



# Please Note

---

This presentation is for educational and informational purposes only.

**This is is NOT medical advice.**

It is always wise to check with your doctor before adding any new medicine, herbs, or treatments to your health care regimen. At CannyNurse®, we believe that You are the ultimate authority on your own body and are responsible for your own health and wellness. In this spirit, we joyfully provide education to help you learn more about your amazing body and all its wonders.



CannyNurse.com

# WHAT IS THE MENOPAUSE?

---

Physiologic Stages and Changes



CannyNurse.com

# GENDER DISPARITY IN HEALTHCARE & RESEARCH

---

- Women's conditions historically (and currently) under-funded

(Duh 🙄)

- But if you want some evidence:
  - Mirin, A. A. (2021). Gender disparity in the funding of diseases by the U.S. National Institutes of Health. *Journal of Women's Health*, 30(7), 956–963.  
<https://doi.org/10.1089/jwh.2020.8682>



CannyNurse.com



# Gender Disparity in the Funding of Diseases by the U.S. National Institutes of Health

Arthur A. Mirin, PhD

## Abstract

**Background:** Gender bias has been an ongoing issue in health care, examples being underrepresentation of women in health studies, trivialization of women's physical complaints, and discrimination in the awarding of research grants. We examine here a different issue—gender disparity when it comes to the allocation of research funding among diseases. **Materials and Methods:** We perform an analysis of funding by the U.S. National Institutes of Health (NIH) to ascertain possible gender disparity in its allocation of funds across diseases. We normalize funding level to disease burden, as measured by the Disability Adjusted Life Year, and we specifically consider diseases for which both disease burden and funding level are provided. We apply a power-law regression analysis to model funding commensurate with disease burden. **Results:** We find that in nearly three-quarters of the cases where a disease afflicts primarily one gender, the funding pattern favors males, in that either the disease affects more women and is underfunded (with respect to burden), or the disease affects more men and is overfunded. Moreover, the disparity between actual funding and that which is commensurate with burden is nearly twice as large for diseases that favor males versus those that favor females. A chi-square test yields a  $p$ -value of 0.015, suggesting that our conclusions are representative of the full NIH disease portfolio. **Conclusions:** NIH applies a disproportionate share of its resources to diseases that affect primarily men, at the expense of those that affect primarily women.

**Keywords:** gender disparity, research funding for diseases, National Institutes of Health

## Introduction

THERE IS LITTLE in the published literature when it comes to gender disparity in the allocation of research funds among diseases. A recent study of the funding of 18 different types of cancers by the National Cancer Institute found that gynecologic cancers (ovarian, cervical, uterine) ranked 10th, 12th and 14th, respectively, in funding normalized to years of life lost, whereas prostate cancer ranked 1st.<sup>1</sup> A study focusing on the disease myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), ~75% of whom afflicted are women,<sup>2</sup> found that disease to be the lowest funded (relative to disease burden) in the National Institutes of Health (NIH) portfolio.<sup>3,4</sup> In carrying out the ME/CFS study, it was observed that some of the lowest funded diseases relative to

disease burden were ones that affect primarily women. We chose to examine this issue in greater depth, leading to the analysis reported herein.

Gender bias has been an ongoing issue in health care and has manifested itself in a number of different ways. Other examples include the underrepresentation of women in health studies, the trivialization of women's complaints, and discrimination in the awarding of research grants.

Historically, the underrepresentation of women in health studies and clinical trials has been pervasive.<sup>5</sup> A well-known example is a 1980s study of whether a daily dose of aspirin would reduce cardiovascular mortality, where all 22,071 subjects were male.<sup>6</sup> In 1985, the Public Health Service Task Force on Women's Health Issues released a report advising that "the historical lack of research focus on women's health

## GENDER DISPARITY IN NIH FUNDING

concerns has compromised the quality of health information available to women as well as the health care they receive."<sup>7,8</sup> In response, the NIH announced a new policy that urged researchers to include women in their clinical studies.<sup>9,10</sup> However, a 1990 Government Accountability Office report found that the NIH failed to communicate its policy to grant applicants and was still instructing reviewers to not consider the inclusion of women as a factor when evaluating scientific merit.<sup>11</sup> That same year, NIH formed the Office of Research on Women's Health, one of whose primary missions has been to ensure that NIH-funded research accounts for sex as a biological variable (see <https://orwh.od.nih.gov/sex-gender/nih-policy-sex-biological-variable>).

An issue commonly faced by women is having their physical complaints trivialized or misdiagnosed as psychologically based. As noted by Tascia et al.,<sup>12</sup> the concept of hysteria as a mental disorder attributable to women goes back 4,000 years and was commonly used to misdiagnose females until the turn of the 20th century; it took until 1980 for hysterical neurosis to be deleted from the *Diagnostic and Statistical Manual of Mental Disorders*. A more recent example is that of the disease myalgic encephalomyelitis (ME), also known as chronic fatigue syndrome (CFS), for which ~75% of those affected are women.<sup>2</sup> After a 1984 outbreak in Ilicine Village, NV, the medical community, unable to identify a specific cause, described the disease as being psychogenic.<sup>13,14</sup> Stephen Strass, an expert virologist working at NIH, stated: "The demography of this syndrome reflects an excessive risk for educated adult white women... A less casual appraisal, however, often uncovers histories of unachievable ambition, poor coping skills, and somatic complaints."<sup>15</sup> In 2015, the Institute of Medicine (now the National Academy of Medicine) issued a comprehensive report characterizing ME/CFS as "a serious, chronic, complex, multisystem disease that frequently and dramatically limits the activities of affected patients,"<sup>16</sup> thereby refuting the prevailing psychogenic characterization.

An additional area of gender bias has been in the awarding of research grants. This is elucidated by Wessel<sup>17</sup> in her analysis of the NIH grant process, where she concludes that women indeed face gender bias, particularly when it comes to renewing grants. Kaatz et al.,<sup>18</sup> in their analysis of NIH reviews, state: "The authors' analyses suggest that subtle gender bias may continue to operate in the post-2009 NIH review format in ways that could lead reviewers to implicitly hold male and female applicants to different standards of evaluation, particularly for R01 renewals." Wittenman et al.<sup>14</sup> conclude from their analysis of the Canadian Institutes of Health Research grant process that "Gender gaps in grant funding are attributable to less favorable assessments of women as principal investigators, not of the quality of their proposed research."

