

The MHT debate

Two articles have appeared this year that draw together reflections on Menopausal Hormone Therapy use. Both are from the United States and both will influence attitudes to MHT in America as well as globally, and as such deserve consideration.

They are:

The Women's Health Initiative Randomized Trials and Clinical Practice. A Review
[Manson et al](#) JAMA 2024 doi 10.1001/jama.2024.6542

Use of menopausal hormone therapy beyond age 65 years and its effects on women's health outcomes by types, routes, and doses

[Baik et al](#) Menopause 2024;31:363-71

To gain perspective it is important to understand that in the United States there are 55 million postmenopausal women who have access to many and varied medical opinions. Medical and moral issues figure largely in the media with social, political and financial aspects never far from the surface. The United States is litigation alert and screening sensitive as well as having pharmaceuticals as its most lucrative industry, so publications like the two featured in this newsletter will be carefully scrutinised and taken on board by a wide array of interested groups, societies and individuals.

Against this background it is easy to understand why accuracy and evidence are paramount as both presentations will be quoted and relied upon to be factually correct.

The first article is from the Women's Health Initiative perspective and covers that organisation's research, which over the years has had more than 150,000 participants. It is from an impeccable stable of scientists, clinicians and statisticians with their findings published and scrutinised by all parties interested in menopausal research.

The review depends heavily on that organisation's flagship piece which was their work focussing on oral conjugated equine estrogens plus medroxyprogesterone acetate for postmenopausal women or conjugated equine estrogens alone for those

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with prior hysterectomy to prevent cardiovascular disease, dementia, or other chronic diseases. The data have been reworked and the original conclusions modified over time to be less intimidating. However, the message that the hormones used then are not the hormones used now (in type, dosage and route of administration) will take a long time to be recognised. Although another randomised trial of such a magnitude will never be repeated, and as such it is a classic, it cannot be held up as an indicator of what women can now anticipate.

Almost every detrimental outcome of that study has had to be rolled-back in the light of new evidence and new medications, but commentators lament the slowness of the more optimistic out-looks getting through to rank-and-file prescribers. Initiating MHT when bothersome symptoms arise is not contentious, but revisiting old data to conclude when to stop therapy is yet to be explored. It should be stated that the authors do not claim to address this aspect of the debate.

The second article uses information gathered from the US Medicare system which is a type of national insurance for people over the age of 65 years. In scrutinising the records of more than 10 million women from 2007 to 2020, the authors have tried to reconcile MHT use (which presumably was started peri-menopausally) with chronic conditions and outcomes.

Their key findings were;

Estrogen Monotherapy: After age 65, usage significantly reduces risks associated with mortality (19% reduction), several types of cancer (breast, lung, colorectal), cardiovascular diseases (congestive heart failure, venous thromboembolism, atrial fibrillation, myocardial infarction), and dementia.

Combined Estrogen and Progestogen Therapy: Shows an increased risk of breast cancer (10% to 20% increase) but also notable reductions in endometrial and ovarian cancer, and some cardiovascular conditions. The increased risk of breast cancer can be mitigated by using low doses of transdermal or vaginal formulations.

The conclusions highlight that MHT benefits vary by the type, dose, and route of administration, with low doses and non-oral routes (vaginal or transdermal) generally providing greater risk reductions. The study supports continued use of MHT beyond age 65 for women with persistent symptoms, emphasising tailored approaches based on individual health profiles and the specifics of the hormone therapy used. Comment on this work echoes the safety of ongoing use of MHT after age 65 as a good option for most women and will “convince the already convinced”.



Editorial opinion: The options for the relief of unwanted menopausal symptoms with hormones are wider and more nuanced than ever and the “cut-off” date seems negotiable which give the patient and her clinician the freedom of choice, provided the situation is monitored. From lifestyle to MHT is a welcome range to offer, and stay with. See also [Iyer et al](#) Menopause 2024;31:359-60).

There is interesting work linking vasomotor symptoms observed at night using skin conductance monitoring with biomarkers of Alzheimer disease ([Thurston et al](#) 2023 AJOG 2023;230:e1-342). It is stated that “Nighttime vasomotor symptoms may be a marker of women at risk of Alzheimer disease. It is yet unknown if these associations are causal.”

Alzheimer biomarkers of amyloid β , tau and glial proteins can identify high-risk women in terms of dementia, which raises “the tantalizing possibility that agents that reduce nighttime hot flashes (including hormone therapy) may lower the subsequent incidence of Alzheimer's disease” ([Kaunitz](#) Medscape 2024).

While on the topic of dementia protection, it was shown that olive oil consumption lowers the risk of dementia-related death by more than 30% ([Tessier et al](#) JAMA Netw Open 2024;7:e2410021).

An early report makes an interesting link between estrogens and head and neck cancers. These malignancies share some characteristics with cervical cancer in that they may have HPV origins and smoking plus alcohol habits are associated with their incidence, and both are squamous cell carcinomas. There is a much greater preponderance of male sufferers but hormonal influences have not been investigated.

Now a large observational study shows that oral contraceptive use in young women is associated with a higher risk of head and neck cancers, but in older women use of menopausal hormone therapy is linked to a lower risk of these malignancies ([Doll et al](#) JAMA Oto Surg 2024;150:378-84).

Athol Kent

Email address atholkent@mweb.co.za

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