Menopause Management
Case history

The case of the perimenopausal woman

Dr Lucy Williams
Gynaecologist/Fertility Specialist

Case history

Ms J.F. DOB 25/2/1980.

She reports her periods are getting much heavier and cycles are erratic. She says she is not feeling herself, irritable and snapping at the kids.

She is also not sleeping well and intermittently waking with hot sweats.

Case history: Ms J.F. DOB 25/2/1980

What would you like to know?

What would you like to know?

Cycles: In the past few years cycles have been changing, in last 6-12m can skip a cycle, flow can be very heavy, lasts up to 10 days

Menopause symptoms: most intense in the week before menses

PMH: Migraine headaches in 20's, advised never to use COCP

Contraception: Mini pill

P3: All vaginal del. at term; 10, 7 and 6 years old.

FH: Breast cancer in maternal aunt.

LS: Non-smoker, drinks within safe guidelines. Overweight and gaining!

SH: Married. Works part-time in HR.

Menopause symptoms

Hot flushes and sweats

Brain Fog

Vaginal dryness
Sex dysfunction

Poor sleep

Low mood anxiety

Increasing PMT

Urinary symptoms

Menstrual changes

Learning point

- Characteristic menopausal symptoms can pre-date the final menstrual period by months to years.

Case history: Ms J.F. DOB 25/2/1980

What are you thinking?

What are your next steps?

Breast cancer and MHT

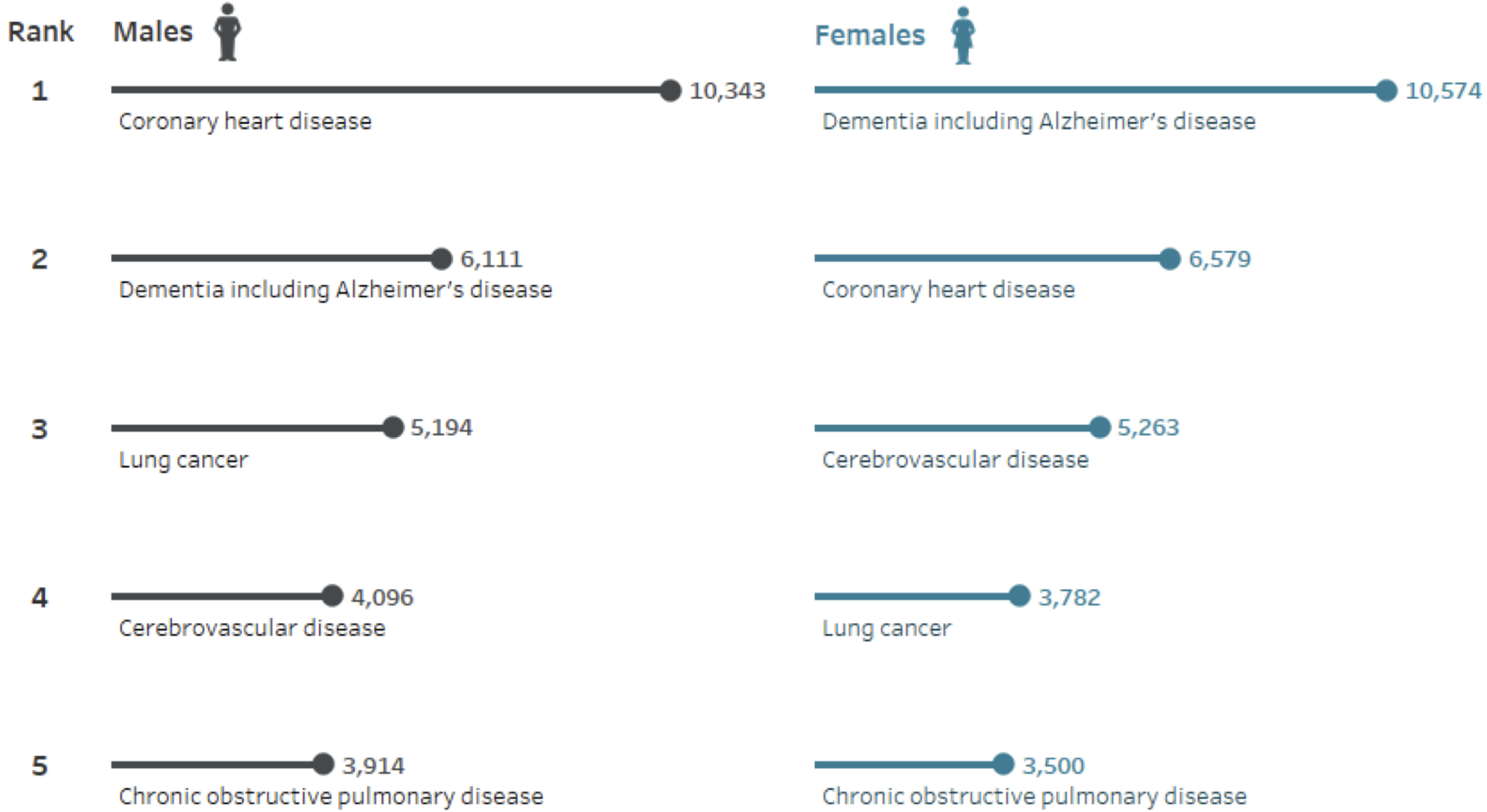
MHT is not advised for women who have had Breast Cancer

- includes hormone receptor positive and negative types

For women who have no history of Breast Cancer

- WHI 50-59 y.o. analysis
  - CEE + MPA – No increased risk
  - CEE only - **Lower** breast cancer risk
- E3N Cohort study - Progesterone type important
  - E2 + micronised progesterone (Prometrium) - No increase in breast cancer
- Educate on modifiable risk factors – alcohol intake, obesity, exercise

Figure 1: Leading underlying causes of death in Australia, by sex, 2023

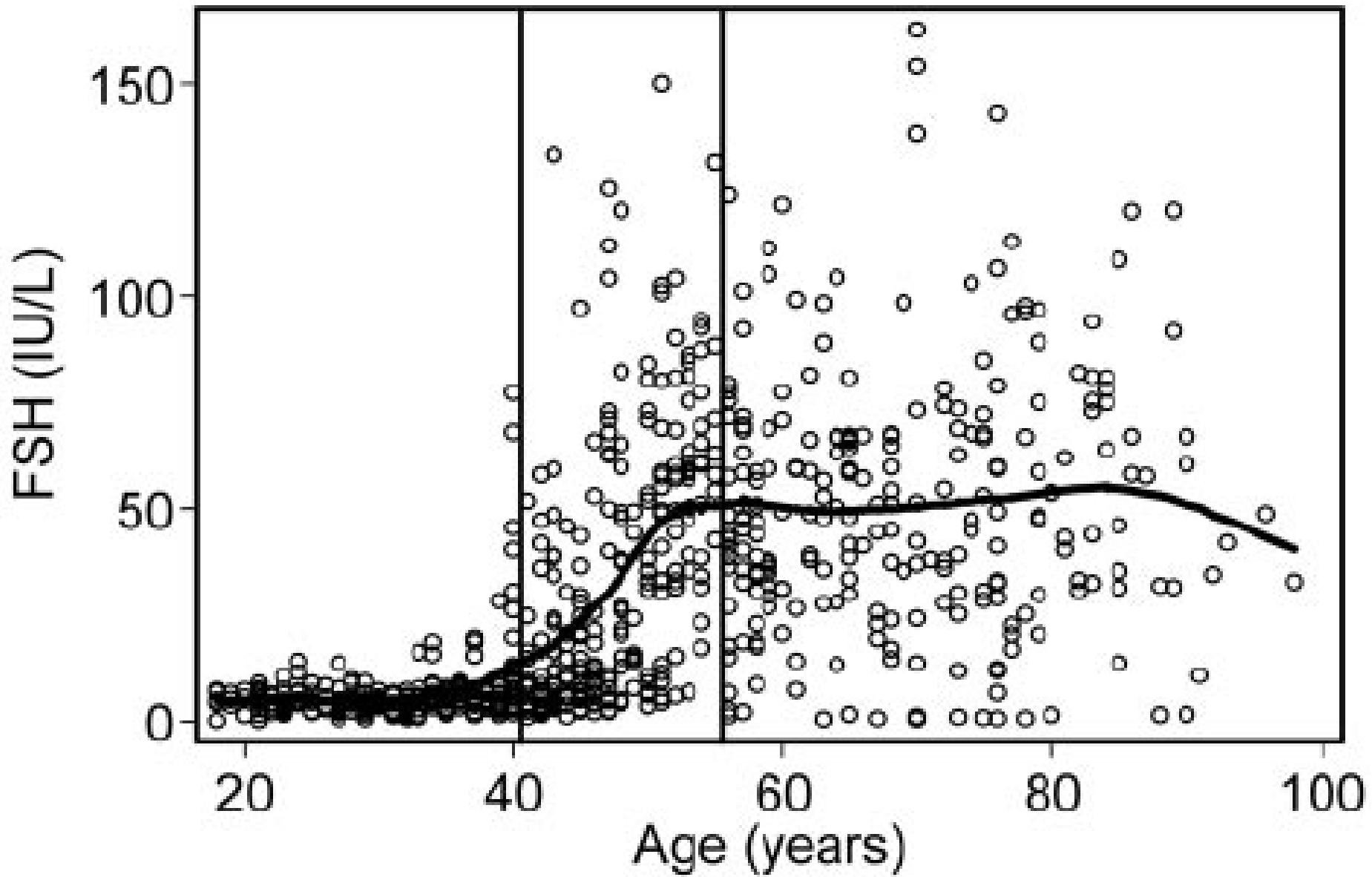


Source: AIHW National Mortality Database; Table S3.1.
https://www.aihw.gov.au

Migraine and MHT

- Migraine with aura is a risk factor for stroke
- Women with history of aura should not use oral oestrogens
- Transdermal oestrogens are safe in women who have migraine even with aura – use lowest effective dose
- Cyclic formulations more prone to trigger migraines – aim to use continuous delivery of both progesterones and oestrogens

Why it is not helpful to measure hormones



Learning points

- Characteristic menopausal symptoms can pre-date the final menstrual period by months to years
- If there is no personal history of Breast Cancer, for most women with menopause symptoms the benefits of MHT outweigh risks
- For women with migraines chose non-oral oestrogen delivery in MHT
- Hormone tests are not usually helpful in diagnosis of menopause

What are your next steps?

- Question about bone health – calcium intake, weight bearing exercise, other risk factors – FHx, malabsorption, weight loss
- Ask targeted questions about sexual function
- Does she have CVD, CVA risk factors
- Clinical examination: pelvis – include CST if not up to date; breast exam
- Check blood pressure, height and weight.

