SAMS South African Menopause Society

MENOPAUSE Matters

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Setting Menopause Research Priorities

Setting priorities for research in any branch of medicine is an important activity for academics, funders, pharmaceutical companies and device makers. Procedures have evolved in recent times which then work to achieve consensus about directions to be followed. But what of consumer opinions? Surely a normal process such as the menopause transition should be addressed by a group of people with lived experience.

The Menopause Priority Setting Partnership is such a team. Technology allows distance and time barriers to be overcome, and virtual methods of group formation are less tedious than gathering people together physically. For example, the Delphi technique now can garner information electronically to facilitate "scoring" rather than people meeting face to face to prioritise topics. The Menopause Priority Setting Partnership was formed in 2021 and has now published the findings of their group (Nash et al. *Lancet*. 2024;404:2535-6).

Most (80%) of the nearly 600 contributors were not healthcare professionals and had lived through the menopause transition. The following were aspects of their experiences that they felt most needed research attention:

Top ten priorities for menopause research

- What are the safest and most effective non-hormone treatments for perimenopause and menopause in people who cannot, or do not wish to take hormone therapy?
- What lifestyle changes benefit people at different stages of menopause? How can people be supported to make these changes?
- Does perimenopause and menopause lead to cognitive problems? If yes, why, and how does this happen? How are these problems best detected and managed? Can they be prevented or reversed?
- Why and how is sleep affected during perimenopause, menopause, and post-menopause? What are the best ways to manage these sleep problems?
- How long should people take hormone therapy? What is the best way to stop hormone therapy?
- What are the best ways to help people prepare for perimenopause and menopause and recognise when it is happening? What helps them know when to seek professional help and make informed decisions about treatment?
- How do menopausal experiences vary across different countries, cultures, and ethnic backgrounds worldwide?
- What are the best ways to manage perimenopause and menopause in people who are living with, or have survived breast cancer?
- Does hormone therapy change the risk of dementia?
- How long can people with a personal risk of heart disease or cancer safely take hormone therapy? If they can, which type and what dose of hormone therapy is best?

Vaginal Laser Therapy for Stress Incontinence

A randomised, double-blinded, sham-controlled trial using laser therapy for stress urinary incontinence was conducted by a Canadian research group (Lee et al. *AJOG*. 2024. doi.10.1016/j.ajog.2024.11.021).

The study involved 144 women with symptomatic incontinence and participants received two sessions of real or sham laser treatment, six weeks apart and follow-up at six weeks and six months. The primary outcome was subjective reporting of urinary continence and secondary outcomes included objective urine loss measurements, incontinence symptom questionnaires, quality of life assessments, and sexual function scores.

At six months, the cure rate was minimal, with no significant difference between the laser group (1.3%) and the sham group (0%). At six weeks, minor differences were noted in a few quality-of-life domains, but no sustained benefits were observed. The findings suggest that Er-YAG laser therapy is no more effective than a sham procedure for treating stress urinary incontinence.

Overactive Bladder Medication & Dementia Risk

Anticholinergic drugs are often used to treat symptoms of an overactive bladder in older adults, but concerns have arisen that they might be linked to a higher risk of dementia. However, it is not clear if some drugs carry more risk than others. A study was carried out gathering data from General Practices in the UK looking at reports from over 170,000 people with dementia and more than 800,000 matched controls (Iyen et al. *BMJ Medicine*. 2024; doi:10.1136/bmjmed-2023-000799). Two thirds of the participants were women, and the mean age was 83 years. The researchers discovered a clear link (about a one fifth rise in risk) between cumulative use of certain drugs—oxybutynin, solifenacin, and tolterodine – and an increased risk of dementia. Other drugs in the same class, like darifenacin, fesoterodine, flavoxate, propiverine, and trospium, did not show the same risk.

These results suggest that clinicians should carefully weigh the risks when prescribing anticholinergic drugs for an overactive bladder, especially for older patients. Exploring alternative treatments that do not carry the same dementia risk might be a safer option which should influence clinical practice, and prescribing guidelines.

More Data about MHT & Cognition

The KEEPS study evaluated the long-term cognitive effects of four years of menopausal hormone therapy initiated soon after the menopause. This observational follow-up to the KEEPS-Cog trial, conducted approximately a decade after the initial study, involved 300 women who were re-evaluated from the original cohort (Gleason et al. *PLOS*. 2024. doi:10.1371/journal.pmed.1004435). Participants had been randomised to oral conjugated

equine estrogens, transdermal estradiol, or placebo. Cognitive outcomes were assessed using test batteries and latent growth models.

The findings confirmed no long-term cognitive benefit or harm associated with menopausal hormone therapy. Baseline cognition and changes during the original trial were the strongest predictors of later cognitive performance. Both active arms performed similarly to placebo in cognitive assessments approximately ten years after treatment cessation. These results indicate that intermediate duration hormone therapy started early, neither preserves cognitive function nor prevents cognitive decline. Hormone therapy was shown to be neurocognitively safe for symptom management in healthy, low-risk women.

These findings are significant for public health, offering reassurance regarding the safety of short-term therapy. However, the study also suggests that hormone therapy should not be recommended for cognitive preservation. Future research should explore other long-term health outcomes, including mood and Alzheimer's disease biomarkers, and assess broader populations.

Warning of Liver Injury in Fezolinetant Use

The United States Food and Drug Administration (FDA) has added a warning about liver injury to fezolinetant, which is prescribed for vasomotor symptoms in menopausal women, according to an FDA statement.

The warning is based on data from a post-marketing report of an individual who experienced elevated liver blood test values as well as symptoms of liver injury after approximately 40 days of taking fezolinetant, according to the statement (Splete. *Medscape*. 2024).

