Menopause and menopausal symptoms

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Menopause
Assessment of the woman algorithm

**Aim:** To identify which assessments are required when a woman presents at the menopause clinic.

### Assessment required at the presentation of the midlife woman

#### Medical history

**Relevant gynaecological facts**
- Bleeding pattern or LMP
- Past surgery (hysterectomy / oophorectomy)
- Current use of hormonal therapy including contraception

**Personal medical issues**
- DVT / PE
- Cancer
  - Type
  - Treatment details
- Cardio / cerebrovascular disease
- Hypertension
- Liver disease
- Osteoporosis / fractures
- Diabetes
- Thyroid disease
- Depression / anxiety / PND
- Recurrent UTI's

**Family history**
- DVT / PE
- Cancer
- Cardio / cerebrovascular disease
- Osteoporosis

**Other**
- Social history
- Current medications (+OTC)
- Smoking
- Alcohol
- Diet
- Exercise
- Allergies

#### Examination

- Height and weight
- Blood pressure
- Breast examination
- Pelvic examination if clinically indicated

#### Investigations required for Menopause Clinic appointment

- FBP and Iron studies
- Lipid profile
- Fasting glucose
- TSH
- U&E, LFT
- Vit D in at-risk women
- Recent MMG (in last 2 years)
- Completed recent cervical screening (CST)

*Note: Female hormone profile not routinely required but is essential if Premature Ovarian Insufficiency (POI) is suspected in women <40 years*

#### Abbreviations:
- CST: Cervical screening test
- DVT: Deep venous thrombosis
- FBP: Full blood picture
- LFT: Liver function tests
- LMP: Last menstrual period
- MMG: Mammogram
- OTC: Over the counter
- PE: Pulmonary embolus
- PND: Postnatal depression
- TSH: Thyroid stimulating hormone
- U&E: Urea & electrolytes
- UTI: Urinary tract infection
Considerations

What to consider

Pre-menopause

Peri-menopause +
early menopause

Post-menopause <60 years
or
Within 10 years since LMP

- General health / disease management
- Lifestyle issues – Smoking, Nutrition, Alcohol, Physical activity, Mental health
- Health concerns
- Family history

Contraceptive needs

Management of
- Menopausal symptoms
- Prevention of osteoporosis
- Genito-urinary syndrome of menopause
- Sexual health concerns
Menopause symptom management

Identify and treat the main issues

**Concerns, no symptoms**
- MHT
- Advice / information on lifestyle
  - Smoking
  - Nutrition
  - Alcohol
  - Physical activity
  - Mental health

**Moderate / severe symptoms**
- Non-hormonal options
- Pharmacological options
  - E+P if uterus
  - E if no uterus
  - Synthetic hormone receptor modulators (e.g. Duavive, Tibolone)
- SSRI / SNRI
- Gabapentin
- Ditropan
- Clonidine

**Genito-urinary symptoms**
- Exclude infection / dermatological cause
- Vaginal E therapy
  - Estriol cream / pessary
  - 17β estradiol vaginal tablet
- Vaginal non - E therapy
  - Lubricants
  - Moisturisers
  - Pelvic floor physiotherapy

**Sexual health concerns**
- Consider bio / psycho / social factors
  - Specific sexual counselling
  - Androgens – considered in Hypoactive Sexual Desire Disorder (HSDD)

**Notes**
- There has recently been supply concerns with many forms of MHT, if required refer to Australasian Menopause Society (AMS): Information Sheets: AMS Guide to Equivalent MHT/HRT Doses Australia only (external website, PDF, 119KB)

**Abbreviations**
- CBT: Cognitive behavioural therapy
- E: Estrogen
- MHT: Menopausal hormone therapy
- P: Progestogen
- SSRI: Selective serotonin reuptake inhibitor
- SNRI: Serotonin–noradrenaline reuptake inhibitor

- Duavive- Tissue selective estrogen complex (TSEC)
- Tibolone- Synthetic steroid with estrogenic, progestogenic and androgenic activity
Peri-menopausal hormone treatment

**PERI-MENOPAUSAL TREATMENT OPTIONS WITH INTACT UTERUS**

- **E+P contraception**
  - Review contraindications
  - Controls PMS / mastalgia/ bleeding
  - Low dose and 17βE preferred

- **Oral or Transdermal E + LNG-IUD**
  - May eliminate bleeding but not cyclical symptoms

