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SHORT REPORT

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State of the art in menopause: current best practice approaches from the IMS World Congress 2024, Melbourne

James A. Simon[a], Susan R. Davis[b], Angelica Lindén Hirschberg[c], Ludwig Kiesel[d], Luciano de Melo Pompei[e], Jean-Yves Reginster[f], Tommaso Simoncini[g] and Timothy Hillard[h]

[a]Department of Obstetrics and Gynecology, George Washington University and IntimMedicine Specialists, Washington, DC, USA; [b]Women's Health Research Program, School of Public Health and Preventive Medicine, Monash University, Melbourne, Australia; [c]Department of Women's and Children's Health, Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden; [d]Department of Obstetrics and Gynecology, University Hospital Münster, Münster, Germany; [e]Departamento de Ginecologia e Obstetrícia, Faculdade de Medicina do ABC, Santo André, Brazil; [f]Biochemistry Department, College of Science, King Saud University, Riyadh, Kingdom of Saudi Arabia; [g]Dipartimento di Medicina Clinica e Sperimentale, Università di Pisa, Pisa, Italy; [h]Department of Obstetrics and Gynaecology, University Hospitals Dorset, Poole, UK

ABSTRACT

The 19th World Congress on Menopause, hosted by the International Menopause Society in 2024, convened global experts to discuss the latest advances in menopause management. This review highlights key focus areas presented at the congress, offering insights into best practices for clinical application. Cardiovascular health remains a priority, with emphasis on recognizing sex-specific risk factors and exploring emerging therapies. Osteoporosis management underscores the role of menopausal hormone therapy (MHT) as foundational, complemented by anti-resorptive and bone-forming agents in high-risk populations and those not candidates for MHT. Addressing genitourinary symptoms and sexual health, vaginal estrogen therapy is confirmed as a safe and effective option with vaginal dehydroepiandrosterone (DHEA) and oral ospemifene as suitable alternatives, while testosterone therapy offers benefits for hypoactive sexual desire disorder in postmenopausal women. Sleep disturbances, depression and workplace challenges linked to menopause were explored, with tailored interventions such as MHT and cognitive behavioral therapy specifically for sleep recommended. Cancer risk management stressed the need for a multidisciplinary approach to risk reduction beginning with lifestyle modification, and with non-hormonal therapies prioritized for symptomatic treatment of menopausal symptoms in those with hormone-sensitive cancers. Lastly, perimenopause management highlighted comprehensive approaches integrating symptom relief and contraceptive needs.

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Introduction

The recent 19th World Congress on Menopause, hosted by the International Menopause Society (IMS), convened more than 2600 delegates and experts from around the globe and provided a valuable platform for reflecting on key themes in menopause management and addressing persistent clinical challenges. Menopausal hormone therapy (MHT) as a cornerstone of symptom management was a central theme, including its role in managing vasomotor symptoms (VMS), the cardinal symptoms of menopause, alongside other key health concerns. Holistic approaches to optimizing women's health during and after the menopause transition were also in the spotlight. This is consistent with recent guidelines from the European Society of Human Reproduction and Embryology (ESHRE) on the vital need for hormone therapy in women with premature ovarian insufficiency (POI), which occurs before the age of 40 years [1]. Updates on emerging areas such as testosterone use in menopause and the role of glucagon-like peptide-1 (GLP-1) agonists for type II diabetes and obesity management were also highlighted at the event. This article presents an overview of current best practice for key focus areas as explored during the congress and offers practical recommendations to support clinical practice, also summarized in Figure 1.

Cardiovascular health in menopausal women

Cardiovascular disease (CVD) is the leading cause of death in women worldwide, with deaths from CVD in women 10 times those from breast cancer in the USA. Factors contributing to women's CVD risk are psychosocial and biological (female-specific) in nature. CVD mortality in women exceeds that in men in low-income countries, in contrast to those in more industrialized, high-income settings. Sex-specific risk factors that need to be identified in women include gestational diabetes, hypertension in pregnancy, preterm delivery and POI.

The adverse cardiovascular effects of the decline in ovarian estrogen production following menopause were reiterated throughout the congress. Estrogen insufficiency

CONTACT James A. Simon jsimon@intimmedicine.com Department of Obstetrics and Gynecology, George Washington University, Washington, DC, USA

enhances CVD risk through increased visceral adiposity, insulin resistance, dyslipidemia, activation of the renin–angiotensin system, chronic inflammation and impaired vascular endothelial function, with estrogen therapy mitigating against these menopause-associated changes [2].

