

## Age at menopause & longevity

Taking the normal range of the menopause transition to be between 45 and 55 years, is the transition outside of these parameters indicative of longevity? A survey from America suggests there is a correlation with premature menopause (before the age of 40) having the strongest association with early all-cause mortality, followed by 40 to 44 years while the transition beyond 55 years appeared to be “protective” ([Xing et al Menopause 2024;31:176-85](#)).

Anti-Mullerian hormone levels are said to be indicators of ovarian reserve but quite what affects such measurements is unclear. Links with serum heavy metal assays indicate that levels of arsenic, cadmium and mercury are raised as the final menstrual period approaches, suggesting that disrupted folliculogenesis is impacted by toxicity of these substances ([Ding et al J Clin Endo Metab 2024 doi 10.1210/clinem/dgad756](#)).

The natural process whereby ovarian function decreases remains obscure apart from chronological ageing. The part played by metals must, at present, remain speculative.

## MHT use in breast cancer survivors

There is a need for relief from menopausal symptoms in breast cancer survivors, either from a natural transition &/or from the anti-estrogen therapies used as part of treatment. However, concerns over the effects of estrogenic hormones on recurrence or mortality has meant that there is caution in their prescription with wide variations in clinical practice.

A “safety report based on a systematic review and meta-analysis” has been published to draw together the latest data ([Coronado et al Menopause 2024;31:234-42](#)). The authors quote 3 randomised clinical trials using combined menopause hormone therapy or tibolone, none of which revealed any significant differences concerning tumour recurrence. A combined analysis of prospective and retrospective work again found no elevated risk of recurrence or death.

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The bottom line is conservative, stating “that MHT could be a viable treatment alternative for breast cancer survivors experiencing menopausal symptoms, especially those with HR-negative tumors.” They also call for further trials “before considering changes to current standards of care” which clinicians will interpret for themselves.

### Plant-based diets & hip fractures

“Previous research has found that vegetarian diets are associated with lower bone mineral density and higher risk of fractures” but the quality and statistical power of these studies has been called into question because diets in general, are now more stringently defined.

The US Nurses’ Health Study has provided a large (70,000 strong) group of reasonably homogeneous participants over a long period of time (more than 30 years) with diligently gathered information which includes details about their diet. Access to this information has allowed the following question to be posed “Are plant-based diets associated with risk of hip fractures in postmenopausal women?” and the answer is intriguing ([Sotos-Prieto et al JAMA Netw Open 2024;7:e241107](#)). The short answer is - no, adherence to a plant-based diet is **not** associated with an increased risk of hip fracture - but the longer answer provides more of interest.

The quality of a plant-based diet can be broadly divided into healthy and unhealthy categories:

- a healthy diet contains foods such as whole grains, fruits, vegetables, nuts, legumes, vegetable oils, and unsweetened beverages, whereas
- an unhealthy diet contains fruit juices, sweetened beverages, refined grains, potatoes, and sweets or desserts

Once the participants were subdivided into healthy and unhealthy groupings, it became apparent that those in the healthiest quintile had a 20% lower risk of fracture and those in the least healthy quintile had a 30% higher risk of fracture. The overall risk was neutral so postmenopausal women can safely continue with their mainly plant-based diets and shift the advantages to themselves and the planet by steering clear of sugary, ultra-processed foodstuffs.

### Cold water swimming

The media have focused on the therapeutic effects of swimming in cold water on perimenopausal symptoms and now data have been published on how women feel about this past-time.

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The statistics are both quantitative and qualitative with information about menstrual and perimenopausal effects ([Pound et al J Post Reprod Health 2024 doi 10.1177/20533691241227100](#)).

It is an interesting article that is “modern” since it was advertised in the social media and more than 1,000 women responded on-line. Most of the respondents said they swam specifically to reduce their symptoms from which they reported improvement as follows - 47% anxiety, 35% mood swings, 31% low mood and 30% hot flushes. The authors ponder whether other forms of exercise would yield similar results but offer no physiological explanations as to the advantages of cold swimming.