- **Continuous E and cyclical P**
  - Irregular bleeding may occur
  - Cyclical symptoms

**Abbreviations:**
- E: Estrogen
- LNG-IUD: Levonorgestrol intrauterine device
- P: Progestogen
- PMS: Pre-menstrual syndrome
Menopausal hormone therapy (MHT)

Uterus intact

A. Combined transdermal patch (E+P)
B. Transdermal (E) patch or gel + Oral P or LNG-IUD
C. Oral E + Oral P or LNG-IUD
D. Synthetic hormone receptor modulators (e.g. Duavive, Tibolone) after 12 months of amenorrhoea

Post-hysterectomy

A. Transdermal E patch or gel
B. Oral E
C. Synthetic hormone receptor modulators (e.g. Tibolone).
N.B. Not Duavive

- Micronised oral progesterone is now available in Australia
- Consider the addition of progestogen for women with a history of deep infiltrating endometriosis

Caution with initiating MHT
- Women > 60 years of age
- >10 years since LMP

Contraindications to MHT *
- Estrogen-dependent cancer
- High risk of DVT / VTE or known thrombophilia
- Undiagnosed vaginal bleeding
- Active liver disease
- Untreated hypertension
- IHD / CVD
- Personal wish not to use hormones

* May be considered following discussion with treating specialist

Abbreviations:
- E: Estrogen
- CVA: Cerebral Vascular Disease
- DVT: Deep vein thrombosis
- IHD: Ischaemic Heart Disease
- LMP: Last menstrual period
- LNG-IUD: Levonorgestrel intrauterine device
- P: Progestogen
- VTE: Venous thromboembolism
Menopause: Review of treatment

**REVIEW OF TREATMENT**

- Non-hormonal therapy
- Menopause hormone therapy
- Vaginal therapy

8-12 weeks

- Symptom relief
  - Review 6 months
    - Symptom relief
      - 6-12 monthly review
      - Discuss ongoing risk / benefit to individual
  - No symptom relief OR Side effects
    - Change dose or therapy
      - Review 6-8 weeks
- No symptom relief OR Side effects
  - Change dose or therapy
    - Review 6-8 weeks

Menopausal symptoms after cancer

Aim
- To guide menopausal symptom management after cancer, including hot flushes, vaginal dryness, sexual dysfunction and bone loss.

Hot flushes
The pathophysiology of hot flushes is poorly understood but may be linked to the instability of the hypothalamic thermoregulatory centre induced by estrogen withdrawal. Low circulating levels of estrogen are not directly related to hot flushes but estrogen may control thermoregulation via serotonin receptors.

Options for medication

Key points
1. The management of menopausal symptoms after breast cancer is best managed with a multidisciplinary approach.
3. Hormone therapy for women with a gynaecological cancer may be considered following advice from the treating Gynaecologic or Medical Oncologist

Indications for treatment
The treatment of menopausal symptoms following cancer should be based on:
- the severity of the symptoms and their impact on quality of life
- evidence for safety following cancer (if available)
Hormonal medications

1. Menopausal hormone therapy (MHT) (previously known as hormone replacement therapy (HRT))

Menopausal hormone therapy containing estrogen is the most effective treatment for menopausal symptoms in healthy women. The evidence suggests that MHT improves vasomotor symptoms, vaginal dryness and reduces the risk of fractures. Unless hysterectomy has been performed, estrogen should be given in combination with progesterone to prevent an increased risk of endometrial hyperplasia or cancer. In postmenopausal women, long-term use (greater than five years) of combined MHT (estrogen and progestogen) appears to increase the risk of breast cancer.

For more information about risk, see also

- Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results From the Women's Health Initiative randomized controlled trial (JAMA)
- Type and timing of menopausal hormone therapy and breast cancer risk: individual participant meta-analysis of the worldwide epidemiological evidence (Lancet)
- Breast cancer risk in relation to different types of hormone replacement therapy in the E3N-EPIC cohort (Fournier et al)

Both estrogen only and combined MHT increase mammographic density, potentially reducing the efficacy of mammogram in detecting breast cancer and increasing the number of false positive recalls. This effect is more pronounced with combined compared to estrogen only MHT.

Previous history of breast cancer and MHT

In women with a history of breast cancer, taking MHT appears to increase the risk of recurrence or development of new breast cancers with a relative risk of 3.4. There is a lack of high quality research because of difficulty in recruiting for randomised controlled trials of MHT versus placebo.

