MENOPAUSE 101 COURSE

Physiology of Menopause 101

Barbara Soltes, MD, FACOG, MSCP. Rush University Medical Center, Chicago, IL

Menopause is a normal but complex physiologic event. It can occur naturally or induced through medical intervention such as surgery, chemotherapy, or radiation. This lecture will cover the basic terminology and definitions of menopause as defined by the STRAW criteria. There will be a review of the stages of perimenopause and menopause based on menstrual status, hormonal criteria, and symptomatology. It will differentiate between Premature Menopause and Premature Ovarian Insufficiency. The review will also address the current understanding of adrenal physiology as a woman transitions from perimenopause into menopause. A knowledgeable menopause practitioner must have a solid understanding of the menopause physiology in order to deliver comprehensive care and discuss options for treatment if needed.

Hormone Therapy 101

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This presentation focuses on the key basics of hormone therapy (HT) prescribing for menopause symptom management. Clinicians typically receive little or no education on menopause management in their training, and HT prescribing rates remain low. Women are undertreated for their symptoms which are known to have significant negative effects on quality of life and are associated with a substantial economic burden in terms of increased health care costs and reduced work productivity. Now, more than ever before, it is possible to individualize the use of HT for women with bothersome menopause symptoms who have a preference to use HT and who are without contraindications to its use. Timing of initiation is important, and there is increasing understanding that both age and time since menopause impact the risk to benefit ratio. In general, the benefits of HT outweigh the risks in women who are under the age of 60 years and within 10 years of menopause onset. There are many HT options available to women, including different formulations, routes of administration, and doses that are government approved such that therapy can truly be tailored to a woman's individual needs. It is advisable to use government approved options rather than custom compounded hormone therapy (which is not government approved) given concerns about purity, potency, efficacy, and safety of non-approved, non-regulated hormones. This presentation will review the various systemic HT options as well as local vaginal therapies. It will also review when a progestogen is needed. Importantly, it will provide practical and evidence-based information on when and how to prescribe HT in women with chronic medical conditions (eg, hypertension, diabetes, rheumatologic disease), particularly given that 4 in 5 50-year-old women have at least one chronic medical condition, and half have two or more chronic conditions.

Vasomotor Symptoms 101

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Vasomotor symptoms (VMS) affect the vast majority of individuals who will traverse menopause in addition to those who take endocrine ablation therapy for a variety of diseases. VMS cause significant disruption of quality of life, impact sleep, and may have long term consequences for cardiometabolic health. They also have a negative impact on women in the workplace, with estimated costs of close $2B per year in lost productivity. Knowledge gained through a number of epidemiological studies of the menopause transition confirms a high prevalence of VMS and has identified participant factors associated with duration and severity. VMS are prevalent even before the menopause transition, with overall greater prevalence among populations of color. VMS increase in prevalence during the early menopause transition and peak in the year before and after the final menstrual period in studies of naturally menopausal women. Surgically menopausal women are believed to have a more severe and prolonged experience with VMS. Longitudinal studies of the menopause transition indicate that the median duration of VMS is 7.4 years, however sociodemographic predictors impact greatly on duration. For example, African American women over a decade's duration VMS, on average, while Chinese American women experience VMS for only about half as long. VMS are effectively treated with hormone therapy. However, risks and benefits for each individual woman need to be assessed and reassessed, as some risks (eg, breast cancer) accrue over time and some women will develop a contraindication to hormone therapy (eg, DVT). Other treatments for VMS have largely been discovered when women with a contraindication to hormone use took a medication for a different reason and noted that their VMS improved. Systematic study of these medications then ensued. In this manner, the SSRI/SNRI class of medications, gabapentin, and oxybutynin have accrued evidence for efficacy for VMS symptoms in many women. However, these nonhormonal alternatives are not as effective as hormone therapy and they often have off-target effects. New to the science of VMS and new to the market, selective neurokinin 3 (NK3) receptor antagonists have been discovered and developed as effective treatments for VMS. Because they target the NK3 receptor proximal to the estrogen mediated pathway, they abrogate hot flashes on a par with hormones in terms of effectiveness.

Genitourinary Syndrome of Menopause 101

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Declining estrogen levels in peri- and postmenopausal women can cause a number of bothersome genitourinary symptoms that negatively impact quality of life at midlife and beyond. Termed the Genitourinary Syndrome of Menopause (GSM), symptoms may include vaginal dryness, irritation or burning, painful sex, dysuria, and urinary tract infections. Up to 50% of women may experience some or all these symptoms, but many do not report symptoms to their healthcare clinicians and/or are not offered treatment. This presentation will help clinicians screen for the symptoms of GSM and differentiate GSM from other conditions that can occur after menopause. An overview of the range of treatment options available for GSM will be discussed including lubricants to use during sexual activity, over the counter vaginal moisturizers, local vaginal estrogen products, vaginal dehydroepiandrosterone, as well as an oral selective estrogen receptor agonist. Laser and radiofrequency treatments are also being studied to treat GSM. At the end of this presentation clinicians should feel more comfortable taking into account individual patient treatment preferences and risk factors such as breast cancer or a history of venous thromboembolism in order to offer treatments to improve genitourinary health and quality of life.

Sexual Function 101

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With life expectancy increasing and the functional health of older adults improving, the identification and treatment of female sexual dysfunction (FSD) represents a great unmet need. Sexual dysfunction in postmenopausal women is a consequence of aging, hypoestrogenemia, medications, and medical comorbidities such as cardiovascular disease, diabetes, and other chronic diseases. In addition, FSD is often a downstream consequence of insomnia, vasomotor symptoms, stress, and generalized musculoskeletal pain. Female sexual dysfunction is divided into four categories: Sexual Desire Disorders, Sexual Arousal Disorders, Orgasmic Disorders, and Sexual Pain/Genito-pelvic pain/penetration disorders. In the post menopause population, it is common for someone to have more than one diagnosis. Hypoactive Sexual Desire Disorder (HSDD) is defined as the persistent or recurrent deficiency or absence of sexual thoughts, fantasies and/or desire for, or receptivity to, sexual activity which causes marked personal distress or interpersonal difficulties and is not better accounted for by another primary disorder, drug/medication, or general medical condition. Diminished or absent libido in menopause is typically multi-factorial and is impacted by psychosocial issues, hormonal changes, medications, depression, sexual pain, alcohol, stress, insomnia, and co-morbidities. Arousal, a primarily vascular function (vasodilation and increased blood flow), is mediated by neurotransmitters but also impacted by vasculopathies, loss of estrogen and the subsequent impact estrogen deficiency has on the endothelial nitric oxide vasodilation pathway. Genitourinary Syndrome of Menopause (GSM) which includes hormonal vestibulodynia and vaginal atrophy is the most common cause of Genito-pelvic pain/penetration disorder. However, painful penetration can also be a consequence of other conditions such as dermatologic pathology, infections, gynecologic or non-gynecologic pelvic conditions, pelvic floor hypertonicity, and/or central sensitization. Vaginismus and pelvic floor tension is typically a secondary consequence of dyspareunia, or other pelvic conditions and is essentially a protective mechanism (ie, to "protect" one from anticipated pain). Even after the initial cause of the pain is treated and eliminated, pelvic floor tension may be persistent, and require pelvic floor physical therapy to erase the "muscle memory." Orgasmic Disorder is defined as the persistence or recurrent delay in or absence of orgasm after normal excitement phase which causes marked distress or interpersonal difficulty. Most menopause women experience acquired, as opposed to primary anorgasmia due to clitoral vasculopathy and neuropathy. Risk factors for orgasmic dysfunction beyond hypoestrogenemia include medications such as SSRIs, pelvic floor disorders, and medical co-morbidities such as diabetes, incontinence, hypothyroidism, and vasculopathies. While there are no FDA approved medications to treat arousal or orgasmic dysfunction there are tools and medications, such as topical vasodilators, which are beneficial. Evaluation of FSD includes a detailed history, and a targeted physical exam. Many women assume that sexual problems are a normal part of aging with no treatment available and therefore do not broach the topic. Therefore, it is incumbent upon the clinician to specifically inquire about sexual concerns since patients rarely initiate a conversation but are willing to discuss the topic once initiated by the clinician. A systematic physical examination of the patient with sexual concerns is an essential and early component of an effective treatment plan. Evaluation without physical examination can result in misdiagnosis and failed treatment. There are safe and effective treatments for virtually every cause of sexual dysfunction, but even the most common cause of postmenopausal sexual dysfunction, vulvovaginal atrophy, is rarely treated. Treatment is dependent on the specific type of dysfunction and cause of dysfunction. Psychosocial, medical and hormonal issues must all be addressed which requires coordination of multiple disciplines including medical clinicians, pelvic floor physical therapists, and sex therapists.

Mood, Sleep, and Cognitive Function 101

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Disruptions in mood, sleep, and cognitive function may occur during the menopause transition and are frequent complaints for many women. These symptoms may persist well into the postmenopause period. The coexistence and interactions of these symptoms can negatively impact quality of life. Disturbed sleep is reported by as many as 69% of women during the menopause transition. Vasomotor symptoms (VMS) account for a third of wakefulness after sleep onset (WASO). Hormonal fluctuations as well as, mood and anxiety symptoms may also disrupt sleep, and lead to complaints of diminished sleep duration, maintenance, and quality. Mood disturbances in the midlife transition may result from sleep disturbance and hormonal fluctuations. Patients with a history of premenstrual dysphoric disorder (PMDD) may experience an exacerbation of mood symptoms during the menopause transition. Those who have a history of major depressive disorder (MDD) are increasingly vulnerable to experience a major depressive episode (MDE) or recurrence of MDD during the menopause transition. New onset MDD may occur in those individuals who are more sensitive to hormonal fluctuations. Estrogen appears to mediate mood regulating neurotransmitters; estrogen therapy (ET) may improve MDD symptoms during menopause transition, but not in the

postmenopause period. While ET is not FDA approved for mood and sleep disturbance in the menopause transition, cognitive behavior therapy is an effective strategy to alleviate sleep disruption, mood disturbance, and VMS. Many women present with cognitive complaints during the menopause transition that include word finding difficulty, declines in memory, and poorer performance on cognitive tests. These complaints too may stem from the intersection of VMS, sleep, and mood disturbances. The relationship between hormone therapy and cognitive performance is complex. The effect appears neutral in the early postmenopause period and varies by formulation in the late postmenopause period. Estradiol has a neutral effect during this period, while conjugate equine estrogens (CEE) combined with medroxyprogesterone acetate appears to have a negative effect. The effect of sleep disruption, mood, and cognitive changes can be profound during the menopausal transition and postmenopause. This presentation will focus on ways to address these symptoms clinically.

Prevention 101

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Menopause marks a significant physiological transition in a woman's life, characterized by hormone changes that often coincide with weight gain and increased health risks. As part of the Menopause 101 course, we will include a presentation on prevention. The presentation will begin by elucidating the relationship between menopause and weight gain, exploring hormonal influences and metabolic shifts that contribute to this phenomenon. Pharmacologic interventions for weight management will be thoroughly reviewed, emphasizing indications, mechanisms of action, and potential side effects, thereby equipping clinicians with evidence-based strategies. We will delve into the heightened risk factors for cardiovascular disease (CVD) and osteoporosis postmenopause, providing an overview of preventive measures and screening protocols essential for early detection and intervention. Detailed discussions on screening guidelines for breast cancer, cervical cancer, colon cancer, osteoporosis, and CVD will ensure attendees are well-versed in current clinical recommendations. Additionally, the role of lifestyle modifications, including exercise and dietary recommendations endorsed by the American Heart Association, will be highlighted as integral components of comprehensive menopause health management. Practical guidelines will be discussed to equip attendees in guiding their patients towards healthier choices. In summary, this presentation aims to equip healthcare clinicians with a comprehensive understanding of menopause-related health issues, and tools available for prevention of the most common diseases postmenopause including cardiovascular disease and osteoporosis. By integrating knowledge on weight management, lifestyle interventions, and disease prevention, attendees will be better prepared to optimize health outcomes for menopausal patients.

