MENOPAUSE MATTERS
AUGUST 2025

Screening for colorectal cancers

All people over the age of 40 years should be screened for colorectal cancer (CRC).

While many cancer rates are stable or decreasing, CRCs are becoming increasingly more common and are presenting earlier. This may be due to rising levels of obesity; diets that are too plentiful in ultra-processed foods or red/processed meats; or sedentary lifestyles but it is now clear that CRC screening should begin at 40 and not 50 years (Chiu et al. *JAMA Oncol.* 2025; doi:10.1001/jamaoncol.2025.1433, Galoosian et al. *JAMA.* 2025; doi:10.1001/jama.2025.12049 & Lee et al. *JAMA*. 2025; doi: 10.1001/jama.2025.7494). There was a slight preponderance of females in these trials.

Screening for these malignancies has the advantage that the testing modalities available can detect neoplasia in pre-cancerous lesions, namely sessile polyps or adenomas so serial testing should be considered preventative as well as diagnostic. At least three quarters of the CRC screening mortality benefit comes from polypectomy rather than early cancer detection.

The difficulty with lowering CRC mortality (it is the second highest cause of cancer deaths in the US) is not the efficacy of the screening tests but the lack of testing in the general population with estimates in developed countries of less than half those eligible availing themselves of opportunities. Reasons given for this reluctance are inconvenience, discomfort, embarrassment, fear of complications and costs or an aversion to dealing with faeces.

The two methods of screening which are proven and effective are endoscopy, in the forms of colonoscopy and flexible sigmoidoscopy and serial occult blood stool testing (the "Faecal Immunochemical Test"). The latter has gained traction, in the US at least, by the introduction of postally delivered and returned stool sampling. Either test is efficient, with cost and convenience being the decisive factors. It is trite but true to say that the best test is the one that actually gets done.

The latest cell-free DNA blood-based test has been evaluated and was found to have "acceptable" accuracy (Shaukat et al. *JAMA.* 2025. doi:10.1001/jama.2025.7515). However, it is expensive, currently not widely accepted, and any positive outcomes will require stringent follow up, and its sensitivity to detect early-stage cancer and advanced cancer precursors is questionable. Expert opinion is that offers of cell-free DNA blood tests should only be made to "those who clearly refuse" endoscopic or FIT strategies (Dominitz et al. *JAMA.* 2025; doi:10.1001/jama.2025.7557).

Butter & plant-based oils for health

Research shows that replacing saturated fats, such as butter, with unsaturated fats, like plant-based oils, reduces cardiovascular disease risk. Now a study has found that higher butter intake was associated with increased total and cancer mortality, while higher plant-based oil consumption correlated with reduced mortality from cancer and cardiovascular disease (Zhang et al. *JAMA Intern Med.* 2025; doi:10.1001/jamainternmed.2025.0205).

The findings suggest that substituting butter with plant-based oils like olive, soy, and canola may reduce premature death risk, supporting current dietary guidelines recommending non-hydrogenated vegetable oils over animal fats for better health outcomes.

Even more specifically, an Italian study has investigated the relationship between olive oil consumption and breast cancer risk. Researchers analysed data from 11,000 women and conducted a systematic review of existing literature which showed that higher olive oil consumption (>3 tablespoons daily) was associated with reduced breast cancer risk, particularly for hormone receptor-negative cancers. (Ruggiero et al. *Eur J Cancer*.2025;224.115520).

Editorial opinion. My personal view is that warnings against dairy products are unwarranted. Excess intake may be harmful but that is true of any foodstuff. I consume full cream milk and freely butter my toast. Margarines in no way carry my endorsement.

Referring specifically to meat consumption, the mechanisms of processing meat involve transformation through salting, smoking, or curing — not just cooking on the grill. As far as colon cancer is concerned, the lifetime risk in healthy individuals is 4%. Daily consumption of 50 g of processed meat increases this risk by a relative 18% (WHO), bringing it to about 5% (McKnight. *Medscape*. 2025).

There are data from a selected group of Americans indicating "a lower risk in vegetarians for all cancers combined, as well as for medium-frequency cancers as a group. Specific cancers with evidence of lower risk are breast, colorectal, prostate, stomach, and lymphoproliferative subtypes." (Fraser et al. *Am J Clin Nutrit*. 2025; doi:10.1016/j.ajcnut.2025.06.006

Don't knock eggs

Cardiovascular disease (CVD) remains a leading cause of morbidity and mortality worldwide, with elevated blood cholesterol levels recognised as a major risk factor. This association has led to advice limiting cholesterol **intake** because of its presumed association with increased low density lipoprotein **plasma** levels. However, recent evidence suggests that saturated fat content in foods, rather than cholesterol content, is more closely linked to adverse changes in blood lipid profiles and CVD risk.