In terms of prevention, despite its beneficial effects on CVD risk factors, estrogen should not be prescribed solely for primary prevention of CVD. Traditional approaches for CVD prevention should be emphasized, including optimizing lipids, blood pressure, weight, physical activity and metabolic health. Recent studies have demonstrated efficacy of low-dose colchicine in the prevention of major adverse cardiovascular events [3], as well as increasing evidence for major adverse cardiovascular event prevention with GLP-1 receptor agonists in non-diabetic people with obesity [4].

A take-home message from the conference was that coronary artery atherosclerosis often occurs in women without standard modifiable risk factors and that a large proportion of CVD risk is still unexplained. Consequently, early and more proactive intervention in women by all members of the practicing healthcare community seems warranted.

Osteoporosis prevention and therapy

The period of menopausal transition is a critical one for bone health, with bone loss starting during perimenopause. In the first 2 years following the final menstrual period, ~2.5% of lumbar spine density and ~1.8% of femoral neck bone density are lost each year [5]. Estrogen mediates the regulation of bone turnover primarily through estrogen receptors, which facilitate both genomic and non-genomic effects [6]. Estrogen deprivation associated with the menopausal transition leads to both increased bone resorption and decreased bone formation and may result in osteopenia and osteoporosis. Women experiencing VMS may face an elevated risk, as they tend to have higher rates of bone turnover [7,8]. In addition to estrogen deprivation, fluctuations in estrogen also contribute to these risks, underscoring the potential benefit of stabilizing estrogen levels through interventions such as estrogen-containing contraception.

MHT is a key intervention for bone health maintenance [9,10], particularly when initiated in early postmenopause and in women aged under 60 years [11]. Regardless of the fall risk or baseline FRAX probability, MHT reduces fracture risk [10,12]. MHT effectively reduces bone turnover, increases bone mineral density and lowers fracture risk at all skeletal sites. Both oral and transdermal administration of MHT at comparable doses provide similar skeletal benefits, with some evidence suggesting that estradiol may be slightly more beneficial than conjugated equine estrogens [13]. The benefits of MHT on bone continue throughout therapy and may persist for some time after treatment is stopped [9]. Non-hormonal treatments for VMS do not provide the same protective effects on bone health.

For women at high fracture risk, anti-resorptive agents (high risk) or bone forming agents (very high risk) offer enhanced fracture prevention, complementing the effects of MHT [14]. A sequential approach of MHT and subsequent use of anti-osteoporosis drugs, overlapping if warranted, can optimize outcomes. Lifestyle measures, such as ensuring adequate vitamin D and calcium intake in addition to weight-bearing exercises, remain essential elements for reducing fracture and fall risk.

Urogenital and sexual health and well-being

In contrast to VMS, which wane in both frequency and intensity in most women over time, genitourinary symptoms are chronic and progressive, affecting a substantial number of postmenopausal women. Symptoms caused by estrogen deficiency, such as vaginal dryness, sexual pain with any touch or penetration, overactive bladder symptoms and increased risk of urinary tract infections, are common but mostly undertreated, with urinary tract infections often treated repeatedly with antibiotics rather than attacking the underlying pathophysiology. This constellation of symptoms affects urogenital and sexual health and well-being of women around the world. Approximately 50% of postmenopausal women over 60 years of age experience symptoms of vulvovaginal atrophy (VVA) [15,16]. Additionally, a healthy vaginal microbiome appears important, as estrogen loss can lead to dysbiosis and increased infection susceptibility [17].

Guidelines recommend local estrogen therapy as an effective means of treating genitourinary symptoms associated with menopause [18] including POI [1]. Vaginal estrogen therapy alleviates vaginal dryness, dyspareunia, urinary urgency and frequency, reduces the risk of urinary tract infections, has been shown to be safe with long-term use and may also improve sexual function overall. Specifically, evidence supports the long-term endometrial safety of low-dose (10 µg twice weekly) vaginal estrogen [19]. Additionally, vaginal dehydroepiandrosterone (DHEA; also called prasterone) and oral ospemifene are suitable alternatives shown to improve dryness, dyspareunia and distress [20]. While laser therapy has been suggested to improve vaginal symptoms, evidence on this remains contradictory and should only be undertaken in research settings.

Breast safety is supported by a meta-analysis of worldwide epidemiological evidence involving 568,814 women by the Collaborative Group on Hormonal Factors in Breast Cancer [21]. However, safety data are limited in breast cancer survivors. As many as three-quarters of breast cancer patients on concomitant endocrine treatment experience vaginal dryness and other symptoms of VVA [22]. For this group, non-hormonal options (physiological moisturizers and 'as needed' lubricants) should be considered as first-line treatment, with low and ultra-low-dose vaginal estradiol, estrone, estriol and estetrol reserved for second-line consideration [18].