COGNITIVE-BEHAVIORAL THERAPY 101

Foundations of Cognitive-Behavioral Therapy

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Cognitive-behavioral therapy (CBT) is an evidence-based psychotherapy widely used for many different psychiatric disorders and psychosocial problems and concerns (Fordham et al., 2021; David et al., 2018). Originating in the work of Aaron T. Beck, the theory and techniques of CBT center around skills-based learning of change in the relationship among thoughts, feelings, and behaviors (Beck et al., 1979). Key tenets of CBT are the identification of and work towards specific and measurable goals, structured process (both within session and between sessions), and a time-limited course. CBT focuses on the individual's present functioning but is also informed by the individual's past; the use of case conceptualization in CBT organizes and elucidates the connection between the present and the past. The relationship between the individual and the therapist is one based in collaboration, with the therapist helping the individual in guided self-discovery, allowing the individual to draw one's own conclusions. CBT uses the process of cognitive restructuring to help individuals evaluate their negative thoughts about themselves, the world and others, and the future and to modify these thoughts to be more helpful or adaptive. In particular, CBT works on three levels of cognition: negative automatic thoughts, maladaptive assumptions, and negative core beliefs. Techniques such as identification of cognitive distortions, exploration and evaluation via Socratic dialogue, and reframing of cognitions to be more adaptive and helpful are used. The behavioral part of CBT includes the learning of new responses and actions, accomplished through such techniques as taking action on reframed thoughts, behavioral activation, exposure to feared stimuli, and relaxation training (Beck, recent 2021). This talk provides an introduction to CBT theory and skills, using examples common to the human condition and sets the stage for its use in working with those in the menopausal transition.

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Cognitive-Behavioral Therapy for Menopause Symptoms

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The menopausal transition, including peri- and postmenopause, occurs in women on average between 40 and 60 years. Although this is a natural experience for all women who reach middle-age, there are a number of adverse physical and emotional difficulties that frequently accompany menopause. One of the most common physical symptoms, and main reason that women seek treatment is vasomotor symptoms, also known as hot flashes and night sweats, occurring in approximately 80% of women. Further, emotional difficulties that are more frequently experienced during menopause are anxiety and depression, with up to 68% of perimenopausal women reporting elevated depressive symptoms along with increased rates of relapse of a major depressive episode. Sleep difficulties, including insomnia, and sexual concerns are also prevalent during the menopausal transition. Perimenopausal women are twice as likely to have sleep difficulties compared to premenopausal women and up to 86% of women going through menopause report some form of sexual concern (eg, low desire, arousal, and pain). Fortunately, a number of pharmacological treatments exist for vasomotor symptoms, depression, anxiety, sleep, and sexual concerns including Hormone Therapy (HT) and Selective Serotonin Reuptake Inhibitors (SSRI's), which are effective for some. However, not all women can utilize these treatments due to contraindications with HT for instance (eg, history of breast cancer, coronary heart disease, stroke related), or intolerable side effects. Importantly, women may prefer not to take medication for their physical and emotional symptoms making the need for non-pharmacological treatments even more critical. Given that women's appraisals of symptoms are highly impacted by psychological and social factors, taking a biopsychosocial approach to guide non-pharmacological treatments for menopausal symptoms is appropriate. Cognitive-behavioral therapy (CBT) is an evidence-based psychological and behavioural treatment that is consistent with the biopsychosocial model. In the general population, is a first line treatment for both anxiety (eg, Panic Disorder, Generalized Anxiety Disorder) and depressive disorders (eg, Major Depressive Disorder). It is also the first-line treatment for Insomnia and there is increasing empirical support for its use with sexual concerns. Interestingly, there is also a strong body of literature demonstrating CBT as an effective treatment for vasomotor symptoms. Indeed, according to the 2023 nonhormone therapy position statement of The North American Menopause Society, CBT for vasomotor symptoms was categorized as a Level I treatment (eg, 'good and consistent scientific evidence'). During this presentation, literature on the use of CBT for vasomotor symptoms will be reviewed as well as CBT for depression, anxiety, insomnia, and sexual concerns during the menopausal transition. Specific cognitive and behavioural strategies that are tailored to meet the unique needs of women during menopause will be highlighted. Considerations for the developmental context of menopause will be emphasized.

Cognitive-Behavioral Therapy for Sexual Dysfunction at Midlife

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Female sexual function is best viewed through the lens of a biopsychosocial model. This is an integrative, fluid model reflecting fluctuations in physical health, neurochemical and hormonal balance, sociocultural factors, psychological issues, and interpersonal concerns. The nomenclature and classification of female sexual dysfunctions (FSDs) varies, but the June 2024 meeting of the International Consensus Conference in Sexual Medicine (ICSM 2024) includes Hypoactive Sexual Desire Disorder (HSDD), Female Genital Arousal Disorder (FGAD), Female Cognitive Arousal Disorder (FCAD), Female Orgasmic Disorders (FOD), Persistent Genital Arousal Disorder (PGAD), and Sexual Pain-Penetration Disorder. Cognitive-behavioral therapy (CBT) has emerged as a prominent psychological intervention for addressing female sexual dysfunctions (FSDs). CBT techniques such as cognitive restructuring, behavioral techniques (e.g. Sensate Focus), and mindfulness approaches, are tailored to target specific cognitive distortions and maladaptive behaviors contributing to FSDs. Key findings indicate that CBT interventions effectively alleviate symptoms and improve sexual functioning by enhancing sexual self-esteem, modifying dysfunctional beliefs and behaviors, and promoting communication skills within intimate relationships. Moreover, the integration of CBT with other therapeutic modalities, such as mindfulness-based interventions and couple's therapy, demonstrates promising results in enhancing treatment outcomes and long-term sustainability. CBT has been evaluated in a number of randomized clinical trials and generally been found to be efficacious in treating FSDs. However, CBT is often most applicable if a woman is open to psychological interventions and to engage in sexual activity (ie how many psychologists does it take to change a lightbulb…), and when there is evidence of psychological, socio-cultural, or interpersonal factors impacting sexual function. One size does not fit all. A biopsychosocial model informs both etiology and treatment. Some women will benefit more from psychotherapeutic options, some from pharmacologic options, and some from an integrated multimodal approach. Implications for clinical practice underscore the importance of personalized treatment plans and the need for further research to optimize CBT protocols tailored to the diverse needs of women experiencing sexual dysfunctions.

Cognitive-Behavioral Therapy and Insomnia During Menopause

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Insomnia is a clinical disorder characterized as difficulty falling asleep, staying asleep, or waking too early. To meet diagnostic criteria for an insomnia disorder, these difficulties must be present for a minimum of three months and cause significant daytime impairment. Insomnia is common in women transitioning through menopause and frequently continues in the years after menopause. Insomnia is likely related to

factors such as aging, hormone fluctuation, hot flashes, other sleep disorders, psychiatric and medical conditions, and psychosocial stressors. Women who report hot flashes are more likely to report insomnia. Insomnia can be part of the clinical presentation of persons suffering from other underlying psychiatric conditions such as depression and anxiety. Cognitive-behavior therapy for insomnia (CBT-I) is a short-term, skill-focused psychotherapy targeting maladaptive behaviors and cognitions contributing to chronic insomnia. Efficacy of CBT-I has been demonstrated in midlife women with insomnia symptoms, including those with hot flashes. Results from randomized clinical trials suggest improvements after CBT-I are equivalent to those achieved during acute treatment with hypnotic medications, and its effects are more durable after treatment discontinuation. The strong evidence for the efficacy of CBT-I led to its recognition as a first-line treatment by a National Institutes of Health Consensus Statement as well as by the American College of Physicians. CBT-I takes a systematic approach to addressing sleep-interfering behaviors and beliefs. Case conceptualization is based on Spielman's Three Factor model of insomnia, which posits that although insomnia usually begins with the combination of a *predisposition* (eg, high emotional reactivity) paired with a *precipitating* event (eg, vasomotor symptoms, depression), the transition to chronic insomnia is usually *perpetuated* by increased sleep effort and compensatory strategies (eg, increasing time spent in bed). Increased effort to induce sleep in response to distress about poor sleep is thought to lead to conditioned arousal (whereby the bed becomes a cue for arousal rather than sleep) and maintains the sleep problem even after the causative factors are eliminated. The core components of CBT-I are delivered across four to six sessions and consist of psychoeducation, sleep restriction, stimulus control, cognitive restructuring, and sleep hygiene education. Throughout treatment, patients are asked to keep a daily sleep log in which they report estimated bed and wake times, time to fall asleep, and length of time they spent awake during the night. Clinicians who suspect insomnia in their patients may consider referring them to a sleep medicine clinic of behavior sleep medicine provider for evaluation. For less-complex patients, clinicians may consider providing self-management resources to their patients. Given the relatively high prevalence rate of sleep complaints in midlife women, clinicians should ask about their patients' sleep patterns and satisfaction with sleep as a part of routine care, and if needed, provide their patients with appropriate resources or referral.

Cognitive Behavioral Therapy in a Clinical Setting

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During perimenopause or menopause, people often experience multiple interacting symptoms and contextual influences. For example, vasomotor symptoms, insomnia, depression, genitourinary symptoms, and pain can all influence one another. Midlife losses, stressors, and role transitions can affect and be affected by all these symptoms. This complexity can lead to fragmentation of care. Coordinated treatment can optimize symptom reduction, functioning, and well-being. Cognitive behavioral therapy (CBT) can promote care integration by alleviating multiple symptoms in perimenopause and menopause. CBT symptom targets can include depression, anxiety, insomnia, vasomotor symptom interference, pain, overactive bladder, and sexual dysfunction. However, there are formidable challenges in access to CBT. These include a shortage of mental health providers, stigma, and treatment burden. The latter is especially relevant to midlife women who are caregivers for family members, often for multiple generations. Integrating CBT into women's health clinical settings (primary care and gynecologic) improves access. This can include co-location and/or virtual teamwork of multidisciplinary clinicians. Collaboration can be fostered via curbside consultations, huddles, shared medical records, and warm handoffs. Steps clinicians can take to promote uptake of CBT include defining treatment targets, engaging patients, and addressing treatment burden. Treatment targets can be developed by multidisciplinary communication and can encompass physical and mental health symptoms of perimenopause and menopause, health promotion (eg, physical activity, smoking cessation, anti-inflammatory diets), and attitudes toward aging. Engaging patients in CBT can begin with psychoeducation, including identifying treatment goals and explaining efficacy of CBT for those goals. CBT can be described in a way that reduces stigma and misperceptions – eg, that it is goal-directed, time-limited, structured, present-focused, and skill-building. Motivational interviewing (discussing pros and cons of CBT in a nonjudgmental way) can be used as needed. Warm handoffs (direct introduction to a mental health clinician by a referring clinician) can further facilitate uptake of CBT. Treatment burden can be reduced by using a modular approach to CBT – delivering different components in different orders, based on patient priorities and preferences. CBT can also be accomplished via telehealth, guided self-help (workbooks or online programs with coaching), or blended modalities (some in-person meetings with a therapist and some online components such as videos, worksheets, and homework).