In this work, we extend the analysis of Mirin et al.<sup>4</sup> to examine gender disparity among the full spectrum of NIH-funded diseases. That analysis used statistical regression to compare funding of diseases relative to disease burden, using NIH data, to develop an estimate of burden-commensurate funding. Actual funding was compared with burden-commensurate funding to determine which diseases are relatively underfunded or overfunded. Here, we correlate the degree of under- or overfunding with the gender prevalence of each disease.

## Case Study

Gatenby, C., & Simpson, P. (2024). Menopause: Physiology, definitions, and symptoms. *Baillière's Best Practice and Research in Clinical Endocrinology and Metabolism/Baillière's Best Practice & Research. Clinical Endocrinology & Metabolism*, 38(1), 101855. <https://doi.org/10.1016/j.beem.2023.101855>



## Menopause vignette

Clara, a 53 year old patient attends clinic reporting increasing symptoms of hot flushes, anxiety and some vaginal dryness. She has been experiencing these symptoms for the past 12 months but feels that they have been worsening recently and are impacting on her ability to function well at work; as a teacher in a local secondary school. Clara also feels that her sleep is poor secondary to the hot flushes mainly happening at night. This negatively affects her concentration making her feel more irritable, which she is quite deeply saddened by.

Clara is not currently taking any medications. She is not allergic to any medications. She is happily married, up to date with her cervical screening and has had three pregnancies with two vaginal deliveries in 2000 and 2006. She has no family history of venous thrombo-embolism (VTE), breast, ovarian or endometrial cancer. Clara reports some dyspareunia and wonders if this could be due to the vaginal dryness she has been experiencing. She has tried using vaginal moisturisers to some benefit.

Clara has previously suffered from migraines and notes that these have been returning recently. She is concerned about using HRT as she was always told that because she had migraines with aura, she could not use the combined oral contraceptive pill. As a result of this, she had a Mirena (LNG-IUS) fitted in 2021 for heavy menstrual bleeding and contraception. She has experienced amenorrhoea with this in-situ.

Clara would really like some help to manage her symptoms and wonders what may be available to her. She has already tried non-pharmacological measures, by reducing her alcohol intake, increasing the amount of exercise she does by taking up running and practising yoga most mornings before work.

Clara's symptoms appear to be related to the menopause. In view of the options available to Clara she could continue to try non-pharmacological measures, or she could try non-hormonal interventions such as a selective serotonin reuptake inhibitor (SSRI) or a serotonin-norepinephrine reuptake inhibitors (SNRI) to help with her anxiety and vasomotor symptoms, although these may only offer mild to moderate improvements for the latter.

Transdermal oestrogen would not be contra-indicated for Clara in view of her migraine with aura history. It may actually provide her with an improvement in her hormone driven migraine symptoms. She could also use vaginal oestrogens to see if this helps with her vaginal dryness symptoms which are likely to be causing the dyspareunia she has described.

Her LNG-IUS (Mirena) is in date and as such, will provide her with contraception (until this is no longer required for contraception at age 55 years) and endometrial protection for up to 5 years. After which, if she remains taking oestrogen HRT, her Mirena would require a removal and refitting of the device.

# WHAT IS THE MENOPAUSE?

(COMMON DEFINITIONS)

- **Perimenopause**
  - The time of life surrounding menopause (*peri* = around)
  - Starts in 30s/ 40s and ends 1 year after the FMP (Final Menstrual Period)
- **Menopause** (*Meno* – [menses] – *pause* [stopping])
  - Per Mayo Clinic: average age in USA = 51 years  
<https://www.mayoclinic.org/diseases-conditions/menopause/symptoms-causes/syc-20353397>
  - Per Gatenby & Simpson (2024, p. 2): Avg age in UK = 51 years, “normal range for symptom onset” = 45-55 years; 25% of symptom experiencers call them debilitating
- **Postmenopause** – the time of life beginning 1 year after the FMP



CannyNurse.com

# WHAT IS THE MENOPAUSE?

(SCIENTIFIC DEFINITION)

- “The menopause transition is a disruptive process that can last for over a decade and causes symptoms in a majority of women” (p.1)
- “Menopause is the final stage of ovarian physiology in women and represents a time when reproductive function is lost due to complete depletion of the finite ovarian follicle supply” (p.2).
- Santoro, N., Roeca, C., Peters, B. A., & Neal-Perry, G. (2020). The Menopause Transition: Signs, symptoms, and management options. *The Journal of Clinical Endocrinology and Metabolism*/Journal of Clinical Endocrinology & Metabolism, 106(1), 1–15. <https://doi.org/10.1210/clinem/dgaa764>



The Journal of Clinical Endocrinology & Metabolism, 2021, Vol. 106, No. 1, 1–15  
doi:10.1210/clinem/dgaa764

Mini-Review

**The Menopause Transition: Signs, Symptoms, and Management Options**

**Nanette Santoro,<sup>1</sup> Cassandra Roeca,<sup>1</sup> Brandilyn A. Peters,<sup>2</sup> and Genevieve Neal-Perry<sup>3</sup>**

<sup>1</sup>Department of Obstetrics and Gynecology, University of Colorado School of Medicine, Aurora, Colorado  
<sup>2</sup>OSMC, Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, New York 10461, and <sup>3</sup>Department of Obstetrics and Gynecology, University of North Carolina School of Medicine, Chapel Hill, North Carolina 27599

**Abbreviations:** 5- $\alpha$ T, testosterone; AMH, anti-Müllerian hormone; CEE, conjugated equine estrogen; CVD, cardiovascular disease; E2, estradiol; FMP, final menstrual period; FSH, follicle-stimulating hormone; GBS, gonadotropin-releasing hormone; GSM, genitourinary symptoms of menopause; HERS, Heart and Estrogen/Progestin Replacement Study; HT, replacement hormone therapy; LH, luteinizing hormone; LOST, trial of oral-pharm; MPA, medroxyprogesterone acetate; NR1, neurexin 1 receptor; NKB, neurexin 1; P4, progesterone; ST/RAW, Stages of Reproductive Aging Workshop; SWAN, Study of Women's Health Across the Nation; T4, thyroxine; WHI, Women's Health Initiative

Received: 16 October 2020; First Published Online: 23 October 2020; Corrected and Typeset: 17 November 2020.