Sexual desire and testosterone

Testosterone has become a prominent topic in women's health, being amplified by social media and drawing substantial attention at sessions during the Congress. Testosterone therapy has shown consistent improvements in sexual desire, arousal, orgasm frequency and reduction of sexual distress in

postmenopausal women with low sexual desire causing distress (hypoactive sexual desire disorder) [23]. Hypoactive sexual desire disorder significantly impairs quality of life, and guidelines support testosterone therapy for postmenopausal women. Importantly, while a range exists for 'normal' testosterone levels in women, there is no specific 'cut-off' level to differentiate women with and without sexual dysfunction. Therefore, testosterone blood levels should only be used to guard against excessive testosterone use and not for any diagnostic purpose as not only is there no 'cut-off', as already noted, but direct testosterone immunoassays, used in most commercial laboratories, are inaccurate for testosterone concentration assessments below 3.5 nmol/l, commonly noted in menopausal women. Tandem mass spectrometry is a more preferable analytical method, particularly for low testosterone concentrations.

Contrary to popular belief, testosterone therapy has not demonstrated significant benefits for well-being, depressive symptoms, cognitive function or musculoskeletal health. Current data are too limited to recommend testosterone for these aspects of menopausal care, emphasizing the need for testosterone research specific to these endpoints [24].

Mid-life changes and work life: sleep, mood and cognition

Sleep

Sleep disturbances often occur during the menopause transition and postmenopause. Frequent awakenings after falling asleep and an inability to fall back to sleep reduce overall sleep quality, causing day-time fatigue and impaired daily functioning. Additionally, sleep disruptions can alter circadian rhythms, which have been associated with increased risks of weight gain, diabetes and other metabolic conditions [25,26]. While often the culprit, not all sleep disorders in menopausal women are directly linked to VMS, and the trajectories of sleep disturbances can vary significantly among individuals. Recent data suggest that sleep duration may impact cognitive health, especially among carriers of the apolipoprotein-E4 (ApoE-ε4) allele [27].

MHT has been demonstrated to improve the quality of sleep alongside improvement in concomitant VMS. Cognitive behavioral therapy, exercise and yoga have both been found to be effective to improve sleep length and quality in postmenopausal women [28,29]. Selective serotonin reuptake inhibitors may also offer some advantage.

Cognitive function

Menopause often brings cognitive challenges, commonly described as 'brain fog', alongside elevated stress, anxiety and depressive symptoms. While mood disorders can exist independently of other menopausal symptoms, they may also be exacerbated by VMS, significantly impacting quality of life. Cognitive symptoms mostly improve during postmenopause, although earlier and more intense symptoms are likely to persist for longer [30]. Addressing these mental health and cognitive struggles is crucial, as they further impact quality of life for menopausal women. Empowering women with knowledge and self-determination, coupled with a combination of lifestyle modifications, MHT and cognitive behavioral therapy, offers comprehensive support for managing these complex changes.

Work life

Menopausal women in the workplace face unique challenges due to severe symptoms, which can reduce productivity and increase absenteeism. Despite these impacts, workplace support remains limited, with workplace-related data and reporting scarce outside western countries. Acknowledging the potential adverse effects of menopausal symptoms on workplace performance and advocating for greater awareness can help mitigate these effects and promote a supportive work environment for menopausal women [31].

Therapeutic management of perimenopause

The menopause transition is a major health milestone for women. However, perimenopause, marked by fluctuating ovarian function and irregular hormone levels, presents unique diagnostic challenges. The severity and duration of perimenopausal symptoms may vary due to a number of factors including body mass index, race/ethnicity and socioeconomic status [32]. Regardless, the Study of Women's Health Across the Nation (SWAN) has shown that perimenopause can significantly impact women's quality of life [33].

Increasing numbers of women are seeking consultations during the late transition phase of perimenopause, often presenting with symptoms that are severe and hard to manage, including VMS, vaginal dryness, adverse mood and sleep changes. In addition to the inconvenience of VMS, studies have shown a correlation between early and frequent VMS and CVD risk [34,35]. Body composition and lipid profile changes also worsen during this transition but stabilize after menopause, shifting to a slower, age-related trajectory [36].

