SAMS
South African Menopause Society

MENOPAUSE Matters

October 2024

Australian Government Senate Committee's Menopause Report

The Australian Government Senate Committee's Menopause Report has been tabled and it is supported by Australasian Menopause Society and their national O&G society. It is a comprehensive document that marks an openness to discuss the subject, starting Chapter One as follows that:

"Menopause is not an illness, and neither is it a medical condition: it is a normal component of the female life cycle; however, it is a women's health issue with social and economic consequences."

Editorial opinion. The willingness to place this topic on the Government's agenda is a signal to other countries and organisations to follow suit. It is a major step towards normalising discussion, legislation and consideration of women's experiences and its appearance is applauded.

Also in the public domain is a summary of *The Menopause Society's* recommendations on:

"Menopause in the workplace".

The Menopause Society's 2024 consensus recommendations address the growing need for menopause support in the workplace. With women over 50 representing a fast-growing demographic in many countries, their experiences during menopause can significantly affect job satisfaction, productivity, and career progression.

Menopause symptoms, such as vasomotor disturbances, genitourinary issues, sleep problems, and mood changes, are linked to adverse work outcomes, including reduced productivity, absenteeism, and even early exit from the workforce. The variability in symptom severity means some women may experience few issues, while others face moderate to severe symptoms for a decade or more, potentially affecting their quality of life and career.

The report also highlights how workplace environments can exacerbate menopause symptoms, such as long work hours, lack of breaks, insufficient restroom facilities, and confined or crowded workspaces. Therefore, tailored workplace solutions are essential to support women's individual needs and work conditions.

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The Menopause Society, with input from medical and legal experts and women's health advocates, recommends that employers create menopause-supportive workplaces. This includes reviewing healthcare plans and policies to ensure they accommodate women with menopause symptoms. Flexibility in work hours, breaks, and other accommodations may be necessary. Additionally, guidance is offered for women to understand workplace resources and advocate for themselves effectively.

Occupational health professionals are urged to be knowledgeable about menopause and provide support for women dealing with bothersome symptoms. These recommendations aim to create an environment where women can thrive in the workforce during this natural life transition, ultimately improving both employee well-being and workplace productivity.

(Editor's note: It is a year ago that the *North American Menopause Society* officially changed its name to *The Menopause Society* to "enhance inclusivity").

Dementia

The female-to-male ratio in dementia, particularly Alzheimer's disease, shows a higher prevalence among women than men. Women account for approximately two-thirds of all dementia cases.

This difference is attributed to a variety of factors, including women living longer, hormonal differences, and biological and genetic predispositions. Health-care workers dealing with women post-menopausally do have an obligation to be conversant with what are indicators, what are markers and what are risk factors for dementia.

Indicators. A patient may present with symptoms of stress at a consultation and these features need to be carefully and sensitively dealt with. Clinical judgement is required to assess whether her complaints are within the spectrum of acceptable changes occurring at this time of transition or are they such that some intervention is required? Is her knowledge of what to expect enlightened?
Do her symptoms bother her to the extent that she needs therapy?

Mood disorders in the perimenopause

Guidance is seldom published on the management of mood disorders during the perimenopause. It is a difficult topic as some degree of mood change is common at this time, so the degree of any negative feelings of sadness or depression being

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experienced need careful evaluation in respect of their duration and the person's history. They are not indicators of dementia.

A speaker at the Santé Paris Femmes 2024 congress, highlighted that women with a history of premenstrual syndrome, postpartum depression, or mood changes while on hormonal birth control may mean the patient is vulnerable to mood disorders (Andre quoted by de Tappie *Medscape* 2024). It was stressed that persistent sadness for more than 15 days should prompt referral to a psychiatrist, as diagnosing depression during menopause can be difficult due to overlapping symptoms.

Menopausal hormone therapy (MHT) could be helpful, as it influences serotonin and GABA cortical pathways, both key to mood regulation. A Canadian study showed that combining MHT with antidepressants leads to significant improvements in depressive symptoms.