Tests

- Pelvic ultrasound
- Blood tests – iron, FBP, TFT's, (Vitamin D), lipids and cholesterol, HbA1c
- MMG, BMD (baseline)

Bone health (do not underestimate osteoporosis)

- Calcium intake met by 3-5 serves dairy/d (one serve = 200ml milk)
- Weight bearing exercise or walking on uneven ground 30 min 5 days/w
- Healthybonesaustralia.org.au

Sexual function

- Vaginal dryness common – silicone-based lubricants, vaginal oestrogens; Low libido also common – start by addressing comfort
- Think of BV, candida, vulval dermatitis, lichen sclerosus

Bone health (do not underestimate osteoporosis)

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Heart disease and MHT

E2 started around time of menopause likely cardioprotective

WHI CEE/MPA RCT – Full cohort trend to increase in cardiovascular disease BUT

WHI CEE/MPA RCT < 60 years - absolute and attributable risks were lower

WHI CEE only RCT < 60 years - **decrease** in coronary events

WHI long-term follow up CEE/MPA and CEE - no change in CVD mortality

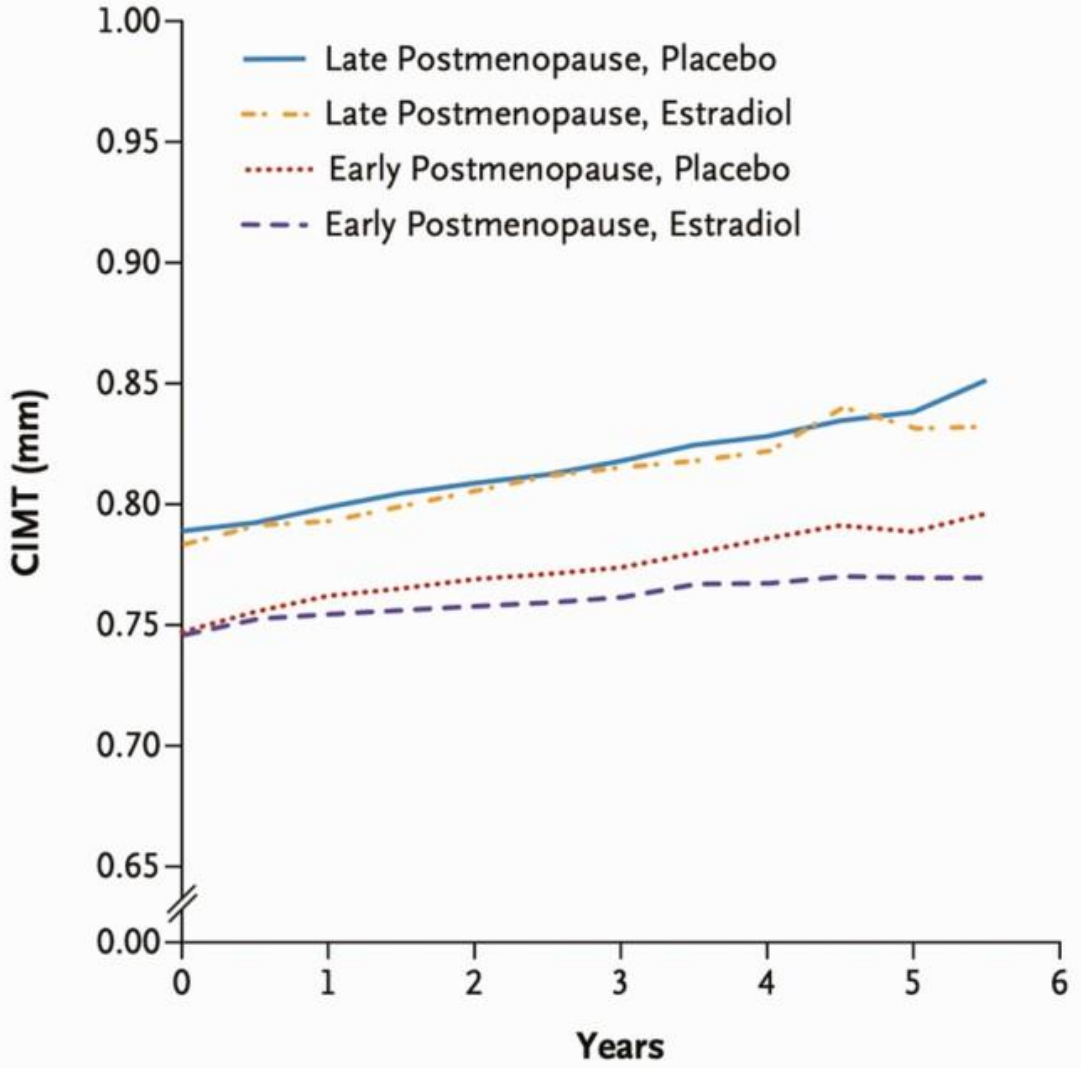
Finnish observational study (489,105 women 1994-2009)

- Users of any HRT >10 years had lower mortality /1000 women - 19 fewer coronary heart disease deaths, 7 fewer stroke related deaths

Cochrane analysis: any HRT started < 60 yo or < 10 yrs FMP

- Reduction in atherosclerosis progression, coronary heart disease, cardiovascular mortality, all-cause mortality.

Lower coronary artery disease risk with early initiation of MHT



No. of Participants							
With CIMT data	643	533	522	515	424	295	56
Who completed or discontinued study	0	106	119	128	215	345	582
Without CIMT data	0	4	2	0	4	3	5

Case history: Ms J.F. DOB 25/2/1980

- Some vaginal dryness, uses OTC lube
- Clinical examination – BP 120/80mmHg; Height 164cm, weight 76kg, BMI 28.3kg/m2; Vulva healthy, pelvis – bulky uterus, else normal, no abnormal discharge; breast exam NAD

Tests

- Pelvic ultrasound: 2 intramural fibroids 2cm & 3cm, endometrium 6mm, no polyp; no adnexal abnormality
- Blood tests: Ferritin 28; FBP, TSH 3.4, Cholesterol 5.7, HbA1C 5.6%
- MMG (Breast screen): Normal but increased density – advised ultrasound – now also completed - NAD
- BMD: mild osteopenia

Learning points

- Characteristic menopausal symptoms can pre-date the final menstrual period by months to years
- If no personal history of Breast Cancer for most women benefits of MHT outweigh risks
- For women with migraines chose non-oral oestrogen delivery in MHT
- Hormone tests are not usually helpful in diagnosis of menopause
- Make direct enquiries about sexual function
- Take every opportunity to educate about and optimise bone and cardiovascular health and other long-term health risks

Case history: Ms J.F. DOB 25/2/1980

What do you advise now?

Choice of MHT

- Take into consideration need to manage menstrual bleeding
- Need for contraception
- Transdermal oestrogens (Ideally for all but in particular with migraine and VTE risks)

MHT is highly effective for Vasomotor symptoms

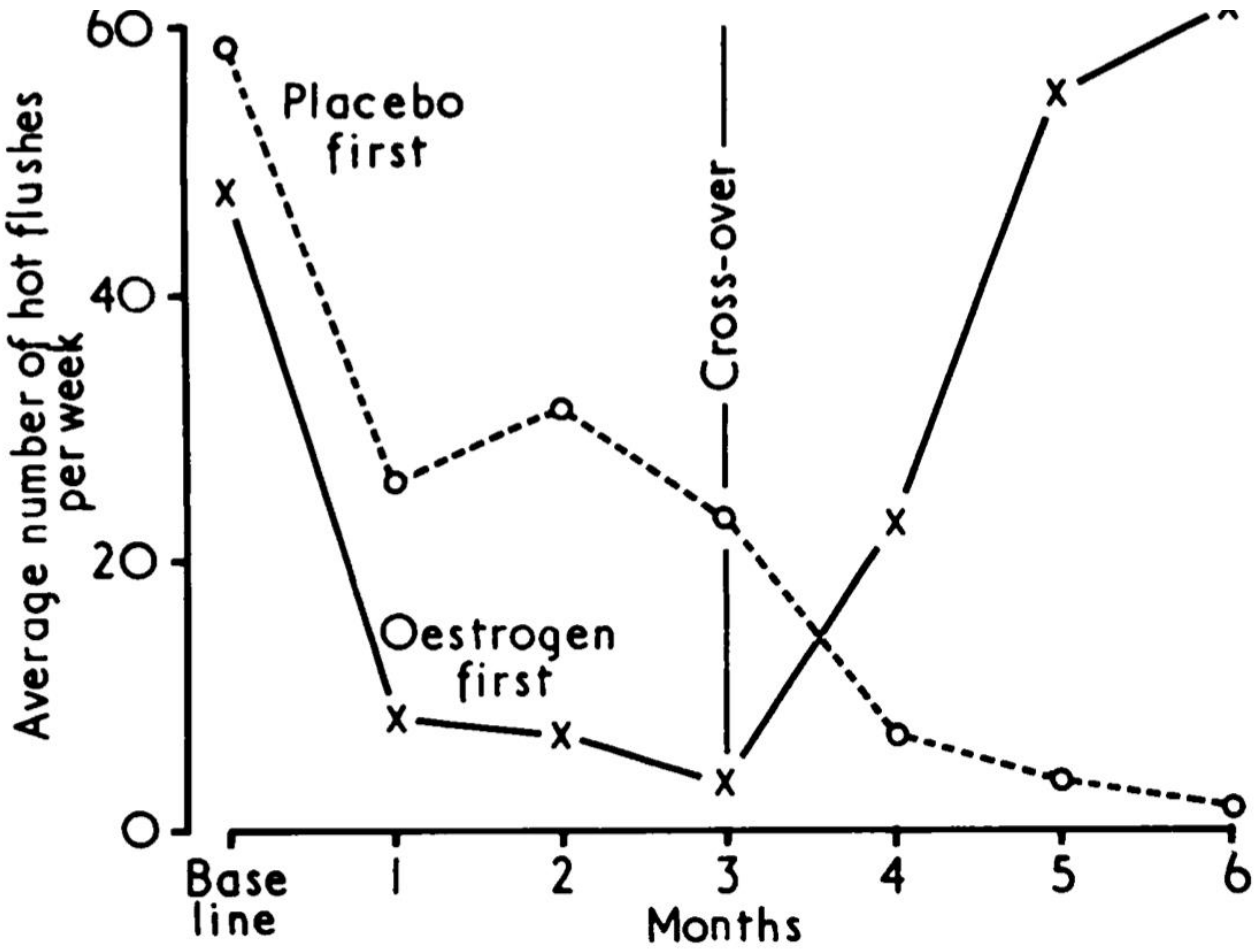


FIG. 2—Average number of hot flushes per week in groups 1 and 2.

MHT is highly effective for symptoms

Cochrane Library

Cochrane Database of Systematic Reviews

Oral oestrogen and combined oestrogen/progestogen therapy versus placebo for hot flushes (Review)

Cochrane Database of Systematic Reviews 2004, Issue 4.
MacLennan AH, Broadbent JL, Lester S, Moore V

Implications for research.

More research is not necessary to confirm the efficacy of oestrogen or combined oestrogen and progestogen in ameliorating hot flushes and night sweats. The effect is very strong.