MHT is considered the mainstay of VMS treatment. Transdermal MHT offers a distinct safety advantage over oral formulations by bypassing first-pass hepatic metabolism, thereby reducing the risk of venous thromboembolism and other cardiovascular complications. While oral MHT remains suitable for women without risk factors for venous thromboembolism or CVD, transdermal MHT is a preferable option for those at higher risk [37].

Non-hormonal treatments for VMS were also highlighted during the congress, such as neurokinin-1 receptor (NK1R) and neurokinin-3 receptor (NK3R) antagonists including elinzanetant and fezolinetant. These emerging therapies offer a targeted approach by modulating thermoregulatory pathways, providing a promising alternative for women who cannot or choose not to use hormonal treatments [38]. Additionally, treatments such as cognitive behavioral therapy provide valuable alternatives for managing VMS and improving quality of life. Lifestyle interventions, including weight-bearing exercise, balanced nutrition and cardiovascular monitoring, further support long-term health and quality of life during the menopausal transition [31].

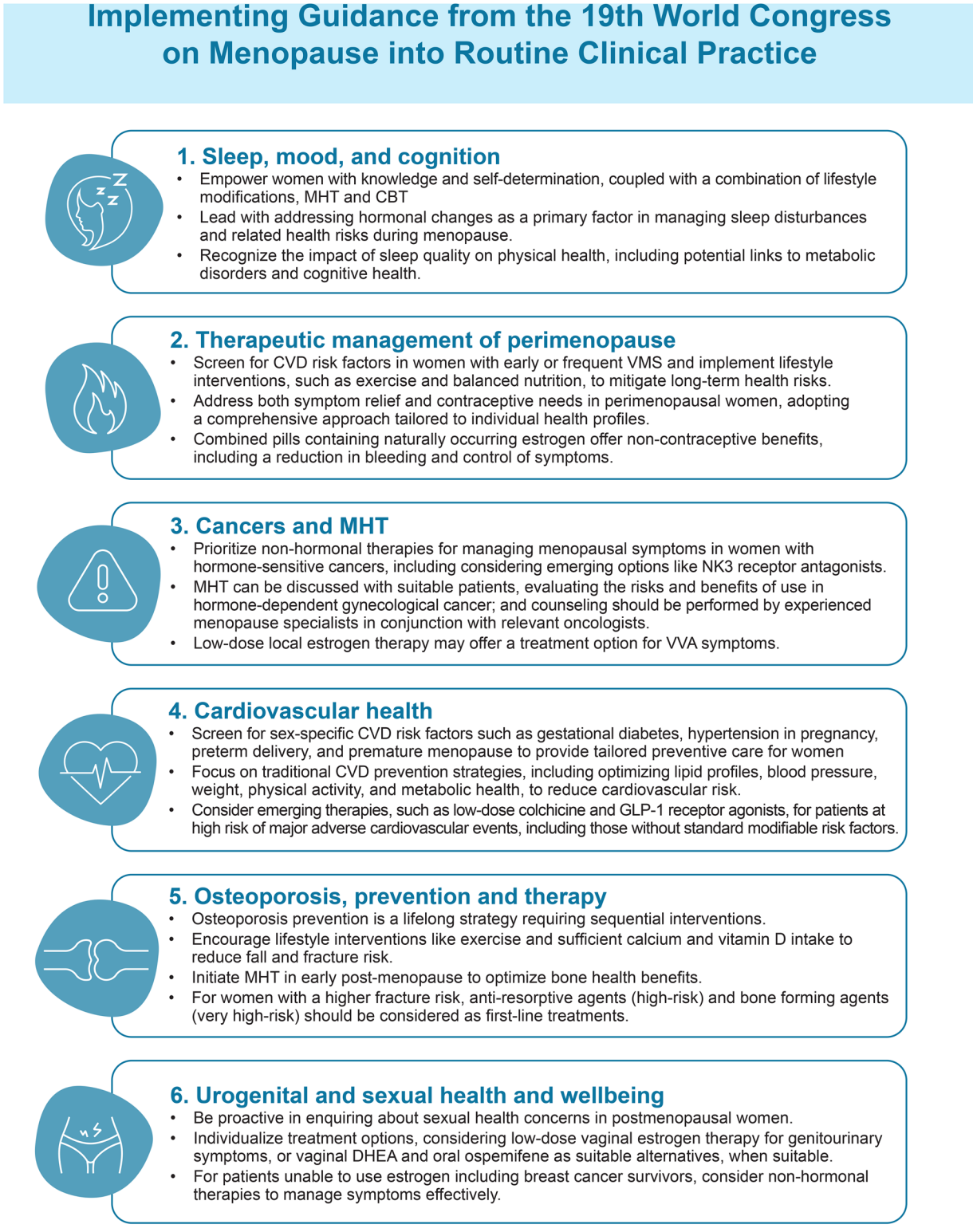

Figure 1. Implementing guidance from the 19th World Congress on Menopause into routine clinical practice.
CBT, cognitive behavioral therapy; CVD, cardiovascular disease; DHEA, dehydroepiandrosterone; GLP-1, glucagon-like peptide-1; MHT, menopausal hormone therapy; NK3, neurokinin 3; VMS, vasomotor symptoms; VVA, vulvovaginal atrophy.

