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California Legislature

Joint Informational Hearing
Senate Health Committee and Assembly Select Committee on Reproductive Health
Menopause: Access to Treatment and Coverage
May 8, 2024 – 10 a.m.
1021 O St, Room 1200

Background

The purpose of this hearing is to examine menopause, its symptoms and available treatments and therapy, knowledge of healthcare providers' patients, disparities in experiences among people of color, and health insurance coverage.

Overview

According to the World Health Organization (WHO), menopause is a natural part of aging that marks the end of a person's reproductive years. Natural menopause occurs after twelve consecutive months without menstruation, in cases where there are no other obvious physiological or pathological causes. Many women experience menopause between the ages of 45 and 55 years, and in North America the average age is 51. Some individuals may experience premature or early menopause due to certain illness and conditions that affect ovarian functions, bilateral oophorectomy (the removal of both ovaries and fallopian tubes) that leads to surgical menopause, or other factors such as family history, smoking, and chemotherapy. Over one million women in the U.S. experience menopause each year, as reported by the National Institute on Aging in 2022.

There are four stages of menopause: pre-menopause, perimenopause, menopause, and post-menopause. Pre-menopause refers to when a person is having their regular menstrual cycle. Perimenopause, also known as the menopausal transition (MT), is the time period from when the signs of gradual changes in the menstrual cycle are first observed to one year after the final menstrual period. Many refer to perimenopause as a "second puberty," as it causes hormonal changes and other symptoms that can last several years and affect a person's physical, emotional, mental, and social well-being in everyday life. Menopause occurs after a person has not had their period for twelve consecutive months; and, post-menopause is the final phase of MT that indicates the official end of ovulation or menstruation for a person.

Knowledge gaps around menopausal symptoms and treatments exist, preventing providers from and midlife patients to prepare for what to expect during MT. This knowledge gap sometimes results in providers being wary of prescribing certain treatments for patients (like hormone therapy (HT) and testosterone) to address menopause symptoms based on flawed studies and stigmatization of treating sexual functioning for women. These gaps also cause some patients to not understand what's happening to their body, and so they're not prepared to engage with their health care team in a helpful way. Additionally, people of color tend to have different experiences

throughout MT compared to white women, including having more severe and intense symptoms as well as entering menopause at an earlier age. Health care providers should take these factors into consideration when determining the best individualized care for their patients, and research needs to prioritize more diverse populations to better understand the disparities among non-white individuals. Investing in more research and improving curriculums for medical students is important to close these gaps to better treat midlife individuals in a new and unfamiliar stage of their life.

Menopause symptoms & the SWAN study

The Study of Women's Health Across the Nation (SWAN) is a multi-site longitudinal, epidemiologic study designed to examine the health of women during their middle years. In 1996, SWAN enrolled 3,302 women between the ages of 42 and 52 at seven geographically distinct sites across the U.S. that: had at least one ovary; were not receiving HT; were not pregnant or lactating; and, had at least one menstrual period in the three prior months. They enrolled white (n=1,550), Black (n=935), Japanese (n=281), Chinese (n=250), and Hispanic (n=286) women. SWAN conducted a baseline visit at enrollment and 16 follow-up visits through 2017 that included interview- and self-administered questionnaires, as well as assessments on relevant medical data. They expanded on the symptoms most commonly associated with menopause, including:

- Changes in the regularity and flow of the menstrual cycle;
- Vasomotor symptoms (VMS), defined as hot flashes and night sweats;
- Difficultly sleeping;
- Vaginal dryness, pain during sexual intercourse, and incontinence;
- Decrease in sexual desire and functioning; and
- Changes in mood, depression, and/or anxiety.

VMS. Up to 80% of women that participated in SWAN reported VMS at some point during MT, with the highest reporting throughout perimenopause. They found that the median total duration of hot flashes and night sweats was 7.4 years – far longer than the perceived time duration of these symptoms. A 2021 study conducted by American Heart Association's *Circulation* journal found that frequent VMS or persistent VMS over midlife are associated with a 50% to 77% increase risk of future cardiovascular disease events, such as strokes or heart failure. This may have correlation to the sleep disruption caused by night sweats, which can also pose significant increase in risk of cardiovascular disease for midlife women.