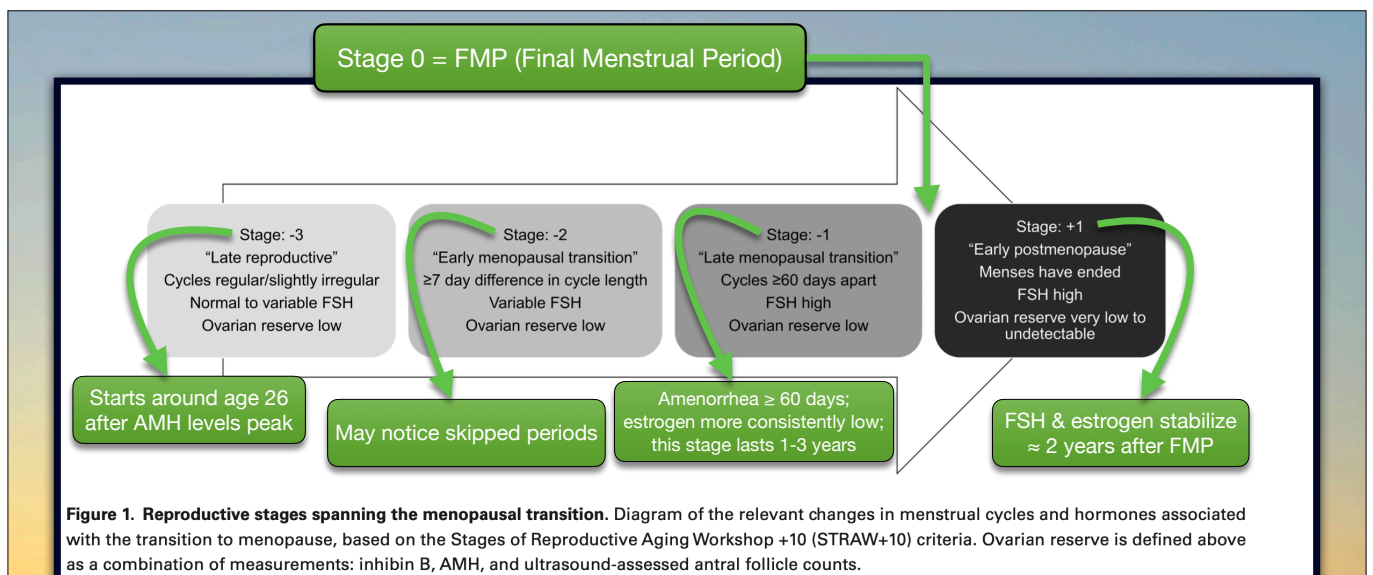
# THE MENOPAUSE TRANSITION

(FROM SANTORO ET AL., 2020)

- **Phase 1: Early Transition**
  - Minimal impact on menstrual cycle (1 cycle per 3 months)
  - Elevated FSH (compensating for low numbers of ovarian follicles)
- **Phase 2: Late Transition**
  - Substantial evidence of estrogen deficiency
  - Increased symptoms
  - Bone mineral loss becomes detectable



CannyNurse.com



**Figure 1. Reproductive stages spanning the menopausal transition.** Diagram of the relevant changes in menstrual cycles and hormones associated with the transition to menopause, based on the Stages of Reproductive Aging Workshop +10 (STRAW+10) criteria. Ovarian reserve is defined above as a combination of measurements: inhibin B, AMH, and ultrasound-assessed antral follicle counts.

FROM "THE MENOPAUSE TRANSITION: SIGNS, SYMPTOMS, AND MANAGEMENT OPTIONS" BY SANTORO ET AL., 2020  
GREEN BOXES ADDED FOR MORE DETAIL BY ARIANA AYU



CannyNurse.com

## FACTORS THAT MAY IMPACT THE TRANSITION

---

- Obesity / BMI — r/t later onset of transition, but not duration\*
- Smoking (tobacco) — r/t earlier entry into transition, shorter duration\*
- Race / Ethnicity
  - African American women: longer duration than white women\*
  - Increased probability of anovulatory cycles: White, Chinese, Japanese\*
  - Decreased probability of anovulatory cycles: African American, Hispanic\*
  - Asian women may have fewer VMS (Gatenby & Simpson, 2024, p.5)
- Alcohol & Caffeine consumption
- *Ariana's Note: Not mentioned in article, but fertility treatments might impact*

## CNS CHANGES DURING THE TRANSITION

---

- HPA axis loses sensitivity to estrogen feedback
- Hypothalamic structure changes
  - Declining hypothalamic sensitivity to estrogen ⇔ hot flashes/ night sweats
  - “In humans, **KNDy-like neurons are also thought to regulate body temperature and play a role in thermoregulation and the emergence of vasomotor symptoms** (hot flashes and night sweats (28), the hallmark manifestations of the menopausal transition. Though typically attributed to estrogen withdrawal, vasomotor symptoms begin before women become floridly and consistently hypoestrogenic and are not necessarily related to ambient estrogen or menstrual cycle patterns (23, 32, 33), suggesting **vasomotor symptoms may also be a manifestation of declining hypothalamic sensitivity to estrogen (23)**” (p.5).





### PRIMARY STUDY

#### A Potential Involvement of Anandamide in the Modulation of HO/NOS Systems: Women, Menopause, and "Medical Cannabinoids"

**Key Findings:** This animal model of estrogen deprivation found that estrogen withdrawal led to a decrease in both heme oxygenase (HO) and nitric oxide synthase (NOS) systems, and similar results in the TRPV1/CGRP pathway, suggesting a potential therapeutic target in estrogen-deficient conditions

**Type of Study:** Animal Study

**Study Result:** Positive

**Study Location(s):** Hungary

**Year of Pub:** 2020

**Cannabinoids Studied:** Anandamide (AEA), Endocannabinoid (unspecified)

**Phytocannabinoid Source:** Not Applicable

**Receptors Studied:** TRPV1, GPCR

**Ligands Studied:** Estrogen

**mg** **Dosage:** AEA (1.0 mg/kg)

**Route of Administration:** Injection

## ANANDAMIDE & MENOPAUSE SYMPTOMS?

- "Our results support the fact that the endocannabinoid system plays a role in the regulation of cardiovascular signaling pathways and could be a therapeutic target for menopause-associated cardiac pathologies.
- The main finding of this study is that **administration of the endocannabinoid AEA restored the estrogen loss-induced adverse effects** via the NOS/HO systems and the activation of the TRPV1/CGRP pathway. **The similarity** between AEA- and estrogen-induced changes **suggests estrogen-like effects of AEA in estrogen-depleted conditions**. However, the combined use of AEA and E2 was not able to amplify the individual estrogen or AEA actions."
- Szabó, R., Börzsei, D., Szabó, Z., Hoffmann, A. N., Zupkó, I., Priksz, D., Kupai, K., Varga, C., & Pósa, A. (2020). A potential involvement of anandamide in the modulation of HO/NOS systems: women, menopause, and "Medical cannabinoids." *International Journal of Molecular Sciences*, 21(22), 8801. <https://doi.org/10.3390/ijms21228801>