OPENING SYMPOSIUM

How Artificial Intelligence is Being Applied in Clinical Practice

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Artificial intelligence (AI) is rapidly transforming healthcare, with applications ranging from predictive analytics to advancing imaging techniques to personalized genomic medicine. This talk provides an overview of AI's growing role in obstetrics and gynecology, emphasizing both its potential to improve clinical outcomes and the challenges posed by data limitations, particularly in menopause care. We begin with an overview of AI applications across healthcare, including machine learning and the emerging field of generative AI. This section highlights how these technologies are being used to enhance diagnostics and patient management across various medical specialties. The discussion then transitions to a review of existing uses of AI in obstetrics and gynecology, with a particular focus within obstetrics on advancing ultrasound diagnosis. Within gynecology, the focus shifts to the early applications of AI across the field including in endometriosis, infertility, and our own early work in developing generative AI for cervical cytology. Finally, we will describe considerations for applying AI to the field of menopause health. Despite the profound impact of menopause on women's health, it remains underrepresented in medical research and AI model development, potentially due to difficulties in data acquisition and interpretation. We explore how – if these data problems can be resolved – future applications might include better predicting and managing symptoms of menopause, personalizing hormone replacement therapy, and otherwise individualizing care. The talk will also address the ethical considerations and potential biases associated with AI in healthcare, emphasizing the importance of comprehensive data collection and ongoing validation to prevent AI from reinforcing existing disparities. Clinician involvement in AI development is crucial to ensure these technologies enhance, rather than replace, human judgment. This presentation aims to demonstrate the transformative potential of AI in both gynecology and obstetrics while highlighting the urgent need for improved data and research in menopause to fully harness these technologies.

Artificial Intelligence and Cardiopulmonary Illness

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Modern computational technologies and the ever-increasing storage of healthcare data has allowed for the rapid advancement of artificial intelligence as an active area of research within the medical realm. Deep learning methodologies are a popular choice, due to their ability to discover features (useful measurements and combinations of measurements) from raw data, removing the need for domain expertise. The trade-off is that deep learning algorithms need large datasets (tens of thousands to hundreds of thousands of examples) to generate high performing models, and as a result, data scientists routinely use tangentially related data sources to meet the data needs. This inherently biases the models and consequently, these models may not perform as expected in the actual intended use populations or in clinically relevant populations. Another concern with deep learning models is the interpretability of the prediction mechanism, including the lack of knowledge of the learned features and their importance, which is an area of active research; however, as of yet, no reliable and generalizable method exists to make transparent the mechanisms of the "black-box." Conversely, supervised machine learning uses a known, or man-made, set of input features instead of relying on deep learning for feature learning, which reduces data needs by magnitudes, and can still produce high performing models. This alleviates the data needs that deep learning has in complex medical applications where the amount of ground-truth data is limiting, expensive to acquire and difficult to find retrospectively as properly labelled. The final models generated are transparent and allow understanding of the physiological mechanisms underpinning the output. However, developing significant and relevant features requires a thorough understanding of signal processing, mathematics and medicine. Furthermore, selecting the best sub-set of features for each specific clinical application requires an understanding of the clinical population that one intends to treat, and the appropriateness of statistical techniques used to select the subset of features. Based on both European Society of Cardiology and American College of Cardiology (ACC) guidelines, standard point-of-care testing for coronary artery disease (CAD) is typically followed by a more complex and rigorous assessment, involving a new encounter at a different care center. Over 80% of the patients are evaluated with single photon emission computed tomography (SPECT) and/or coronary computed tomographic angiography (CCTA), which can expose the patient to significant radiation and/or stress (pharmaceutical or exercise-induced). Testing may take place over a period of days to weeks, and positive/inconclusive results may result in referral to gold-standard invasive coronary angiography (ICA) and possible intervention (i.e., catheter-based coronary intervention or coronary artery bypass graft surgery) if indicated by the presence of obstructive CAD. Diagnosis of CAD has been skewed between the sexes. Specifically, risk stratification for CAD is less effective for women, resulting in lower angiographic diagnostic yield, which may be an overcompensation for the historic underdiagnosis of heart disease in women. Indeed, a large registry review of almost 400,000 patients undergoing ICA found that while women were referred at a similar rate as men (47% vs. 53%), only 27% of women were found to have obstructive CAD (vs. 47% of men). This indicates that non-invasive testing results, which are used to justify sending patients to ICA, fall short in women. Pulmonary hypertension (PH) affects women to a greater extent than men. PH is definitively diagnosed using invasive right heart catheterization. Echocardiography is used as a front-line non-invasive test but is not usable in ~40% of the incoming population because a key measurement made by echocardiography, tricuspid regurgitant velocity, to determine likelihood of PH cannot be made. There is an immediate need for accurate and accessible non-invasive testing for both conditions. Described here is the development and validation of a non-invasive, point-of-care diagnosis platform that can assess for CAD (with similar performance to standard of care tertiary center testing) and PH, simultaneously.

Electroencephalography in the Development of Objective Neurotechnology in Depression

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Since its inception in 1924, electroencephalography (EEG) has been a pivotal tool for exploring brain-behavior relationships and assessing the neurobiological effects of psychiatric interventions, including those for major depressive disorder (MDD). MDD is a highly prevalent condition, affecting over 300 million people globally. Despite the availability of antidepressant treatments, the dependence on a trial-and-error treatment

prescription prolongs the duration of untreated depression. Moreover, 30-50% of patients fail to respond to first-line treatments, such as cognitive behavioral therapy (CBT) or selective serotonin reuptake inhibitors (SSRIs), leading to treatment-resistant depression (TRD). This underscores the urgent need for objective biomarkers to predict treatment responses and identify novel therapeutic targets, particularly for TRD. EEG-based biomarkers offer a promising avenue for developing diagnostic tools and personalized treatment strategies to reduce the duration of untreated depression. Over the past decade, my lab has focused on advancing EEG-based brain mapping technologies and biomarker discovery with potential clinical applications. Our research has leveraged multi-site, longitudinal EEG recordings from antidepressant clinical trials to identify candidate biomarkers for predicting and monitoring responses to first-line treatments, such as CBT and SSRIs, in MDD. Additionally, we have integrated EEG with Transcranial Magnetic Stimulation (TMS-EEG) to develop diagnostic, predictive, and mechanistic biomarkers, as well as new treatment targets for TRD. In this presentation, I will review the candidate EEG predictors of treatment response identified through our work in the Canadian Biomarker Integration Network in Depression (CAN-BIND). I will also discuss the potential of multi-modal EEG-based biomarkers in guiding the development of new antidepressants for TRD. Finally, I will outline the next steps for validating these biomarkers through multi-site, biomarker-informed, randomized controlled trials, paving the way for their clinical implementation.

Responsible Artificial Intelligence Use Cases in Women's Health

Andrea Barrett, PA, MHA. Microsoft, Westwood, MA

As 'femtech' puts women's health in the spotlight, large and small language artificial intelligence (AI) models that bridge Data, Equity, and Trust are being built to help women navigate life transition from menstruation to menopause. This presentation will explore responsible AI use cases in clinical practice that assist in managing menopause symptoms, enhancing women's healthcare experience, supporting better outcomes, and restoring the joy of medicine to clinicians in fields dedicated to serving women.

Voice as a Predictor of Health During Menopause

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An important symptom in perimenopausal women that is often underdiagnosed and disregarded is voice change that coincide with the prime of their working and active years. Over 60% of women going through menopause report symptoms of dysphonia or "abnormal voices" that can cause a significant impact on quality of life, mood and work efficiency, and are often unrecognized or minimized by the medical community. While a drop in vocal pitch is typically the hallmark sign, many women also notice that their voice becomes raspier and in some, the hoarseness leads to a persistent cough and pain. To counteract symptoms of shortness of breath and vocal fatigue, some women adopt inefficient clavicular breathing techniques which when utilized for prolonged periods of time can also lead to increased head, shoulder, and neck muscle tension. All this to say that the hormonal changes associated with (peri)menopause set off a series of physiological, biomechanical, as well as gross and fine motor disruptions. For a subset of women, the Voice Superusers, vocal changes aren't just quality of life and health issues, they impact their livelihood and economic independence. Voice Superusers are our teachers, 75% of whom are women in the US; news anchors (51% women), coaches (41% women), voice artists (41% women), professional singers (31% women) and other such professions. In fact, 50% of teachers need to miss work due to voice related issues, an occupational hazard further exacerbated by the (peri)menopause. For voice performers and personalities, even subtle changes can have a significant impact on maintaining and advancing their careers. Moreover, while an increasing number of women chose hormone replacement therapy to alleviate their symptoms of menopause, they are rarely counseled on the effect of these treatments on their voice. In fact, certain estrogen-based therapies have positive effects on female voice by increasing hydration of the larynx while testosterone-based HRT can have detrimental effects including lower voice pitch and roughness, leading women to seek medical attention for their voice changes due to significant impact on their quality of life. Although voice changes can be a burden to these women, they can also become valuable biomarkers of hormonal changes. Voice biomarkers could help monitor hormonal fluctuations, screen for early signs of menopause, and help develop personalized treatments. This presentation will review the impact of hormonal changes in menopause on voice and respiratory function and discuss how vocal biomarkers could be used for diagnosis and treatment monitoring. We will also review current treatments and management options for voice changes during menopause and future work needed to push the field forward.

MENOPAUSE RESEARCH: FUNDING, METHODS, AND CAREER ADVICE

Menopause Research: Pilot Funding, Basic Research Methods, and Career Advice

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The new initiative on Women's Health Research by the White House announced on November 13, 2023, and the executive order signed by President Biden on March 18, 2024, providing an investment of $12 billion for women's health research underscores the critical need to advance science for the health of women. As part of this initiative, the Office of Research on Women's Health and the Office of Disease Prevention launched events to bring attention to female-specific health conditions including the menopause transition and future health. Over the past 20 years, longitudinal studies of women transitioning through menopause have contributed substantially to our understanding of the relationship between the menopause transition and future health. Even with the progress made, key research questions are still left unanswered. This session targets early career scientists interested in studying the menopause transition. Early career investigators will learn about a new funding opportunity provided by The Menopause Society for small pilot awards to enhance opportunities to receive independent funding through federal organizations. The session will cover basic research methods needed when studying the menopause transition along with resources and biobanks that host data and biospecimens relevant to the menopause transition research. A presentation from a mid-career investigator in this field will describe their journey and provide tips towards a successful career in menopause research. A panel discussion of senior and mid-career investigators is included to answer questions about career decisions, strategies for obtaining funding, and resources and research methods employed in menopause transition research.

PLENARY SYMPOSIUM #1

Opportunity to Reimagine Personalization for Breast Cancer Treatment, Screening, and Prevention

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Breast cancer remains a feared disease in women. In the US alone, the incidence is now almost 300,000 per year, a rate that has nearly doubled in the last 30 years. The majority of women survive, but 40,000 women a year still die of their disease. It is the most commonly diagnosed cancer among women and the second leading cause of cancer death. Progress has been made in understanding and treating breast cancer, which has led to lower mortality rates. In the past several decades, we have developed a considerably better understanding of the heterogeneity of breast cancer. There are many types of breast cancer, influencing the aggressiveness and recurrence risk. At its most basic, tumors are classified as hormone negative/positive and HER2 positive/negative. Hormone positive tumors are generally considered slower growing but have a risk of distant recurrence that extends for many years, where hormone negative and HER2+ cancers are considered faster growing, and their recurrence risk is largely confined to the 5 years after diagnosis. Improved tumor classification has led to the development of targeted therapies, including HER2 directed therapies for HER2 overexpressing tumors, endocrine therapies for hormone driven tumors, and immune directed therapies in combination with chemotherapy for fast growing tumors. These targeted therapies have revolutionized how we treat breast cancer, leading to greater response and higher survival rates. We will discuss how trials such as I-SPY 2, that change the order of treatment (starting with neoadjuvant or systemic therapy before surgical excision) has led to improvements in our ability to learn which treatments are successful and for whom, and how response to therapy can enable tailoring of adjuvant therapy, de-escalating treatment in the setting of complete pathologic response and escalating therapy in the setting of poor response. We will also review important updates on new treatment approaches to precancerous lesions such as ductal carcinoma in situ (DCIS), including active surveillance and intratumoral immunotherapy trials. DCIS should be reframed as an opportunity to better understand prevention of invasive cancer. The advances in treatment provide important information about how we can tailor risk assessment tools, prevention interventions and manage the treatment of breast cancer survivors. We will introduce the national WISDOM study (Women Informed to Screen Depending on Measures of Risk). Breast cancer is not one disease, and women have varying risk, and therefore a one size fits all approach to screening is not sensible. We are working to reframe our approach by starting with risk assessment. Taking inspiration from the field of cardiologists where a decades long concerted effort to bring down the death rate from cardiac disease started with risk assessment that transitioned to routine risk assessment and management as part of primary care. It is important to use what we know about genetic risk (mutations and polygenic risk) as well as breast density, and other risk models, adjusted for race and ethnicity. Opportunities to further improve risk assessment by considering risk for fast or slow growing tumor types will be reviewed (WISDOM 2.0). The impact of screening strategies on the cost and burden of screening should be an additional consideration. The range of economic impact varies from 12-36 billion annually in the US, depending on the strategy considered. The resources spent on screening, in aggregate, are enormous. One of the biggest potential benefits of shifting to a process where risk assessment is the first step, is that it should enable us to integrate risk reduction, which, in the long run, should become more important than screening. Our goal should be to decrease the incidence of breast cancer, It is critically important that we change our approach in medicine to one where we integrate care and research so that we learn and improve in real time. Innovative trials that embrace the learning engine concept will enable us to continue to refine and continuously improve options for patients. The money is already in the system (as illustrated by the resources expended for screening). We need to continue to work to find ways to reallocate resources to learn at a faster pace.