### Digital assistance for overactive bladder management

Much can be achieved in the management of an overactive bladder by understanding the disorder and using a logical approach to its control. This is conventionally carried out with the assistance of a urogynaecologist or trained therapist but such help may not be local or affordable, so a remote system of interaction using a telehealth system or chatbot is a potential solution.

A digital conversational agent has been devised where the patient remotely enters personal data and gets real-time responses to their queries. They can have their progress in symptom severity recorded and the chatbot responds with advice and encouragement. A commercial product (CeCe) has been tested and shown to decrease unwanted interference in patients' lifestyles ([Sheyn et al Urogynecology 2023 doi 10.1097/SPV.0000000000001428](#)).

*Editorial comment. This information is not unexpected. Artificial Intelligence can provide algorithms that follow logical pathways gathered from other patients' experiences, collate these and offer next steps and feedback. Perhaps urogynaecology groups are already considering how this technology can be incorporated into supporting their work?*

### Mammography screening

#### Whose responsibility?

If a woman of average risk is referred for mammography cancer screening, the person initiating the screening should be aware of the process that follows such a decision.



It is not a question of sending her off to the screening clinic and letting them take it from there, hoping that the clinic or radiology department will deal with any follow-up. The referring practitioner remains the core professional responsible for seeing that the patient gets the results, interprets any ambiguities and schedules (or confirms) her next appointment.

If abnormal results do occur, then oncological assistance may be required to decide whether to repeat the imaging, proceed with more definitive investigations such as aspiration, biopsy etc but these can be anxiety provoking and need explanation, so the referring doctor remains central to the process. If a cancer is diagnosed - the oncologist or "breast cancer treatment group" - will take over but the original referrer becomes part of that team.

Those taking a special interest in menopausal medicine are increasingly becoming holistically involved in their patient's well-being and are seen as "general practitioners" who are responsible for serial care which builds relationships and with it, the reward of continuing care. That means staying "abreast" of mammography information.

### AI & reading mammograms

Will Artificial Intelligence prove to be a boon in the reading of mammographic screening results?

If the repetitive task of interpreting mammograms can be done as efficiently by AI algorithms as by radiologists, then time can be saved and potentially money as well. The efficiency of the performance of AI was researched using a series of normal, benign and malignant images that had been evaluated by a large number (>500) of experienced professionals. The outcome was that the "Diagnostic performance of AI was comparable with that of the average human reader when evaluating cases" ([Chen et al Radiology 2023 doi 10.1148/radiol.223299](#) & [Philpotts Radiology 2023 doi 10.1148/radiol.232034](#)). AI is "non inferior" to human efficiency and does not detect cancer, it detects abnormal images that need investigation, and as such can save human time.

Considering that the US health-care spending in the next decade is projected to account for \$1 in every \$5 spent - that is 20% of the entire economy - savings by using machines could be vital ([Harris JAMA 2023; 330:210](#)). In 2021 a breast screening episode cost more than US\$400 ([Richman et al JAMA Intern Med 2021;181:1665-8](#)).

### When to start & when to stop mammography



In the United States there is a lively debate about at what age mammography should start. Resident experts are advising lowering the recommended age of initiation from 50 to 40 years. This will bring 20 million more women into their screening programmes but the arguments in favour are based on scientific modelling rather than randomised or clinical trials. This change is the recommendation of the powerful US Preventative Services Task Force so it is a serious proposal. It has attracted dissenting views which are being aired by the journals ([Woloshin et al NEJM 2023](#); 389:1061-4 & [Brooks Medscape 2023](#)).

At the other end of the spectrum, the age at which to stop screening is under discussion. Most recommendations suggest 70 to 74 years as the upper limits of routine screening but many people continue to be monitored. Some used 10 years of life expectancy to inform cessation but this creates uncomfortable judgements by those doing the referring and real fears of over-screening ([Schoenborn JAMA Intern Med 2022 doi 10.1001/jamainternmed.2022.4316](#)).

Overdiagnoses - that is the risk of detecting and treating cancers that would never have caused issues in a person's lifetime - increase with age and are estimated to constitute 30% of all breast cancer diagnoses for those in their early 70s rising to more than 50% for those older than 85 years ([Richman et al Ann Int Med 2023 doi 10.7326/M23-0133](#) & [Otto Medscape 2023](#)).

