Document 6: Menopause after Breast Cancer diagnosis

2025

When a person develops symptoms that may be attributable to menopause/perimenopause there are many well established therapies available. There is no single, best answer when it comes to maintaining wellbeing and improving symptoms in menopause, but the fact remains HRT has been proven most effective for vasomotor symptoms caused by hormonal fluctuations at this transitional time[1]. But what can we suggest for people who have been advised to avoid HRT?

Research on peri menopause/menopause and HRT and their impact on serious medical conditions is staggeringly poor. We are only beginning to see female biological variables being taken into consideration as part of mainstream health research & pharmaceutical studies[2].

On top of that, menopause and its symptoms can be triggered or worsened by the medical interventions for breast & other hormone sensitive cancers. People with female hormone-sensitive cancers may undergo oophorectomy (removal of the ovaries) on medical advice which can cause sometimes very troublesome menopausal symptoms and; if done before 40 years of age, could go on the undermine future health outcomes[3].

Pelvic radiotherapy and certain forms of chemotherapy can cause temporary or even permanent ovarian failure. Anti-endocrine therapies are often recommended for estrogen sensitive malignancies - most commonly but not exclusively, breast cancer. These medicines improve cancer outcomes but (depending on the patient) the side effects and the menopausal symptoms they can trigger disimprove quality of life and often limit compliance with the prescribed therapy[4].

Being diagnosed with cancer when already using HRT may become a problem and oncologists might sometimes advise discontinuation of the HRT leading to a rapid return of menopausal symptoms.

---

[1] *Maclennan AH. Evidence-based review of therapies at the menopause. Int J Evid Based Health. 2009 Jun;7(2):112-23. doi: 10.1111/j.1744-1609.2009.00133. x. PMID: 21631851*

[2] *Yakerson, A. Women in clinical trials: a review of policy development and health equity in the Canadian context. Int J Equity Health 18, 56 (2019)*

[3] *ESHRE guideline group. ESHRE Guideline: management of women with premature ovarian insufficiency. Hum Reprod. 2016 May;31(5):926–37.*

[4] *Meade E, et.al. Survivorship care for postmenopausal breast cancer women in Ireland: What do women want? Eur J Oncol Nurs. 2017 Jun; 28:69–76.*

What can be done? What options do I have?

Logically, if you have had a cancer that had hormone receptors on it you would probably want to avoid putting more of that hormone in your body. The worry is some residual cancer cells may be influenced by the additional hormone and cause the tumour to come back. We do not have high quality medical studies on the pros and cons of HRT use after breast cancer and we probably never will. What we do know for sure is that surgery, radiation, chemotherapy and adjuvant hormone therapies for breast cancer can all have a negative impact on your quality of life and some breast cancer therapies can increase your risk of diseases such as osteoporosis and cardiovascular disease. This all needs to be considered with your oncology team when you are ready for that discussion.

Lifestyle changes may help with menopause symptoms such as mood changes, flushes, sweats, poor sleep etc. We have had some success in symptom reduction with options including: minimising alcohol, cigarettes and incorporating a daily movement regime. There is a growing list of therapies and medications that have been shown to be useful in relieving some of the symptoms of menopause for people who are either on anti- estrogen therapies or who have been advised to avoid standard HRT.

The British Menopause Society offers guidelines on their "Tools for Clinicians" document.

1. CBT- Cognitive behavioural Therapy

Interestingly, it appears that one of the most successful management options with the best range of meno symptoms relief is **Cognitive Behavioural Therapy**- it has been shown to be effective over placebo in helping with vasomotor flushing and sweating, fatigue, weight gain, musculoskeletal (MSK) pain and sexual function[5].

Access to one-to-one, in person CBT can be limited, so some people may be directed to online therapy and/ or smart phone apps to seek relief.