AI & Osteoporosis – Too much of a Good Thing?

A conundrum arose in an Australian research centre where the investigators found they did not have sufficient recruits for an osteoporosis trial. The team wanted to "close the gap" between the occurrence of osteoporosis and its treatment, so they asked to review some hospitals' radiology records (Larkin. *Medscape*.2025).

They were looking for vertebral fractures diagnosed and reported in older women, in the hope of finding volunteers for a preventative treatment trial. Unfortunately, the actual reporting of vertebral fractures was either not noted or not found in enough cases, so they enlisted the assistance of AI tools to scan image libraries. They got more than they bargained for.

These tools reliably identified undiagnosed cases, revealing the disorder's widespread underreporting. If they contacted all those "uncovered", the surge in identified patients would overwhelm the health-care systems, as organisational workflows and funding lagged

behind the technology's capabilities. The leader of the team, Christopher White from Sydney, emphasised that technology must align with infrastructure, education, and funding to address the osteoporosis treatment gap effectively, urging caution with AI's rapid implementation (See also the FDA's role in this regard: Warraich et al. *JAMA*. 2024; doi:10.1001/jama.2024.21451).

Editorial comment. The situation raises many questions, not least of which are confidentiality, privacy and medico-legal implications. "Mining" hospital records and radiology departments' images by using new technologies is a potential source of data for re-examination, but it is also thwart with issues arising from unexpected findings (such as misdiagnoses, unrecognised incidentalomas like coronary calcification) that create matters that the investigators have to resolve.
Be careful what you wish for.

Zoledronate & Vertebral Fractures

Zoledronate is a potent bisphosphonate used to manage and treat conditions that involve excessive bone resorption. Its mechanism of action involves inhibiting osteoclast-mediated bone breakdown, thereby preserving bone density and strength, and is administered as an intravenous infusion.

A 10-year, double-blind, placebo-controlled trial assessed the efficacy of infrequent zoledronate administration in preventing vertebral fractures in early postmenopausal women with bone mineral density T scores between 0 and −2.5. Participants received either two doses of zoledronate (baseline and year 5), one dose followed by placebo, or placebo only. Among 1,000 women, 95% completed the study (Bolland et al. *NEJM*. 2025; doi:10.1056/NEJMoa2407031).

Morphometric vertebral fractures occurred in 6.3% of the two-dose group, 6.6% of the one-dose group, and 11% of the placebo group. Zoledronate significantly reduced the risk of vertebral fractures compared to placebo (relative risk [RR], 0.56). Secondary outcomes showed reductions in fragility fractures (RR, 0.72), any fractures (RR, 0.70), and major osteoporotic fractures (RR, 0.60) with two doses versus placebo. One-dose effects were slightly weaker.

Zoledronate, given at 5-year intervals, effectively prevents vertebral fractures in early postmenopausal women, with sustained benefits over a decade.

US Recommendations for Osteoporosis Screening

The USPSTF reviewed evidence on osteoporosis screening for adults 40 years or older without prior osteoporosis or fragility fractures. They found moderate benefits in screening women 65+ and postmenopausal women under 65 at increased risk, recommending it for these groups. (US Preventive Services Task Force Recommendation Statement. *JAMA*. 2025; doi:10.1001/jama.2024.27154). These findings aim to guide targeted screening strategies to reduce fracture risk in high-risk populations.

The Polypill Revisited

Many of us remember the Polypill that was introduced as a panacea for cardiovascular disease some decades ago. With the widening of socio-economic gaps come thoughts of resurrecting the concept and approaching disadvantaged groups.

This has been done in the US with an economic evaluation assessing the cost-effectiveness of a cardiovascular polypill—a single pill combining a statin and three half-dose antihypertensives—compared with usual care in a low-income, majority Black population (Kohli-Lynch et al. *JAMA Cardiol*. 2025. doi:10.1001/jamacardio.2024.4812). Using a computer simulation, the polypill was estimated to cost $8,560 per quality-adjusted life-year (QALY) gained, well below the high-value threshold of $50,000 per QALY. The polypill remained high value in 99% of simulations.

The intervention is projected to improve adherence, reduce cardiovascular risk factors, and address disparities in healthcare access. These findings support the polypill as a cost-effective strategy for reducing cardiovascular health disparities in certain populations and may gain traction in the US.
Editorial comment. The study population was mainly women (60%) with a mean age of 57 years, which makes one think about targeting a similar group for menopausal intervention using the social media as a recruitment mechanism. Yes, it will take a champion person or organisation to try it, but more outrageous ventures have succeeded.

Do Supplements Improve Physical Vitality?

The VITamin D and OmegA-3 TriaL (VITAL) examined whether vitamin D3 (2,000 IU/day) and/or omega-3 fatty acids (1 g/day) supplementation over two years improves physical performance in older adults (Chou et al. *J Clin Endo & Met*. 2025; doi:10.1210/clinem/dgae150).

Conducted as a placebo-controlled trial in more than 1,000 participants, the study assessed changes in grip strength, walking speed, balance, repeated chair stands, and Timed-Up and Go. All groups showed declines in walking speed and test performance over two years, with no significant differences in physical performance between vitamin D3, omega-3, and placebo groups. Results were consistent across subgroups defined by sex, age, BMI, and baseline levels of vitamin D or omega-3s. Interestingly, participants with higher baseline vitamin D levels experienced a slight worsening in short distance movement tasks with vitamin D supplementation. Overall, the study concluded that neither vitamin D3 nor omega-3 supplementation improved physical performance in this generally healthy cohort.

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