Alongside symptom relief, perimenopausal women frequently require ongoing contraception, remaining at risk of spontaneous ovulation and pregnancy. Contraception is necessary for women over the age of 50 years for 1 year after menopause and for women under 50 years for 2 years after menopause [32,33]. Considering each woman's need and following a risk assessment, options include long-acting reversible contraception methods, such as copper or levonorgestrel

intrauterine devices and progestogen-only implants, with injectables recommended only until around age 50 years due to potential bone density loss. Oral contraceptives include progestogen-only pills and combined estrogen–progestogen pills. Combined pills containing body-identical estrogen offer a potentially safer option with additional non-contraceptive benefits, including a reduction in bleeding and control of symptoms associated with fluctuating estradiol levels. Tailored contraception counseling can help women transition smoothly through perimenopause while managing symptoms [39].

Cancers and MHT

Nearly 10 million women globally are diagnosed with cancer each year, and more than 60% are expected to survive long-term; many living with the consequences of cancer treatment, including early onset of menopause. Managing cancer risk and symptoms in menopausal women requires a personalized, multidisciplinary approach, especially for those with genetic predispositions such as BRCA1/BRCA2 mutations, which significantly increase the risk of breast and ovarian cancers [40]. Side effects of cancer treatments include vaginal dryness and other symptoms of VVA, which occurs in 50–75% of women undergoing endocrine therapy for breast cancer [22]. Treatment can also often induce POI, impacting general health, particularly bone and cardiovascular health, and exacerbating menopausal symptoms [41].

In hormone-sensitive cancers, particularly estrogen receptor-positive breast cancer, systemic MHT is generally contraindicated [41] and non-pharmacological and non-hormonal therapies should be considered for first-line treatment [42]. Newer options like NK1R and NK3R antagonists are emerging as potential alternatives for managing VMS in these patients but are not yet licensed for this use. For patients with non-hormone-sensitive cancers or early-stage hormone-dependent cancers, including certain endometrial and ovarian cancers, limited use of MHT may be considered depending on the stage, grade and surgical status, but remains a cautious option [41,42]. HPV-related cervical cancers are not hormone-dependent and MHT may be prescribed [42]. Symptoms of VVA affect a high proportion of women receiving endocrine treatment. Vaginal estrogen, estriol in particular, offers a potential safe treatment option for breast cancer survivors, as systemic absorption is very low (off-label) [42,43]. Clinicians should always assess individual recurrence risks when balancing symptom management and quality of life with cancer treatment goals, clearly communicating them to the patient as part of the shared decision-making process [42].

Disclosure statement

The following conflict of interest was reported by the authors:

J.A.S. receives grant/research support from AbbVie, Inc., Bayer Healthcare LLC., Daré Bioscience, Mylan/Viatris Inc. and Myovant Sciences; serves as a consultant and/or on advisory boards with Ascend Therapeutics, Bayer HealthCare Pharmaceuticals Inc., Besins Healthcare, Biote Medical, LLC, Daré Bioscience, Femasys Inc., Khyria, Mayne Pharma, Inc., Pfizer Inc. and Vella Bioscience Inc; contributes to Speaker's bureaus with Ascend Therapeutics, Mayne Pharma, Inc., Myovant Sciences, Inc., Pfizer Inc. and Pharmavite LLC; and currently holds stock in Sermonix Pharmaceuticals.

S.R.D. reports having received honoraria from Abbott Laboratories, Besins Healthcare and Mayne Pharma; has served on Advisory Boards for Mayne Pharma, Astellas Pharmaceuticals, Gedeon Richter, Theramex and Besins Healthcare; and has been an institutional investigator for OvocaBio.

A.L.H. receives honorariums for lectures, presentations or educational events from Astellas, Besins, Gedeon Richter and Bayer; and participates on a data safety monitoring board or advisory board for Astellas, Besins and Exeltis.

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