### False positives

One of the pitfalls of mammographic screening is a "false positive" result. This occurs when the scan reveals a "lesion of interest" that needs to be investigated, so a definitive diagnosis can be made. Of 20 such outcomes, on average only one turns out to be a "true positive" so most patients will be told that they do not have a malignancy.

False positives occur frequently with the statistical chances of this happening being between 2.5% (European data) and 10% (United States data). Depending on whether the woman is screened yearly or every 2 years, she will have at least 10 scans over her "contact years" from 50 to 74 years old. The cumulative risk of a false positive is between 20% and 50%.

But does a woman who has a false positive revert to the risk category she was in prior to this "wrong diagnosis"? To answer this 45,000 Swedish women who had a false positive result were followed up and compared with the same number of controls



who did not have a false positive result. After 20 years, those who did **not** have a false positive had a 7.3% incidence of breast cancer, and those who **did** have a history of a false positive had a 11.3% incidence of breast cancer. They also were at an elevated risk of dying from breast cancer and these increases were highly significant.

The risk was higher in those between 60 and 75 years old and in those with less dense breasts ([Mao et al JAMA Oncol 2023 doi 10.1001/jamaoncol.2023.4519](#)). The authors conclude that the following implications flow from their findings for women who have received a false positive result:

- Older age and less dense breast tissue indicate a need for “individualised surveillance”
- The next 2 screening rounds are imperative
- All those who receive the diagnosis need to be counselled about their raised risk.

Also in the category of false positives are the group of patients in whom a lesion is found, investigated and on aspiration has cells present that are atypical but are not classified as cancerous and are classified as being of uncertain malignant potential. A cohort of 3,200 patients with these characteristics has been followed up in England over the last 20 years and it was found - at least in the few years following the atypical findings - that the incidence of breast cancer diagnosis was low ([Freeman et al BMJ 2024;384:e077039](#)). The authors do not recommend surgical excision or annual mammography and call for on-going surveillance.

### Genetic assistance

Is there genetic assistance on the horizon to forecast those at high or low risk of developing breast cancer? The answer is by no means binary but there are situations where knowing the person's genetic profile can be helpful.

**High risk.** Scientists can identify pathogenic germline variants which are known to be associated with high incidences of breast (and other) cancers. Examples are BRCA1, BRCA2, PALB2, ATM, and CHEK2 and these are sought in members of families with a history of malignancies plus any patient with an already diagnosed cancer to find out whether they are at risk of other tumours.

Incidentally, patients presenting with interval breast cancers (those appearing between screening appointments) were found to have a higher probability of these high-risk genetic variants ([Rodriguez et al JAMA Oncol 2024 doi 10.1001/jamaoncol.2023.6287](#)).



In future it looks as though population genetic screening will be cost effective. The modelling is complex but if the cost is below US\$800 there is merit in testing “unselected women” for breast and ovarian cancer predisposition ([Guo et al JAMA Netw Open 2024;7:e2356078](#)).

**Low risk.** It is feasible to select women at low risk of breast cancer by genetic testing. They must not have the high-risk variants mentioned above and have a low polygenic risk score which is a combination of various single-nucleotide variants – a process which is both theoretically feasible and was shown to work “in the field” ([Bloze et al JAMA Oncol 2023 doi 10.1001/jamaoncol.2023.5468](#)). It may be that these women could delay their mammogram screening debut by 5 to 10 years, but this is for future confirmation.

*Editorial comment: Your editor has publicly presented the case against the mammographic screening process. This, he understands is a minority view but it does not stop him following and summarising developments in the literature. It should be noted that this is a personal view and does not necessarily reflect those of the SAMS organisation or its office-bearers.*

*What is presented here are developments in the field which can be incorporated into any decision to embark on, or proceed with, mammographic screening. He hopes these excerpts in Menopause Matters will be helpful in promoting the debate.*

*His view is that*

- *The harms outweigh the benefits at every age*
- *There is no reduction of all-cause mortality (and this has never been claimed)*
- *Prevention by maintaining a normal weight, exercising, and not smoking is essential*
- *Education and self &/or professional examination has produced as good or better outcomes than screening ([Miller et al BMJ 2014;348:g366](#)).*

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

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