## ANANDAMIDE & MENOPAUSE SYMPTOMS?

---

- “Although both HRT and AEA treatments possess advantageous and disadvantageous effects, the examination of AEA-induced pathways may provide new targets and mechanisms of hemodynamic regulation.
- In this regard, Underdown et al. found that AEA treatment reduced infarct size in rat isolated heart by interaction with one or more mechanisms of cannabinoid action [32]. Tuma and Steffens summarized that **the mechanisms by which endocannabinoids are cardioprotective** include **decreased inflammation and oxidative stress as well as increased activation of cardioprotective signaling pathways through activation of CB1 and CB2 receptors** [33].
- CB1 receptors are predominantly expressed in the central nervous system but also present at much lower levels in the myocardium, postganglionic autonomic nerve terminals, and vascular endothelial and smooth muscle cells [27]. **Our current findings show that the presence of CB1 receptors was reduced in the cardiac tissue of the OVX animals; however, AEA treatment restored it.**” (Szabó et al., 2020, p.7)



CannyNurse.com

## ANANDAMIDE & MENOPAUSE SYMPTOMS?

---

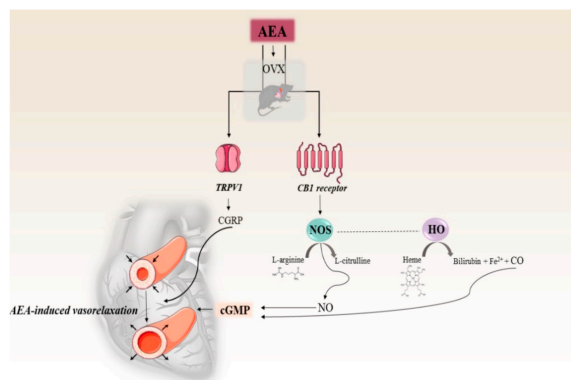
- “Accumulating evidence indicates that **AEA-induced vasorelaxation and cardioprotection** can be mediated via alternative receptors, such as TRPV1. TRPV1 is located predominantly in nerve fibers that innervate the cardiovascular system, and its activation stimulates the release of a dilator neuropeptide, CGRP.
- In a previous study, Ross analyzed the interaction of AEA with TRPV1 and reported that **AEA-induced CGRP release may induce a potential endogenous myocardial protective response** [35]. Our results clearly showed that the TRPV1/CGRP system was underactive in estrogen-depleted conditions; however, these **unfavorable changes were reversed as a result of both AEA and estrogen treatment.**
- **Furthermore, our data proved that AEA and estrogen treatments not only upregulate the activity** and expressions of HO and NOS enzymes, but also induce CGRP release. In accordance with Peng et al. who examined the co-mediated effects of HO and CGRP, we can presume a potential interaction in biological effects of CO, NO, and CGRP [36]. ” (Szabó et al., 2020, p.7)



CannyNurse.com



An overview of the AEA-induced cardiac effects on NOS/HO systems and the TRPV1/CGRP pathway in estrogen-deficient conditions is summarized in Figure 6.



**Figure 6.** Effects of anandamide on NOS/HO systems, and TRPV1/CGRP pathway in an estrogen-deficient rat model. short arrows indicate changes of the diameter of the vessels. AEA= anandamide, OVX= surgical ovariectomy, TRPV1= transient receptor potential vanilloid 1, CGRP= calcitonin gene related peptide, CB1 receptor= cannabinoid 1 receptor, cGMP= cyclic guanosine monophosphate, NOS= nitric oxide synthase, HO= heme oxygenase, NO= nitric oxide, CO= carbon monoxide.

## ANANDAMIDE & MENOPAUSE SYMPTOMS?

- What can we take from this article?
- Author's Conclusions
  - "In this scenario, we proved that two weeks of either AEA or E2 treatment enhanced the NO and HO enzyme systems via CB1R activation, and this tendency was also shown for the TRPV1/CGRP pathway. Furthermore, AEA-induced alterations were similar to the effects of the estrogen replacement therapy, which suggests **AEA estrogen-like role in this model.**" (Szabó et al., 2020, p.11)
- Could we guess that taking THC might potentially help cardiovascular health in menopausal/ post-menopausal women? Maybe...? 🤔

# SIGNS & SYMPTOMS OF THE MENOPAUSE

---

Experiencing the Change



CannyNurse.com

(\*FROM SANTORO ET AL., 2020)

## SIGNS & SYMPTOMS OF THE MENOPAUSE

---

- Early menopause = onset before age 45\*
- Average duration of the transition = 4 years\*
  - Stage -2 (early) plus Stage -1 (late) to FMP\*
- Symptoms typically start as mild/ infrequent then increase to their “most prevalent and severe” during the first 1-2 years after FMP\*
- Earlier symptom development ⇔ longer symptom duration\*
- Per Gatenby & Simpson (2024), early menopause starts between age 40-45, if before age 40 = Primary Ovarian Insufficiency (p.3)



CannyNurse.com



**Table 1**

Some of the most widely reported symptoms of menopause.

Type of symptom	Examples patients may describe:
<b>Psychological and cognitive</b>	Low mood Anxiety Altered sleep patterns and insomnia 'Brain fog' – memory and concentration issues
<b>Vasomotor</b>	Night sweats Hot flushes
<b>Urogenital</b>	Dyspareunia Low libido Vaginal dryness Genital itch Vulvo-vaginal atrophy Increased frequency of urinary tract infections Polyuria, nocturia Urgency and incontinence
<b>Others</b>	Reduced energy levels Palpitations Increased frequency of migraines Headaches Myalgia and joint aches

## CAM, CANNABIS, & THE MENOPAUSE

- “Approximately 51% of women use CAM and more than 60% perceive it be effective for menopausal symptoms. However, the majority of women using CAM do not discuss it with their health care providers. Women often report feeling confused about their options and rely on the internet as their primary source of information” (p.1)
- CAM Interventions: mind-body practices, natural products, other systems (TCM)
  - Johnson, A., Roberts, L., & Elkins, G. (2019). Complementary and alternative medicine for menopause. *Journal of Evidence-based Integrative Medicine*, 24, 2515690X1982938. <https://doi.org/10.1177/2515690x19829380>
- Article doesn't include cannabis, but as an herbal medicine, it fits with CAM