MHT is highly effective for symptoms

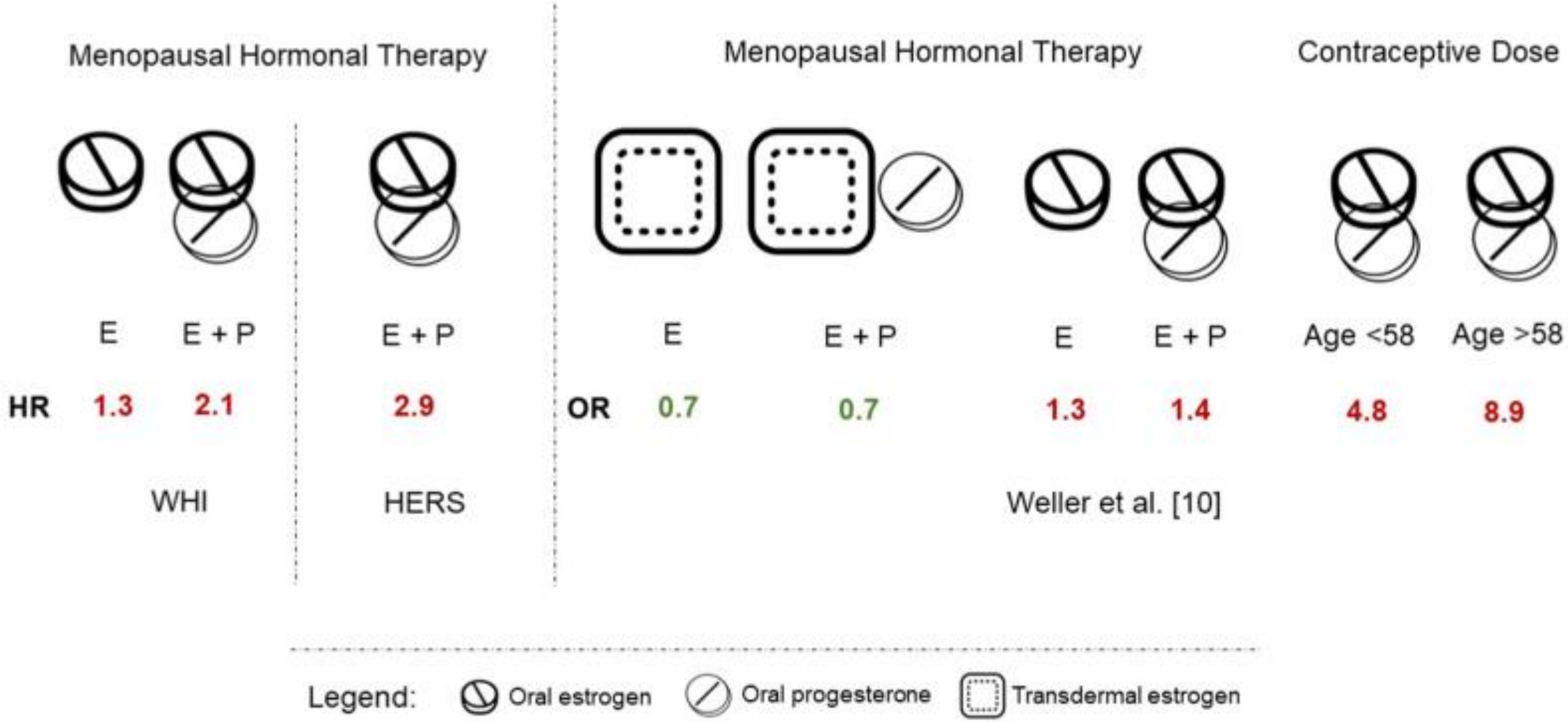
NICE: Menopause, Diagnosis and Management – from Guideline to Practice Guideline Summary

Offer HRT first line for menopause related vasomotor symptoms and low mood

Hormone therapy and HMB

- Mirena IUD + estrogen gel, patch (or oral E2 if no CI)
- Androgenic progestagen gives better cycle control than other progestagens
  - Provera 10mg + estrogen gel, patch, tablet
  - Primolut 5mg + estrogen gel, patch, tablet
- COCP preparations with levonorgestrol/norethindrone
  - Good cycle control (not suitable with migraines)
  - Ideally not to use beyond 50 but if used long-term and no risk factors can continue till 55
  - EE substantially increased VTE risk compared to oral oestradiol

MHT type and VTE risk



MHT and weight gain

Change of fat distribution from the hips to the abdomen with hormonal changes of perimenopause and menopause

Ageing, social, lifestyle and medical factors are the main causes of midlife weight gain - less active, lower metabolic rate

Users and non-users of MHT have same weight change

MHT when also contraception needed

- MHT preparations containing Mirena IUD, Slinda* or use of COCP preparations all suitable in the symptomatic woman needing contraception

- Androgenic progestagen with oestradiol NOT suitable when need for contraception

*Slinda “off label” in MHT

What oestrogen formulation?

Many options available

Most common

- Transdermal - Patches and Gels
- Oral

Less used

- Implants

Not recommended

- Buccal troche

Estrogen dosing

Low dose

1mg oral/1 pump gel/25mcg patch 2x/w

Medium dose

2mg oral/2 pumps gel/50mcg patch 2x/w

High dose

3-4 pumps gel/75-100mcg patch 2x/w

What progestagen to use?

Biological activities of progestins and interaction with the steroid receptors other than progesterone receptors

Progestogens	*Androgenic*	*Antiandrogenic*	*Glucocortcoid*	*Antimineralocorticoid*
Progesterone	neg	pos/neg	pos	pos
(and dihydroesterone)				
Older progestins				
MPA	pos/neg	neg	pos/neg	neg
Norethisterone	pos	neg	neg	neg
Levonogestrel	pos	neg	pos/neg	neg
Newer Progestins				
Dienogest	neg	pos	neg	neg
Drospirenone	neg	pos	neg	pos++

Case history: Ms J.F. DOB 25/2/1980

- She has had a Mirena IUD inserted in the office
- Pipelle endometrial sample collected at the time – NAD
- She commenced a 50mcg patch

Case history: Ms J.F. DOB 25/2/1980

- She has had a Mirena IUD inserted in the office
- Pipelle endometrial sample collected at the time – NAD
- She commenced a 50mcg patch

Review appointment 6 weeks later

- She is so pleased – she says she feels herself again and cannot thank you enough!!

Learning points

- MHT is safe and appropriate treatment for most women with menopausal symptoms
- MHT is not the cause for mid-life weight gain
- Transdermal is preferred option for most but oral oestradiol is also very safe for the majority
- Select progestogen carefully based on individual woman's needs

Resources

Australasian Menopause Society

- http://www.menopause.org.au

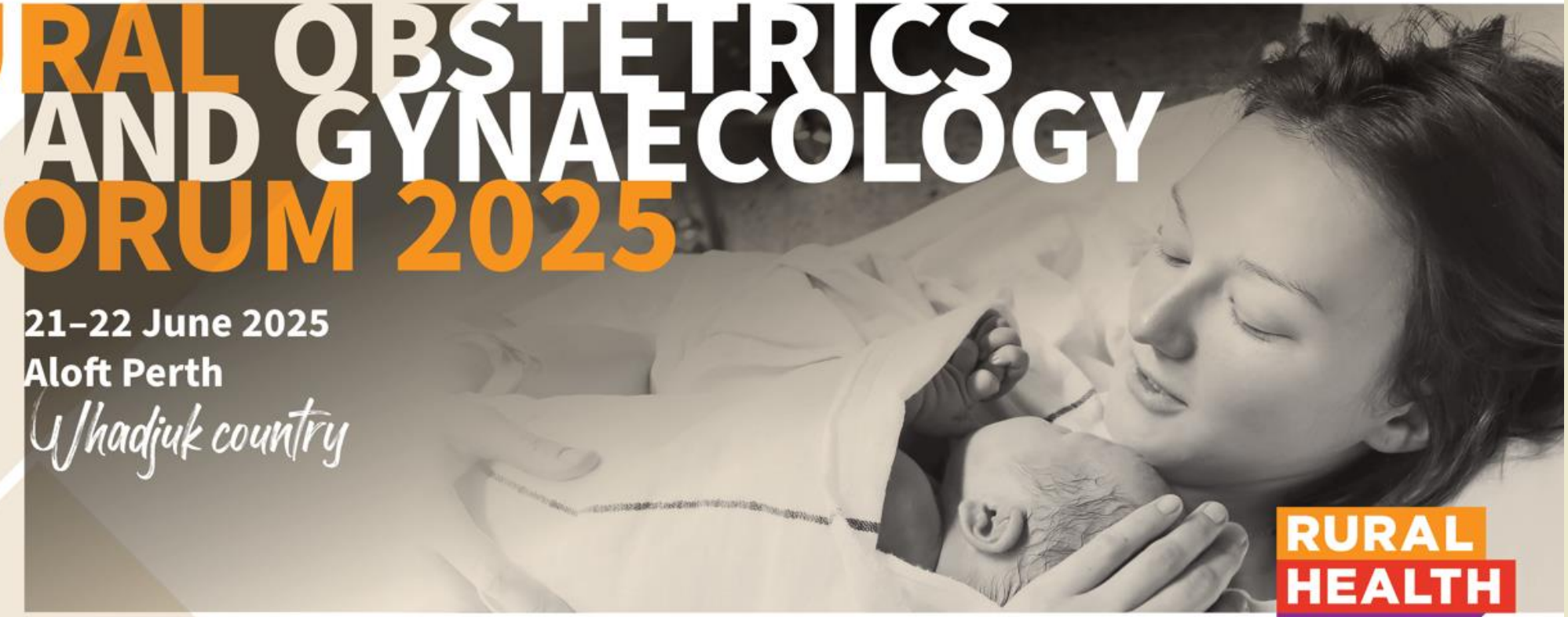
Jean Hailes Foundation

- https://jeanhailes.org.au

KEMH Menopause services

- Menopause Clinic/ Menopause Symptoms after Cancer (MSAC) Clinic/ Young Age at Menopause (YAM) Clinic
  - Nurse Practitioner support – MSAC and Menopause
  - Multidisciplinary meetings for case management

RURAL OBSTETRICS AND GYNAECOLOGY FORUM 2025



21–22 June 2025

Aloft Perth

Whadjuk country

RURAL HEALTH WEST

Government of **Western Australia**
WA Country Health Service

This forum is delivered by Rural Health West in partnership with WA Country Health Service

Rural Health West's education and skills development program is made possible by funding from WA Country Health Service and the Australian Government Department of Health, Disability and Ageing.

RURAL OBSTETRICS AND GYNAECOLOGY FORUM 2025

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RURAL HEALTH WEST

Management of menopause after cancer

Dr Manju Ambekar

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King Edward Memorial Hospital

Government of Western Australia
WA Country Health Service

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Background

- Globally, over 9 million women are diagnosed with cancer each year.
- Breast cancer is the most common cancer worldwide, followed by colorectal cancer in high-income countries and cervical cancer in low-income countries.
- Survival from cancer is improving and more women are experiencing long-term effects of cancer treatment, The extent of ovarian damage depends on the age and pre-treatment ovarian reserve of the woman, type of chemotherapy or radiation field & cumulative dose.
- Amenorrhoea may be permanent or temporary with subsequent development of POI/ early menopause. Predictive AMH after 30/12?
- Menopausal symptoms after cancer are more severe than natural menopause transition and overlap with effects of cancer treatment

Menopause and cancer

- Treatment induced- POI/early menopause
- Ovarian removal/ suppression/ chemotoxicity or radiation toxicity
- Abrupt withdrawal of MHT at cancer diagnosis
- Aromatase inhibitor treatments
- Menopause symptoms are overlapped with adverse effects of shock diagnosis, chemoradiation ,recovery from surgery and ongoing endocrine treatment – fatigue, foggy brain, joint stiffness, low mood, and sexual dysfunction.
- **Health risks from premature ovarian insufficiency: implications on fertility, bones, urogenital, musculoskeletal, cardiovascular, mental and cognitive health**

Case 1: Sarah M

- 34 year old , para 1
- Referred for severe vasomotor symptoms and insomnia
- H/o Breast cancer 8 months ago
- Currently on monthly Goserelin and Letrozole

How will you treat her?

Other information?

