any benefits over other forms of breathing. (Level I; not recommended)
- **Relaxation**
  - Evidence is limited and inconsistent on relaxation for hot flashes. (Level II; not recommended)

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MIND-BODY TECHNIQUES KEY POINTS

- CBT has been shown to reduce the bother and interference associated with VMS.
- Clinical hypnosis has been shown to reduce VMS frequency and severity.
- MBI for the management of VMS are limited by sample size and lack of control groups and are not designed to consider VMS; therefore, there are not enough data to recommend treatment.
- Paced breathing and relaxation techniques do not alleviate VMS and are not recommended.

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PRESCRIPTION THERAPIES

- Many nonhormone prescription therapies have been evaluated and found to significantly reduce VMS in symptomatic menopausal women.
- Only paroxetine mesylate at 7.5 mg daily is FDA approved for this indication.
- Other medications that reduce VMS include selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), gabapentin, and oxybutynin.
- Suvorexant has been shown to reduce insomnia severity, and findings in a small study of menopausal women showed that it led to reductions in nighttime VMS frequency compared with placebo and was well tolerated. Suvorexant did not improve daytime VMS.
- Neurokinin B antagonists are nonhormone therapeutic agents under development for the management of VMS, but they have not received FDA approval.

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PRESCRIPTION THERAPIES (CONTD)

SUGGESTED DOSING RANGES FOR NONHORMONE PRESCRIPTION THERAPIES

SSRIs		
Paroxetine salt	7.5 mg	Single dose, no titration needed
Paroxetine	10-25 mg/d	Start with 10 mg/d
Citalopram	10-20 mg/d	Start with 10 mg/d
Escitalopram	10-20 mg/d	Start with 10 mg/d (for sensitive or older women, start with 5 mg/d for titration, but this dose has not been evaluated for efficacy)
SNRIs		
Desvenlafaxine	100-150 mg/d	Start with 25-50 mg/d and titrate up by that amount each day
Venlafaxine	37.5-150 mg/d	Start with 37.5 mg/d
Gabapentinoids		
Gabapentin	900-2,400 mg/d	Start with 100-300 mg at night, then add 300 mg at night, then a separate dose of 300 mg in the morning (start 100 mg if concerned about sensitivity)

SNRIs, serotonin-norepinephrine reuptake inhibitors; SSRIs, selective serotonin reuptake inhibitors.

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PRESCRIPTION THERAPIES KEY POINTS

- SSRIs and SNRIs are associated with mild to moderate improvements in VMS.
- Gabapentin is associated with improvements in the frequency and severity of VMS.
- Pregabalin is not recommended for VMS because of adverse events (AEs) and controlled-substance prescribing restrictions.
- Because of significant AEs and no recent studies showing greater benefit than placebo, clonidine is not recommended.
- Oxybutynin has been shown to reduce moderate to severe VMS, although in older adults, long-term use may be associated with cognitive decline.
- Given limited data, suvorexant is not recommended.
- Neurokinin B antagonists have not received FDA approval.

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DIETARY SUPPLEMENTS

- **Managing VMS with dietary supplements is complex and challenging because there are limited rigorous randomized, clinical trial data from which to evaluate supplements and a lack of government regulation to ensure their purity and safety. These over-the-counter products remain widely marketed through direct-to-consumer marketing. They are permitted to market toward specific claims of alleviating symptoms despite limited evidence as long as there is no claim to provide disease benefit.**

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DIETARY SUPPLEMENTS (CONTD)

- **Dietary supplements with limited or inconsistent evidence of benefit**
  - **Soy foods and soy extracts**
  - **Soy metabolite equol**
  - **Pollen extract**
  - **Ammonium succinate**
  - ***Lactobacillus acidophilus***
  - **Rhubarb**

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DIETARY SUPPLEMENTS (CONTD)

- **Dietary supplements without demonstrated evidence of benefit**
  - **Black cohosh**
  - **Wild yam**
  - **Dong quai**
  - **Evening primrose**
  - **Maca**
  - **Ginseng**
  - ***Labisia pumila*/*Eurycoma longifolia***
  - **Chasteberry**
  - **Milk thistle**
  - **Omega-3 fatty acids**
  - **Vitamin E**

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DIETARY SUPPLEMENTS (CONTD)