The Rationale for Population Genetic Testing and Polygenic Risk

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Guidelines for breast cancer screening are ever evolving as breast cancer is now the most common type of cancer diagnosed in women in the US, with trends showing increasing incidence rates, including in younger women. Breast cancer risk assessment can be challenging with a variety of medical societies and evidence-based guideline groups

making different recommendations for breast cancer risk assessment and screening. Compounding this challenge is the existence of a variety of available risk models based on different study populations, input variables, and with different performance statistics. Two types of genetic testing can inform individual breast cancer risk: One is traditional germline testing for high-risk genes such as BRCA1 and BRCA2, in addition to more moderate-risk genes such as CHEK2 and ATM. The other is with polygenic risk scores (PRS). Germline testing has historically been available only to those who meet specific risk criteria predominantly based on either already having had a diagnosis of breast (or ovarian, or other) cancer and/or family history characteristics. However, population studies of the prevalence of these genes in the population have consistently shown that most mutation carriers are unaware of their mutation until *after* a cancer diagnosis, and that using family history criteria to limit access to germline testing prevents those with small families, those who don't know biological family medical history, or those with few female relatives from accessing insurance coverage for these tests. In the WISDOM study (wisdomstudy.org), we found that out of 23066 participants undergoing germline screening for a nine gene panel including BRCA1 and BRCA2, 3.1% were found to carry a mutation in a breast cancer pre-disposing gene, and 22-46% of those with mutations reported having no family history of breast cancer. These findings support consideration of germline testing of younger women for at least higher-risk genes in the general population as there are interventions proven to improve morbidity and mortality in those at highest risk. Conversely, polygenic risk scores (PRS) use many genetic variations (hundreds to thousands) that are scattered across the genome: Individually these variants confer a negligible contribution to breast cancer risk, but when combined to generate a PRS, those individuals at the highest end of the PRS distribution have breast cancer risks similar to those who have mutations in moderate-risk genes. While our initial data from the Wisdom study shows that women with higher PRS have some enrichment for breast cancer family history, using family history alone is not predictive of PRS and we are continuing to study how to refine the use of PRS in the WISDOM study, with next steps including the development of PRS for more aggressive breast cancer risk vs slower-growing breast cancer risk, as well as continuing to study how to best incorporate ancestry into PRS development given that the specific genetic variants that comprise PRSs are dependent on ancestral background in many cases. Incorporating genetic information into personalized risk assessments is now more cost-effective than ever, and population-based studies are demonstrating that risk management can incorporate both types of genetic information. Studies such as WISDOM that look at both types of genetic information to personalize screening recommendations are ongoing as the combination of genetic information with traditional risk factors continues to evolve. Our overarching goal is to accelerate the earlier identification of those at elevated risk of breast cancer at a young age and/or more aggressive breast cancers, while simultaneously identifying those who are likely to have lower risks for younger/more morbid breast cancers to aid in informed decision-making about breast screening.

Transitioning Mammographic Artificial Intelligence from a Research Tool to Everyday Practice: What Will It Take?

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Artificial intelligence algorithms trained to read mammograms are increasingly being shown to be a better predictor of a woman's future breast cancer risk than breast cancer risk assessment tools that have been used for decades. Our research demonstrates risk-related imaging biomarkers seen on mammograms — that computers can identify and use to generate a risk score — may help doctors provide women with more personalized breast cancer screening recommendations. We have performed several retrospective studies among over 200,000 women who had a mammogram that found no sign of visible breast cancer at Kaiser Permanente Northern California. None of the women had previously had breast cancer or had been diagnosed with a genetic mutation that increases breast cancer risk. Over the next 15 years, over 8,000 of the women were diagnosed with breast cancer. We compared 5 AI algorithms risk prediction score from the mammography images made for these women. We then compared this to a standard clinical risk model, the Breast Cancer Surveillance Consortium (BCSC) clinical risk model to assess each woman's risk of developing breast cancer. The BCSC model predicts risk using age, race or ethnicity, first-degree family history of breast cancer, number of prior benign breast biopsies, and mammographic breast density. The area under the curve (AUC) was used to compare how well each risk model predicted which women would be diagnosed with breast cancer up to 15 years in the future. An AUC result can range from 0.0 (no correct predictions) to 1.0 (all predictions were correct). The BCSC model had an AUC of 0.61. In comparison, the AI models had a risk prediction result that ranged from 0.63 to 0.67. Findings suggest that AI used alone or combined with current risk prediction models provides a new avenue for future risk prediction.

You've Identified a High-Risk Patient: Now What?

Olufunmilayo I. Olopade, MD, FACP. Section of Hematology/Oncology, Center for Clinical Cancer Genetics and Global Health, The University of Chicago Medicine, Chicago, IL

Analysis of cancer genomes has provided fundamental insights into the process of malignant transformation, and cancer genomes have rapidly become an integral part of the practice of clinical oncology, with implications for prevention and early detection. I will discuss the basic concepts of this rapidly expanding field, offering an understanding of the roles of both germline and somatic genomic analysis in clinical practice. Inherited and sporadic cancers often share common mutational events. When inherited mutations are identified, comprehensive cancer risk assessment and cascade testing of unaffected family members are essential components of care. I will discuss efforts to streamline genetic counseling and testing, examine the role of genetic counseling for cancer patients and identify barriers to its broader application for population risk stratification exemplified by the Wisdom Study. As technology advances, new models incorporating Artificial Intelligence and Deep Learning for management of high-risk patients will transform Precision Prevention in primary care settings. I will discuss the Chicago Alternative Prevention Study and new models of care available to women at risk of premature deaths from pathogenic variants in *BRCA1* and *BRCA2* genes.

WISDOM: How Can You and Your Patients Participate?

Allison Stover Fiscalini, MPH[1,2]. [1]Department of Surgery, University of California San Francisco, San Francisco, CA; [2]On behalf of the WISDOM study investigators and collaborators., San Francisco, CA

Forty years ago, when breast cancer screening was first introduced, there was little understanding of the heterogeneity of breast cancer. Today, we know better, and treatment is tailored to tumor biology. However, screening has not evolved accordingly, and our strategies remain largely to screen all women the same. In the United States, the variation between guidelines focuses on the age to start and frequency to pursue mammograms, however, screening has not evolved to address the issues of overdiagnosis, low cancer to biopsy yields, and the failure to identify fast-growing tumors at an early stage. The WISDOM Study is the first large-scale study of a risk-based approach to breast cancer screening. The goal is to understand if a risk-based approach can improve our ability to identify those at risk for faster growing tumors while minimizing the harmful effects of screening – overdiagnosis and overtreatment among them. WISDOM 1.0 was implemented from August 2016 until March 2023 as a preference-tolerant randomized trial enrolling over 45,000 participants ages 40-74 across the United States. Starting in June 2023, WISDOM 2.0 launched with the aim to improve our risk classifications to determine if early genetic profiling and targeting of the population at risk for the fastest growing tumors can improve our ability to proactively detect these cancers and optimize prevention strategies based on the degree and type of risk. Key changes in WISDOM 2.0 include lowering the enrollment age to women ages 30-39, removal of the randomized arm and expansion to low-pass whole genome sequencing (instead of a limited single nucleotide polymorphism panel). Over the past year, WISDOM 2.0 has registered an additional 12,000 participants, with over 9,000 consented and nearly 8,000 enrolled. Main enrollment methods during this period included: invitations through doctors/medical centers (including MyChart and VA passive outreach), family/friend referrals, news/social media, and other community partnerships. WISDOM is a pragmatic, virtual trial that is open to those ages 30-74 without a prior history of breast cancer or ductal carcinoma in situ, regardless of insurance or location of care. The study can be completed from a smartphone, tablet or computer from the comfort of home. Those in the Personalized Arm of the study are mailed a saliva-based genetic testing kit, with prepaid envelope to return the completed sample. Based on the WISDOM comprehensive risk assessment, which incorporates risk factors such as age, prior biopsies, breast density, race/ethnicity, family history, and genetics (minimum of 9 breast cancer specific genes and over 300 single nucleotide polymorphisms – SNPs) to determine a personalized screening frequency and modality. To date, over 60% of participants with a positive breast cancer gene mutation did not have a first-degree family member with breast cancer, and therefore would not be offered genetic testing as part of clinical care. WISDOM provides high risk breast consultations using a WISDOM Breast Health Decisions tool to review risk in context and strategies to reduce risk, including risk reducing medications and procedures for those at highest risk. Participants in WISDOM receive a Screening Assignment Letter (which includes their risk-based screening recommendation), genetic testing results (for those in the Personalized Arm), access to the Breast Health Decisions tool, and a Breast Health Specialist consultation (for those identified as high risk). Our goal is to enroll 72,000 participants, with at least 25% identifying as non-White. The virtual, centralized approach enables women nationwide to join, and we encourage providers to help share WISDOM with their patients to help guide their individual screening choices as well as contribute to this critical area of research. Future directions include collection of environmental exposure history data and geocoding, ancestry and tumor-biology based approaches to polygenic risk, and Artificial Intelligence (AI) models for mammography and risk prediction. Our long-term goal is to iteratively reduce breast cancer mortality, while demonstrating the value of a risk-based approach to breast cancer screening and prevention.