Sleep. The most common characteristics related to sleep difficulties for menopausal women includes trouble falling asleep, waking up several times, and waking up earlier than planned at least three nights weekly. SWAN found that late perimenopause and natural postmenopausal women reported more sleep difficulties than premenopausal women did. According to a 2024 study published in the *Circulation* journal, poor sleep for midlife women can be associated with a 70% to 75% increased risk of cardiovascular disease.

Vulvovaginal symptoms and sexual functioning. Vaginal dryness increased across MT, from approximately 19% in pre- and early perimenopause to 34% in postmenopausal years. This can contribute to pain during sexual intercourse. At the baseline reporting of the SWAN study, sexual

functioning was reported as an important component of 75% of the participants' lives. Over MT, pain during sexual intercourse increased, while sexual desire decreased. A decline of sexual functioning became evident 20 months before the final menstrual period and slowed one year following the final period. They concluded that MT is most likely the primary cause of this decline as opposed to other factors such as poorer health, VMS, vaginal dryness, depression, or partner status.

Depressive symptoms and anxiety. SWAN used the Center for Epidemiological Studies of Depression's (CES-D) scale for measuring depressive symptoms throughout the study. Factors outside of MT such as stressful life events, financial strain, and low social support are also strong contributors to depressive symptoms and/or anxiety. There is not sufficient data to directly correlate MT and depression based on SWAN. Among women who did not have anxiety preceding menopause, there was a greater likelihood of reporting anxiety throughout the stages of menopause, regardless of independent factors. Those who already experienced consistent anxiety before menopause did not report any changes. Hormone fluctuations, life stressors, VMS, and natural aging can all cause emotional distress that may lead to mood swings throughout MT. The North American Menopause Society highlights that 23% of individuals with menopause report mood changes.

Cognitive performance. Approximately 60% of midlife women report memory problems during MT, but SWAN found that age-related decline in cognitive performance was most likely caused by chronological age, not MT. The SWAN study clarified that there was no association between cognitive performance and either VMS or poor sleep. However, midlife women with depressive symptoms did score lower in cognitive processing and those with higher symptoms of anxiety had worse verbal episodic memory. A 2021 *Alzheimer's & Dementia* study found that almost two thirds of adults with Alzheimer's disease are women. A November 2023 article in *The New York Times* flags that there is a growing consensus that menopause may be a significant risk factor for the development of dementia later in life, since the natural decline of estrogen during MT poses a threat to the brain's ability to defend itself against aging and damage. A 2023 *Neurology Journals* article links VMS with an increased amount of tiny lesions in the brain, which is a sign of declining brain health. However, most people's brains and cognitive functions stabilize in post-menopause.

Cardiovascular and cardiometabolic health. SWAN documented sharp increases in total cholesterol, low-density lipoprotein cholesterol (LDL-C), and apolipopriotein B levels over MT. Acceleration in LCL-C was associated with greater risk of carotid plaque later in life. MT was also correlated to fat redistribution that extends to other critical locations, such as heart fat within and outside the pericardial sac, which have been associated with worse cardiovascular disease risk factors and events.

Knowledge gaps

The 2022 KFF Women's Health Survey found that 35% of women ages 40-64 say that their health care provider never talked to them about what to expect in menopause. To further evaluate the knowledge and training for menopause management in postgraduate residents, the *Mayo Clinic Proceedings* performed a survey in 2017 that included 183 residents representing 20 U.S. residency programs. They found that while 93.8% of respondents believed it was important or very important

to be trained in managing menopause, only 6.8% reported feeling adequately prepared to manage women experiencing menopause. *The Journal of The Menopauses Society* conducted a survey in 2022 that was completed by 99 U.S. OB/GYN residency program directors. They found that only 31.3% reported having a menopause curriculum in their residency program and only 29.3% reported that trainees had dedicated time assigned to a menopause clinic.