- Tumour details and cancer treatment details?
- Chronology of symptoms?
- Any symptomatic treatments tried over 8 months? Benefit?
- Medical , surgical and family history? Genetic testing?
- Fertility and sexual history? Lifestyle factors?
- Any other symptoms?
- Support systems? Ability to cope?
- Background knowledge about menopause and health awareness?
- Expectation from appointment?

Tumour and treatment details for Sarah

- 30 mm Grade 3 IDC,ER positive PR positive >90%, Her 2- negative
- WLE and SLNB , LN – micro metastasis
- Dose dense chemo, followed by radiation,
- Currently on Monthly Goserelin and Letrozole
- GP started Venlafaxine, stopped after a week due to feeling unwell
- Also c/o dyspareunia, urinary burning, joint pains, low mood, insomnia, brain fog, fatigue, weight gain
- relationship strain, fear of recurrence

Who's managing menopausal symptoms? Breast Cancer Network Australia (BCNA) survey

In a 2021 community-based survey (n=524), the prevalence of menopausal symptoms in survivors of breast cancer 5.7 years after diagnosis was:

- 90% had vasomotor symptoms or sleep disturbance,
- 75% had vaginal dryness,
- 62% had mood swings,
- 59% had sexual difficulties.
- Less than a third were offered treatment and less than half found this to be effective. Majority - 60% wanted more support to manage their symptoms

Breast cancer res treat 2021: Michelle Peate , Christobel Saunders · Paul Cohen , Martha Hickey

Management of menopause after Breast cancer

- Systemic HRT is generally avoided in breast cancer patients regardless of tumour receptor status.
- Discuss non-hormonal options for vasomotor symptoms, sweating, low mood, GSM and joint pains
- Multidisciplinary care : dietician, psychology, physiotherapy , geneticist, cardiology, haematology, physician as needed

Liaise with Oncologist to consider:

- Alteration to adjuvant anti-estrogen treatment? change of tamoxifen brand/ dose splitting/ tamoxifen holiday to assess benefit? change of AI/ AI holiday to assess benefit
- Long term health and wellbeing in hypoestrogenic women

Non-hormonal options

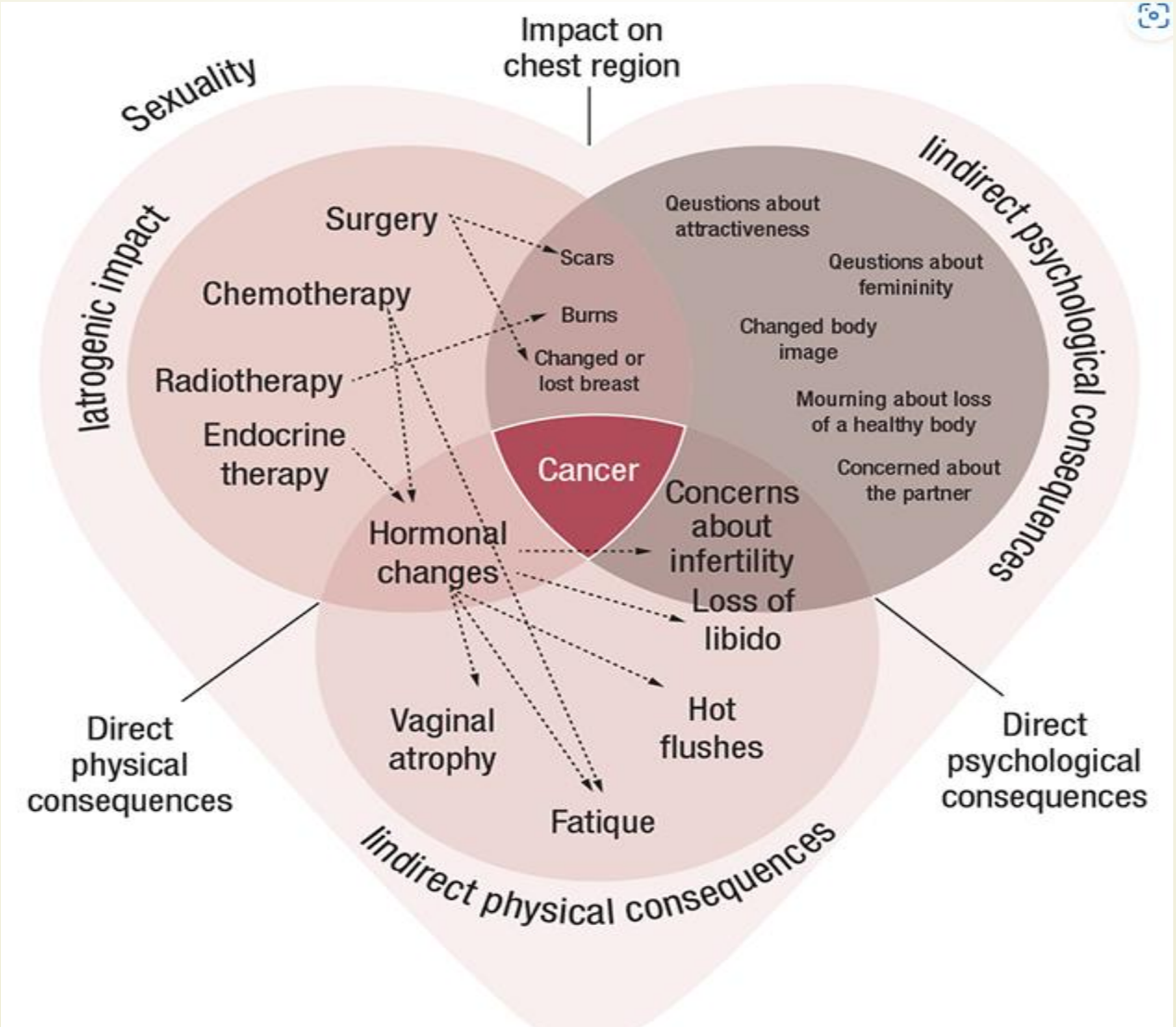
- Lifestyle modification, reduce alcohol, improve fitness, support groups, Life now programs
- Avoid triggers, sleep hygiene, sleep apps,
- Cognitive behavioural therapy (CBT) helps to alleviate anxiety, vasomotor symptoms, low mood and sleep difficulties
- Clinical Hypnosis has shown to reduce frequency ,severity of VMS.
- Phyto-estrogens should be discouraged for women who had hormone-sensitive tumours if formal HRT is contraindicated.
- Cannabinoids are not recommended
- St John's Wort should be discouraged due to its drug interactions, especially with chemotherapy or PARP inhibitors.

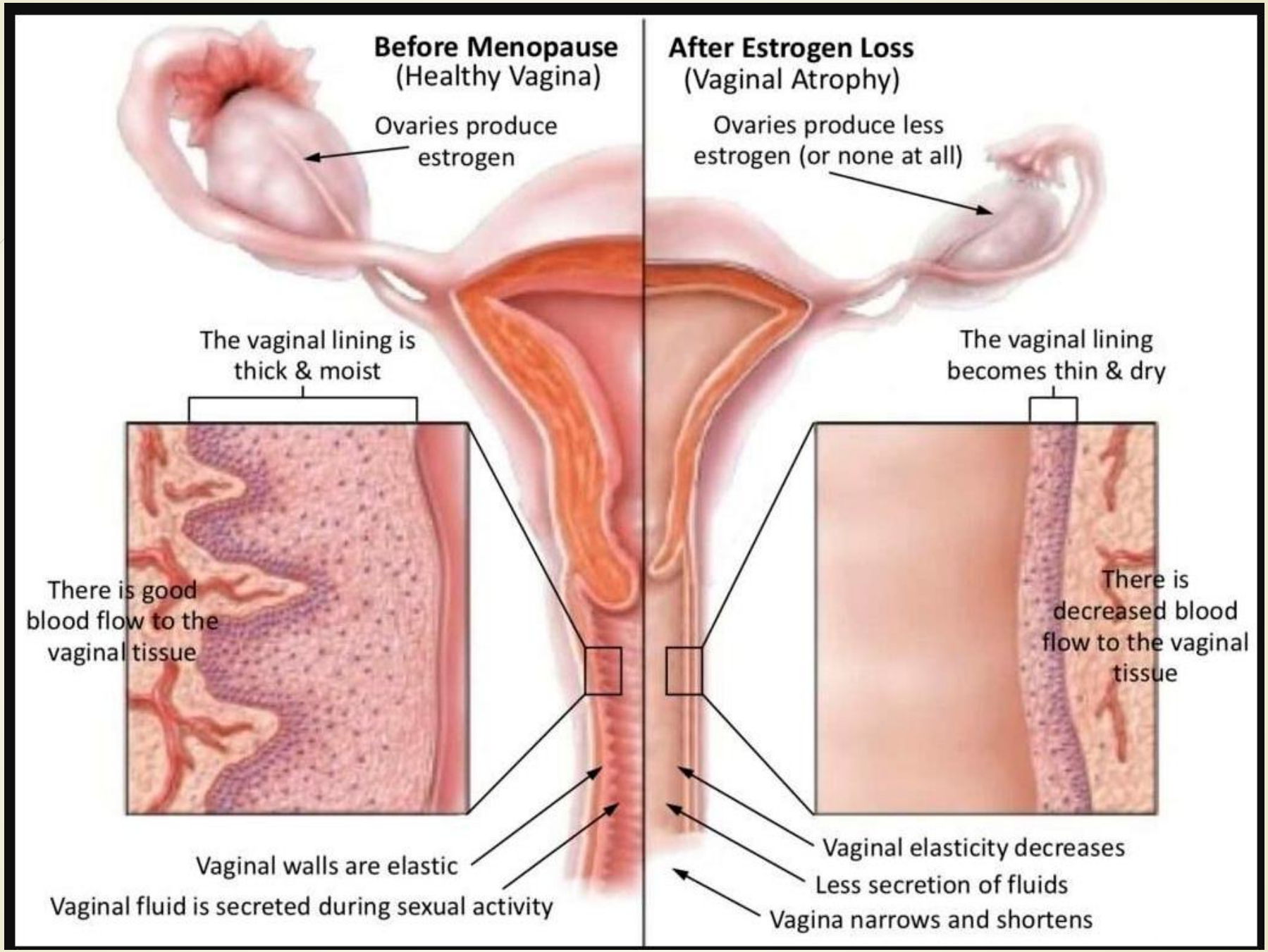
Non hormonal medication

- SSRI s such as paroxetine, citalopram and Escitalopram,

  SNRIs, such as venlafaxine, Desvenlafaxine , Duloxetine for mood stabilization and off-label for vasomotor symptoms
- Avoid fluoxetine and paroxetine as they inhibit metabolism of tamoxifen to its active metabolite
- Gabapentin- 100-900 mg- off label for vasomotor symptoms, improves sleep and reduces musculoskeletal pain
- Oxybutynin 2.5-5 mg BD if sweats are troublesome
- NK3 antagonists- fezolinetant - off label ,after discussion with oncologist, needs baseline liver and kidney function tests and close monitoring

Sexual dysfunction in cancer survivors




Before Menopause
(Healthy Vagina)
Ovaries produce estrogen
The vaginal lining is thick & moist
There is good blood flow to the vaginal tissue
Vaginal walls are elastic
Vaginal fluid is secreted during sexual activity
After Estrogen Loss
(Vaginal Atrophy)
Ovaries produce less estrogen (or none at all)
The vaginal lining becomes thin & dry
There is decreased blood flow to the vaginal tissue
Vaginal elasticity decreases
Less secretion of fluids
Vagina narrows and shortens

GSM- Genitourinary Syndrome of Menopause

- Lower estrogen levels cause urogenital atrophic symptoms: vaginal dryness, pain, dyspareunia, dysuria and UTI
- First line management: explanation, avoid irritation, vaginal and vulval care, moisturisers ,silicone based lubricant for intimacy
- Oncologist may consider switching/stopping AI , Tamoxifen has a beneficial agonist effect at vaginal estrogen receptors
- Topical ovestin after consultation with oncologist if symptoms severe and persistent
- pelvic physiotherapy and sexual counselling as required.
- **Treatment needs to be maintained for continued beneficial effects.**

Safety of vaginal Estrogen/ DHEA in breast cancer patients?