PLENARY SYMPOSIUM #2

Recognizing and Managing Irregular Menstrual Bleeding During The Menopause Transition

Steven R. Goldstein, MD, MSCP, CCD, FACOG, FRCOG(H). New York University Grossman School of Medicine, New York, NY

This lecture will cover basic physiological changes in the endometrium as a result of stimulation by estrogen and will give the learner a better understanding of when the endometrium bleeds, and why it bleeds. The endometrium consists of a basalis and a functionalis. Estrogen causes the functionalis to proliferate. Progesterone, or in sequential hormone therapy, the use of a progestogen will convert an estrogen primed functionalis to a secretory phase. After shedding of the functionalis the basal endometrium that remains is initially quite thin. In menopause, there is no estrogenic stimulation of the functionalis, and the endometrium is atrophic. To our patients, all the blood that comes out of their vagina is their period. To us as healthcare providers, however, a menses is a bleed, preceded two weeks before by ovulation. The hallmark of ovulatory cycles is their predictability, regularity, and occurrence 14 days after ovulation if no pregnancy ensues. The hallmark of anovulatory cycles ("an" from the Greek meaning "without") is their variability. They can be irregular, heavy, or light, with or without cramps, more often or less often. We know that menopause is defined as no bleeding for 12 months due to a depletion of ovarian follicles. This is an arbitrary definition. The average age is

51.4 years. Perimenopause is characterized by oligo- and anovulation. Cycles are irregular. There is also an increase in many psychosocial symptoms, such as mood swings, anxiety, memory changes, sleep disturbances, "brain fog," etc. Vasomotor symptoms are variable. In many respects perimenopause is the mirror image of adolescence. This lecture will cover the nomenclature of PALM-COEIN to define abnormal uterine bleeding. The old terminology of menorrhagia and metrorrhagia will also still be discussed. Any postmenopausal bleeding must be evaluated to rule out endometrial hyperplasia or even carcinoma. In addition, ACOG guidance tells us that, in any woman over 40 who has abnormal uterine bleeding, endometrial evaluation is essential. We will cover various diagnostic techniques for the proper diagnosis of endometrial pathology or the lack thereof. Specifically, the lecture will highlight an ultrasound-based approach to abnormal uterine bleeding, using transvaginal ultrasound and saline infusion sonography when appropriate. It will also discuss the potential pitfalls of blind endometrial sampling, which can be a starting point, but, if negative, will not always be a stopping point. New disposable hysteroscopes that can easily be used in an office setting will be introduced. In terms of treatment for menopausal symptoms, such as hot flashes, and night sweats, as well as prevention of bone loss it is well known that this is accomplished with menopausal hormone therapy (MHT). However, the mainstay of treatment in perimenopausal patients should be suppression of erratic ovarian function, and substitution of a stable amount of estrogen and progestogen all month long. This is different than replacement when there is no more ovarian function. In such perimenopausal patients this is best accomplished with low dose birth control pills as long as there are no contraindications to them. Although vasomotor symptoms can be treated with estradiol and a progestogen releasing IUD, this will not control AUB the way oral contraceptive pills will. There are certain myths and preconceptions about birth control pills that we need to help our patients appreciate. These pills suppress ovarian function. They are not on top of endogenous occurring hormonal levels. Patients do not seem to understand that. In addition, suppressing the ovarian cycle is closer to natural than what we have socialized into. As higher order primates nature expected women to have 8 children, nurse them all for 12-15 months (no bottle or formula in nature), along the way have 2-3 miscarriages, have no more than 250 menstrual cycles. Modern women are having close to 500 menstrual cycles and the incidence of gynecologic cancers are on the rise in modern industrialized nations because of this increase in menstrual cycles. One can never forget that the individual sitting opposite us in the consultation room is an "n" of one.

Near-Term and Future Options for Management of the Menopause Transition and Menopause

Joshua Johnson, PhD. Obstetrics and Gynecology, University of Colorado School of Medicine, Aurora, CO

Significant physiological and metabolic changes occur during reproductive aging that can modify the impact of chronological aging on organ systems. While our understanding of how individual primordial ovarian follicles (PFs) are "selected" for growth and loss, it has not been clear how the behavior of the ovarian reserve relates functionally to the timing of reproductive aging landmarks. Using a combination of wet laboratory[1] and mathematical modeling[2-4] approaches, we have recently linked loss patterns of PFs to the timing of the menopausal transition (MT; onset of menstrual irregularity)[4,5] and the age of natural menopause (ANM; 12 months without a menstrual period). Briefly here, we found that as the ovarian reserve declines, increasingly unpredictable "gaps" in days where no PFs begin to grow become more common. We showed that gaps in the growing follicle supply correspond to increasing disruptions in endocrine signaling required for regular menstrual cycles (the MT) and afterwards, disrupted endocrine signaling required for any menstrual cycles (menopause onset). Despite this improved understanding of why the MT and menopausal onset occur when they do in individuals, it is still not clear how alterations in the pattern of growing follicle supply result in the symptoms characteristic of the events. We thusly consider available evidence for how unpredictable disruptions in the growing follicle supply and increasingly unpredictable follicular endocrine activity contribute to symptoms, particularly during the MT. Last, there are strategies on the horizon that can plausibly extend the duration of ovarian function for women.[6] These strategies are currently experimental and promise to either slow the rate of PF loss, or to deliver additional PFs that will presumably delay the MT and menopause and their symptoms. We have extended our mathematical modeling approach so that we can simulate how these different strategies are likely to perform and can test feasibility given different patient characteristics. To date, it has not been clear exactly who such interventions are likely to benefit, and we will discuss the risks versus theoretical rewards of extending ovarian function. Perhaps such technologies are only suitable for women facing early ovarian demise as in primary ovarian insufficiency. Any interventions designed to slow ovarian aging must be considered in terms of improving patients' health and well-being while first minimizing risk. REFERENCES 1. Llerena Cari et al., *Mol Hum Rep*, 2021, https://doi.org/10.1093/molehr/gaab050. 2. Johnson, Emerson, and Lawley, *PeerJ,* 2022. https://doi.org/10.7717/peerj.13941. 3. Lawley and Johnson, *Biol Reprod*, 2023. https://doi.org/10.1093/biolre/ioad022. 4. Lawley, Sammel, Santoro, and Johnson., *Sci Advances*, 2024. https://doi.org/10.1126/sciadv.adj4490. 5. Paramsothy et al., *Menopause*, 2017, https://doi.org/10.1097/gme.0000000000000736. 6. Johnson, Lawley, Emerson, and Oktay, *AJOG*, 2024. https://doi.org/10.1016/j.ajog.2023.12.037.

PLENARY SYMPOSIUM #3

Cognition and Hormone Therapy: Helpful or Harmful?

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All estrogen preparations in the United States have a black box warning of an increased risk of dementia. At the same time, there is widespread public messaging encouraging women to use hormone therapy for the primary prevention of dementia. The goal of this presentation is to inform menopause practitioners of the strengths and weaknesses in the quality of the existing data on cognition, dementia, and hormone therapy so that they can better guide their patients in shared decision making. We will present an overview of the major studies bearing on this issue, prioritizing randomized clinical trials and drawing on observational studies where randomized trial data are lacking. Regarding hormone therapy and cognitive function, clinical trial evidence supports the use of hormone therapy in women experiencing early menopause, though the studies are small. Four large, randomized trials in naturally menopausal women show that hormone therapy has a neutral effect on cognitive function across a variety of domains, including memory. In younger postmenopausal women studied within 10 years of the final menstrual period, neutral effects are observed regardless of hormone therapy formulation. Hormone therapy also appears to have neutral effects on cognition in older women, except that conjugated equine estrogen plus medroxyprogesterone acetate (CEE+MPA) treatment led to small but significant cognitive declines. We will point to a critical gap in the literature, which is that there are no large, randomized trials of the effect of hormone therapy on cognitive function in women with bothersome hot flashes. This is a notable gap because of evidence linking hot flashes to memory dysfunction, alterations in brain function and structure, and Alzheimer's disease biomarkers. The Women's Health Initiative Memory Study (WHIMS) found a doubling of the risk of all-cause dementia with CEE+MPA and remains the only randomized trial of hormone therapy for the prevention of dementia. To address the question of whether other formulations of hormone therapy might also confer risk, it is necessary to consider observational studies of hormone therapy and Alzheimer's disease. While the two-fold increased risk observed in WHIMS with CEE+MPA is not observed in the observational studies, a small but statistically significant elevated risk of dementia is found with other hormone formulations. For most women, that risk is not of a magnitude sufficient to recommend avoiding the use of hormone therapy for the treatment of VMS. Overall, we conclude that hormone therapy should not be used to treat or prevention cognitive decline or dementia, recognizing that we do not yet know the effects of hormone therapy on cognition in women with bothersome VMS.

Cognition and Hormone Therapy: Helpful or Harmful?

Jacob van Doorn, MS. Graduate Program in Neuroscience, University of Illinois, Chicago, IL

In survey research, about 40-60% of midlife women report cognitive difficulties. There is considerable variation in the public messaging about how menopause might affect cognition and brain function, ranging from the view that menopause may fundamentally change brain function and structure in a way that predisposes women to Alzheimer's disease to a view that cognitive changes at menopause are minimal. The goal of this presentation is to inform menopause practitioners of the strengths and weaknesses in the quality of the existing data so that they can better counsel their patients. We will present an overview of the research studies to date bearing on these questions, and critically evaluate the extant literature. Regarding cognitive changes, we will show reliable evidence of menopause-related changes in verbal and memory coming from prospective studies following large cohorts of women from the pre- to perimenopause. From cross-sectional and experimental studies, we will present evidence that the factors contributing to those changes include not only changes in estradiol but also menopause symptoms, specifically sleep disruption, hot flashes, and mood. Next, we will review the neuroimaging literature related to brain changes at menopause. We will focus on the central critique of the extant literature that there are yet no longitudinal studies of brain health in women across the menopause transition. We will review cross-sectional evidence that raises hypotheses about what aspects of brain health might relate to menopause, and the factors that might contribute to those changes. We will conclude that there is accumulating evidence of menopause-related changes to memory circuits in the brain, particularly in the hippocampus, and that cross-sectional data on other aspects of brain health requires further validation in longitudinal studies.

What Causes Depression During Menopause?

Alison Shea, MD, PhD, FRCSC, MSCP. St. Joseph's Healthcare, Department of Obstetrics and Gynecology, McMaster University, Hamiton, ON, Canada

Mental health challenges are prevalent during and immediately after the menopause transition, impacting up to 50% of women. While a history of major depression significantly increases the risk of mood and anxiety disorders during this transitional period, other critical factors also play a role. This session will delve into how physical symptoms and social determinants of health contribute to the emergence of anxiety and depressive symptoms. We will explore the physiological effects of hormonal fluctuations and the impact of stressful life events on mood state and regulation. Findings from prospective as well as cross- sectional studies will be presented to understand potential mitigating factors. Additionally, we will discuss a comprehensive approach to assessing and treating patients with mental health symptoms, emphasizing a biopsychosocial model for promoting mental wellness.

What Causes Depression During Menopause?

Claudio N. Soares, PhD, FRCPC, MBA. Department of Psychiatry, Queen's University School of Medicine, Kingston, ON, Canada

The burden and costs (personal, societal) associated with depression are undeniable, as this condition is estimated to affect one in every 5 adults in North America. For decades, we have known that women are disproportionately more affected by depression than men, likely due to a variety of factors, including cultural, behavioural, hormonal, and gender-related determinants of health. Moreover, experimental, clinical, epidemiologic evidence suggests that some women may experience an increased vulnerability for depression at certain reproductive stages (or windows of vulnerability) across their life span. As such, depression (new onset, recurrence) could be expressed among women reporting dysphoria or irritability during luteal phases of their menstrual cycles; low mood, cognitive changes during puerperium; or anhedonia during the menopausal transition (MT). Cross-sectional studies suggest that depressive symptoms might be endorsed more often by women during perimenopause compared with premenopausal years, whereas cohort studies indicate a higher risk for major depressive episodes (MDE) among perimenopausal women with prior history of MDD – ie, increased risk for recurrent MDEs, rather than new onset of MDD among never-depressed individuals. We have often categorized risk factors for menopause-related depression into 2 groups: (1) continuum-related risk factors and (2) window related risk factors. Continuum-related risk factors are moderating factors, impacting one's risk for depression throughout their lives (eg, socioeconomic, health-related, psychosocial factors), as well as history of hormone-related mood symptoms (eg, premenstrual dysphoric disorder, postpartum depression). Window-related risk factors are context-related, likely to act as mediating or precipitating factors – eg, concomitant/bothersome vasomotor symptoms and sleep disturbances. But what exactly causes depression during menopause, and how different can menopause-related depressive episodes be compared to those at experienced at any other given time in life? For some, different profiles 'estradiol sensitivity' profiles could explain the occurrence and clinical characteristics of depression during the MT. The E2 sensitivity model has been successfully tested in clinical experiments, both in 'at risk' populations (ie, women with history of hormone-related mood symptoms) and in sub-samples of healthy, younger (premenopausal) women – when those were submitted to 'hormone withdrawal' experiments mimicking sudden E2 increases/decreases. This framework also helped us explore "windows of opportunity" for E2-based therapies for depression during midlife years, and the use of E2 as a preventative strategy – given the evidence that E2 has stabilizing effects on mood during this period in life. Despite our better understanding of potential mechanistic pathways and vulnerability factors contributing to depression during midlife years, many questions remain unanswered. Existing frameworks are somewhat simplistic and have not fully incorporated the complex interplay between various neuroendocrine factors. It is still challenging to disentangle the contributions of various menopause-related symptoms to depression (VMS, sleep, anxiety, sexual) and the extent to which they should inform treatment. Clinical trials designed specifically to address menopause-associated depression are limited in number, sample sizes and therapies; they often lack proper characterization of hormone status, chronicity/severity of symptoms or psychosocial impairment. Studies investigating hormone-based therapies for depression were absent or stalled for more than a decade as a direct result of the lingering, detrimental effects of WHI findings. Lastly, it is extremely important to emphasize that most women will NOT experience clinical depression or significant depressive symptoms during menopause, so a conscious effort should be made to avoid over-medicalizing this period in life. At the same time, the burden associated with depression during midlife years shouldn't be trivialized either. Clinicians should be prepared to pro-actively address them, engaging patients in a shared decision-making process in the pursuit of best, comprehensive therapeutic options.