The largest randomised control trial to address this question showed that, after a median follow up of 2.1 years, 14.9% of MHT users and 4.09% taking placebo had either a recurrence or development of a new breast cancer.

Note:

It is not known whether the type or regimen of MHT and the estrogen/progesterone receptor status of the breast cancer have implications for the safety of use of MHT. Similarly, very little is known about the interaction between MHT and endocrine therapy for breast cancer. However, since endocrine therapy is essentially anti-estrogen, it is certainly possible that MHT may undermine the effects of endocrine therapy.
Recommendations for practice

- MHT should not be used as first line management for menopausal symptoms following breast cancer.
- Use of MHT may be justified to improve quality of life reasons when all other interventions have failed and the woman is clearly informed of the potential increased recurrence risk.
- MHT may be considered for women with metastatic disease where attainment of quality of life overrides all.
- MHT may be considered after some gynaecological cancers following discussion with Gynaecological or Medical Oncologist.
- For further information regarding products, dosing and administration, refer to [KEMH Adult Medication Monograph: Estrogen (Oestrogen) MRT](#).

2. Progestogens

High doses of progestogens have been used to treat advanced breast cancer. Progestogens at lower doses are effective in reducing menopausal hot flushes, but are not as effective as estrogen or estrogen and progestogen in combination. A small study (2006) suggests that one dose of depomedroxyprogesterone acetate (DMPA) may also be effective.

The safety of progestogens for the treatment of menopausal symptoms following breast cancer is not known.

Recommendations for practice

- Progestogens are not recommended for the treatment of vasomotor symptoms as safety is uncertain and efficacy is likely to be less than that of estrogen and progestogen in combination, or estrogen alone.

3. Synthetic hormone receptor modulators

Tibolone (Livial®) is a synthetic compound with weak estrogenic, progestogenic and androgenic properties. There have been no large studies assessing the impact of tibolone on the risk of breast cancer in healthy women. Tibolone does not appear to:

- stimulate breast cells in vivo
- increase mammographic density or increase the false positive recall rate for mammograms.

Tibolone has an unfavourable effect on serum cholesterol by reducing HDL cholesterol. While it has been known to improve bone density, its effect on fracture reduction is yet to be confirmed.
The researchers from the LIBERATE Trial (Organon) 2008, conclude “Tibolone increases the risk of recurrence in breast cancer patients, while relieving vasomotor symptoms and preventing bone loss”. Therefore the use of Tibolone for women with a known, past or suspected breast cancer will remain contraindicated.

4. Testosterone / androgen therapy
Testosterone may exert biological effects by acting directly on the androgen receptors or indirectly through conversion to estrogen by the aromatase enzyme. This mechanism is blocked by aromatase inhibitors. Levels of testosterone reduce gradually throughout adult life. Early or surgical menopause may be associated with a greater reduction in testosterone and its effects.

The Endocrine Society’s Clinical Guidelines recommend against making a diagnosis of androgen deficiency in women at this time because there is neither a well-defined clinical syndrome nor normative data on testosterone or free testosterone levels in women across their lifespan that can be used to define the disorder. The safety or efficacy of testosterone supplementation following breast cancer is not known.

Recommendations for practice
- The generalised use of testosterone by women after breast cancer is NOT recommended because the indications are inadequate and evidence of safety in long term studies is lacking.
Non-hormonal medications

1. Gabapentin
   See
   - Pharmacy Medication Monograph Gabapentin
   - Consumer brochure Menopausal Symptoms - Gabapentin

2. Selective Serotonin / Noradrenaline Re-Uptake Inhibitors (SSRI / SNRI)
   See
   - Pharmacy Medication Monographs
   - Consumer brochure Menopausal Symptoms - Antidepressants

3. Clonidine
   See
   - Pharmacy Medication Monograph: Clonidine
   - Consumer brochure Menopausal Symptoms - Clonidine

Oxybutynin
   See
   - Consumer brochure Menopausal Symptoms - Oxybutynin

Non-hormonal medications
Most studies have only shown efficacy for 4-12 weeks durations. This is limited by the duration of the studies themselves. Benefits are often seen for longer periods of time, but response is an individual one.

What is the appropriate length of therapy?
Non-hormonal treatments for hot flushes appear to be effective in 1 to 2 weeks. If no clinical response is seen over this period treatment approaches should be modified. The mean duration of hot flushes is around 5 years for spontaneous menopause.8 It is not known whether hot flushes after cancer treatment have a similar duration.