- Limited direct evidence suggests little or no adverse effect of use of low dose topical estrogen on breast cancer outcomes, even potentially during use of AI (McVicker,Jama Oncology Nov 2023)
- Vaginal DHEA /Prasterone is converted intra-cellularly within the vaginal mucosa to estradiol and testosterone and is currently contra-indicated for breast cancer survivors.
- Emerging data shows use of low-dose 3.2 mg vaginal prasterone in select women with breast cancer who are at low risk of recurrence is reasonable if they are on AIs
- No evidence for safety and efficacy for vaginal laser treatments

Key messages

- Individualised, integrated and multidisciplinary care
- Fertility preservation options prior to chemotherapy
- Contraception: non-hormonal methods - barrier / copper IUCD,
- Discuss GSM , vulvovaginal care and pelvic physiotherapy, sexual counselling and local vaginal estrogen if needed.
- Non-hormonal options for VMS, sleep, mood, joint pains.
- After trying lifestyle and all non hormonal options, if severe refractory symptoms persist, MHT is a last resort to maintain QOL.
- Decision to start MHT is taken in consultation with patient, oncologist and managing GP/ menopause specialist.

Case 2: Jenny

- 35 yr old para 2
- Referred to surgical menopause clinic
- Awaiting completion surgery – Lap Total Hysterectomy, omentectomy, peritoneal washings , Rt oophorectomy
- H/O Left ovariectomy for Mucinous Borderline ovarian tumour
- Private genetic testing- BRCA 1 mutation carrier
- What should we discuss with Jenny?

Consultation with Jenny

- BRCA 1 mutation: counselling and implications on future health.
- High risk breast clinic referral for discussion of options regarding surveillance , tamoxifen, and Risk reducing Bilateral mastectomy.
- Complete medical assessment for suitability for HRT.
- Discussion of surgical menopause with its effect on vasomotor symptoms, mood, sleep, Genitourinary health
- Implications for Bone health, cardiovascular health and cognition
- Patient preferences and discussion of treatment options for surgical menopause

Primary Cancer	Subtype or Risk Group	Systemic HRT	Vaginal Estrogen
Ovarian Fallopian tube Primary peritoneal	High grade serous		
	Low grade serous stage 1		
	Low grade serous stage 2+		
	Endometrioid stage 1		
	Endometrioid stage 2+		
	Clear cell		
	Mucinous		
	Granulosa cell stage 1		
	Granulosa cell stage 2+		
	Germ Cell		
	Borderline tumour: No residual disease		
	Borderline tumour: Peritoneal implants, microinvasive disease, residual disease, recurrence		
Endometrial	Low and intermediate risk		
	High-intermediate risk		
	High risk: ER/PR negative		
	High risk: ER/PR positive		
	Advanced and metastatic		
Cervical	All		
Vulval	All		
Vaginal	All		
Uterine sarcoma	Leiomyosarcoma		
	Endometrial stromal sarcoma		

	Benefits usually outweigh risks. Suitable for non-specialist use.
	Refer to text of BGCS BMS guidelines. Discuss benefits and risks for the individual patient. Consider specialist advice.
	Not recommended. Refer for specialist advice if non-hormonal approaches are not effective.

HRT for women with an increased risk/genetic predisposition to develop breast, ovarian and/or endometrial cancer

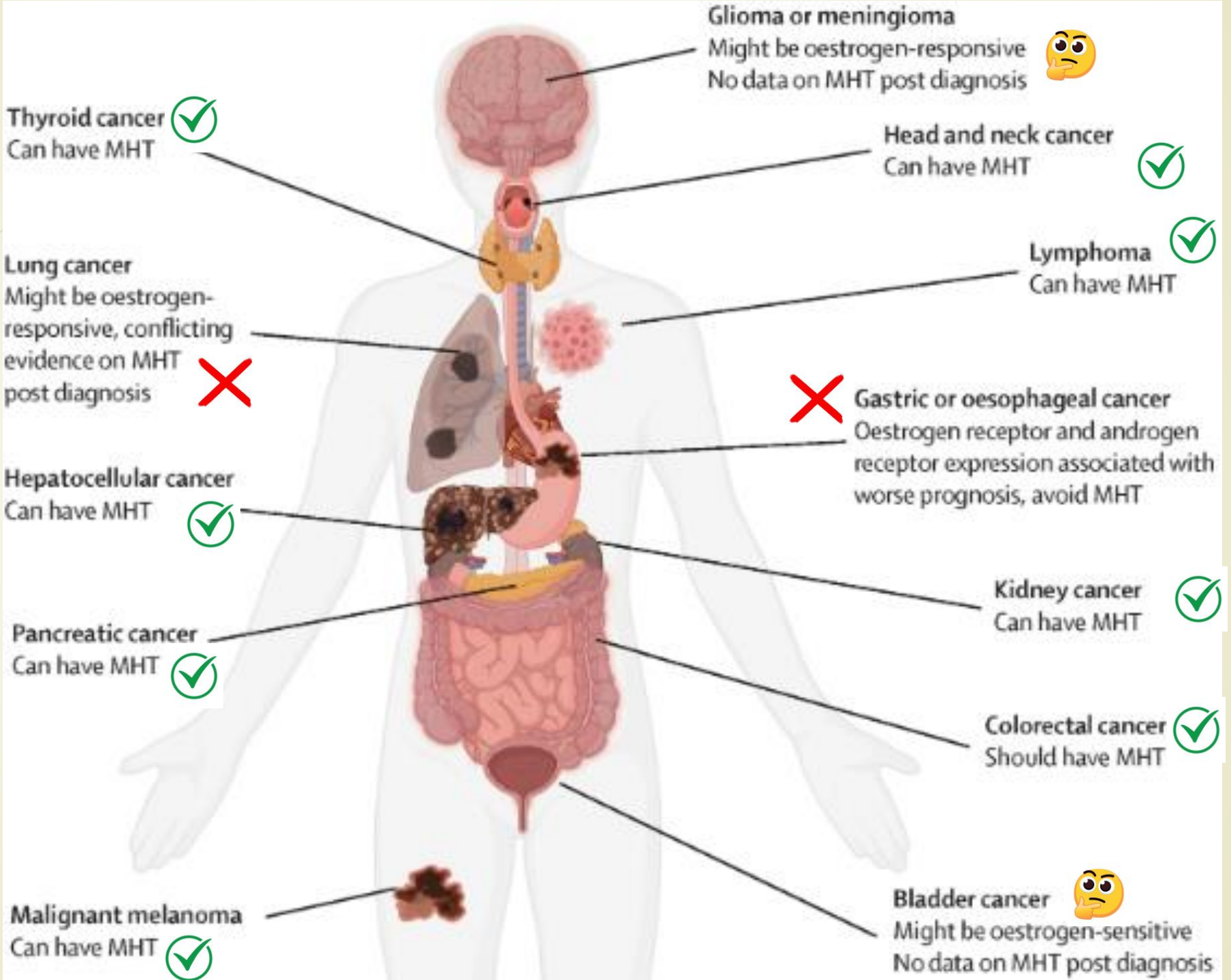
- Premenopausal women need careful counselling ,access to evidence based information and discussion of treatment options prior to decision-making for risk-reducing surgery.
- Following premenopausal oophorectomy, HRT should be offered until the usual age of the natural menopause, unless there is a personal history of breast cancer.
- Continuation beyond this age lacks an evidence base and is not routinely recommended. However, continuation can be considered depending on the individual balance of risks and benefits in women who have had bilateral risk reducing mastectomy.
- Women with Lynch syndrome or BRIP1 mutation are not at an increased risk of breast cancer. HRT use beyond the usual age of menopause for these women should be governed by the same principles as for population-based risk.

When to start MHT and for how long?

- For premenopausal women, if tumour is not hormone-sensitive and if there are no contraindications, MHT is recommended and should be commenced as soon as clinically appropriate.
- For complex or a potentially hormone-sensitive cancer, such as ER-positive endometrial cancer, the final pathology and staging is required before considering MHT. There may also be an advantage to delaying MHT in peri-menopausal and older women, to evaluate the need for HRT to treat menopausal symptoms.
- MHT can be commenced during chemo /radiation treatment, provided there are no contraindications.
- MHT in younger women replaces ovarian hormones and should be continued at least until the age of natural menopause. Compliance is necessary to minimize the consequences of surgical POI.
- MHT needs to be reviewed annually and can continue as long as the benefits outweigh the risks for the woman.
- If vaginal estrogen therapy is appropriate this therapy can be started once the vagina has healed from any surgical intervention.

Bone health

- Baseline BMD by DEXA scanning should be arranged for premenopausal women with treatment induced menopause or women commenced on aromatase inhibitors.
- Baseline 25-OH vitamin D level measurement or blanket vitamin D supplementation of 1000 IU/day should be considered for women at higher risk of bone loss.
- Weight-bearing exercise, smoking cessation, reduced alcohol intake and adequate dietary calcium intake should be encouraged.
- For women under 50, HRT is recommended for prevention of bone loss, if not contraindicated.
- Tamoxifen is bone protective.


Glioma or meningioma
Might be oestrogen-responsive
No data on MHT post diagnosis
Thyroid cancer
Can have MHT
Head and neck cancer
Can have MHT
Lymphoma
Can have MHT
Lung cancer
Might be oestrogen-responsive, conflicting evidence on MHT post diagnosis
Gastric or oesophageal cancer
Oestrogen receptor and androgen receptor expression associated with worse prognosis, avoid MHT
Hepatocellular cancer
Can have MHT
Kidney cancer
Can have MHT
Pancreatic cancer
Can have MHT
Colorectal cancer
Should have MHT
Malignant melanoma
Can have MHT
Bladder cancer
Might be oestrogen-sensitive
No data on MHT post diagnosis

Key messages

- Gynecological malignancy is not an automatic contraindication to HRT.
- Treatment-induced menopause and treatment options including HRT should be discussed with pre- and peri-menopausal women prior to cancer treatment.
- Women with treatment-induced premature ovarian insufficiency are at increased risk of osteoporosis and reduced overall survival from other causes; HRT should therefore be considered.
- Women with intact uterus following chemoradiotherapy for cervical cancer need continuous combined HRT for endometrial protection.
- Women should be asked about urogenital and menopausal symptoms at their follow up appointments.
- Vaginal estrogen is safe for the majority of women after treatment for a gynecological malignancy.

