Menopause:
Navigating from Symptoms to Solutions

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Menopause has entered the chat. The subject of a recent Oprah Winfrey special, outspoken celebrity confessions, and the focus of institutional and startup investors clamoring for a piece of this more than $15 billion market, menopause is finally being noticed for the hidden phenomenon it is.[1] Consider that every day in the U.S. alone, approximately 6,000 women become menopausal. That translates to about 1.3 million women annually crossing this biological threshold.[2]

However, to think of menopause as a moment is misleading. Given a life expectancy of 81, women can spend more than a third of their lives in a menopause-related state.[3] The term itself refers to the day that marks one year from the last menstrual cycle, but the transition can involve 10-15 years of physiological changes on either side of that day, thanks to wavering estrogen production by the ovaries.[4] A woman experiencing perimenopause in her 40s could live the second half of her life with fundamentally different physiology compared to her first.

While often still siloed as a gynecological specialty, there are few body systems beyond the reach of estrogen or the cascade of hormonal changes that follow its decline. The almond-sized hypothalamus gland at the base of the brain stem requires estrogen to play a coordinating role not only in body temperature but also heart rate, hunger, thirst, sleep and a dozen other autonomic processes. Estrogen receptors play active roles in the brain, heart, lungs, bones, muscles, adipose tissue and even within immune system signaling pathways.[5]

Put simply, there is no way to discuss or treat age-related conditions without understanding the menopause transition.

But further statistics paint a troubling picture of subject matter neglect, even within the specialty most closely connected. A recent survey of gynecological residents found that while nearly all strongly agreed that they should have access to a standardized menopause curriculum, only about a third reported receiving this during their residency.[6] Even the foundational biological research is lacking. A research review in *Nature Aging* found that while 70% of the top age-related diseases in women are influenced by the systemic effects of declining estrogen, preclinical studies modeling those conditions make up less than 1% of published aging biology research.[7]

Gaps in medical research, understanding and education lead to gaps in care. The result is predictable: More than 50% of women aged 50 to 64

report that no provider discussed with them what to expect during the menopause transition.[8] These realities contribute to high costs: Menopause-related symptoms affect women in the workplace, resulting in the U.S. in an estimated $1.8 billion in lost work time per year and $26.6 billion annually when combined with medical expenses, according to recent research published by the Mayo Clinic.[9]

When we consider the downstream health consequences, the true cost of inadequate menopause care becomes exponentially higher. This is not a niche issue affecting a small subset of patients, nor is menopause a condition that can be fully supported by only one specialty. To understand why menopause care demands a comprehensive, system-based approach, we must first dig deeper into the remarkable reach of estrogen throughout the human body and the realities of its decline.

LONG-TERM HEALTH IMPACTS

Increased Cardiovascular Risk

Prior to menopause, women enjoy relative protection from cardiovascular disease compared to age-matched men. This advantage evaporates in the postmenopausal period. Estrogen exerts protective effects on the vascular lining, promotes favorable cholesterol makeup, reduces oxidative stress, and regulates inflammatory responses.[10]

With estrogen's decline, women experience accelerated arterial stiffening and increased abdominal fat — both of which contribute to heightened cardiovascular risk.[11] Women experiencing premature menopause (before age 40) or early menopause (between ages 40-45) due to the necessity of surgical procedures or medical treatments face even higher risks of cardiovascular disease than their natural menopause-matched peers, but might be overlooked for cardiovascular screening due to their younger age.

Accelerated Bone Loss

The skeleton represents another major estrogen target. Estrogen inhibits osteoclast (bone-resorption) activity and supports osteoblast (bone-building) function. In its absence, this balance shifts dramatically toward bone resorption, or the breaking down of bone.

Attributing bone loss simply to older age does not accurately represent the data: Women lose up to 20% of their bone density in the first five to seven years following menopause (regardless of age or cause), with the most rapid loss occurring in the immediate aftermath. This accelerated bone loss translates directly into fracture risk later.

According to the Bone Health and Osteoporosis Foundation, half of all women over age 50 will experience an osteoporosis-related fracture in their lifetime; in fact, a woman's likelihood of a hip fracture is equal to the combined risk of breast cancer, uterine cancer and ovarian cancer.[12] While all fractures can lead to other medical conditions and difficulties, hip fractures carry significant morbidity and mortality, loss of independence and financial burden.[13] Despite this, the *Journal of Women's Health* reports that up to 91% of women over 65 years old with a previous low trauma fracture are not screened for osteoporosis.[14]

Beyond bones, estrogen influences muscle mass and strength, connective tissue integrity and joint health. The increase in musculoskeletal pain, joint stiffness and conditions like frozen shoulder during the menopausal transition reflects estrogen's broader role in maintaining musculoskeletal strength and flexibility.[15]

Neurological and Cognitive Deficits

Estrogen influences neurotransmitter systems, promotes neuroplasticity and exerts neuroprotective effects. Its decline removes these advantages and can lead to atrophy and degeneration.