- **Cannabinoids**
  - **The data evaluating the relationship between cannabinoids and menopause symptoms is very limited. This lack of evidence is particularly notable because more than one-quarter of women have used or are using marijuana to treat their menopause symptoms. A systematic review found only three small studies that evaluated cannabis use and its associations with menopause symptoms, including VMS, insomnia, mood, and depression/anxiety. Based on the lack of available evidence, cannabinoids cannot be recommended for the treatment of VMS.**

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DIETARY SUPPLEMENTS KEY POINTS

- Given mixed evidence of benefit for VMS, soy foods, soy extracts, and the soy metabolite equol are not recommended.
- Given the lack of rigorous, evidence-based scientific research supporting the use of any over-the-counter supplements and herbal therapies for the management of VMS, these remedies are not recommended.
- Cannabinoids are not recommended for the treatment of VMS.

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ACUPUNCTURE, OTHER TREATMENTS, AND TECHNOLOGIES

- **Acupuncture**
  - **A component of the ancient practice of traditional Chinese medicine in which thin needles are inserted into the skin at key points in the body and activated through specific movements (manual acupuncture) or with electrical stimulation (electroacupuncture).**
  - **Existing evidence does not support the use of traditional acupuncture for the treatment of VMS, neither for midlife women nor for VMS in survivors of breast cancer. (Level I; not recommended).**
  - **The use of electroacupuncture, although more promising, still warrants further investigation. (Level II; not recommended)**

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ACUPUNCTURE, OTHER TREATMENTS, AND TECHNOLOGIES (CONTD)

- **Stellate ganglion block**
  - **Stellate ganglion blockade has emerged as a potential treatment option for VMS in both midlife women and those with breast cancer**
  - **Stellate ganglion blockade might help alleviate moderate to very severe VMS in select women. Given that stellate ganglion blockade is a procedure that involves potential risks and adverse events, its potential use for VMS should be carefully evaluated. (Levels II-III; recommended)**

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ACUPUNCTURE, OTHER TREATMENTS, AND TECHNOLOGIES (CONTD)

- **Calibration of neural oscillations**
  - A closed-loop acoustic stimulation neurotechnology based on the principle of allostasis. Given the lack of controlled trials, high-resolution, relational, resonance-based electroencephalic mirroring is not recommended for treatment of VMS. (Level II; not recommended)
- **Chiropractic intervention**
  - There have been no clinical trials of chiropractic interventions for VMS, and epidemiologic survey data show no association between use of such interventions and VMS. (Level II; not recommended)

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ACUPUNCTURE, OTHER TREATMENTS, AND TECHNOLOGIES KEY POINTS

- Existing evidence does not support the use of traditional acupuncture for the treatment of VMS; electroacupuncture requires more rigorous study before it can be recommended.
- Stellate ganglion blockade might alleviate moderate to very severe VMS in select women but is associated with potential risk.
- Calibration of neural oscillations and chiropractic interventions are not recommended for treatment of VMS.

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CONCLUSIONS

- Hormone therapy remains the most effective treatment for VMS in menopausal women within 10 years of their final menstrual periods.
- For women who are not good candidates for HT because of contraindications (eg, estrogen-dependent cancers or cardiovascular disease) or personal preference, it is important for healthcare professionals to be well informed about nonhormone treatment options for reducing VMS that are supported by the evidence.
- Evidence-based review of the literature resulted in several nonhormone options for the treatment of VMS.

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RECOMMENDED

- Cognitive-behavioral therapy (Level I)
- Clinical hypnosis (Level I)
- Selective serotonin reuptake inhibitors/serotonin-norepinephrine reuptake inhibitors (Level I)
- Gabapentin (Level I)
- Oxybutynin (Levels I-II)
- Weight loss
- Stellate ganglion block (Levels II-III).

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NOT RECOMMENDED

- Paced respiration (Level I)
- Supplements/Herbal remedies (Levels I-II)
- Cooling techniques, avoiding triggers, exercise, yoga, mindfulness-based intervention, relaxation, suvorexant, soy foods and soy extracts, soy metabolite equol, cannabinoids, acupuncture, calibration of neural oscillations (Level II)
- Chiropractic interventions(Levels I-III)
- Clonidine (Levels I-III)
- Dietary modification (Level III)
- Pregabalin (Leve III)

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