References

- Managing menopause after cancer - The Lancet
- Australasian menopause society- www.menopause.org.au
- https://www.healthtalkaustralia.org/
- www.jeanhailes.org.au
- British Menopause Society- www.thebms.org.uk
- National Institute of Care and Excellence www.NICE.org.uk
- Daisy Network- www.daisynetwork.org.uk
- Women's Health Concern -www.womens-health-concern.org
- North American Menopause society- MENO_230215 573..590-
- International menopause society-https://www.imsociety.org/

MHT after Endometrial cancer

- Women with low-risk endometrial cancer, who are pre-menopausal or have significant menopausal symptoms, should have discussion about the advantages and disadvantages of HRT after hysterectomy. Limited evidence shows no increased risk of recurrence with HRT.
- HRT is not recommended for women with high risk, advanced or metastatic disease that is expressing hormone receptors.
- Women with advanced disease, where treatment is with palliative intent, should have careful consideration of all treatments to improve quality of life, which may include HRT depending on symptoms.
- Women diagnosed with endometrial cancer whilst on tamoxifen for breast cancer should be discussed with their breast oncology team, with consideration being given to either switching to an aromatase inhibitor or discontinuation of endocrine therapy.

MHT after uterine sarcomas

- Uterine leiomyosarcomas are aggressive, can be hormone sensitive, and therefore HRT should be avoided
- For women with significant menopausal symptoms following treatment for leiomyosarcoma, HRT should only be considered if alternative options have been ineffective.
- Women should be advised to avoid HRT after treatment for endometrial stromal sarcoma, unless the individual the benefits outweigh the risk.

MHT after cervical, vaginal and vulval cancer

- Treatment induced menopause is a significant problem after cervical cancer treatment, especially in women diagnosed at a young age and with a good prognosis. Increased awareness of the significant health benefits of HRT for this patient group is needed.
- HRT is not contraindicated after treatment for cervical ,vaginal or vulval cancer
- Estrogen-only HRT should be offered after hysterectomy and bilateral salpingo oophorectomy for cervical cancer in premenopausal women.
- Continuous combined estrogen-progestogen HRT or Tibolone is recommended after chemoradiotherapy to the pelvis for pre-menopausal women.
- Evidence from cutaneous melanoma at all sites does not support or contradict HRT use following treatment for melanoma of the vulva.

MHT after Ovarian cancer/PPC/FTC

- Majority of high grade serous and endometrioid ovarian cancers express estrogen receptors, however, limited randomised controlled trial data do not suggest an increased risk of disease recurrence with systemic HRT.
- Non-hormonal options should be offered in the first instance to women who do not have the health impacts of an early menopause.
- HRT is not recommended for women with FIGO stage II-IV or recurrent low grade serous ovarian cancers, as the disease is hormone sensitive and there is an advantage to estrogen suppressing treatment.
- HRT should be offered to women who have menopausal symptoms following treatment for borderline ovarian tumours and actively recommended for those with surgical menopause resulting from completion treatment for early-stage disease.
- HRT should be offered to women who have premature ovarian insufficiency following treatment for germ cell tumours.
- Limited evidence does not demonstrate harm with HRT following treatment for stage I granulosa cell tumours, but these tumours are hormone-sensitive and women should be counselled regarding the uncertainties and limited data of safety.

Non-hormonal options

- For women on tamoxifen, venlafaxine, escitalopram and citalopram can be offered but paroxetine, sertraline and fluoxetine are contra-indicated due to cytochrome P450 interactions.
- Pregabalin and gabapentin are effective alternatives to manage vasomotor symptoms as well as improving sleep and musculoskeletal issues but can be very sedative. Start at lower doses in elderly patients
- Oxybutynin may improve generalized sweating and vasomotor symptoms, but caution should be exercised in the older population due to toxicity profile including cognitive impairment.
- Neurokinin 3 receptor antagonists can be considered for treatment of moderate to severe vasomotor symptoms. Check drug interactions CYP1A2 enzyme induction
- Clonidine and Hypnotherapy is modestly more beneficial than placebo.

What about Testosterone?

- Sexual dysfunction is very common in women who have had treatment for cancer and is often multi-factorial. Access to Bio - psycho-sexual services is strongly recommended.
- Testosterone replacement therapy can be considered, if indicated, for women in whom estrogen replacement has been optimised and other causes have been assessed.
- Testosterone is only indicated for hypoactive sexual desire disorder. There is insufficient evidence to recommend testosterone for other indications, including brain fog and lack of energy.
- Testosterone should not be offered if estrogen replacement is contraindicated as long term effects on cardiovascular , metabolic risks and breast are unknown.

Premature ovarian insufficiency

Ashley Makepeace

Endocrinologist

Fremantle and Fiona Stanley Hospitals

Conflicts of interest

Nil

POI

Amenorrhoea due to loss of ovarian function before the age of 40

Observational studies have shown that POI is associated with an increased risk of:

- Type 2 diabetes and cardiovascular disease
- osteoporosis
- depression and anxiety
- cognitive dysfunction and dementia
- increased mortality

Hormone therapy can mitigate some of these effects, questions remain regarding the optimal management

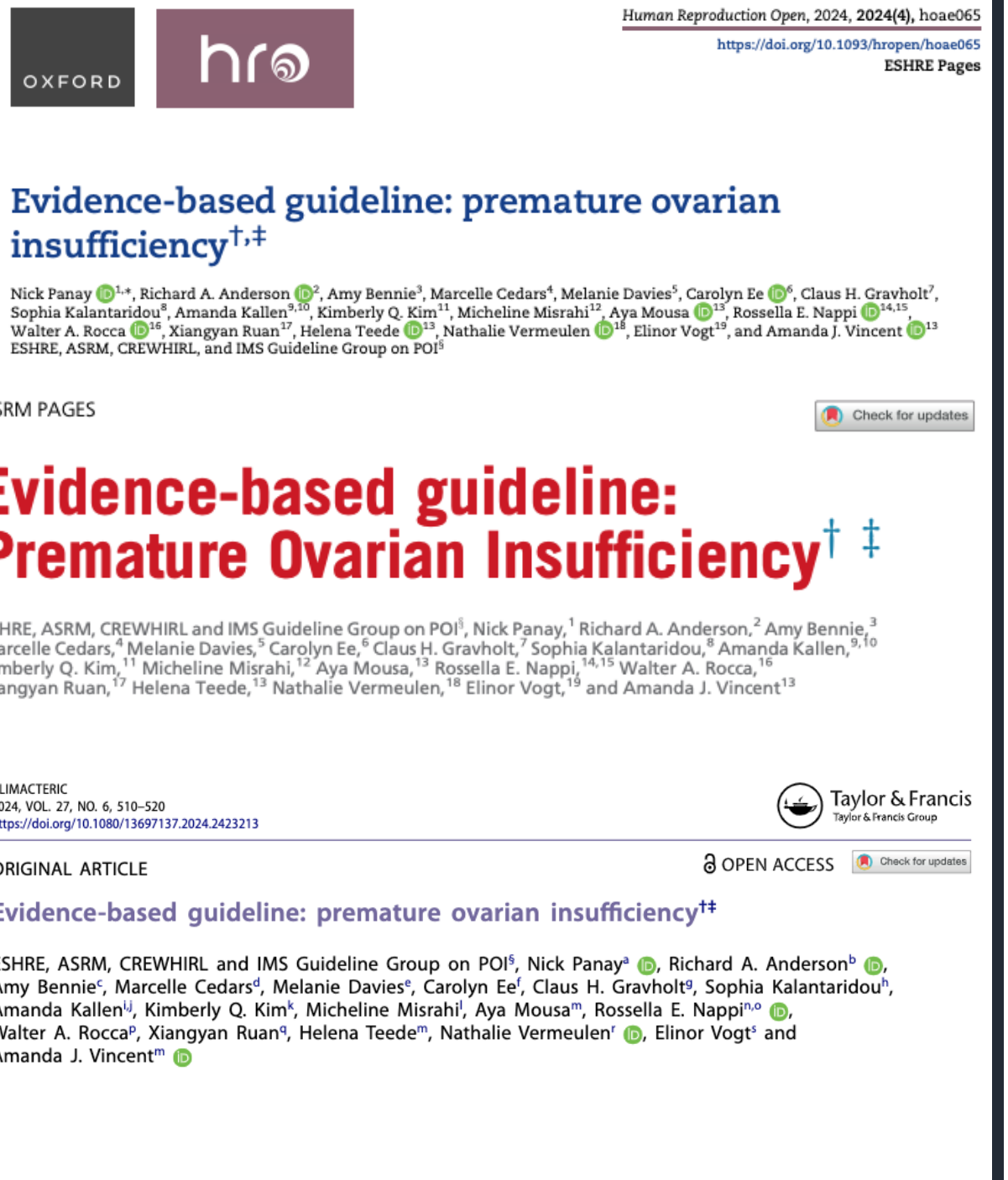
Table: Longterm consequences

	Increased risk of:	
	**Cardiac**	• Hypertension • Coronary artery disease, heart failure, • Atrial fibrillation • Stroke
	**Metabolic**	• Diabetes mellitus • Dyslipidemia • Metabolic syndrome
	**Musculoskeletal**	• Decreased bone density and osteoporosis • Decreased muscle mass and strength
	**Psychological**	• Anxiety • Depression • Poor self-esteem, body image • Decreased quality of life
	**Brain**	• Cognitive impairment • Dementia • Parkinsonism
	**Infertility**	
	**Life expectancy**	• Reduced life expectancy with untreated POI mainly to cardiac disease

POI Guidelines 2024

- **40 key questions**
- **145 recommendations**
  - 92 supported by research
  - 53 good practice points

Based on best available evidence, including extrapolated from natural or early menopause or guideline working group consensus



Human Reproduction Open, 2024, 2024(4), hoae065
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ESHRE Pages

Evidence-based guideline: premature ovarian insufficiency†,‡

Nick Panay[1,*], Richard A. Anderson[2], Amy Bennie[3], Marcelle Cedars[4], Melanie Davies[5], Carolyn Ee[6], Claus H. Gravholt[7], Sophia Kalantaridou[8], Amanda Kallen[9,10], Kimberly Q. Kim[11], Micheline Misrahi[12], Aya Mousa[13], Rossella E. Nappi[14,15], Walter A. Rocca[16], Xiangyan Ruan[17], Helena Teede[13], Nathalie Vermeulen[18], Elinor Vogt[19], and Amanda J. Vincent[13]
ESHRE, ASRM, CREWHIRL, and IMS Guideline Group on POI[§]

ASRM PAGES

Check for updates

Evidence-based guideline: Premature Ovarian Insufficiency† ‡

ESHRE, ASRM, CREWHIRL and IMS Guideline Group on POI[§], Nick Panay,[1] Richard A. Anderson,[2] Amy Bennie,[3] Marcelle Cedars,[4] Melanie Davies,[5] Carolyn Ee,[6] Claus H. Gravholt,[7] Sophia Kalantaridou,[8] Amanda Kallen,[9,10] Kimberly Q. Kim,[11] Micheline Misrahi,[12] Aya Mousa,[13] Rossella E. Nappi,[14,15] Walter A. Rocca,[16] Xiangyan Ruan,[17] Helena Teede,[13] Nathalie Vermeulen,[18] Elinor Vogt,[19] and Amanda J. Vincent[13]

CLIMACTERIC
2024, VOL. 27, NO. 6, 510–520
https://doi.org/10.1080/13697137.2024.2423213
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ORIGINAL ARTICLE

