MENOPAUSE MATTERS

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Is Age at Menopause Socially Driven?

An observational study examined how neighbourhood social status affects menopause timing and symptoms (Lin et al. *JAMA Netw Open.* 2025; doi:10.1001/jamanetworkopen.2025.12075). In the US a group of 700 women were followed from their last pregnancy to midlife for more than 2 decades. Researchers used the Social Vulnerability Index (SVI) to categorize neighbourhoods from very low to very high, and track participants at regular intervals.

The study found that women living in very high vulnerability areas experienced natural menopause approximately two years earlier than those living in very low vulnerability areas. The median age of menopause was around 51-52 years for high-vulnerability residents versus 53-54 years for low-vulnerability residents. Notably, living conditions showed the strongest association with early menopause when measured after the age of 40. However, no relationship was found between neighbourhood vulnerability and menopausal symptom severity.

The findings suggest that addressing local disadvantages through community interventions and policy changes could help achieve more equitable reproductive health outcomes and potentially delay menopause onset in high-risk women.

How Women Age Healthily

High quality carbohydrate intake plays a crucial role in the future health of middle-aged women.

Diet is the most readily controlled factor in staying healthy and the Nurses' Health Study from the US provides rigorous data as to how past and present dietary habits predict a woman's future wellbeing (Korat et al. *JAMA Netw Open.* 2025; doi:10.1001/jamanetworkopen.2025.11056 and Tessier et al. *Nature Medicine*. 2025; doi:10.1038/s41591-025-03570-5).

In modern Western diets nearly half of all calories consumed are derived from carbohydrates, but it is the quality of these carbohydrates that dictates the risk of chronic illnesses and mortality rates. These foods also contain high levels of fibre which is independently associated with healthy ageing. Poor quality carbohydrates are refined, ultra-processed foods, while high quality carbohydrates are found in whole grains, legumes, fruits, and vegetables. The intake of high-quality carbohydrate sources are consistently associated with healthy ageing and a better quality of life.

*Editorial comment. Diet is one of the most difficult domains in which to conduct research as controlled trials are nigh impossible. Modern science may provide biomarkers to measure ultra-processed food proportions in diets – but this is for future researchers to quantify (*Abar et al. *Plos Medicine*. 2025; doi:10.1371/journal.pmed.1004560). In the meanwhile, t*he Nurses' Health Study has accurate records of nearly 50,000 women over 30 years. The data presented are unequivocal – eat healthy carbs to age healthily.*

What Prevents Muscle Loss in Older Women?

It would be highly desirable if there were an easy way to prevent muscle loss in older women. The loss of lean muscle, loosely called sarcopenia if it is age related, can impede normal function so elixirs are sought by science and commercial interests. A three-year trial investigated whether vitamin D (2,000 IU/day), omega-3s (1g/day), and/or a home exercise programme could guard against muscle loss in older women living in the community (Eggimann et al. *JAGS*. 2024; doi:10.1111/jgs.19266).

Despite participants being predominantly active, they experienced modest muscle loss over 3 years of just over 1% with none of the interventions, alone or combined, significantly improving outcomes compared to controls.

Many products are marketed to persuade people to buy their way to health, but this scientific study does not support vitamin D or omega-3s, or for that matter, home exercise programmes, as the way to preserve muscle mass.

Is there any protection against dementia?

Biomarkers as prognostic tools in forecasting dementia remain elusive. Until such time as genetic risk profiles or other mechanisms are identified to predict those who are likely to develop dementia, efforts to protect against cognitive decline remain speculative. Two candidate mechanisms may be:

Medications:
A systematic review and meta-analysis study has examined whether two diabetes medications—GLP-1 receptor agonists (GLP-1RAs) and SGLT2 inhibitors (SGLT2Is)—affect Alzheimer's disease and related dementia (ADRD) risk (Tang et al. *JAMA Neurol.* 2025; doi:10.1001/jamaneurol.2025.0353).

One study involved over 33,000 patients with type 2 diabetes and results showed both medications were associated with significantly reduced ADRD risk compared to other glucose-lowering drugs. These findings were consistent, suggesting both medications may have neuroprotective effects that could potentially be leveraged for dementia prevention strategies (Seminer et al. *JAMA Neurol.* 2025; doi:10.1001/jamaneurol.2025.0360).

Vaccinations:
Two articles suggest the Herpes Zoster vaccination may have a protective effect against dementia: *A natural experiment on the effect of herpes zoster vaccination on dementia*. Eyting et al. *Nature*. 2025; doi:10.1038/s41586-025-08800-x and *Herpes Zoster Vaccination and Dementia Occurrence* Pomirchy et al. *JAMA*. 2025; doi:10.1001/jama.2025.5013

Editorial comment: While neither mode is evidence-based proof of protection, it is difficult not to be swayed towards using the medicines or the vaccination in situations of "marginal indication". By this I mean that if there are some reasons for using, say GLP-1 drugs, or possible recommendations to give the vaccine – one might be tipped from equipoise to commitment knowing that one or other of these treatments may lower future risk of dementia.