## SIGNS & SYMPTOMS OF THE MENOPAUSE

- **Vasomotor symptoms (Hot flashes / Night sweats)** 🌡️😓🔥
  - “Affect the majority of women undergoing the menopause transition and can significantly impair quality of life”  
(\*FROM GATENBY & SIMPSON, 2024, P.5)
  - Last several minutes, may persist 4-10 years (or up to 15 years after the transition\*)
  - African American women — “longest and most intense symptomology”
  - “thought to occur due to a physiologic narrowing of the hypothalamic thermoregulatory system that regulates core body temperature in response to estrogen deprivation.”
  - “severe and prolonged VMS” assoc. with ↑ cardiovascular risk burden / future events
  - “Most effective intervention”: HT (hormone replacement therapy) with estrogen

## STANDARD TREATMENT

<https://www.joinmidi.com/what-we-treat>



### Hot flashes + night sweats

Dealing with hot flashes that come out of nowhere and night sweats that wreck your sleep? We'll work with you to find the right evidence-based solutions—from prescription meds to supplements and lifestyle hacks.

#### TREATMENT OPTIONS CAN INCLUDE:



Hormones: HRT



Prescriptions: Gabapentin, Venlafaxine (Effexor), etc.



Supplements: Recommendations customized by your clinician



Lifestyle: Diet changes, stress management, acupuncture, etc.



## COULD CANNABIS HELP?

---

- Vasomotor symptoms (Hot flashes) 🌡️🔥

- Hopegood, R. (2024, April 5). Will cannabis help my menopause symptoms? Oprah Daily. <https://www.oprahdaily.com/life/health/a60353700/cannabis-menopause-symptoms/>
- “For each symptom, there is a scientific explanation of why it is plausible that cannabis actually makes a difference,” explains Streicher, who is also the medical director of education and community outreach for Midi Health. For example, the human body produces a chemical compound called **anandamide** that **is important for temperature control**. “The levels of anandamide are going to get thrown off when you’re no longer making estrogen, which may be one of the reasons women get hot flashes,” says Streicher. Anandamide is an endocannabinoid, a molecule produced in the body that is strikingly similar to the cannabinoids found in cannabis. “So **theoretically, if a woman has hot flashes, and if she uses a cannabis product with THC, that should help her. The sad part about this is that we don’t have the data to support it. This has never been proven or disproven.**”



CannyNurse.com

## OTHER COMPLEMENTARY & HOLISTIC TREATMENTS

---

- Vasomotor symptoms (Hot flashes) 🌡️🔥

- “Women are advised to minimize stress, sleep next to a fan, dress in layers, consume cold beverages, and avoid potential dietary triggers such as caffeine, spicy food, and alcohol.” (Santoro et al, 2020, p. 11)
- “For patients who are not eligible for HRT or prefer alternative therapies, lifestyle modifications can prove to be beneficial. Strategies to consider are: reducing alcohol intake, increasing exercise and physical activity levels and reducing their weight” (Gatenby & Simpson, 2024, p.5).
- “The placebo effect has been demonstrated to reduce hot flashes on average in RCTs by 25%, and previous research indicates a 50% reduction in hot flash frequency to be a clinically meaningful change” (Johnson et al., 2019, p.2).



CannyNurse.com

## OTHER COMPLEMENTARY & HOLISTIC TREATMENTS

- **Vasomotor symptoms (Hot flashes)** 🌡️🔥🔥
  - Recommended:
    - Hypnosis, Cognitive Behavioural Therapy (CBT)
  - May help but evidence is insufficient:
    - Relaxation techniques, aromatherapy in addition to other CAM, reflexology, acupuncture, Traditional Chinese Medicine
  - Does not appear to help with VMS:
    - Mindfulness-based stress reduction (MBSR), yoga, homeopathy, electroacupuncture

## CAM FOR MENOPAUSE

(JOHNSON ET AL., 2019, P.7)

- **“Mind-body interventions have few negative side effects and seem to provide safe treatment options worthy of consideration.**
- **The effects and safety of herbal preparations is difficult to ascertain due to large variations in the RCTs** that have been conducted. Investigations of standardized herbal preparations may provide a path for better understanding their effects and safety. There are no herbal treatments that have demonstrate consistent clinically meaningful benefits for menopausal symptoms.
- This **lack of consistent evidence** may not be due to the ineffectiveness of the treatments, rather it may **indicate the need for more rigorously conducted RCTs** regarding each of these modalities on menopausal symptoms.
- Some CAM interventions show promise (e.g. aromatherapy, acupuncture, reflexology), but lack empirical support due to the limited number of studies. **Health care decisions regarding CAM therapies for menopausal symptoms can be informed by existing scientific evidence for effectiveness and safety.”**

## SIGNS & SYMPTOMS OF THE MENOPAUSE

---

- **Genitourinary symptoms** 🌸🌸🌸

- “Symptoms include atrophy of the vulva and vagina, vaginal dryness, vaginal narrowing and shortening, uterine prolapse, and urinary incontinence (56). These changes can cause **dyspareunia [painful intercourse], irritation, and increased risk for urinary tract infections.**

Estrogen deprivation reduces blood flow to the vagina, which reduces vaginal secretions, increases vaginal pH, decreases surface epithelium and increases parabasal cells.

Connective tissue dehydration leads to architectural narrowing of the vagina and vestibule, and atrophy of the vulva (57).” (Santoro et al., 2020, p.6)



CannyNurse.com

## COULD CANNABIS HELP?

---

- **Genitourinary symptoms** 🌸🌸🌸 (below from Gatenby & Simpson, 2024, p.6)

- Vulvovaginal atrophy (thinning, drying, inflammation of vulva/ vagina)
- Vaginal dryness / itch, ⬆ risk of urogenital prolapse
- Painful urination, excessive urination, incontinence, urinary urgency, ⬆ risk of UTIs
- Dyspareunia (pain with intercourse), post-coital bleeding
- **Standard Treatment:** “**Estrogen replacement** has been shown to alleviate most GSM symptoms except for urinary incontinence.” (Santoro et al., 2020, p.6)
- Also: vaginal lubricants (OTC) & moisturizers (“Vaginal moisturizers can be applied with an applicator up to 3 times a day and can alleviate dyspareunia” (Santoro et al., 2020, p.11)



CannyNurse.com



## STANDARD TREATMENT

<https://www.joinmidi.com/what-we-treat>

### 🔗 Painful sex, vaginal dryness + libido change

Half of menopausal women experience painful sex and vaginal dryness, which often go hand in hand with low libido. Yet this is one of the most treatable symptoms of hormone change. We'll work with you to make it better.