PLENARY SYMPOSIUM #4

Bone Health

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At age 50, women who have survived to that age can expect to live another 34 years. Unfortunately, not all these will be healthy years. The last 19 years are often unhealthy, and the last four years may be fraught with disability severe enough to require institutional care. The main cause of this severe disability is musculoskeletal disease, closely followed by dementia. This presentation is not about dementia. This presentation will be about the twin sisters, osteoporosis and sarcopenia, and how they contribute to severe disability as we age. If we consider our peak bone mass to be our "retirement income," it is somewhat disheartening to understand that after age 30, we can't make any further deposits. During the 30s and 40s, our goal needs to be protecting and stabilizing our capital investment. This may be done through lifestyle changes such as appropriate diet, weight bearing and muscle building exercise, and avoidance of habits which may withdraw from our bone bank. The late perimenopause and early postmenopause may represent a golden opportunity to protect our investment. On average, from the late perimenopause to early postmenopause, a woman loses 6-10% of her total bone mass. Some women lose more. After this time, the rate of loss slows to 0.5 to 1% per year. Use of menopause hormone therapy, in those without contraindications, offers the opportunity to delay this loss for years. In most countries, medical therapies are indicated for the treatment of osteoporosis—we must develop the disease state before treatment is initiated, and we must be at moderate to high risk of fracture to start medication. It is counterintuitive to wait for moderate to severe fracture risk before instituting therapy to slow the loss of bone. Perhaps a more common-sense approach would be to monitor the trajectory, and intervene if trouble is ahead, rather than waiting for it. Sarcopenia is the second important component to musculoskeletal disease. Sarcopenia is low muscle mass with low muscle strength and low muscle performance. Muscle mass decreases progressively over time. Sarcopenia may predispose to falls (due to decreased core strength and related balance issues) and much of the frailty associated with older age. It is often not assessed, not recognized, and not treated. Those with both osteoporosis/osteopenia AND sarcopenia appear to be most at risk of severe disability. In order to decrease severe disability and need for institutional care, a more proactive, lifelong plan for musculoskeletal health needs to start prior to menopause and needs to be thoughtfully developed.

Immunization of Midlife Women

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Midlife is often defined as age 50 and above and is a period of life when patients commonly access the healthcare system, having recognized the need for various preventions. The Women's Health Initiative (WHI) identified cardiovascular disease (CVD), cancer, and osteoporosis as the most common causes of morbidity, disability, and poor quality of life in postmenopausal women.[1] Healthcare professionals routinely screen patients with risk factors for these diseases and offer prevention and treatment to improve their quality of life. However, recommendations for immunizations are often neglected leading to unnecessary morbidity and mortality in our midlife and aging population. In Canada, it is estimated that 20,000 hospitalizations related to influenza occur each year[2] and that 4,000 to 8,000 Canadians die from influenza-related complications alone.[2,3] Vaccines can prevent the debilitating and fatal effects of infectious disease,[4] yet clinical evidence has revealed an adult immunization gap.[5] Midlife screening and intervention should serve as an immunization checkpoint, providing an opportunity for healthcare professionals to optimize quality of care and health maintenance in older patients. While we have excellent guidelines in both Canada and in the United States, the general population is under immunized for every routine vaccine. Part of the solution is to improve both understanding of specific vaccines, increase knowledge and awareness of age and risk and appreciate the impact of a healthcare provider's recommendation to their specific patient. This presentation will review the general issues and focus on the current guidelines for some routine immunizations in midlife women 1. WHI Clinical Trial and Observational Study (1993-2005). 2. Public Health Agency of Canada. (2011). Statement on seasonal influenza vaccine for 2011–2012. *Canada Communicable Disease Report, 37*(ACS-5). Retrieved from http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/11vol37/acs-dcc-5/assets/pdf/acs-dcc-5-eng.pdf 3. Stevenson CG, McArthur MA, Naus M, Abraham E, McGeer AJ. Prevention of influenza and pneumococcal pneumonia in Canadian long-term care facilities: how are we doing? *CMAJ*. 2001 May 15;164(10):1413-9. 4. US Department of Health and Human Services. Healthy People 2010. 2nd ed. Understanding and Improving Health and Objectives for Improving Health. 2 vols. 5. CDC. Adult vaccination coverage—United States, 2010. *MMWR Morb Mortal Wkly Rep* 2012;61:66–72.

Hair Loss

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Female pattern hair loss or androgenetic alopecia is the most prevalent hair loss condition during the menopausal transition, typically affecting women starting ages 45 to 55. This condition is primarily driven by the marked decline in estrogen and progesterone levels, hormones crucial for maintaining hair growth and density. The reduction of these hormones leads to the miniaturization of hair follicles, resulting in thinner hair shafts and increased telogen effluvium. Concurrently, the relative rise in androgens, such as testosterone, can further exacerbate follicular miniaturization, contributing to the overall thinning of the scalp hair. Exogenous factors such as psychosocial stress, nutritional deficiencies, and genetic predispositions can intensify this hair loss. Clinically, patients may present with diffuse hair thinning, increased shedding, and noticeable reduction in hair volume, primarily affecting the frontal and parietal regions – the clinician must rule out other inflammatory, scarring hair disorders such as frontal fibrosing alopecia. Management of menopausal hair loss involves a multifaceted approach. Minoxidil remains a cornerstone of treatment, promoting hair regrowth and reducing hair shed. Hormone replacement therapy (HRT) may be considered for its potential benefits on hair density, though it should be carefully evaluated against its risks. Nutritional optimization, ensuring adequate intake of biotin, iron, and vitamins A, C, and E, plays a supportive role. Anti-inflammatory medications are helpful in managing inflammatory or scarring hair diseases. It is imperative for healthcare providers to adopt a personalized treatment plan, considering the patient's overall health, hormone levels, and specific etiological factors contributing to the hair loss. Collaboration with dermatologists and endocrinologists can enhance the management outcomes for patients experiencing menopausal hair loss.

PLENARY SYMPOSIUM #5

Beyond the Scale: The Importance of Food and Nutrition for the Menopausal Transition

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Menopause represents an inflection point in the life course of women. Many women experience symptoms such as hot flashes and insomnia, and an acceleration of the onset of chronic conditions occurs following the menopausal transition. During this time frame, optimal nutrition is vital for women as nutrient needs evolve, including increased requirements for calcium and magnesium for bone health to prevent osteoporosis and a reduced need for iron. These changes coincide with a decline in gut microbiome diversity, potentially diminishing nutrient absorption. Evidence suggests that nutritional

strategies must address these changing dietary needs and metabolic function rather than merely focus on calorie reduction. The menopausal transition is accompanied by metabolic changes that elevate the prevalence of metabolic syndrome, characterized by increased blood pressure, elevated blood sugar, central adiposity, and elevated cholesterol and/or triglyceride levels. These metabolic factors contribute to a heightened risk of obesity, cardiovascular disease and diabetes. Excess weight in midlife is also associated with a higher risk of developing Alzheimer's disease and dementia. Dietary counseling, modifications to dietary patterns and individual nutrients, and adjustments in exercise duration and intensity can lead to significant improvements in metabolic profile for women during the menopausal transition. Weight gain related to menopause stems from decreased circulating estrogen levels due to the progressive loss of ovarian function. This hormonal decline, along with reductions in basal metabolic rate (BMR), can lead to increased waist circumference and overall body mass. Additionally, many women experience reduced physical activity and increased caloric intake (as estrogen suppresses hunger), further exacerbating physiological changes that facilitate weight gain during the menopausal transition. On average, women gain 12 pounds within eight years of menopause onset. Weight gain during the menopausal transition can alter the course of women's post-menopausal health. Longitudinal study data indicates that a weight increase of 8 to 20 pounds in women aged 34-59 correlates with a 27% rise in cardiovascular disease risk. Altogether, changes in metabolism and nutritional needs during the menopausal transition can alter women's post-menopause health trajectories significantly. Future research in menopausal health should include studies to better understand the nutritional needs of midlife women, and nutritional interventions to promote healthy aging.

Obesity and GLP-1: Artificial Intelligence and the Future of Obesity Care

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Obesity is the most prevalent serious chronic treatable disease of our time. If you consider overweight and patients with abnormal metabolic health (prediabetes, metabolic associated steatohepatitis, metabolic syndrome, increase waist to height ratio), the disease affects over 70% of the US population. Today we have many factors in our environment that promote adverse metabolic health. Many lifestyle factors are modifiable, however in practice can be challenging given how routine they are in our daily lives. Menopause is a life transition that adds to metabolic changes that promote weight gain. Understanding the complex physiology of obesity and how to apply treatment strategies using all four pillars of treatment, nutrition, physical activity, behavioral health, and medical management using medications and surgery is important if we are going to succeed in treating this epidemic. The advent of more potent medications that are nutrient stimulating hormones such as those that activate the GLP-1 receptor has propelled obesity treatment into general practice and obesity treatment as commerce. Understanding how to deliver this care empathetically, comprehensively, and longitudinally will be necessary to see improvement in long term outcomes. We will discuss the basics of obesity care delivery, medication, and other treatment options as well as how to personalize care in a shared decision-making patient centered care model specifically focused on the midlife women's health patient for now and a glimpse of the future as more artificial intelligence tools come to the market.