To explore whether dietary cholesterol or dietary saturated fats were responsible for raised LDL levels, an Australian study examined the independent effects of dietary cholesterol and saturated fat on LDL concentrations (Carter et al. *Am J Clin Nutrit*. 2025; doi:10.1016/j.ajcnut.2025.05.001). Their conclusion was "Saturated fat, not dietary cholesterol, elevates LDL cholesterol. Compared with consuming a high-saturated fat diet with only 1 egg/wk, consuming 2 eggs daily as part of a low-saturated fat diet lowers LDL concentrations, which may reduce CVD risk."

Recurrent UTI management

Recurrent urinary tract infections are common, and their treatment can be tedious. Resort to repeated urinary cultures and antibiotic therapy often occurs but recent publications suggest both a scientific approach (as in the European Urological Guidelines) and non-antibiotic solutions (Loewy. *Medscape*. 2025). The non-antibiotic approaches include:

Behavioral Changes
Recommendations include drinking at least 1.5 L of water daily, emptying the bladder regularly, maintaining good hygiene, urinating after sexual intercourse, and avoiding spermicides, diaphragms, tampons, tight clothing, and douching.

Cranberries, probiotics, D-mannose and methenamine have their protagonists with pH changes and the prevention of bacterial adhesion to local cells given as their rationale for efficacy.

Estrogens
Vaginal estrogens increase glycogen levels in the vaginal epithelium, which stimulates *lactobacillus* colonisation, lowers pH, and prevents the growth of local uropathogens. A meta-analysis of eight studies involving approximately 5,000 women found that vaginal estrogen significantly reduced recurrent UTIs compared to placebo. Adverse effects, including vaginal discomfort, irritation, and itching, were mild. No benefits were observed with the administration of oral estrogens.

A recent US study of primary care providers reported that the vast majority (more than 90%) are in favour of prescribing vaginal estrogens for recurrent UTIs, which makes it the leading nonantibiotic treatment option in clinical practice.

Hyaluronic Acid/Chondroitin Sulphate. The evidence is stronger for combining hyaluronic acid and chondroitin sulphate than for using either alone.
Phage therapy uses bacteriophage viruses that cause rapid bacterial cell death and alter the microbial population. However, it is used more frequently for treatment, than for prevention.

Estrogens & "Black Box" warnings

In the United States topical vaginal estrogen therapy comes with "Black Box" warnings. These are statutory warnings that declare these products "increase the risk for other cardiovascular disorders, breast cancer, endometrial cancer, and probable dementia" which is incorrect for local applications used for the relief of the Genitourinary Syndrome of Menopause, "in fact, a large body of research has shown that these hormones do not increase these risks" (Manson quoted by Brooks. *Medscape*. 2025).

Such misleading information is harmful to women seeking symptomatic relief from local symptoms and there are strong moves to have the warnings removed, spearheaded by FDA experts and authorities such as Faubion and Manson.

The issue has come under the spotlight following an article from Denmark showing that women who had a previous stroke were not at risk from having a repeat stroke if they used vaginal estrogen therapy (Haddadan et al. *Stroke*.2025; doi:10.1161/STROKEAHA.125.050986). This supports the concept that these products, whether tablets or creams, are safe and effective, even in high-risk situations.

Editorial opinion. I agree with Faubion who is reported as saying that vaginal estrogens are "dramatically under-prescribed" and that clinicians should be discussing vaginal – and urinary – issues with their patients proactively and not waiting passively for these to be volunteered.
More freely available purchasing should the aim all of those involved in decision-making.

Women & Post CABG Surgery

A systematic review analysed survival outcomes after coronary artery bypass grafting (CABG) compared to the population as a whole. The authors examined outcomes for 142,000 patients over 20 years and found both men and women who underwent CABG had worse overall survival expectations than the general population (Kirov et al. *Am J Cardiol*. 2025; doi:10.1016/j.amjcard.2025.06.007).

However, a time-sensitive analysis revealed no survival difference in the first ten years post-surgery. Beyond the first decade survival deteriorated compared to the general population, with men experiencing slightly worse outcomes than women. The authors suggest this late decline may result from graft occlusions. The findings indicate CABG provides comparable life expectancy to the general public for the first decade, but long-term survival advantages diminish over time, especially in men.