#### TREATMENT OPTIONS CAN INCLUDE:



Hormones: Vaginal estrogen, testosterone, etc.



Prescriptions: Flibanserin (Addyi), bremelanotide (Vyleesi), DHEA



Supplements: Recommendations customized by your clinician



Lifestyle: Sex therapy, use of lubricants, vaginal dilators

## SIGNS & SYMPTOMS OF THE MENOPAUSE

- **Mood symptoms** 🙄😞😓😭😩
  - “increased depression and anxiety” (Santoro et al., 2020 p. 6-7)
  - “16% prevalence of new-onset depression and/or anxiety” (Santoro et al., 2020 p. 6-7)
- **Standard interventions:** “HT may improve mood” (Santoro et al., 2020 p. 6-7); also HRT, CBT, SSRIs, and/or SNRIs (Gatenby & Simpson, 2024 p.5); Yoga (Johnson et al, 2019, p.3)
- **Ariana’s Note:** *Panic attacks can be another sudden, new, and terrifying experience during this transition — google menopause and panic attacks/ anxiety to read a wide variety of people’s personal accounts*

## STANDARD TREATMENT

<https://www.joinmidi.com/what-we-treat>

### Moodiness, anxiety + depression

Ups and downs in mental wellbeing—even drastic ones—are a natural part of hormonal change. We'll help you regain control, and feel like yourself again.

#### TREATMENT OPTIONS CAN INCLUDE:



Hormones: HRT for moodiness



Prescriptions: SSRIs and SNRIs for anxiety and depression



Supplements: Recommendations customized by your clinician



Lifestyle: Physical activity, mindfulness, CBT, sleep hygiene



CannyNurse.com

## PATIENT STORY

Patient  
Story

- “For Michele Wilson, 40, her most troubling perimenopausal symptom was the sudden onset of severe anxiety and drastic mood changes. “It was extreme,” she says. “It would be a lump in the throat and a tightness in the chest that was there constantly. They don’t prepare you enough for the anxiety that just suddenly hits you.”
- Hopegood, R. (2024, April 5). Will cannabis help my menopause symptoms? Oprah Daily. <https://www.oprahdaily.com/life/health/a60353700/cannabis-menopause-symptoms/>



CannyNurse.com

(FROM STUDY, 20, P.)

## COULD CANNABIS HELP?

---

- **Mood symptoms** 🙄😞😡😭😞
- CBD is excellent for anxiety and depression
- THC can uplift mood



CannyNurse.com

(FROM STUDY, 20, P.)

## OTHER COMPLEMENTARY & HOLISTIC TREATMENTS

---

- **Mood symptoms** 🙄😞😡😭😞
- Mindfulness-based stress reduction (MBSR)



CannyNurse.com



# SIGNS & SYMPTOMS OF THE MENOPAUSE

## • Cognitive symptoms 🧠🙄

- “Cognitive decline is mostly associated with somatic aging rather than menopause. Several studies have refuted the benefits of estrogen on cognitive function.” (Santoro et al., 2020, p.7)
- “cognitive functioning declines during the menopause transition, but appears to return to baseline by the transition’s end.”(Santoro et al., 2020, p.7)
- “patients often reporting; ‘brain fog’, word-finding difficulties, increasing forgetfulness amongst low mood and increased anxiety symptoms (Gatenby & Simpson, 2024 p.5)
- *Ariana wonders: Is “menopause brain” myth or fact? And is it possible I would be better suited to answer this question after I finish my own Menopause?*



CannyNurse.com

# STANDARD TREATMENT

<https://www.joinmidi.com/what-we-treat>



## Brain fog + memory lapses

Words and names—not to mention keys and phones—go missing. Focus is a challenge. Women often panic about early Alzheimer’s at midlife, but hormone change is the likely culprit. Research-backed solutions can help to clear your mind.

### TREATMENT OPTIONS CAN INCLUDE:



Hormones: HRT



Prescriptions: SSRIs and SNRIs (if associated with mood changes)



Supplements: Recommendations customized by your clinician



Lifestyle: Sleep hygiene, physical activity, brain games, etc.



CannyNurse.com

## COULD CANNABIS HELP?

---

- **Cognitive symptoms** 🧠🤔👁️
  - CBD has shown promise for other brain-related issues, so could potentially help



CannyNurse.com

(FROM SANTORO ET AL., 2020, P.7)

## SIGNS & SYMPTOMS OF THE MENOPAUSE

---

- **Sleep-related symptoms** 😴🛌🤔
  - Sleep difficulty correlates with timing of menopause transition (independent of age)
  - Appears early in the transition, peaks late in the transition, stabilizes in postmenopause
  - Postmenopause — ⬆️ difficulty falling asleep, ⬆️ likelihood of obstructive sleep apnea



CannyNurse.com

## STANDARD TREATMENT

<https://www.joinmidi.com/what-we-treat>



### Trouble sleeping

A full 61% of women report difficulty sleeping during the menopause transition. Maybe you struggle to fall asleep, or find yourself wide awake in the middle of the night. Your energy might be low, even after a solid eight hours. Let's solve your sleep mystery and get you the rest you deserve.

#### TREATMENT OPTIONS CAN INCLUDE:



Hormones: HRT, progesterone in perimenopause



Prescriptions: Gabapentin, Tricyclics (Elavil)



Supplements: Recommendations customized by your clinician



Lifestyle: Sleep hygiene, mindfulness, caffeine management, etc.

(FROM STUDY, 20, P.)

## COULD CANNABIS HELP?

- **Sleep-related symptoms** 🤔🚗🤔
  - Cannabis for insomnia? Yes!
  - CBD at high doses (above 160mg per study, but anecdotally, the threshold may be lower for some patients)
  - THC at low-moderate doses



(FROM STUDY, 20, P.)

## OTHER COMPLEMENTARY & HOLISTIC TREATMENTS

---

- **Sleep-related symptoms** 🤔🛌😴
  - MsFLASH studies found the following effective (Santoro et al., 2020, p.11):
    - CBT-I (Cognitive behavioural therapy for insomnia)
    - Yoga
    - Aerobic exercise



CannyNurse.com

(FROM SANTORO ET AL., 2020, P.7)

## SIGNS & SYMPTOMS OF THE MENOPAUSE

---

- **Libido-related symptoms** 🤔💋😴
  - Decreased sexual desire (more prevalent in ages 45-64, per PRESIDE study)
  - Thought to be due to low estrogen / testosterone
  - *Ariana's Common Sense Observation: Considering the GSM symptoms, decreased libido seems to make perfect sense....*
- Standard intervention: Hormone replacement



CannyNurse.com

## STANDARD TREATMENT

<https://www.joinmidi.com/what-we-treat>

### ⑧ Painful sex, vaginal dryness + libido change

Half of menopausal women experience painful sex and vaginal dryness, which often go hand in hand with low libido. Yet this is one of the most treatable symptoms of hormone change. We'll work with you to make it better.