OPEN ACCESS Check for updates

Evidence-based guideline: premature ovarian insufficiency†‡

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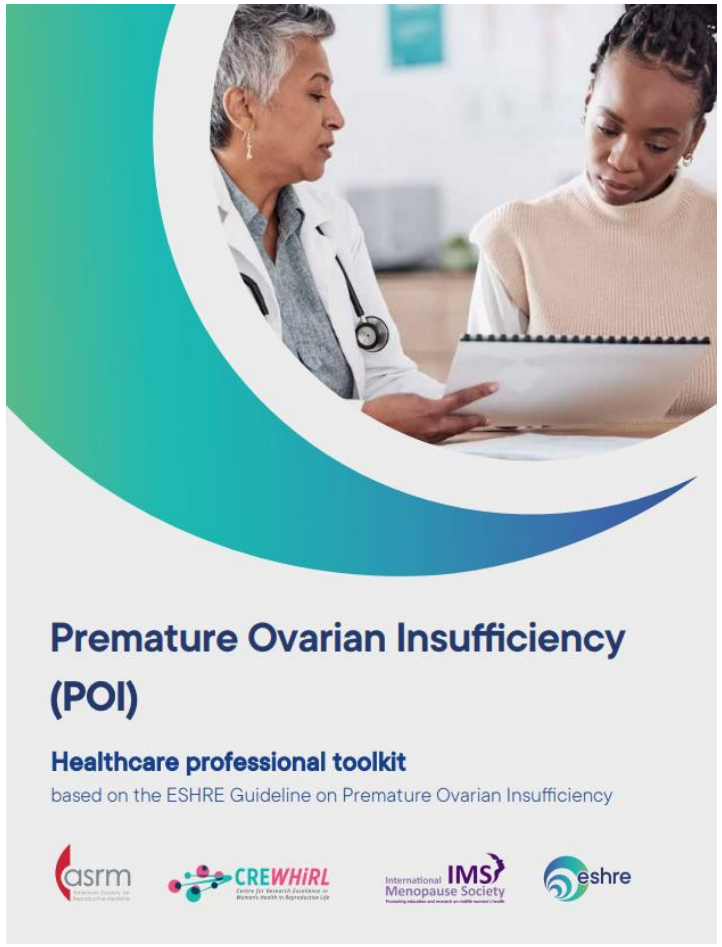
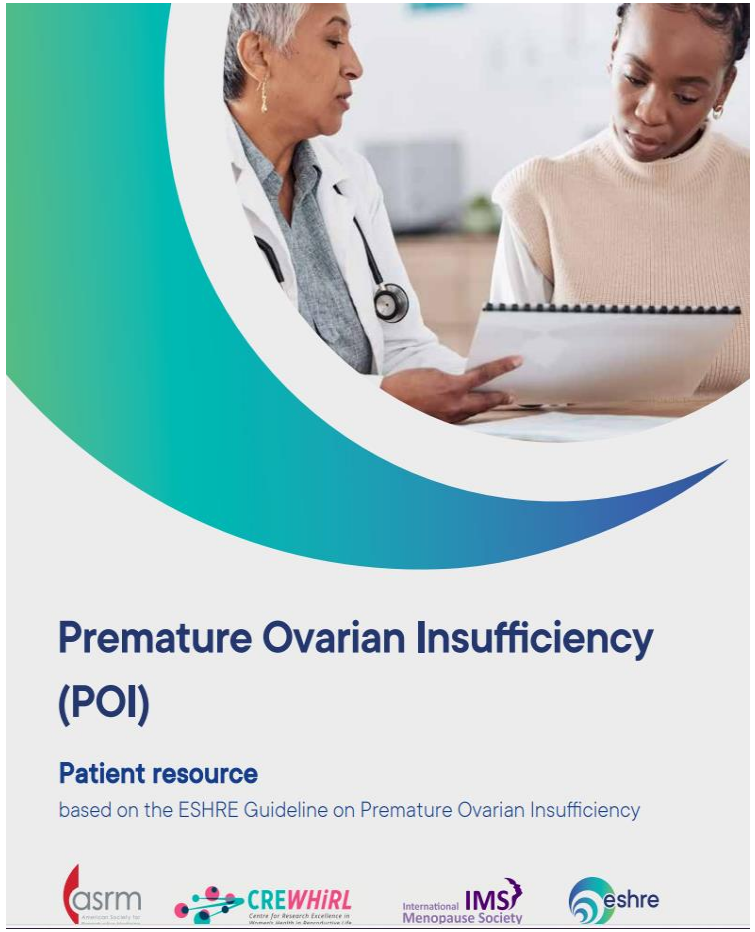
Resources


Premature Ovarian Insufficiency (POI)
Healthcare professional toolkit
based on the ESHRE Guideline on Premature Ovarian Insufficiency
asrm
CREWHiRL
International IMS Menopause Society
eshre


Premature Ovarian Insufficiency (POI)
Patient resource
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eshre

Amy, 37

4 months amenorrhoea since ceasing the COCP

Menarche at 13, periods were fairly regular

COCP use from age 18 for contraception, ceased before with return of menstrual cycle

Never pregnant, no STIs

BMI 22, 125/70 mmHg

2-3 standard drinks 2-3 nights a week

Regular exercise – gym, pilates, walking

Full time work, office based, normal hours

Up to date with immunisations and cervical screening

Started a pregnancy supplement after pre-pregnancy check 9 months prior.

Amy, 37

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Started a pregnancy supplement after pre-pregnancy check 9 months prior.

Would you think differently if:
Amy was 24 with 4 months amenorrhoea after a break from the COCP to see what her natural cycle was like, keen to return to COCP as in a new relationship?

Amy, 37

4 months amenorrhoea since ceasing the COCP

Menarche at 13, periods were fairly regular

COCP use from age 18 for contraception, ceased before with return of menstrual cycle

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BMI 22, 125/70 mmHg

2-3 standard drinks 2-3 nights a week

Regular exercise – gym, pilates, walking

Full time work, office based, normal hours

Up to date with immunisations and cervical screening

Started a pregnancy supplement after pre-pregnancy check 9 months prior.

'**Post pill amenorrhoea**' – Not a diagnosis, but a symptom.

Possibly related to older higher dose COCP.

Unrelated to duration of use

Reduced conception rates possibly in the first months, normalized by 12 months.

Work up for secondary amenorrhoea

Serum HCG

FSH, LH, Oestradiol, Progesterone (useful if amenorrhoea)

Prolactin

TSH

Testosterone, SHBG, FAI

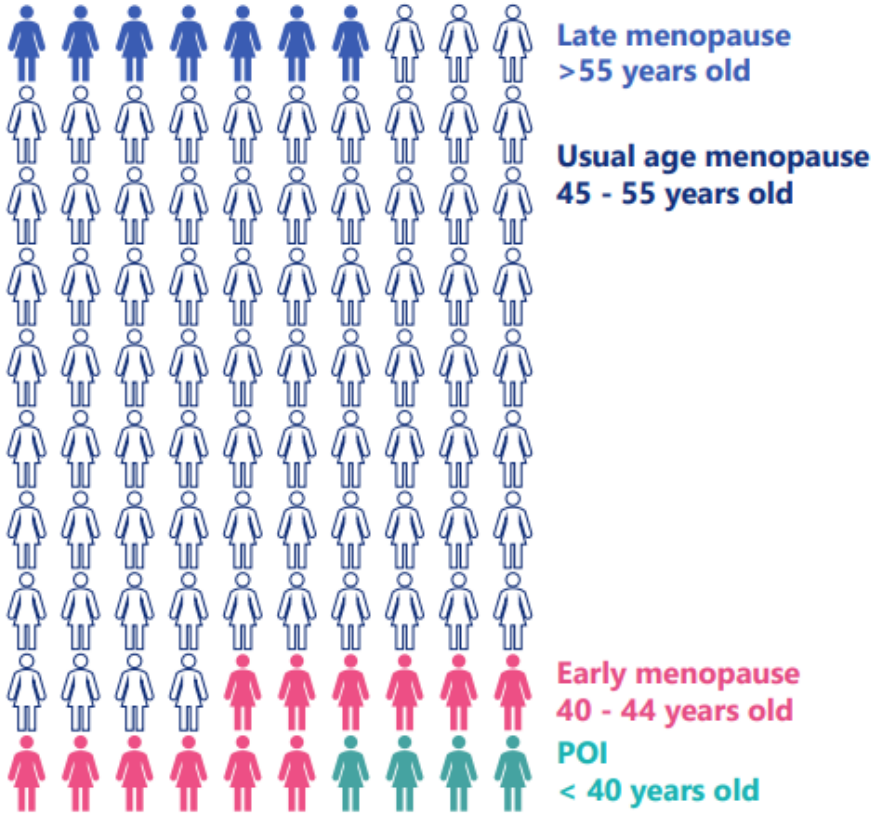
Imaging – pelvic ultrasound

POI Prevalence

More common than previously thought

- Non-iatrogenic POI affects 3.7% of women globally
  - Higher in low and medium Human Development Index populations
- Earlier the onset the rarer the condition

PCOS prevalence 8-13 % reproductive aged women



100 women and the prevalence of POI (3.7%) and early menopause (12.2%)

Prevalence

More common than previously thought

- Non-iatrogenic POI affects 3.7% of women globally

No way to predict onset of POI

Risk factors POI/early menopause/early age of menopause:

- presence of specific genetic variants
- family history of POI
- autoimmune diseases
- medical treatments - chemotherapy, radiotherapy, pelvic surgery
- earlier menarche
- low BMI*
- ethnicity (lower prevalence with Asian background)
- socio-economic status
- smoking*
- alcohol*
- early life exposures* associated with early menopause: mother who smoked, multiple birth, prematurity

Causes

1. Iatrogenic
   Secondary to medical treatments, including chemotherapy, radiotherapy or surgery

2. Non-iatrogenic
   Genetic, chromosomal, autoimmune, infectious

Non-iatrogenic causes	
Idiopathic	**most common cause (>60% cases)** thought to be secondary to non-syndromic polygenic mutations
Genetic Chromosomal	approximately 10–15% cases
	X chromosome • Turner syndrome • Fragile X premutation (*FMR1* gene) • Trisomy X Other: *FOXL2, NR5A1, BMP15, FSHR*
Autoimmune	approximately 10–20% of cases more frequent in women with POI than general population,
	• **Addison's disease** – primary adrenal insufficiency • **Autoimmune polyglandular syndrome 1 and 2 (*AIRE* gene)** • Autoimmune thyroid disease • Other: coeliac disease, T1DM, myasthenia gravis, connective tissue disorders, pernicious anaemia, Crohn's disease, PBC, vitiligo
Infectious	Mumps oophoritis, HIV, tuberculosis, cytomegalovirus, shigellosis, varicella
Metabolic	Galactosaemia (*GALT* gene), 17α-hydroxylase deficiency

Clinical presentation is variable

Menstrual disturbance is a characteristic feature, oestrogen deficiency symptoms are not