Menopausal symptoms as indicators of dementia

Are menopausal symptoms an indication of future dementia? Some symptoms during the perimenopause are so common as to be considered normal and part of the hormonal changes taking place. But what of abnormal symptoms in terms of severity or duration?

An article in *Menopause* recently stated in its "Conclusion" that "Severe menopausal symptoms in postmenopausal women were associated with cognitive impairment." (Calle et al. *Menopause*. 2024. doi:10.1097/GME.0000000000002422).

Such a statement in isolation can have misinformation repercussions unless it is read in context. That context is given in the body of the work which states that there are many other factors that are linked to or associated with cognitive decline and dementia. Recognising the possibilities of misinterpretation a balanced view is expressed by Manson in a piece in *Medscape* entitled "Hot Flashes: Do They Predict CVD and Dementia?" She says "It is quite plausible that hot flashes could be a marker for increased risk for cognitive impairment. But the question remains, are hot flashes associated with cognitive impairment independent of these other risk factors?"

Where menopausal symptoms do impair a woman's quality of life it is vital to treat them – as it is important to address wider issues that may arise during a consultation but vasomotor symptoms *per se* are not indicators of future dementia.

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Severe vasomotor symptoms should be treated but at our present state of knowledge they do not constitute "risk factors" for dementia.

Markers for dementia

It remains one of the holy grails of medical research to discover markers of early dementia. Be these psychological, psychiatric, genetic, biological or biophysical, they are yet to be defined and found to be useful. Nothing so far suggests that interrogation of the menopause holds clues in this direction.

Risk factors for dementia

There are various risk factors for developing dementia – some of which are alterable, and some are not. Unalterable factors are age, female sex and genetic predisposition, but many others are amenable to lifestyle alterations and medical management.

Lifestyle factors.

Earlier this year The Lancet published a report: Dementia prevention, intervention, and care
Livingston et al. *The Lancet*. 2024;404:572-628

It was remarkable in that the authors concluded that "that close to 50% of cases of dementia worldwide can be prevented or delayed by improving 14 modifiable risk factors.

Evidence is increasing and is now stronger than before that tackling the many risk factors for dementia that we modelled previously (ie, less education, hearing loss, hypertension, smoking, obesity, depression, physical inactivity, diabetes, excessive alcohol consumption, traumatic brain injury, air pollution, and social isolation) reduces the risk of developing dementia.
To this list must be added elevated LDL cholesterol and untreated vision loss."

Diet and physical activity are within the persons control and can be risk factors or preventable factors for dementia. These two topics will be addressed in subsequent issues of *Menopause Matters*.

When to stop MHT

The case for continuing menopausal hormone therapy beyond the age of 65 years was made at the *Menopause Society* annual meeting last month. There was a report on more than 100 women who were being follow-up in a Canadian tertiary centre, all

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of whom had initiated their MHT close to their menopause and had no contra-indications to ongoing treatment (Frellick *Medscape* 2024).

Their reasons for continuing were given as the return of vasomotor symptoms on the cessation of therapy plus quality-of-life factors. The lead author was quoted as saying no major adverse events had been encountered and that most women used transdermal patches, with few using "synthetic progestins". The potential benefits such as bone, cardiovascular and cognitive effects were not quoted as considerations.

Other comments were that it was not logical to limit the duration of therapy because of the individual's age or her duration of usage, as there is no evidence that continuing MHT endangers the recipient, and benefits may accrue.

These data are in tune with the findings earlier this year (Baik et al. *Menopause* 2024 doi: 10.1097/GME.0000000000002335). These were that the risk reductions of MHT use beyond the age of 65 years appear to be greater with low rather than medium or high doses, vaginal or transdermal rather than oral preparations, and with E2 rather than conjugated estrogen.
They also are in keeping with the research of biological and chronological ageing found by Liu et al (*JAMA Netw Open*. 2024;7(8):e2430839).

MHT and head and neck cancers

Head and neck cancers (HNCs) are associated with human papilloma infections. So are genital malignancies and although head and neck lesions are commoner in males (possibly due to higher preponderances of cigarette and alcohol use), it is not established whether hormone intake in women affects HNC rates.