Patient information
See above
Summary of management for hot flushes after cancer

**MANAGEMENT OF HOT FLUSHES AND NIGHT SWEATS AFTER CANCER**

- Assess the severity and impact of symptoms
- Educate the woman
- Provide evidence-based information

**Lifestyle changes**
- Weight loss
- Dress in layers
- Stop smoking
- Reduce alcohol/caffeine
- Avoid spicy food
- Encourage exercise

**Behavioural therapies**
- Cognitive Behavioural Therapy
- Mindfulness therapy

**Complementary therapies**
- Hypnosis
- Yoga
- Acupuncture

**Prescribed non-hormonal medications**
- Clonidine (0.05 -0.15mg/day)
- Venlafaxine XR (37.5-75mg/day)
- Desvenlafaxine (100-150mg/day)
- Escitalopram (10-20mg/day)
- Gabapentin (300-900mg/day)
- Ditropan (2.5-10mg/day)

*See options for medication

**MHT -**
If deemed safe by the treating specialist/ oncologist

- Emerging evidence of reducing distress related to symptoms and improved sleep quality

The above medications can be considered for moderate to severe symptoms following a diagnosis of cancer.

Avoid Paroxetine in women taking Tamoxifen

Emerging evidence of reducing distress related to symptoms and improved sleep quality

Not evidence based BUT unlikely to be harmful and may assist symptoms
Vaginal dryness

1. Vaginal lubricants

Vaginal lubricants are designed for use during sexual intercourse. Examples of these include Astroglide® or silicone-based lubricants such as Pjur®.

2. Vaginal moisturisers

- Vaginal moisturisers are developed to provide relief from the symptoms of vaginal atrophy such as dryness, itching and irritation and dyspareunia.
- Replens® is a long-lasting, hormone free vaginal moisturiser that is applied internally three times a week. Replens® is available at community pharmacies without a prescription in packs of 10.
- Aci-Jel Restore® is a similar product
- Women who do not achieve relief with Replens may consider hormone-free, paraben-free hyaluronic acid gel (Hyalofemme®). Hyalofemme® is a Special Access Scheme (SAS) Category B medication, that requires a prescription and an SAS Category B form to be completed before supply can be obtained.
- A compounded preservative free hyaluronic acid product is also available under special circumstances. The compounded product takes approximately a week to order and has an expiry of only one month. A prescription and an Individual Patient Application (IPA) form must be completed before supply of the compounded product can be obtained.

3. Vaginal estrogen

Evidence suggests that topical estrogen effectively alleviates vaginal dryness and reduces dyspareunia. As topical estrogen does not appear to stimulate the endometrium, additional progestogens are not required.

Although short term use of topical estrogen has not been shown to be associated with increased risk of breast cancer recurrence, recent data suggests that for women on aromatase inhibitors serum estradiol rises. This effect reverses the estrogen suppression achieved by aromatase inhibitors and may partially negate the benefit of aromatase inhibitors. For more information regarding products, dosing and administration, refer to KEMH Adult Medication Monograph: Estrogen (Oestrogen)- Vaginal

Recommendations for practice

- Topical estrogens in the form of estriol (e.g. Ovestin) may be used following treatment for breast cancer in women who are prescribed Tamoxifen.
• Women using aromatase inhibitors should be advised that vaginal estrogen may impact on the efficacy of their endocrine therapy.8
• Topical estrogen is not necessarily contraindicated following a gynaecological malignancy. Discuss with treating Gynaecologic Oncologist / Oncologist.

Sexual dysfunction

Sexual dysfunction is commonly associated with menopause and cancer. After menopause, vaginal dryness, lack of arousal, dyspareunia and difficulty with orgasm are common. Women who have had treatment for cancer may have issues with body image, health concerns and fatigue. These factors and others can affect libido and sexual satisfaction.

As part of the routine assessment obtain:
• Sexual history and any relevant issues
• All potential physical, psychological and social factors.

Non-medical interventions

• More time for oral/manual stimulation
• Increased communication between partners
• Sensual massage/warm bath
• Change of sexual routine
• Read appropriate literature e.g. Dr Rosie King’s “Good Loving, Great Sex”

Recommendations for practice

• Consider referral to psychological medicine services, such as Breast Cancer Clinical Psychology Services (RPH, FSH, SCGH), WA Psycho-Oncology Service (WAPOS) or a Sex / Relationship Counsellor for further intervention.
• Note: The use of testosterone / Viagra for sexual dysfunction following treatment for breast cancer is not supported by the evidence therefore is NOT recommended.