The case against menopausal hormone testing

An article from Canada has appeared discussing the problematic trend of routine hormone testing for menopause management (Christakis et al. *BMJ.* 2025; doi:10.1136/bmj.r1695). This has emerged alongside increased demand for menopausal hormone therapy (MHT) in North America.

The authors argue that while cultural awareness of menopause benefits has grown dramatically—with MHT prescribing rising up to 50% in recent years—this has been accompanied by the commercialisation of expensive hormone testing panels costing hundreds of dollars. These tests, often promoted by direct-to-consumer digital health services in the expanding $28 billion "femtech" market, are promoted as necessary for "individualising" hormone therapy.

However, major clinical guidelines agree that menopause should be diagnosed clinically, based on symptoms in women over 45, not through hormone testing. The fluctuating nature of hormone levels during the perimenopause makes such testing unreliable and potentially misleading. Normal hormone levels can lead to underdiagnosis, while abnormal results may prompt inappropriate treatments such as unregulated compounded hormones.(See the SAMS guidelines on unregulated compound MHT https://www.menopause.co.za/wp-content/uploads/2024/09/231020-FINAL-The-South-African-Menopause-Society-SAMS-Statement-on-Compounded-Bioidentical-Menopausal-Hormone-Therapy-18-October-2023.pdf)

The authors advocate a symptom-driven, patient-centred approach to menopause care, emphasising that effective treatment begins with listening to patients rather than relying on commercially driven testing.

Editorial opinion. The need for hormone measurement in the perimenopause is limited and should not be part of standard advice or management – anywhere in the world.

Multiple Sclerosis & MHT

Multiple Sclerosis (MS) is an autoimmune disease that affects the central nervous system with the individual's immune system targeting the myelin of nerve fibers, causing inflammation and scarring. It has a 3:1 female to male predominance and presents in adulthood with symptoms that include fatigue, numbness, tingling, muscle weakness, vision problems, balance and coordination issues, cognitive difficulties, and bladder dysfunction.

There have been encouraging advances in the treatment of episodes of symptoms (Vermersch et al. *NEJM*.2024; doi:10.1056/NEJMoa2309439) and the question of augmenting remissions with hormonal therapy at the time of the perimenopause has been raised previously (Bove et al. *Neurology*. 2016; doi:10.1212/WNL.0000000000003176). Experts in MS management are now debating hormone use again and its ability to add quality of life for their patients (Bosworth. *Medscape*. 2025).

Gynaecological rare cancer treatment

There are rare but aggressive gynaecological cancers of the cervix and ovary. These are clear-cell malignancies that do not respond well to chemotherapy so research in their treatment is of interest.

An Australian group has trialled an immunotherapy combination that appears to offer “encouraging activity with a high rate of durable responses” in patients with advanced tumours of this kind (Goa et al. *JAMA Oncol*. 2025; doi:10.1001/jamaoncol.2025.1916). They used a blockade of nivolumab and ipilimumab "checkpoint inhibitors".

For those who are not familiar with these drugs or their mode of action, the following is a plain English explanation.

Our immune systems are extremely efficient at protecting our bodies from foreign agents, such as bacteria and viruses. When these invade, they are recognised as “non-self” agents and antibodies are produced to destroy them.

Our immune systems have to recognise what is “self” and “non-self”. This is done by control mechanisms that prevent our immune cells from attacking our own healthy tissue. These are called “checkpoints”.

If this mechanism goes awry, it can result in the checkpoints failing to recognise parts of our bodies as “non-self” and attacking “self” giving rise to auto-immune disorders.

There is another way in which problems arise, and that is when malignancies appear.

Cancerous cells are produced as part of cell reproduction but the vast majority of these “variants” are detected by our immune systems as “non-self”. The checkpoints are performing their function, and these malign cells are eradicated before they can go on to multiply in an uncontrolled fashion.

However, some of these malignant cells produce signals which fool our immune systems into **not** attacking them. These are fake signals which prevent the cancer from being recognised as “non-self”. The checkpoints thus malfunction. A way of allowing the immune system to function normally is to **inhibit the checkpoints** in these circumstances.

Nivolumab and ipilimumab are “checkpoint inhibitors”. They block the signals that cancer uses to evade immune cells destroying them. They work by targeting different "brakes" the cancer is applying to the immune system. This is called immunotherapy and essentially gets the immune system back full capacity.

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