2. SSRI's & SNRI's

These are a class of mood drugs ('Selective Serotonin Reuptake Inhibitors' and 'Serotonin Noradrenaline Reuptake Inhibitors') which appear to help some people with vasomotor symptoms, mood changes and joint aches and pains. While these medications are more typically used for people with disorders of mood such as depression, anxiety, phobia, etc. there are a number of good-sized Randomised Controlled

[5] *Franzoi MA, et al Evidence-based approaches for the management of side-effects of adjuvant endocrine therapy in patients with breast cancer. Lancet Oncol. 2021 July*

Trials (RCT's) that have shown these medications to be effective for menopause relief. One particular brand of SSRI, 'Paroxetine' (7.5 mg at night) has a license from the FDA in the US for the management of moderate to severe vasomotor flushes but most of these drugs are used in an off label or off license capacity* (see below for "off label" discussion)

We are told to avoid this formula of SSRI for people on Tamoxifen so another popular option is the SNRI, 'Venlafaxine'; usually 37.5 mg a day, which is considered safe to take along with Tamoxifen.

There can be side effects from SSRI and SNRI medicines, Nausea, dizziness, fatigue, restless legs, and more have been reported, but they are generally well tolerated in lower doses.

There can be drug interaction problems with these medicines (just like there can be with HRT) so people need to be sure and go through all their other medicines with the prescribing doctor or nurse beforehand if you are interested in trying one of these medications.

SSRI's in general should not be used at all if you are already taking anti-psychosis medicines such as MAOI's (monoamine oxidase inhibitor), thioridazine & pimozide.

Certain SSRI's should be avoided if using tamoxifen because they block the actions of the liver enzyme 'CYP2D6' which is essential for the activation of Tamoxifen. It is considered acceptable to use SSRI's like escitalopram, citalopram and any of the SNRI's with Tamoxifen as they are much less likely to interfere with its estrogen receptor blocking action.

Potent Inhibitors	Moderate Inhibitors	Weak Inhibitors	No Activity CYP2D6
Fluoxetine	Sertraline	Citalopram	Venlafaxine
Paroxetine	Duloxetine	Escitalopram	Desvenlafaxine
Bupropion	Fluvoxetine		Mirtazapine

Kelly CM, Juurlink DN, Gomes T, et al. Selective serotonin reuptake inhibitors and breast cancer mortality in women receiving tamoxifen: a population based cohort study. BMJ.

3. Anticonvulsants/ neurological pain medications such as Pregabalin or Gabapentin may help with vasomotor flushing & joint pain.

4. Antispasmodics, anticholinergic medicines such as Oxybutynin can also help with both vasomotor flushing and urinary issues.

5. Antihistamines with sedating properties may help with sleep disruption.

Other options that have shown benefit include yoga and acupuncture, gently physical activity and exercise and hypnosis[6].

6. New medical therapies designed to reduce vasomotor symptoms (VMS) like flushing and sweating may eventually be approved for use for people with a breast cancer diagnosis.

One of the main causes of VMS appears to be linked to heightened signalling of certain neurotransmitters (particularly neurokinin B & its receptor (neurokinin 3 & 4 receptors) - these affect the autonomic thermoregulatory pathway. A group of drugs known as the NK3/4 receptor antagonists can block NK3/4R related VMS seemingly as effectively as HRT. The Oasis 4 trial is helping to explore one of these NK antagonist drugs. Recently, an NK3R antagonist has been made available in Ireland under the name Veoza. It has not been licensed for use after a breast cancer diagnosis but it may be used off label in those circumstances[7].

In Summary

In our Complex Menopause Clinic at The National Maternity Hospital we aim to offer patients time to discuss the symptoms of menopause. We try to validate the patients' individual experience (as some people sadly seem to have been given little forewarning about possible menopausal symptoms that may result from procedures and treatments for cancers). We explore lifestyle issues and offer support there where we can. We take our patients through the varied non-HRT strategies that could bring them some relief and possibly allow them to improve their Quality of Life. We prescribe where appropriate and review, usually after 3-4 months, to see if there is any improvement - if they are still struggling we try something else.

Some of our patients never really regain their optimal quality of life - some we barely help at all I think - but most patients have expressed a gratitude for having been given a safe space to be listened to, to discuss their symptoms and worries and to be offered treatments wherever we have them.

The BMS has published a detailed guideline on managing menopause symptoms after a diagnosis of breast cancer.

Their main suggestions include:

[6] *Franzoi MA, et al Evidence-based approaches for the management of side-effects of adjuvant endocrine therapy in patients with breast cancer*

[7] *David PS, et al A Clinical Review on Paroxetine and Emerging Therapies for the Treatment of Vasomotor Symptoms. Int J Women's Health. 2022 Mar 10; 14:353-361. doi: 10.2147/IJWH.S282396*

- Patients should be referred to a healthcare professional with expertise in gynaecological endocrinology for counselling about the possible consequences of their breast cancer treatment.