PLENARY SYMPOSIUM #6

Menopause and the Workplace: The Menopause Society Perspective

Stephanie S. Faubion, MD, MBA, FACP, MSCP, IF[1,2]. [1]Mayo Clinic, Jacksonville, FL; [2]The Menopause Society, Cleveland, OH

Menopause is a universal life transition experienced by half the global population. The symptom experience during the menopause transition is highly variable, with some women experiencing few or no symptoms and others experiencing moderate to severe symptoms for a decade or longer. These symptoms can be disruptive, negatively impacting relationships, quality of life, work productivity, job satisfaction, and even opportunities for career advancement. Menopause symptom severity has been shown to correlate with adverse work outcomes such as lower work productivity, reducing hours of work, missing days of work, and quitting or retiring from the workforce early. While vasomotor symptoms, in particular, have been associated with adverse work outcomes, sleep, mood, joint, genitourinary, and total menopause symptom burden have also been linked with adverse work outcomes. In addition, the relationship between menopause symptoms and the workplace appears to be bidirectional. The work environment may also negatively impact a woman's experience of menopause symptoms, with factors such as insufficient restroom facilities, unpredictable or long work hours, inability to take breaks, poor workstation design, high levels of noise, frequent interruptions, stressful or boring work, and hot, unventilated, confined, or crowded work spaces contributing to a greater menopause symptom burden. Women have also indicated that improvements in the workplace would help them better manage their menopause symptoms, including control over the temperature, flexible work hours, education for their supervisors and managers, and having a supportive supervisor. Further, shift work has been linked with irregular menstrual cycles, and night shift work, specifically, has been associated with an earlier onset of menopause in some studies suggesting that disruption of Circadian rhythms may impact the hypothalamic-pituitary-ovarian axis. Not only do menopause symptoms have the potential to impact work productivity, but they also result in a substantial economic burden to women, employers, and society in general. The Menopause Society has developed and published consensus recommendations on menopause and the workplace to provide recommendations to employers, women employees, and healthcare professionals who care for midlife women. The consensus recommendations provide employers with suggestions to review policies and healthcare plans and benefits and to consider flexibility and accommodations that may be needed for women with menopause symptoms. In addition, the consensus recommendations provide guidance for women with menopause symptoms that affect them at work in terms of understanding their resources and empowering them to be self-advocates. The consensus recommendations also outline what occupational health professionals should know and do for women with bothersome menopause symptoms in the workplace. In addition to the consensus recommendations, The Menopause Society will introduce its employer designation program designed to help employers take action to ensure that they are a workplace that "makes menopause work" and they are supporting their women employees during this important life stage.

Menopause and the Workplace: UK and Global Perspectives

Nick Panay, BSc, MBBS, FRCOG, MFSRH. Menopause and PMS Centre, Imperial College Healthcare NHS Trust, London, United Kingdom

Too many women with menopause related symptoms are still "suffering in silence" in the workplace, and either underperforming professionally, or leaving work, due to lack of support and information about management options. The issue of "Menopause in the Workplace" has therefore been brought to the forefront of the Women's Health agenda in the UK. My lecture will illustrate the steps that have been taken in the UK to bring this to the attention of the government, healthcare providers and the public. I will also discuss what actions are now required to ensure that the recommended next steps are effectively implemented. These are the four key steps recommended by the UK Government[1] 1. Sharing of employer best practice on a portal that is accessible to all employers, whether large or small, free of charge. 2. A national sector-specific allyship programme, which ensures no one is isolated and everyone has someone available to talk to. 3. Menopause-friendly employers who will support, share, and advocate across their sector – retaining and attracting talent to the sector; and 4. A communications plan to improve the working lives of women in their sector, achieved by amplification through strategic partnerships. As President of the International Menopause Society (IMS), it is my role to spearhead its vision that all women across the world have easy and equitable access to evidence-based knowledge and health care, enabling them to make fully informed midlife health choices. Empowering women to thrive in all aspects of their lives, including the workplace, is the cornerstone of our work at IMS. I will discuss how IMS intends to disseminate information about menopause in the workplace globally, both to healthcare professionals and also "direct to consumer," through our new Menopause Info[2] website. Menopause Info offers trusted information to inform health choices and to be shared with colleagues and employers to increase knowledge in the workplace. Key References https://assets.publishing.service.gov.uk/media/65e1bc003f69450011036077/shattering-silence-menopause-12-month-report-march-2024.pdf https://www.menopauseinfo.org/

Menopause and the Workplace: Canadian Perspective

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In Canada, women 40 years and over account for a quarter of the workforce with many of these women experiencing perimenopause or are postmenopausal. The fastest growing sector is women who are between the ages of 45 to 55 years, with expectations to expand by nearly 30% in the workforce in the next 15 years. Unfortunately, the subject of menopause is still too often a taboo subject especially in the work environment. Many women suffer unnecessarily with menopause symptoms with their work productivity impacted. Women often do not share with their employers due to shame or fear of repercussion, nor do they discuss these impacts with their health care providers. The report, Menopause and Work in Canada in 2023 from the Menopause Foundation of Canada (MFC) shed light on the impact of menopause on Canadian women in their prime working years.[1] The report highlighted the results of a 2022 survey of over 1000 women between the ages of 40 to 60 years. The economic impact of unmanaged menopause symptoms in Canada is estimated to cost an astounding $3.5 billion dollars per year through lost days of work, lowered productivity or lost income (due to working less hours or leaving their jobs). One third of working women indicated that menopause symptoms negatively impacted their productivity at work and one quarter said they hid their symptoms from their employers. An unbelievable 1 out of 10 women will leave the workforce due to unmanaged symptoms. Recommended support systems identified by women include policies incorporating menopause such as flexible working schedules, adjustments in the workplace to accommodate menopause, menopause education sessions, and toolkits to help employers. The most recent report Menopause and Nursing in Canada, a partnership between the MFC and BC Nurses Union, highlighted the physical, mental and emotional impact of menopause symptoms on nurses in their work environment.[2] A common thread was to normalize the menopause conversation in the workplace. Several suggestions in supporting nurses were made including improved working conditions, providing benefits in relation to menopause, menopause education and better working culture. In this presentation, I will discuss the efforts currently happening in Canada to bring awareness to menopause in the workplace, to provide education to empower women and inform workplaces, and to develop policies, support systems and tools for menopause inclusive workplace. References Menopause Foundation of Canada. 2023; https://menopausefoundationcanada.ca/menopause-and-work-in-canada-report Menopause Foundation of Canada 2024; https://menopausefoundationcanada.ca/pdf_files/MenopauseNursingInCanada_EN_2024.pdf

PLENARY SYMPOSIUM #7

Genitourinary Syndrome of Menopause

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Genitourinary syndrome of menopause (GSM) encloses an array of anatomical and functional changes in the urogenital tissues (the labia majora/minora, clitoris, vestibule/introitus, vagina, urethra, and bladder) mainly related to the hypoestrogenic state occurring in postmenopausal women. A connection also exists between GSM and reduced androgen [testosterone and its precursors dehydroepiandrosterone (DHEA) and androstenedione] levels, as well as the aging process *per se*. GSM represents an expansion of the previous term "vulvovaginal atrophy (VVA)," which was replaced in consensus documents by The North American Menopause Society (now The Menopause Society) and the International Society for the Study of Women's Sexual Health (ISSWSH). The prevalence of GSM is highly variable depending on study design, age of the study samples and other confounders, with women complaining of at least one symptom (among vaginal dryness, irritation, itching, and dyspareunia) ranging from 14% to 87%. A fair estimation based on available data is that 40% to 60% of interviewed women report GSM symptoms. Country-comparisons of some of these studies underline the importance of conducting research with a multi-cultural approach. Signs visible during pelvic examination are chronic and progressive and may be associated with a constellation of genital, sexual and urinary symptoms showing an impact on quality of life. The terms VVA and GSM are not interchangeable. VVA is the anatomical substrate of genitourinary and sexual dysfunctions, but GSM is a large basket encompassing signs and symptoms related also to clinical conditions with other etiologies. For instance, hypoactive sexual desire disorder (HSDD) may be linked to GSM and specific treatments are required. When clinical signs of GSM at physical examination are more evident, sexual function seems more impaired, but severity of signs and symptoms does not always go in parallel. Proper patient-reported outcome measures (PROMs) have been recently identified to measure pain with sexual activity and distress, bother or interference from genitourinary symptoms properly. This a very important step in the individual care of menopausal women and will guide healthcare professionals (HCPs) to make tailored evidence-based treatment choices.

Hypoactive Sexual Desire Disorder

Sheryl A. Kingsberg, PhD. Division of Behavioral Medicine, Department of Ob/Gyn, University Hospitals Cleveland Medical Center, Case Western Reserve University School of Medicine, Cleveland, OH

Numerous surveys have documented that sexuality and sexual activity is important to women in midlife and beyond. Genitourinary syndrome of menopause (GSM) and hypoactive sexual desire disorder (HSDD) are common disorders in postmenopausal women and may occur together, or one condition may be the primary dysfunction but lead to the development of symptoms of the other. For example, a woman with HSDD may engage in sex despite no interest and as a result will have little genital arousal. Without adequate arousal she will likely have vaginal dryness resulting in pain with penetration. Similarly, a woman with GSM may lose desire for sexual activity if she experiences recurrent pain. Hypoactive sexual desire disorder (HSDD) can be described as the persistent deficiency or absence of sexual interest or desire that causes personal distress. It is best understood using a biopsychosocial model that underscores the interaction of physiologic, psychologic, sociocultural, and interpersonal factors. The highest estimated prevalence of HSDD is in midlife women, ranging from 14.5% to 33%. Healthcare professionals should routinely screen for sexual concerns and identify and differentiate these conditions using a biopsychosocial assessment. An initial assessment can be accomplished quickly during any office visit. A statement validating the woman's right to have healthy sexual function can be followed by a few directed questions that focus on past and present sexual desire, arousal, orgasm, and pain. Medical, psychological, and social histories, a list of prescription and over-the-counter medication, and substance use/abuse may help identify contributing factors. Screeners such as the validated Decreased Sexual Desire Screener (DSDS) are also useful to quickly identify HSDD and can be incorporated into an electronic medical record. Although a physical examination is not required to make the diagnosis of HSDD, it may help when differentiating HSDD and GSM. Treatment for HSDD may include education, modification of contributing factors, psychotherapy, pharmacotherapy, or a combination of treatments, and can be initiated in conjunction with treatments for GSM if they are co-occurring.

PLENARY SYMPOSIUM #8

Cannabis

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The rapidly expanding legalization of cannabis products has resulted in decreased stigma, increased access, and prevalent cannabis use among US adults across the lifespan. Research suggests many individuals perceive cannabis as safer or more natural than other substances, with recent evidence that more adults in the US report daily cannabis use than daily alcohol use. Midlife and older adults are the fastest growing population of individuals using cannabis, and cannabis is increasingly marketed to midlife women for the management of menopause symptoms. In a nationally representative sample of 5,174 midlife US women, almost half reported ever using cannabis, with most women ingesting cannabis via smoking or consuming edible products. Of those who reported ever using cannabis, almost one third reported daily or near daily use for over a one-year period. One in ten participants reported cannabis use in the past month, with many women reporting daily or near-daily use. Over half (53%) of midlife women with a history of cannabis use reported therapeutic use, most commonly for the management of pain (28%), mood (26%), sleep (22%), and menopause symptoms (7%). While there is some evidence to support the efficacy of cannabis use for pain management, evidence for the efficacy of use for these other common targets is mixed or non-existent. Furthermore, cannabis use may have unintentional negative health impacts. Smoking remains the most common form of cannabis use and has been linked to impaired lung health and cardiovascular disease. Readily available cannabis has markedly high THC potency; average THC content has risen from 4% in 1995 to 20% today, and frequent and/or high potency use contributes to risk for anxiety, psychosis, tolerance, and dependence. An estimated 30% of individuals who use cannabis meet criteria for Cannabis Use Disorder. Given increasingly widespread use of cannabis products for symptoms and issues common among women in midlife, with limited evidence for benefit and potential for harm, awareness and discussion of cannabis use is an important consideration for healthcare providers. Clinical considerations may include psychoeducation, screening for higher risk cannabis use and cannabis use disorder, and identification and referral to evidence-based treatment options for cannabis use disorder and related comorbidities.

Alcohol and Opioids

Sarah Wakeman, MD. Mass General Brigham, Program for Substance Use and Addiction Services, Mass General Addiction Medicine Fellowship, Harvard Medical School, Boston, MA

Substance use related health harms have been rising nationally, and in particular among women. Alcohol related mortality has been rising among women more rapidly than among men, with a 35% increase in mortality between 2016 and 2021. Opioid-related overdose deaths are also increasing. Between 1999 and 2017 there was a 260% increase in opioid overdose mortality among female Americans. Alcohol, opioid and other types of substance use disorder are treatable, good prognosis health conditions. Yet most individuals affected do not receive treatment. There are unique issues in treatment for women across the lifespan as well. This talk will describe the current epidemiology of addiction and overdose among women, review screening and diagnosis, and explore treatment issues for substance use disorder among women.