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The neurological manifestations of menopause extend well beyond the infamous hot flashes and night sweats experienced by up to 80% of women. During a hot flash, blood vessels rapidly dilate, dropping the blood pressure while quickly bringing blood to the face, chest, back, stomach and legs. Body temperature rapidly rises, and measurable sweat is produced in episodes that can last 10 minutes or more and recur dozens of times a day.[16] These autonomic disruptions can significantly impair sleep, creating a cascade of mood and cognitive decline.

Dr. Rhonda Voskuhl, professor of neurology at UCLA and founding faculty neurologist of UCLA Health's Comprehensive Menopause Program, studies the impact of estrogen and sex-based genetics on the brain alongside treating patients in the multispecialty clinic. Separate from vasomotor symptoms, she said, large areas of the brain express abundant estrogen receptors, particularly in regions important for memory, focus and processing speed.

"Brain fog occurs in 70% of healthy women as they go through menopause," said Voskuhl, specifically causing challenges with verbal memory and concentration. "It's not global IQ, they're still smart," said Voskuhl. "They're still able to do complex decision-making, but they have these domain specific problems." Voskuhl lamented that often her patients are at the height of their careers, may have more time for themselves and then find themselves struggling to retrieve words or respond as quickly, often undermining confidence. A woman deserves to understand how this experience may be related to her estrogen levels, said Voskuhl, and how she might address it to live the life she desires.

Genitourinary Decline

Unlike vasomotor symptoms, which often improve with time, genitourinary syndrome of menopause tends to worsen progressively without treatment, said Dr. Harmony Schroeder, a gynecologist who focuses on menopause care at PeaceHealth in Washington state. The vulvovaginal lining, bladder and urethra are especially sensitive to estrogen. Without it, these tissues atrophy: The lining thins and loses elasticity and lubrication, and vaginal pH changes, becoming more susceptible to infection and contributing to the increase of urinary tract infections (UTIs), which sometimes require hospitalization.

Schroeder said that symptoms such as vaginal dryness, dyspareunia (painful intercourse), urinary urgency and frequency, and recurrent UTIs significantly impact both sexual function and quality of life for many postmenopausal women.

Metabolic and Body Composition Changes

Schroeder said that many women are surprised during the menopausal transition by other unexplained body changes. The characteristic redistribution of body fat from a gynoid (peripheral or "pear-shaped") to an android (central or "apple-shaped") pattern often happens even with no weight gain. The "menopot" (as Schroeder's patients call it) occurs independently of aging and is directly related to estrogen deficiency.

Without any increase of net calories, women often gain an average of 5-7 pounds during the menopausal transition. More concerning than weight gain itself is the accompanying metabolic dysregulation. Insulin sensitivity decreases, glucose metabolism becomes less efficient, and the risk of type 2 diabetes increases, even when a woman's weight stays relatively stable. These metabolic changes, combined with the adverse cardiovascular and bone health effects already described, create a perfect storm for accelerating chronic disease development in the postmenopausal years.[17]

Thinning Skin and Gums

As if these internal changes were not enough, menopause changes the appearance and health of the skin and teeth. With less estrogen, skin ages faster as collagen falls by almost one-third in the first five years after menopause. As a result, the skin thins and becomes stretchier, easier to break or tear and takes longer to heal.[18]

Oral health deteriorates as the outer layer of the gums undergo atrophic changes alongside bone loss affecting the jaw and teeth. Postmenopausal women have an increased risk of periodontal disease, dry mouth and altered taste perception. These seemingly marginal concerns can significantly impact self-esteem and quality of life, contribute to loss of teeth and increase in infection, yet they're rarely addressed in clinical menopause discussions or patient education. Earlier detection of periodontal disease or jawbone loss gives more options for successful intervention.[19]

TREATMENT OPTIONS EXPAND

From head to toe, women are undergoing shifts to their very sense of identity and personality as

they experience autonomic, metabolic, mood, neurological, vascular and physical changes they have little control over, even as they access other medical advancements that keep them living longer. How can health care providers be better equipped with the knowledge and tools to support patients through this decades-long period?

Hormone therapy remains the most effective way to eliminate or reduce vasomotor symptoms and genitourinary syndrome, as well as relieve the many other possible effects of estrogen loss. Yet its use has plummeted.