#### TREATMENT OPTIONS CAN INCLUDE:



Hormones: Vaginal estrogen, testosterone, etc.



Prescriptions: Flibanserin (Addyi), bremelanotide (Vyleesi), DHEA



Supplements: Recommendations customized by your clinician



Lifestyle: Sex therapy, use of lubricants, vaginal dilators



CannyNurse.com

## COULD CANNABIS HELP?

### • Libido-related symptoms 🤔👉👎

- “Of the 373 participants, 34.0% (n 1/4 127) reported having used marijuana before sexual activity. Most women reported **increases in sex drive, improvement in orgasm, decrease in pain, but no change in lubrication.**
- After adjusting for race, women who reported marijuana use before sexual activity had **2.13 higher odds of reporting satisfactory orgasms** (adjusted odds ratio 1/4 2.13; 95% CI 1/4 1.05, 4.35) than women who reported no marijuana use.
- After adjusting for race and age, **women with frequent marijuana use**, regardless of use before sex or not, **had 2.10 times higher odds of reporting satisfactory orgasms** than those with infrequent marijuana use (adjusted odds ratio 1/4 2.10; 95% CI 1/4 1.01e4.44).” (p. 192)
- Lynn, B. K., López, J. D., Miller, C., Thompson, J., & Campian, E. C. (2019). The Relationship between Marijuana Use Prior to Sex and Sexual Function in Women. *Sexual Medicine*, 7(2), 192–197. <https://doi.org/10.1016/j.esxm.2019.01.003>



CannyNurse.com

## SIGNS & SYMPTOMS OF THE MENOPAUSE

- **Bone-related symptoms** 🧠📊🔧
  - Low estrogen ⇒ increased bone resorption ⇒ decreased bone density
  - “Osteoporotic fractures affect half of women after age 50” (Santoro et al., 2020, p. 7)
  - “Rates of bone loss increase dramatically starting a year before the FMP and persist up to 3 years with rates of bone loss as high as 5% per year, then slows again to approach the rate of loss prior to menopause” (Santoro et al., 2020, p.7-8)
- **Standard intervention:** Calcium/ Vit. D supplementation, exercise (strength training, weight-bearing, balance exercises), HT/ HRT



CannyNurse.com

## STANDARD TREATMENT

<https://www.joinmidi.com/what-we-treat>



### Joint pain, bone loss + fracture risk

On average, women lose up to 10% of their bone mass in the first five years after menopause. Testing and preventative treatment can help you reverse that, and protect your long term bone health.

#### TREATMENT OPTIONS CAN INCLUDE:



Hormones: HRT, SERMs (Evista)



Prescriptions: Bisphosphonates (Fosamax, Actonel)



Supplements: Recommendations customized by your clinician



Lifestyle: Weight-bearing exercise, diet changes



CannyNurse.com



## COULD CANNABIS HELP?

---

- **Bone-related symptoms** 🦴🦴🦴
  - “Interestingly, CBD promoted a bloom in *Lactobacillus* species. Prior studies indicated that probiotic *Lactobacillus* treatment may protect against bone loss by reducing gut permeability and levels of proinflammatory cytokines in the gut, circulation, and bone” (Sui et al., 2022, p.12)
  - CBD partially reversed whole body areal bone mineral density (aBMD) + vBMD; Completely reversed ↓ whole body bone mineral content (BMC) (Sui et al., 2022, p.5-6)
  - Standard intervention: pharmaceuticals, calcium/ vit. D supplements, HRT

## OTHER COMPLEMENTARY & HOLISTIC TREATMENTS

---

- **Bone-related symptoms** 🦴🦴🦴
  - Supplementation with *Lactobacillus* probiotics to reduce bone loss and inflammation (Sui et al., 2022, p.10)
  - “gut microbiota is a regulator of bone mass” (Sui et al., 2022, p. 12)

## WHAT ABOUT CARDIOVASCULAR HEALTH?

---

- “the reduction in the production of oestrogen can result in endothelial dysfunction [2], **potentially resulting in hypertension, endothelial plaque accumulation and thus increased CVD risk**” (Gatenby & Simpson, 2024, p.6)
- “**HT should not be used for the primary or secondary prevention of CVD**....The conclusion from more than 2 decades of study suggest that HT does not prevent CVD, and it should not be prescribed for this purpose. Alternatively, studies have not demonstrated mortality differences in women who do and do not take HT; an important point to understand and impart on patients prescribed HT for symptomatic purposes.” (Santoro et al., 2020, p.8)
- “The influence of HRT in relation to CVD reduction is however, **time dependent** [2]. **When HRT is commenced soon after or during menopausal transition, it is protective against CVD however, if commenced in the postmenopausal period, the beneficial effect of HRT is lost and may increase CVD risk, especially if commenced greater than 10 years since their last menstrual period (LMP).**” (Gatenby & Simpson, 2024, p.6)



CannyNurse.com

## WHAT ABOUT CARDIOVASCULAR HEALTH?

---

- “evidence demonstrates that **lifestyle discussions and interventions for middle-aged and elderly women will improve a patients’ overall health**, reducing the burden of CVD thus, reducing their associated morbidity and mortality....Lifestyle interventions should include discussion regarding regular exercise, reducing alcohol and caffeine intake and dietary improvements to reduce BMI, if raised.” (Gatenby & Simpson, 2024, p.8)
- Ariana wonders: THCV has shown promise in metabolic conditions, maybe an area for future research?



CannyNurse.com

# STANDARD TREATMENT

<https://www.joinmidi.com/what-we-treat>



## Weight + body changes

Shifting hormones can cause you to gain weight, add belly fat, lose muscle tone, or (sorry!) all three. We'll work with you on solutions, which range from lifestyle tweaks to prescription medication.