The Journal of the North American Menopause Society asserts that federal investment in menopause research must be prioritized to close the knowledge gap in the field. To illustrate, of the estimates of funding for various research, condition, and disease categories reported by the National Institutes of Health, menopause is not once listed as a primary topic of research areas (out of 315) between the years of 2015 and 2022. A further search of the National Institutes of Health grants funded in 2019 revealed only 28 project titles that included the term "menopause" or some variation, compared to more than 300 that included "pregnancy." The *Journal* published an article in 2021 regarding a menopause working group conducted by the Society for Women's Health Research to address unmet needs in clinical care, education, and access to treatment to improve quality of life for individuals during MT. They article includes multiple priority recommendations for a menopausal care model and further research to improve quality of life during and after MT:

- View menopause as a normal part of life;
- Prepare women as young as 35 years old on MT and post-menopause;
- Explore alternative interventions for individualized care;
- Gather additional data to address menopause-related health disparities and better inform insurance coverage, affordability, access, and education; and
- Develop interdisciplinary cross-sector coalitions to address individual and systemic needs in the healthcare and workforce landscapes.

The American College of Obstetricians and Gynecologists guidelines. The American College of Obstetricians and Gynecologists (ACOG) is a professional membership organization for OB/GYNs that produces guidelines for healthcare professionals and educational materials for patients. ACOG recently released an updated guideline on the Management of Menopausal Symptoms for healthcare providers outlining MT, as well as various clinical considerations and recommendations in treating the needs of menopausal patients.

ACOG states that VMS and vaginal symptoms are primary symptoms that menopausal patients most frequently request treatment for. The guidelines list HT as the most effective therapy for VMS related to menopause, but emphasizes that low-dose and ultra-low systemic doses of estrogen is safer than prescribing standard doses. For non-hormonal medications effective in treating VMS, the guidelines highlight low dosages of antidepressants, clonidine, and gabapentin. The guidelines state that alternative methods such as herbal supplements, vitamins, and lifestyle modifications are not proven to assist with alieving severity of the symptoms.

Treatments for menopausal symptoms
Some common treatments for MT symptoms include:

- HT: Also known as, estrogen therapy, this treatment reduces symptom frequency and intensity by nearly 90% within one month of initiation. Many providers recommend estrogen in the lowest dose and the shortest period needed to provide symptom relief;
- Vaginal estrogen: This treatment helps relieve vaginal dryness and is often administered directly to the vagina using a vaginal cream, tablet, or ring;
- Low-dose antidepressants: Selective serotonin reuptake inhibitors (SSRIs) are associated with managing VMS, particularly for those who cannot take estrogen for health reasons;
- Testosterone: Levels of testosterone gradually decline during MT, which can affect sexual function and general well-being for individuals. Testosterone supplementation can be considered for menopausal women with low libidos if HT alone is not effective;
- Fezolinetant: A hormone-free option for treating VMS; and
- Ospemifene: An oral medication used to treat pain during sexual intercourse for those who are post-menopausal.

In 2022, a study of 283 health care providers and 1,016 patients' electronic health records was conducted to determine the use of prescription and nonprescription therapies by providers for women experiencing VMS associated with menopause. The data included women who sought care between January 2016 through December 2019, were 40 to 60 years of age, and reported bothersome VMS at least twice within 24 days. The study found that nearly 40% of women had no prescription medication documented, and approximately 13% had no therapy documented. A total of 86.9% of women had documentation of at least one therapy or intervention for VMS associated with menopause in their records. Nearly 50% of patients delayed seeking care for more than six months despite experiencing VMS.

HT. HT is a medical treatment that delivers estrogen to the body through gels, creams, patches, pills, or devices fitted inside the uterus to help relieve the symptoms of menopause and perimenopause, such as VMS, that has existed since the 1960s. It is considered as the most effective treatment option for relieving VMS. According to ACOG, there are two types of HT: estrogen only and estrogen plus progestin, also referred to as combined HT. The latter helps reduce the risk of uterine cancer that can occur when estrogen is used alone. The 2020 Scientific Statement of the American Heart Association stated that MT is a major risk factor for cardiovascular disease, and that initiating HT within ten years of menopause appears to be associated with lowering that risk for menopausal women. A System Review article from the *Frontiers Aging Neuroscience Journal* published in 2023 found that HT initiated during the critical window of MT, particularly during younger ages, may help support neurological function and reduce the risk of future Alzheimer's and dementia among some women.