It should also be remembered that treating hearing loss might delay dementia for a large number of older adults (Ishak et al. *JAMA Oto Head Neck Surg.* 2025; doi:10.1001/jamaoto.2025.0192). Public health interventions targeting clinically significant audiometric hearing loss might have broad benefits for dementia prevention. Ref WHO and the Lancet guidelines for addeded emphasis

(Livingston G, et al. Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. Lancet. 2024;404(10452):572-628. And WHO 2019 guidelines

Biomarkers & Alzheimer's Disease

This is an Editorial opinion. Is it true that the holy grail of Alzheimer's Disease research is the finding of a biomarker that will accurately predict who will develop the disorder?

Given the option, would healthy, low-risk people want to know if they are destined to become Alzheimer's sufferers? As someone with "insatiable curiosity" my initial response is "Yes please." But reading the results of research into the reactions of volunteers taking part in a longitudinal ageing study, I was given pause for reflection.

A group of 270 participants with a mean age of 75 years were offered the results of their investigations, which included sophisticated Alzheimer's biomarkers, but 40% declined the opportunity (Goswami et al. *JAMA Netw Open.* 2025; doi:10.1001/jamanetworkopen.2025.2919). These people were presumably altruistic otherwise they would not be involved, but they were aware of the psychosocial harms of learning one is at risk of a "feared and incurable disease", knowledge they felt they could live without. The authors emphasise the ethical autonomy of each person's right to know – and right not to know.

Also flashing are warning lights about over-the-counter tests for AD and their potential for disinformation which may sound attractive by do have significant downsides in terms of costs and sequalae (Widera et al. *JAMA Intern Med*. 2025; doi:10.1001/jamainternmed.2025.0976).

Testosterone to Promote Hip Fracture Healing?

Hip fractures represent an increasing public health problem. As the number of older adults continues to grow, the burden of care for patients with hip fracture is expected to expand as three quarters of them experience functional loss despite receiving rehabilitation as part of their fracture management.

Whether adding topical testosterone to women patients' post-fracture care improves outcomes is unknown, so a trial was conducted in the US on a group of women with a femoral fracture. Half had testosterone added to their management and half had standard care (Binder et al. *JAMA Netw Open.* 2025; doi:10.1001/jamanetworkopen.2025.10512). After six months, those receiving testosterone and those on routine treatments had equivalent outcomes but "testosterone combined with exercise might benefit physical performance and mobility for short distances and warrants further study".

Breast Cancer Screening Study in Older Women

A cohort study from the US examined 13,000 women aged 70+ with screen-detected breast cancer to determine associations between prior screening history and outcomes (Huang et al. *JAMA Netw Open.* 2025; doi:10.1001/jamanetworkopen.2025.5322). The researchers found that women with screening mammography history within the five years before diagnosis had more favourable outcomes compared to those without prior screening.

Key findings:

- Three quarters of women had at least one prior screening
- Prior screening was associated with 50+% lower odds of later-stage cancer diagnosis

- Prior screening was linked to a one third lower breast cancer-specific mortality
- Having 3-4 prior screenings showed a one third reduced mortality compared to just one prior screening

While these findings support routine screening's potential to improve breast cancer outcomes in women 70+, the authors acknowledge limitations due to potential selection bias between screening and non-screening groups. This research addresses an important evidence gap, as the USPSTF currently cites insufficient evidence for screening recommendations in women 75+.

Real World Hormone Therapy Over 3 Decades

Historically the last thirty years will be recorded as the most turbulent as far as menopausal hormone therapy (MHT)use is concerned. The impression is that at the turn of the century, MHT was surging in its acceptance and uptake, only to have this trend reversed by the adverse publicity surrounding the WHI Report. This was followed by the development of newer medications and methods of administration being tried but what actually happened to prescribing patterns?

An observational study analysed hormone replacement therapy (HRT) patterns using Welsh healthcare data covering most of the population and including nearly 300,000 women who took oral or transdermal HRT over the 3 decades under review (Andrews et al. *BJOG*. 2025; doi:10.1111/1471-0528.18220).

Key findings revealed contrasting trends with oral prescriptions declining post-2002 and transdermal HRT prescriptions increasing exponentially after 2021. Discontinuation rates followed a U-shaped pattern, peaking at ages 40-43 and mid-50s onward, but decreasing during mid-40s to early 50s. Oral HRT showed better adherence than transdermal formulations.

Socioeconomic deprivation emerged as a significant barrier to HRT access overall. Discontinuation rates increased markedly after 2001, with the highest rates post-2021, reflecting the impact of publicised safety studies and media coverage on patient and physician perceptions. The researchers conclude that prescribing disparities were prompted by safety concerns, with women experiencing natural menopause showing better adherence, particularly to oral preparations. They emphasise the need for strategies addressing socioeconomic inequalities and improving cost-effective HRT prescribing practices.

Recommended reading

An authoritative article has appeared this month entitled:

Nonhormonal Treatment of Menopausal Vasomotor Symptoms
Haung et al. *JAMA Intern Med.* 2025; doi:10.1001/jamainternmed.2025.0990

It mentions some behavioral and Complementary Therapies with details for printing out for patients with an in-depth interest in the topic.

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