- Ideally, people diagnosed and treated for breast cancer should be encouraged to try non-HRT remedies for both systemic symptoms and genito urinary problems like vaginal dryness.

- If these are ineffective, systemic hormone replacement therapy or low-dose topical (applied into the vagina) estrogen may be considered, but only after taking specialist advice, i.e. from an oncologist or menopause expert.

- Switching breast cancer hormone treatments might also be suitable, but this needs to be discussed with your oncologist.

What about using Local Vaginal Estrogen after Breast cancer?

The BMS suggests offering non-estrogen remedies for the vagina first (there are a multitude of over the counter products that act to moisturise and lubricate the vagina) and if they are not successful we can offer local vaginal estrogen if your oncology team does not have an objection.

Local Vaginal Estrogen is considered to be relatively safe for use after breast cancer diagnosis as there is minimal absorption of the estrogen hormone form the vaginal wall into the blood stream. It can relieve many of the genitourinary symptoms that can affect menopausal patients such as vaginal dryness, painful intercourse, passing urine too often or at night, leaking urine and more.

No evidence of breast cancer spread or recurrence has ever been liked to local vaginal estrogen use. Be aware though that all local vaginal estrogen preparations will say “do not use after breast cancer” on their product information leaflets.

The only caveat about local vaginal estrogen products is for women using an aromatase inhibitor medication. A small study from 2006 suggested an increase in the level of estrogen in the blood in some women using both an Aromatasc Inhibitors (AI) and vaginal estrogen products. Another publication in 2022 also raises a concern about the small absorption of intravaginal estrogen into the blood for people on AI therapy and what they might mean for their recovery. For this reason, the BMS usually advise that you switch from an AI to tamoxifen (if that is feasible) as it may have less of a negative impact on the vagina and pelvic structures and if you are still symptomatic we can add in some local estrogen at that point. But in practice very few breast oncologists would object to the use of local vaginal estrogen for their patients on an AI and using them both together is usually not a problem.

What about using Testosterone after Breast Cancer?

This is another area where we have lots of questions and very few answers.

Testosterone and other androgens are produced naturally by the ovaries and are an important group of sex hormones for females. In Perimenopause and Menopause, the loss of circulating androgens can result in a decline in sex drive for some people (particularly for people who experience menopause when very young). Offering testosterone replacement medicine has become an accepted part of HRT therapies. It is only indicated for the treatment of low desire and has not been shown to benefit other menopause symptoms[8].

Unfortunately, some breast cancer cells do have androgen (male hormone) receptors on them - they are rarely tested for though. So it is unclear what if any impact using testosterone might have on your future breast cancer risk. Studies have indicated that people diagnosed with ER negative or triple negative breast cancer are more likely to have had androgen receptors on the cancer cells but what this might mean for people who choose to try testosterone HRT we do not know.

We do sometimes prescribe off label testosterone for people with a breast cancer diagnosis but we do so with the understanding that this is not first line. All other options should have been discussed and at least considered first. But as with everything else in menopause care after breast cancer, each person is an individual and no absolutes apply.

* What is off-label or off-license prescribing?

Off-label prescribing is when a doctor or nurse uses an authorised medicinal product (a "licensed drug") outside the terms of its marketing authorisation (MA) license. Meaning, the medicine is approved and licensed but NOT for the condition we trying it for.

The Irish Medical Council allows doctors to prescribe off- label but the UK's General Medical Council goes further and says we should only prescribe licensed medicines outside the terms of the license if:

A. We believe it would better serve our patient's needs better than an appropriately licensed alternative

B. We are satisfied that there is a sufficient evidence base and/or experience of using the medicine to demonstrate its safety and efficacy

C. We can take responsibility for prescribing the medicine and for overseeing the patient's care, monitoring and any follow up treatment

D. We explain the situation to our patient, why we are suggesting this medicine for their conditions and how to take it correctly.

[8] *Climacteric global consensus position statement on the benefits of testosterone therapy for women www.doi.org/10.1080 and 2. BMS recommendations on HRT 2016*