However, after a 2002 study from the Women's Health Initiative Investigators reported that the overall health risks exceeded benefits from the use of estrogen for longer than five years among postmenopausal women, providers became reluctant to prescribe HT. Following this publication, the *Journal of Clinical Oncology* released a report in 2006 stating that the use of HT in Northern California had declined by 68%, most likely as a result of the study findings. The study conducted by the Women's Health Initiative Investigators was later found as flawed because both the study population and interpretations were skewed. The participants' average age was 63 years old, while

the typical person is around 50 years old when they first begin MT. There were also multiple external factors in the group of participants that could have influenced study results, such as weight and smoking habits. Despite the flaws in this decades-old study, providers remain hesitant to prescribe HT to treat menopausal symptoms.

Testosterone. The *International Journal of Impotence Research* found that testosterone is a vital hormone in women to maintain sexual health and function, rendering testosterone replacement therapy (TRT) an effective treatment option for menopausal people with reduced libidos. However, testosterone is only FDA-approved for use in men who have low testosterone levels in conjunction with an associated medical condition. Women can be prescribed a fraction of the dose often prescribed for men. Many report difficulties getting TRT covered for menopause-related healthcare even though men's sexual functioning is frequently deemed as "medically necessary" by insurance carriers.

Non-medicine therapy. The American Psychological Association (APA) highlighted multiple psychology-based tools to help individuals through MT. In addition to acts of self-care, APA recommends different forms of therapy to offer greater comfort, ease, and insight to individuals going through this stage of menopause. As MT is commonly associated with loss of sleep, and loss of sleep in midlife is associated with a higher risk of cardiovascular disease, APA emphasizes considering cognitive behavioral therapy (CBT) and brief behavioral therapy for insomnia. CBT can also help regulate emotions and distress as it targets stress, low mood, and sleep problems. A 2021 *PLOS One Journal* article found that stress can increase the frequency of VMS; in fact, those who reported having endured a stressful event experienced 21% more VMS than those who had not experienced any significant life stressors. An updated 2023 statement from North American Menopause Society reiterates that while HT is the most effective treatment for VMS, CBT is still an effective option for reducing symptoms. However, those who still struggle with severe VMS after trying CBT should still consider prescribed medicine such as HT or low-dose antidepressants.

Disparities

Limitations of SWAN study. Of those screened for the study, Black women had nearly double the risk compared to all other racial and ethnic groups of being ineligible for the study due to having surgical or natural menopause prior to ages 42-52. Japanese women had the highest proportion eligible to participate in the study at 54.4%, while Black women had the lowest at 38.9%. In fact, research shows that Black women begin MT between 8.5 months and 1.2 years earlier than white women, according to journal articles published in 2021 by *Women's Midlife Health* and in 2023 in the *International Journal of Epidemiology*. Hispanic women followed a similar trend of an earlier natural menopause compared to white women by an average of six months.

SWAN acknowledges that a large limitation includes the limited sample size of Hispanic participants; which could have reduced their ability to detect significant differences in MT characteristics among this ethnic group. The 2023 article highlights that if certain populations experience menopause earlier than the recruitment age requirement for the study, then the results could overestimate the average age of MT and underestimate disparities of experiences for non-white individuals.

Premature/early menopause. Individuals who reach menopause under the age of 40 years are categorized as premature menopause, and those who reach menopause before the age of 45 are considered as early menopause. The *American Journal of Epidemiology* examined factors related to age at natural menopause in a 2013 journal article based on the results of the SWAN study. They found that the factors with the greatest association between age and menopause are (from greatest to lowest significance): smoking habits, health status at baseline visit, education status, and weight at baseline. At the baseline visit, Black women were more likely to smoke than white women (24.1% vs. 16.6%) as well as more likely to be exposed to passive smoke for at least five hours weekly (39.4% vs. 29.1). Additionally, Hispanic women were the least likely to have a college degree at the baseline visit (10.1%) and white women were the most likely (53.3%). Almost one-third of Black women in the study had a college degree and 49.2% of Chinese women had a degree. The *Journal of Thoracic Disease* also asserts that many young women are at increased risk for entering menopause prematurely following treatment for breast cancer because the change in hormone levels and estrogen depletion caused by chemotherapy or hormonal therapy often triggers early menopause. A 2023 *Archives of Medical Science* article concluded that those who experience premature and early menopause have a significantly increased risk of cardiovascular disease before the age of 60 in comparison to those who reach menopause at the age of 50-51.