Useful links

 Refer to Australasian Menopause Society (AMS): Information Sheets (external website):
• Genito-urinary syndrome of menopause (external website)
• Vaginal health after breast cancer: A guide for patients (external website)
Bone loss

Recommendations for practice

Consider bone densitometry (DEXA) in women:

- Following treatment for cancer with chemotherapy, ovarian suppression (or removal), Tamoxifen or Aromatase inhibitors
- With a personal or family history of osteoporosis
- With other risk factors for osteoporosis, such as POI, low BMI, smokers, malabsorption syndromes, certain anti-epileptic medications and corticosteroid or GnRH agonist use.

Provide the woman with information regarding:

- Calcium intake
  - Recommended daily intake of 1200mg / day. For further information see also Healthy Bones Australia (external website)
  - May require supplements if unable to have adequate dietary intake of calcium
- Adequate Vitamin D
  - Ensure adequate safe sunlight
  - May require supplementation
  - For further information, see KEMH Adult Medication Monograph: Colecalciferol (Cholecalciferol)
- Weight bearing exercises
  - Regular walking
  - Resistance / weights training
- Avoid smoking and excessive caffeine and alcohol consumption.
**Bone loss flowchart**

**MANAGEMENT OF BONE HEALTH IN WOMEN WITH BREAST CANCER**

**Risk stratification**

- Identify osteoporosis risk factors
- Assessment of hip and spine BMD by DEXA
- Exclude secondary causes of bone loss
- X-ray screen for vertebral fractures
- Falls risk assessment

**Lifestyle approaches**

- Optimise calcium intake 1200mg/day
- Adequate Vitamin D >50nmol/l
- Exercise 3 hrs/week
- Avoid excess alcohol
- Stop smoking

**Initiate antiresorptive therapy or endocrinology referral**

**Pre-menopausal women**
- Z-score < -2.0
- Z-score < -1.0 and 5-10% decrease in BMD in 1 year
- Prevalent fragility fracture

**Post menopausal women**
- T-score < -2.0
- T score < -1.0 with 2 or more osteoporotic risk factors present*
- Decrease of 5-10% in BMD in 1 year

*Risk factors and aromatase inhibitor treatment: Age >65, BMI <20, T-score < -1.5, FH of hip fracture, personal history of minimal trauma fracture after age 50, oral steroid use > 6 months, current or ex-smoker


**Abbreviations:**
- BMD: Bone mineral density
- BMI: Body mass index
- DEXA: Dual-energy X-ray absorptiometry
- FH: Family history
References


Bibliography


Jane F, Davis S. A practitioner’s toolkit for managing the menopause. Climacteric, 2014;17:1-16.


Related WNHS guidelines

Perioperative Services: Day Surgery Unit: Stellate Ganglion Block for menopausal symptoms
KEMH Pharmacy Medication Monographs

Resources

- Individual Patient Application (IPA) form

Keywords: Menopause symptoms, hot flushes, bone loss, menopause after cancer, menopause, menopausal symptoms, Menopause medication, complementary therapy for menopause, MHT, menopausal hormone therapy, HRT, hormone replacement therapy

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| 1              | April 2018 | First version.  
**History:** In April 2018 amalgamated 6 individual guidelines relating to menopause and menopausal symptoms after cancer (from section B – Gynaecology dated from June 2007) into one document:  
1. Menopause: Assessment Algorithm  
2. Hormonal Treatment  
3. Review of Treatment  
4. Symptom Management  
5. Menopause Symptoms After Cancer (Breast): Management  
6. MSAC Medication Options |
| 1.1            | Sept 2018  | Hyperlinks fixed and minor wording change- Replens |
| 2              | Oct 2021   | • Reviewed newer evidence. Condensed content about non-hormonal medications, instead links to consumer information  
• Menopausal hormone therapy (MHT) replaces term 'HRT'  
• Menopause symptom management flowchart updated- with non-pharmacological options  
• Added synthetic hormone receptor modulator  
• Menopause- Review time period changed to 8-12 weeks  
• Broader scope to be inclusive of several cancers  
• Links to more information added for MHT breast cancer risk |

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