PLENARY SYMPOSIUM #9

Sleep Disturbance in Women with Breast Cancer

Kathleen Van Dyk, PhD[1,2]. [1]Department of Psychiatry and Biobehavioral Sciences, UCLA David Geffen School of Medicine, Los Angeles, CA; [2]UCLA Semel Institute for Neuroscience and Human Behavior, UCLA Jonsson Comprehensive Cancer Center, Los Angeles, CA

Sleep disturbance is a common occurrence in breast cancer survivorship, with estimates that up to 60% of breast cancer survivors have sleep difficulties. Sleep disturbances can be an acute effect of many breast cancer therapies including surgery, radiation, and chemotherapy. On top of those risks, another primary contributor to such sleep disturbance is anti-estrogen endocrine therapy, which is indicated for 75% of breast cancer patients and recommended for 5-10 years. Endocrine therapies downregulate estrogen function in the body in order to prevent recurrence of hormone-receptor positive breast cancer. Sleep problems following endocrine therapy can vary from mild to more severe symptoms of insomnia, and can have a substantial impact on women with breast cancer. Sleep disturbances in breast cancer survivorship can reduce quality of life, impair functioning, and even have adverse effects on survival rates. Women on anti-estrogen endocrine therapy often experience symptoms similar to menopause and there are likely similar mechanisms underlying sleep disturbances for both menopause and women on these medications. Hot flashes are commonly experienced during endocrine therapy treatment and may contribute to sleep disturbance through nighttime awakenings. Evidence is also emerging that hot flashes can affect arousal. In addition, estrogen is involved in regulating circadian rhythms and the rapid disruption of estrogen signaling with endocrine therapy can affect sleep cycling. By examining sleep disturbance in breast cancer survivors through the lens of women's health and menopause, we can better understand how to effectively diagnose and manage these disruptive symptoms.

Pharmacologic and Behavioral Approaches to Treating Menopause-Associated Insomnia

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Sleep disturbance affects 40-60% of people in the menopausal transition and postmenopause. Insomnia symptoms, specifically nocturnal awakenings and difficulty returning to sleep, are endorsed as the most bothersome symptoms, and improving sleep is the most important attribute for peri and postmenopausal people in selecting among treatment choices. While vasomotor symptoms are experienced by up to 80% of peri- and postmenopausal women and are associated with insomnia symptoms in some, but not all studies, there are multiple other factors (eg, aging, sleep apnea, mood disturbance) that contribute to insomnia that begins or accelerate with perimenopause and early menopause, and which can occur in the absence of hot flashes. Insomnia has also been associated with a higher risk of cardiovascular disease among women. Despite the pervasiveness of menopause-associated insomnia as well as guidelines recommending behavioral treatments for insomnia in the setting of comorbid conditions and data supporting the short-term efficacy of behavioral and pharmacotherapies for insomnia among peri- and postmenopausal women, there are limited data on the best treatment approaches to treating menopause-associated insomnia. The first step in treating patients

with sleep disturbance is to perform a comprehensive evaluation to evaluate for factors contributing to insomnia, such as active medical, psychiatric, or sleep disorders, with recommended directed therapy of contributing factors. Clinical testing is recommended if the patient is at risk for sleep apnea or another sleep disorder. Among peri- and postmenopausal people, the evidence guiding the treatment of insomnia is more limited and stems from data from single RCTs supporting the short-term (4-12 weeks) efficacy of pharmacotherapies (ie, benzodiazepine receptor agonists; dual orexin antagonists) and behavioral treatments (8 weeks-6 months). Additional evidence comes from the Menopause Strategies: Finding Lasting Answers for Symptoms and Health network studies, comprising three RCTs testing six interventions to treat VMS and a fourth RCT targeting insomnia symptoms among women with VMS (n=546). In analyses across the seven interventions, compared to placebo, CBT-I resulted in the greatest reduction in insomnia symptoms (−5.2 points, 95% CI −7.0, −3.4). Clinical guidelines, specific for women with bothersome nighttime VMS, also support hormone therapy based on limited or inconsistent evidence. Emerging data suggest neurokinin receptor antagonists improve sleep among people with menopause-associated VMS. In the general population, which includes peri- and postmenopausal people, data from randomized controlled trials (RCTs) support the efficacy for treating insomnia with CBT-I (including among patients with comorbid medical and psychiatric conditions), benzodiazepine receptor agonists (eg, zolpidem; eszopiclone), doxepin, and a dual orexin receptor antagonist. It is important to note that the American Academy of Sleep Medicine guidelines recommend that clinicians not use sleep hygiene as a monotherapy for insomnia. There is insufficient evidence on the efficacy of trazodone and melatonin for insomnia. This approach to treating menopause-associated insomnia is justified by the preponderance of evidence for a bidirectional relationship between hot flashes and sleep impairment. It is further supported by clinical trial data showing that targeting sleep in peri- and postmenopausal women with hypnotic medications (i.e., zolpidem, eszopiclone, suvorexant) improves sleep at one month, while cognitive behavioral therapy for insomnia compared to placebo improves a myriad of patient-reported sleep outcomes and sleep duration at six months. Substantial data demonstrate that insomnia can be improved even in the setting of common comorbid conditions in midlife, including sleep apnea, depression, and anxiety. This approach is supported by clinical guidelines that support the efficacy of treating insomnia in the context of comorbid medical and psychological conditions. However, despite the availability of existing guidelines, given the limited comparative effectiveness studies, the best treatment approaches still need to be clarified and thus require a shared decision-making approach.

PLENARY SYMPOSIUM #10

Menopause: Are We Doing Too Much or Not Enough?

Marla Shapiro, CM, MDCM, CCFP, MHSc, FRCPC, FCFP, MSCP. University of Toronto, Toronto, ON, Canada

A recent Lancet publication titled: An empowerment model for managing menopause (Hickey M, et al. An empowerment model for managing menopause. *Lancet* 2024;403:947-957) created a great deal of controversy in practitioners of midlife women. Among its key messages were that most women navigate menopause without the need for medical treatments and over-medicalization of menopause can lead to disempowerment and over-treatment. This presentation will review the historical approach to the evidence and knowledge of menopause management and review concepts of medicalization and empowerment. Are we doing too much or not enough? This presentation will challenge you to decide.

Menopause: Cutting Through the Noise With Science

Rebecca C. Thurston, PhD, FABMR, FAPS. Psychiatry, Psychology, Epidemiology and Clinical and Translational Science, Women's Biobehavioral Health Research Program, Cardiovascular Behavioral Medicine Research Training Program, University of Pittsburgh, Pittsburgh, PA

Menopause is a transition experienced by almost all women as they age. Historically, menopause has been cloaked in popular and public silence. However, recent years have brought increased popular - and commercial - attention to menopause. Such attention has sparked a debate, with contrasting approaches to this life transition. Some perspectives assert that menopause is a "natural" midlife transition that most women experience without incident and without need for intervention; these perspectives seek to avoid pathologizing a near universal life transition, reduce fear, and reduce predatory actors seeking to capitalize on recent attention to menopause. Other perspectives assert that menopause can be a symptomatic and stressful transition which, for many women, warrants attention and medical management; these approaches seek to elevate women's often neglected concerns, spur new treatment development, and expand the access to existing treatment options. This talk seeks to address these perspectives, presenting science about key biological and psychological changes of the menopause transition; the prevalence of symptoms, particularly interfering symptoms; and the consequences and correlates of these symptoms. In addition, this talk will present data on how midlife can be a positive life transition for many women. Leveraging science, this talk seeks to take a balanced perspective, with the ultimate goal of optimizing women's health and functioning during midlife and beyond.

KEYNOTE ADDRESS

Virtually Better: The Potential of Virtual Reality as an Adjunctive Therapy for Menopause Symptoms

Brennan Spiegel, MD, MSHS. Department of Medicine, Cedars-Sinai, Los Angeles, CA

Virtual Reality (VR) has emerged as a powerful tool in modern medicine, with over 30,000 studies revealing its potential to lower pain, calm nerves, and boost mental health without pharmacotherapy. For decades, scientists have been quietly discovering the surprising health benefits of VR for a wide range of ailments. Despite these promising findings, the technology historically remained too expensive and unreliable for widespread clinical application. Recent advances in delivering low-cost, portable, and high-quality VR have now spawned a new field the FDA calls Medical Extended Reality (MXR). MXR encompasses the use of VR and related technologies in medical settings, offering innovative solutions for a variety of health conditions. In this lecture, Dr. Brennan Spiegel will describe frontline stories of using VR in over 3,000 patients at Cedars-Sinai Medical Center and will review his lab's latest clinical research, including a trial testing VR in the hospital setting, a new virtual clinic for patients with chronic abdominal pain, and NIH-sponsored research testing VR for managing other forms of pain. These experiences have paved the way to direct these innovative techniques toward managing symptoms associated with menopause. Menopause brings a variety of challenging symptoms, such as hot flashes, mood swings, sleep disturbances, and cognitive changes. Leveraging the immersive and therapeutic potentials of VR, new pathways are emerging to provide relief and improve the quality of life for menopausal women. This includes VR experiences designed to induce relaxation, simulate environmental cooling to alleviate hot flashes, and employ cognitive-behavioral strategies to manage mood changes and insomnia. By integrating AI with spatial computing, we are enhancing the delivery of cognitive-behavioral therapy (CBT), a well-known support for menopause. Attendees will gain insights into how VR, combined with AI-driven CBT, is poised to become a transformative tool in the treatment arsenal for menopausal symptoms, offering a non-pharmacological option tailored to individual needs.

THE MENOPAUSE SOCIETY/PFIZER WULF H UTIAN ENDOWED LECTURE

Emerging Strategies to Postpone Menopause: Ovarian Tissue Cryopreservation and Beyond

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Since the report of the first successful autologous ovarian tissue transplantation which restored ovarian function in a menopausal patient in 2000 by Oktay et al, ovarian tissue cryopreservation has evolved to be an effective fertility preservation method before ovarian damaging treatments. The success with medical indications prompted its recent use to delay menopause and reproductive aging in healthy women. We have developed a mathematical model utilizing biological data to predict that menopause can be significantly delayed and even eliminated by ovarian tissue cryopreservation and later transplantation near menopausal age. Our recent laboratory research also identified compounds that can slow down primordial follicle loss from the human ovary and potentially medically delay menopause. This lecture will cover the background on ovarian tissue cryopreservation and transplantation, and its recent use in delaying menopause. We will also review our recent research on potential medical treatments to delay menopause.

THE MENOPAUSE SOCIETY/KLEINMAN ENDOWED LECTURE

The White House Initiative on Women's Health Research

Carolyn M. Mazure, PhD. Chair of the White House Initiative, Women's Health Research, Psychiatry and Psychology, Yale University, New Haven, CT

Despite making up more than half the population, women have historically been understudied and underrepresented in health research. The first-ever White House Initiative on Women's Health Research was launched by President Biden in November 2023 to fundamentally change how we approach and fund women's health research, and pioneer the next generation of discoveries in women's health. The Initiative is led by Dr. Jill Biden in collaboration with the White House Gender Policy Council and is chaired by Dr. Carolyn M. Mazure. The members of the Initiative include executive departments and agencies across the Federal government, such as the U.S. Departments of Health and Human Services, Defense, and Veterans Affairs. This presentation will describe the work of the Initiative in: integrating women's health across the federal research portfolio so that federal funding is leveraged for health research to improve women's health; prioritizing new investments and encouraging innovation in women's health research; galvanizing new research on women's midlife health for which research gaps are especially acute; and assessing unmet needs in women's health research by evaluating gaps in federal funding and identifying changes that are needed to support women's health research.