Severity of symptoms. SWAN documented multiple, significant disparities among racial and ethnic groups in the severity of symptoms related to MT:

- For menopausal symptoms, Black women experience a longer MT duration than white women do by approximately 3.5 years. SWAN also found that Black women had the highest prevalence and highest duration of VMS, and were the most bothered by their hot flashes and night sweats. Women in lower socioeconomic positions as well as women with a history of childhood abuse or neglect were more likely to have VMS, regardless of race or ethnicity. The study established that several other factors were associated with greater reporting of VMS, including education status, smoking, greater depressive symptoms, greater anxiety, and higher symptom sensitivity.
- In addition to disparities in intensity of VMS, the study found that Black women are less likely to experience increases in depressive symptoms due to MT, while Hispanic women are more likely to consistently experience depressive symptoms over midlife. It is important to note that stressful life events, financial strain, low social support, sleep issues, and low physical activity are also important contributors to depressive symptoms.
- Black and Hispanic women also have shorter sleep duration and less efficient sleep relative to white women, with financial hardships, increasing health problems, and VMS having the most impact. According to the American Heart Association's *Circulation* Journal, poor sleep for midlife women can be associated with a 70% to 75% increased risk of cardiovascular disease.
- Lastly, Black women were half as likely to use HT to treat menopausal symptoms as white women, despite having greater symptom burden.

Insurance coverage

A 2024 report released by the California Health Benefits Review Program highlighted baseline estimates of health coverage of specific prescription drugs and therapeutic categories of drugs for

treatment of menopause symptoms by state-regulated health insurance plans. Currently, coverage base by these insurance plans for HT in the forms of estrogen only, progesterone only, combination estrogen-hormone; topical systemic; and low-dose vaginal estrogen is 100%. The only two exceptions are high dose vaginal estrogen and compounded bioidentical hormones. The coverage percentage of those two hormonal drug therapies are, respectively, 8% and 91%. For non-HT, their baseline coverage is 100% for low-dose antidepressants, anticonvulsants, and drugs to prevent or treat osteoporosis. However, for fezolinentant, it is 7%, and for ospemifene, it is 13%.

Conclusion

Menopause will occur in half of the world's population, with more than one million experiencing it each year in the U.S. This unfamiliar stage of midlife significantly disrupts a person's everyday life through its multitude of physical, emotional, and mental changes. MT symptoms are not just psychological – they can cause hot flashes and night sweats that cannot be ignored and obstruct sleep for years on end, all of which can pose a higher threat to cardiovascular health. MT is also associated with causing emotional distress and temporarily worsening cognitive performance that is compounded as a person struggles to balance MT and their lives. These symptoms inevitably creep into a person's work life, at times impacting the ability to perform their job. To demonstrate, a 2023 cross-sectional study of 407 menopausal employees working in a hospital found that common menopause symptoms impacted 65% of employees and affected their overall work performance. The symptoms that affected them the most while at work were: fatigue (54%), difficulty sleeping (47%), poor concentration (44%), and poor memory (40%). A 2024 qualitative study from the *Maturitas Journal* reported that individuals whose roles were "client-facing" (such as educators) or entailed physical labor (hospitality workers) expressed greater concerns of the physical effects of MT (such as VMS) that impact their ability to do their job. Many who work in this field are also unable to take appropriate breaks while experiencing hot flashes throughout the work day. On the other hand, individuals working in office jobs were more concerned about the cognitive and emotional impacts of MT as well as their perceived competence by their boss and co-workers. The stigma surrounding menopause, among other female health issues, often prevents people from discussing it in the first place, forcing them to work through bothersome symptoms without taking the appropriate breaks to take care of themselves and their health. As this issue will impact half of the world's population, the state should prioritize destigmatizing menopause by improving the educational curriculum for health care providers, researching the impact of menopause on a person's health, understanding the disparities of experiences among people of color, and continuing coverage of treatments proven to effectively treat MT symptoms.