### TREATMENT OPTIONS CAN INCLUDE:



Hormones: HRT, to improve bothersome symptoms associated with weight gain



Weight loss medications: GLP-1's: Semaglutide (Wegovy, Ozempic), Tirzepatide (Mounjaro); naltrexone/bupropion HCL (Contrave), metformin, Zepbound (tirzepatide)



Supplements: Recommendations customized by your clinician



Lifestyle changes: Prediabetes counseling, personalized eating and activity recommendations, sleep optimization



CannyNurse.com

# STANDARD TREATMENT

<https://www.joinmidi.com/what-we-treat>



## Hair + skin changes

Estrogen plays a significant role in the health of your hair and skin, so when it declines during the menopausal transition, you may see the aging process pick up speed. Changing your care routines, as well as medications and supplements, can help.

### TREATMENT OPTIONS CAN INCLUDE:



Hormones: Compounded estrogen face cream



Prescriptions: Retinol, minoxidil, ketoconazole shampoo, etc



Supplements: Recommendations customized by your clinician



Lifestyle: Sunscreen and moisturizer use



CannyNurse.com



## CANNABIS & THE MENOPAUSE

---

How much evidence do we have?

(Not enough. 😬😂)



CannyNurse.com

## CBD AND MENOPAUSE?

---

- Improvements from taking CBD (animal study):
  - glucose tolerance, energy metabolism, intestinal inflammation markers, gut barrier permeability, femoral markers of bone resorption/ inflammation (suppressed), bile acid changes consistent with ↓inflammation/ ↑ glucose/bone metabolism
- Sui, K., Tvester, K. M., Bawagan, F. G., Buckendahl, P., Martinez, S. A., Jaffri, Z. H., MacDonell, A. T., Wu, Y., Duran, R. M., Shapses, S. A., & Roopchand, D. E. (2022). Cannabidiol-Treated ovariectomized mice show improved glucose, energy, and bone metabolism with a bloom in lactobacillus. *Frontiers in Pharmacology*, 13. <https://doi.org/10.3389/fphar.2022.900667>



CannyNurse.com



**PRIMARY STUDY**

**Cannabidiol-Treated Ovariectomized Mice Show Improved Glucose, Energy, and Bone Metabolism With a Bloom in Lactobacillus**

**Key Findings:** In this mouse model of post-menopausal syndromes such as osteoporosis, insulin resistance, and inflammation found that CBD treatment resulted in increased bone volume, improved glucose tolerance, and reduced inflammation, suggesting a potential alternative to oral estrogen replacement therapies for such conditions.

**Type of Study:** Animal Study  
**Study Result:** Positive  
**Study Location(s):** United States  
**Year of Pub:** 2022



**Cannabinoids Studied:** Cannabidiol (CBD)  
**Phytocannabinoid Source:** Isolate  
**Chemotype:** Chemotype III  
**Receptors Studied:** CB1, CB2, GPCR 55, TRPV1, GPCR 55 antagonist  
**Ligands Studied:** Estrogen, Insulin, Pro-inflammatory cytokines

**DOSING DETAILS**

**Study Dosing Objective:** Effective Dose  
**Established Protocol:** Effective dose  
**Route of Administration:** Oral (Ingestion)  
**Cannabinoid Ratio:** (CBD) 0  
**Dosage Form:** cannabidiol dissolved in sesame oil  
**Dosing Regimen:** CBD (25 mg/kg) 5 days per week  
**Treatment Duration:** 5 days per week for 18 weeks  
**Clinical Relevance:** In ovariectomized mice, cannabidiol (CBD) treatment positively affected the immune system and the gut microbiota. This data supports the possible use of CBD to improve energy metabolism and bone homeostasis and alleviate several chronic disease symptoms of postmenopause via modulation of the gut-bone axis.

## PHYSIOLOGICAL CHANGES & CBD

- Estrogen decline leads to ↑ risk for: weight gain, cardiometabolic disease, osteoporosis (starts with rapid bone loss), GI disorders, altered gut microbiota, metabolic dysregulation, leaky gut
- Chronic low-grade inflammation ⇔ metabolic disease/ bone loss
- CBD effects of interest: antioxidant, anti-inflammatory, gut barrier improvement, protection from collagen-induced arthritis, reduced bone loss (Sui et al., 2022, p. 1-2)

## EXPECTATIONS OF CANNABIS THERAPY IN THE PAUSE

---

- **“women expected MJ to improve joint/muscle discomfort, irritability, sleep problems, depression, anxiety, and hot flashes, but not decreased libido, heart discomfort, exhaustion, vaginal dryness, and bladder problems.** Regression analyses and a bootstrapping technique found that expectancies mediated the links between menopause symptoms and monthly use.” (p. iii) (meaning: people use more cannabis when they expect it to work)
- “Clinical lore suggests that cannabis dries mucous membranes and exacerbates vaginal dryness, but the effect does not appear in every study” (p.6)
- Slavin, M. N. (2017). Expectancy mediated effects of marijuana on menopause symptoms. *Legacy Theses & Dissertations (2009 - 2024)*. Retrieved May 30, 2024, from <https://scholarsarchive.library.albany.edu/legacy-etd/1949>



CannyNurse.com

## EXPECTATIONS OF CANNABIS THERAPY IN THE PAUSE

---

- “individuals who believed that MJ would help their menopause symptoms were significantly less likely to experience cannabis-related problems” (Slavin, 2017, p.12) (*maybe because this is a medical use mindset?*)
- “Average intoxication—a proxy for MJ quantity, was the only variable to significantly and positively predict problems in an equation that also included menopause symptoms, expectancies, and frequency of use” (Slavin, 2017, p.13)
- “the current data suggest that women expect medical MJ to alleviate a subset a menopause symptoms. Their symptoms predict their monthly use, and this link is mediated by expectations of MJ-induced relief. Expectancies, symptoms, and monthly use do not correlate with problems, suggesting that MJ might have potential in making the menopause experience less aversive without creating negative consequences.” (Slavin, 2017, p.15)



CannyNurse.com



## CANNABIS USE DURING PERI-/POSTMENOPAUSE

---

- Dahlgren, M. K., El-Abboud, C., Lambros, A. M., Sagar, K. A., Smith, R. T., & Gruber, S. A. (2022). A survey of medical cannabis use during perimenopause and postmenopause. *Menopause*, 29(9), 1028–1036. <https://doi.org/10.1097/gme.0000000000002018>
- “Of the 499 current cannabis users, over 75% were using cannabis for medical purposes. Most common reasons for current use were sleep (65%), anxiety (45%) and muscle/joint achiness (33%). **In current users, 74% indicated that cannabis was helpful for symptoms.** Current cannabis users were more likely to report experiencing menopause symptoms compared with non-users.” (p.1)