A study investigates the link between exogenous estrogen and the development of HNC in women (Doll et al. *JAMA Otolaryngol Head Neck Surg*. 2024;150:378-84). It showed that women using oral contraceptives had a higher risk of HNC compared to those not using OCs (RR, 1.47). Conversely, postmenopausal women on menopausal hormone therapy had a lower risk of HNC compared to those not using MHT (RR, 0.77). This suggests that exogenous estrogen may influence HNC risk.

Non-hormonal treatment for GSM

The efficacy of vaginal hyaluronic acid (HLA) was compared to vaginal estrogen in treating genitourinary syndrome of menopause in a small randomised trial (Agrawal

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et al. *Menopause*. 2024. doi:10.1097/GME.0000000000002390). Forty-nine women received either HLA vaginal suppositories or vaginal estrogen cream over 12 weeks.

The primary outcome, assessed using a vulvovaginal symptom questionnaire, showed no significant difference between the two groups. Both treatment groups experienced symptom improvement according to the questionnaire, and secondary outcomes, including the vaginal symptom index, the female sexual function index, and vaginal pH, also improved without differences between the treatments. More than 90% of participants reported improvement on the patient global impression scale and no serious adverse events were observed. The study concluded that vaginal HLA could be a promising non-hormonal alternative to vaginal estrogen with comparable efficacy.

Readers are reminded that a study showed no evidence of increased early breast cancer-specific mortality in patients who used vaginal estrogen therapy compared with patients who did not use MHT (McVicker et al. *JAMA Oncol*. 2024; doi:10.1001/jamaoncol.2023.4508).

Thickened endometrium – biopsy necessity?

A study has explored the necessity of performing a biopsy in asymptomatic postmenopausal women with an incidental finding of thickened endometrium. The retrospective analysis included 580 women, all with an endometrial thickness (ET) of ≥4 mm (Wang et al. *Euro J Obs Gyn Reprod Bio.* 2024. doi:10.1016/j.ejogrb.2024.08.016).

The researchers aimed to establish a threshold for ET that would prompt a biopsy and develop a risk prediction model for endometrial malignancy. The findings revealed that an ET of 8 mm was the optimal cutoff, with reasonable predictive accuracy. The model also identified other risk factors for malignancy, including diabetes, a raised BMI, and hypertension.

The study concluded that it is reasonable to perform hysteroscopy and biopsy in women with an ET of 8 mm or more. For those with an ET between 4 and 8 mm, decisions regarding biopsy should be based on individual risk factors, such as endometrial blood flow and other malignancy risks. This approach helps tailor management to minimise unnecessary procedures while addressing the potential risk of malignancy.

Weight loss

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Depot semaglutide. Research has inevitably been looking at ways of delivering GLP-1 agonists with less hassle than is involved in daily pills, or daily/weekly injections. Research in animals shows that it is feasible to deliver depot injections using hydrogel impregnated with semaglutide that releases the active substance over a month (Marechal et al. *Euro Ass Stud Diab.* and *Medscape* 2024}. The hydrogel is absorbed as it is biodegradable which allows reliable usage – at least experimentally. This will theoretically improve control and compliance and hopefully lower costs while increasing availability.

Appetite suppression with bitter hops. Bitter-tasting plant extracts have traditionally been used for appetite suppression, and recently in a trial (involving men only) had promising results. A randomised trial of New Zealand women has been published which suggests that a bitter hops extract could be effective in reducing the desire for calorie intake in those undertaking acute 24-hour fasting regimens (Walker et al *Obesity Pillars.* 2024. doi:10.1016/j.obpill.2024.100117).

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Menopause Matters is a monthly review of matters menopausal that have recently appeared in the journals. These summaries and opinions do not necessarily reflect the views of the South African Menopause Society. Any clinical decisions made on the data presented are exclusively at the reader's discretion. ChatGPT has been used to assist with the production of some of the summaries.

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