In 2002, clinical trials conducted on the use of hormone replacement medications, known as the Women's Health Initiative (WHI), were stopped prematurely due to an observed increase in the rate of breast cancer detection in the test group. The interpretation of the WHI findings and the ensuing media coverage created misunderstanding that persists today, leaving countless women with symptoms that medical professionals now say are often treatable.[20]

Twenty years of subsequent analysis and additional trials have provided crucial context. The WHI trials studied primarily older women (average age 63) without differentiating time since menopause. Hormone supplementation was initiated for most participants many years after menopause. Additionally, subjects within the study used a specific, now outdated regimen (conjugated equine estrogens containing additional forms of estrogen not found in the human body) that was taken orally. Medical research now indicates that timing, dose and delivery mechanism matter profoundly.

Detailed analysis of both the WHI trials and subsequent research suggests that hormonal treatment initiated within 10 years of menopause, or before age 60, provides cardiovascular and neuroprotective benefits, while initiation in older women (or further from menopause) may have increased risk. Impact on all-cause, cardiovascular or cancer mortality rates remained neutral when WHI participants were followed for 13 years.

The biggest concern related to the use of hormone replacement — breast cancer — remains nuanced. The difference in absolute number of cases within the WHI test group was calculated at "one per 1,000 women per year," but "with no increased risk of breast cancer mortality."[21] Meta-analysis of 58 studies shows that risk varies based on the estrogen formulation and combination with progesterone. Lastly, in several early studies, "lack of assessment of the effect of underlying breast cancer risk on attributable risk" was "a major limitation."[22]

Contemporary hormonal treatment has evolved significantly, with a much wider array of formulations, delivery methods, dosages and more nuanced risk and benefit guidelines. FDA-approved hormone replacement therapy is recommended as first-line treatment for the relief of certain symptoms and risks of menopause by both American College of Obstetricians & Gynecologists (ACOG) and The Menopause Society (formerly The North American Menopause Society).[23]

Current recommendations favor bioidentical hormone formulations, such as estradiol, and transdermal delivery systems. These patches or creams (in various frequencies and doses) deliver estrogen through the skin into the bloodstream, which avoids metabolism through the liver, lowers the effective dose needed and reduces side effects. Current approved treatments also include varied progestogen options for patients with a uterus.[24] Recent recommendations emphasize that all women be evaluated and treated based on their individual risks and treatment goals, especially those with personal or strong family history of estrogen-receptor positive cancer or other specific risks.

Physicians caring for patients in this stage of life use research-based guidelines, analysis of risks, lab tests, coordination with other specialists, and patient reporting to prescribe and manage treatment. "When needed, I even use an FDA-approved medication for testosterone," said PeaceHealth's Schroeder. "Because there is not an approved dose for women yet, I [prescribe] a tenth of the male dose." She regularly lab tests and tracks symptoms to titrate treatment up or down.

For women whose symptoms are primarily genitourinary, low-dose vaginal estrogen provides highly effective local therapy with minimal systemic absorption. In addition to preventing skin tearing and tissue atrophy, vaginal estrogen prevents recurrent UTIs by restoring a healthy vaginal microbiome and improving urinary tract health.[25] "The data is so clear that the vaginal estrogen does not come with the same risks," agreed Schroeder. To place the highest warnings on this product, she said, is "almost antimedicine."

The FDA now agrees. Following years of advocacy by providers and associations like ACOG

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— DR. HARMONY SCHROEDER

and The Menopause Society, a comprehensive review of the scientific literature prompted an expert panel and public comment period this past summer. In November, the FDA announced the removal of all black box warnings on low-dose vaginal estrogen as well as most systemic hormone replacement therapy products.[26]

For those requiring or preferring nonhormonal treatments, the pipeline has expanded considerably in recent years. Many FDA-approved medications can be used off-label to relieve menopause symptoms including specific antidepressants, certain treatments for overactive bladder and high blood pressure, and others. Multiple new nonhormonal medications have been recently approved for the specific treatment of hot flashes, and there are a variety of treatments on the horizon.[27] UCLA's Voskuhl, for example, is studying other forms of estrogen, including estriol, to gauge its impact on cognitive and neurological symptoms.

Overall, women and providers should "start paying more attention in the 40s to physiological changes," advised Schroeder. "Menopausal medicine is so complex and can be a frustration for a lot of women, so I'm excited that there's more research and tools."

TIME IS NOW FOR CULTURAL CHANGE

The bottom line is that a woman experiencing any of the wide range of consequences resulting from natural, surgical or chemical menopause could present anywhere in the health care system — emergency, primary, cardiology, endocrinology, rheumatology or many other specialties. She requires education, support and access to treatment options from an informed clinician. In many health care systems, providing this kind of care may mean creating new kinds of primary care models or encouraging continuing education for a broader range of clinicians.

Perhaps most fundamentally, women's care seems primed for a cultural change. Menopause is not an inevitable decline requiring resignation or just a gynecological condition, but rather a significant biophysiological shift, deserving competent, compassionate and comprehensive health care.

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NOTES

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