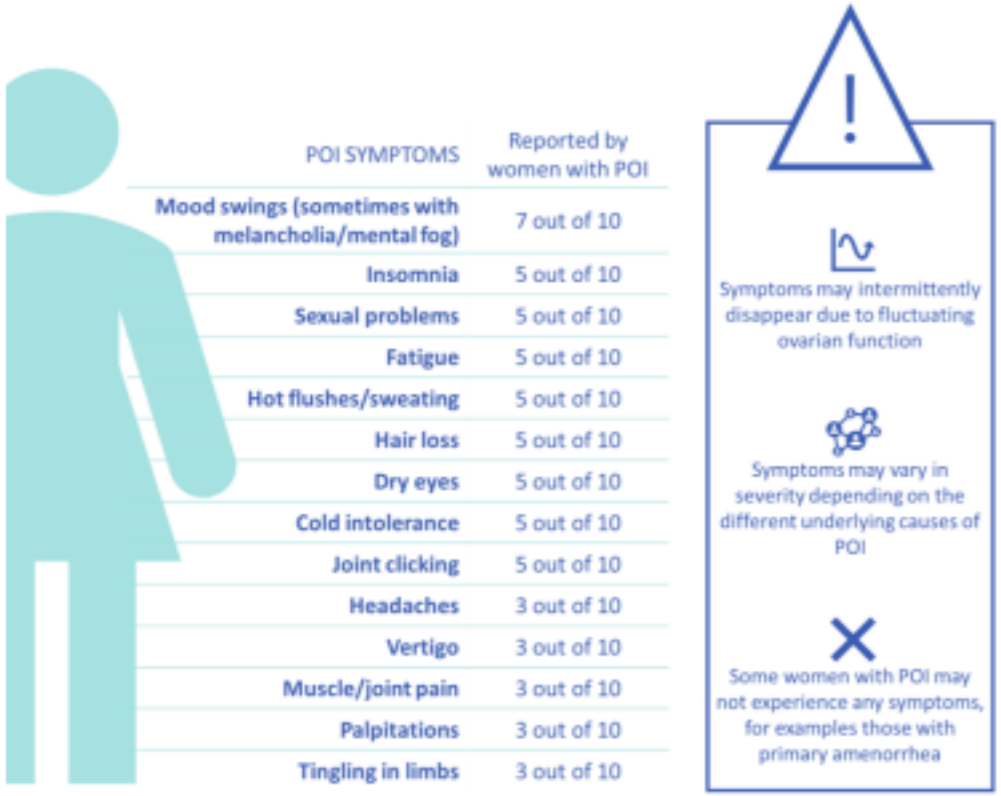
- **Menstrual disturbance : secondary amenorrhoea/ oligoamenorrhoea is most common**

  Primary amenorrhoea occurs in a minority and usually associated with a genetic cause of POI.

- Symptoms and signs related to the cause of POI

  eg Turner syndrome, autoimmune disease, cancer or coexisting co-morbidities

- Symptoms may be more severe in those with iatrogenic POI.



Healthcare professional toolkit

based on the ESHRE Guideline on Premature Ovarian Insufficiency

Diagnosis of POI is based on symptoms and biochemical testing

Diagnostic criteria

1. Disordered menstrual cycles (spontaneous amenorrhea or irregular menstrual cycles) for at least 4 months
2. Elevated FSH concentration > 25 IU/L

Menstrual disturbance is a characteristic feature, oestrogen deficiency symptoms are not

Diagnosis of POI is based on symptoms and biochemical testing

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1. Disordered menstrual cycles (spontaneous amenorrhea or irregular menstrual cycles) for at least 4 months
2. Elevated FSH concentration > 25 IU/L

Symptoms of estrogen deficiency MAY NOT be present

- **Only one elevated FSH >25 IU/L is required for diagnosis of POI**

- FSH testing does not have to be timed to a specific day of the menstrual cycle.
- FSH > 25 is a value greater than the physiological peak seen in premenopausal women
- FSH assessment can be repeated after 4–6 weeks **if there is diagnostic uncertainty**.

Use of hormonal therapy (including oral, injectable, or long-acting contraceptives) may conceal or cause amenorrhea or irregular menstrual cycles, and potentially lower FSH (reduced GnRH pulsatility)
Some hormonal therapy (e.g. combined oral contraceptive) will need to be ceased before diagnosis can be made

Diagnosis of POI is based on symptoms and biochemical testing

Diagnostic criteria

1. Disordered menstrual cycles (spontaneous amenorrhea or irregular menstrual cycles) for at least 4 months
2. Elevated FSH concentration > 25 IU/L

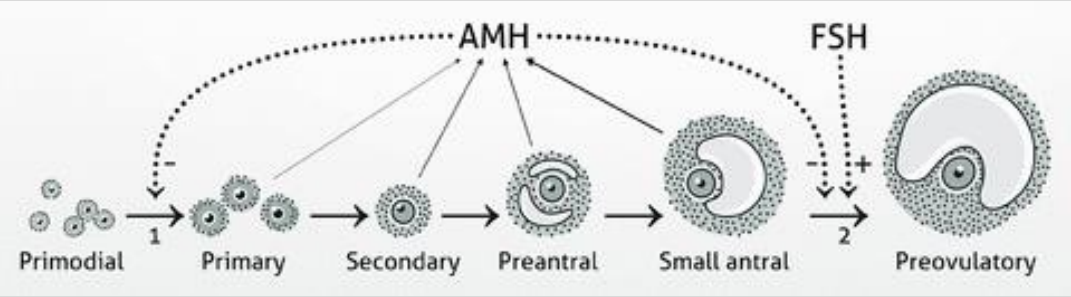
Symptoms of estrogen deficiency MAY NOT be present

Anti-mullerian hormone (AMH) should not be used as a primary diagnostic test

Serum oestradiol concentrations are not needed for diagnosis

Ultrasound may show small volume ovaries/low antral follicle count but is not needed for diagnosis

Anti-Müllerian hormone (AMH)



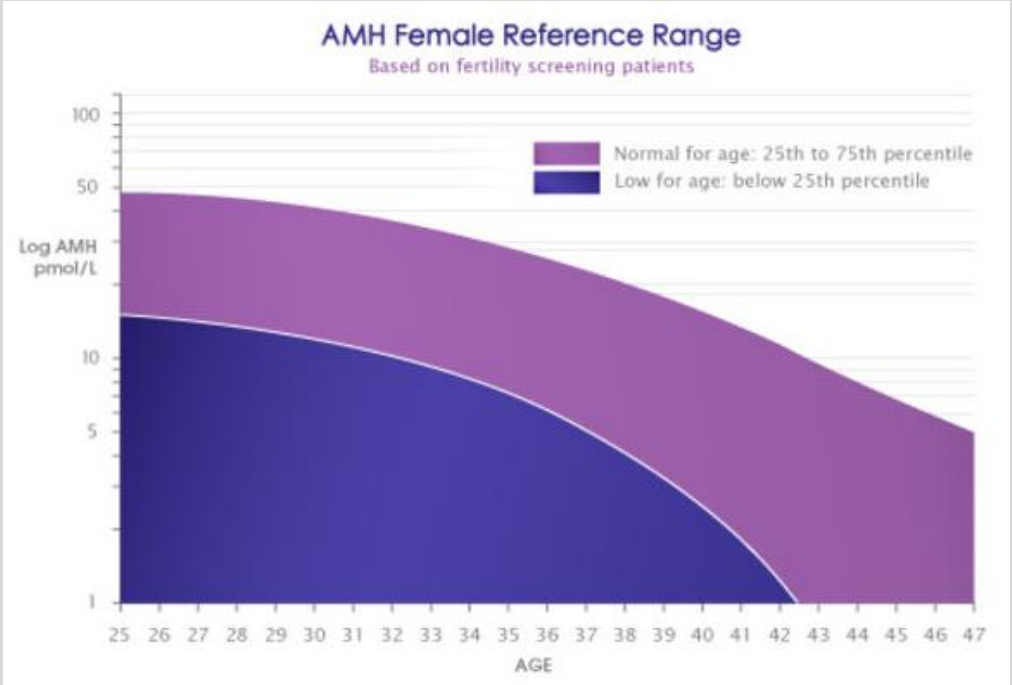
AMH secreted by granulosa cells of growing follicles

Highest level is in preantral and small antral follicles.

AMH:

- inhibits initial recruitment of primary follicles from resting pool of primordial follicles
- inhibits the sensitivity of antral follicles to FSH during cyclic recruitment

->prevents premature depletion of the follicle pool



AMH correlates to antral follicle count on transvaginal ultrasound

AMH levels fall with age, undetectable approximately five years prior rise in FSH

Low AMH can occur in women with regular menstrual cycles despite low ovarian reserve so cannot be used to diagnose menopause.

Anti-mullerian hormone (AMH)

- AMH is decreased with ovarian insufficiency

- Other causes of decreased AMH include **prolonged/severe gonadotrophin suppression, reducing follicular development**:
- oral contraceptive pills (OCP)
- long-acting Gonadotrophin-releasing hormone (GnRH) agonists, hypothalamic amenorrhoea
- Kallmann syndrome, hypopituitarism
- high dose biotin (>5 mg daily)

ANTI-MULLERIAN HORMONE

Keywords: *AMH, Mullerian-inhibiting hormone; MIH; Mullerian inhibiting factor; MIF; Mullerian-inhibiting substance; MIS*

SPECIMEN:	5 mL blood in SST/Serum or lithium heparin tube.
METHOD:	Immunoassay.
REFERENCE INTERVAL:	Age, sex, and method dependent. See laboratory.
APPLICATION:	Anti-Mullerian hormone (AMH) is made by small follicles in the ovary and Sertoli cells in the testes. It can be used to assess follicular reserve, predict ovarian response to fertility treatments, assess indeterminate genitalia, monitor granulosa cell tumours and support a diagnosis of polycystic ovarian syndrome (PCOS).
INTERPRETATION:	AMH is decreased with ovarian insufficiency. Other causes include prolonged/severe gonadotrophin suppression including the oral contraceptive pills (OCP), long-acting Gonadotrophin-releasing hormone (GnRH) agonists, hypothalamic amenorrhoea, hypopituitarism, Kallmann syndrome, and with high dose biotin (>5 mg daily).
RESOURCE:	Pathology Tests Explained - Anti-Mullerian hormone (AMH)
MEDICARE:	Non MBS Rebatable see Medical Benefits Scheme Category 6 Pathology Services
LAST REVIEWED:	02 Jan 2024

RCPA
The Royal College of Pathologists of Australasia

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- Public Pathology Australia
- Pathology Awareness Australia
- Royal College of Pathologists of Australasia

..provide information about pathology testing that you can rely on as being accurate and authoritative.

..provide evidence-based information, free from commercial interest

PATHOLOGY TESTS
EXPLAINED

Information about pathology tests to help everyone take control of their health and make the right decisions about their care.

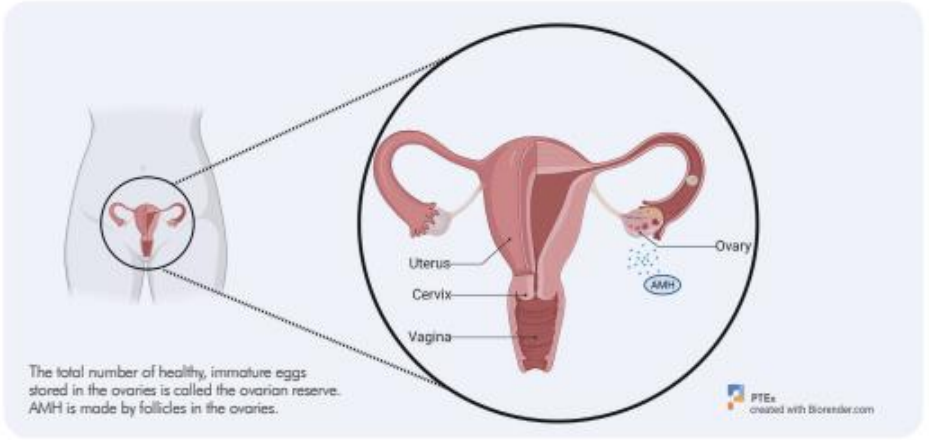
WHAT YOU SHOULD KNOW ABOUT **AMH TESTING FOR ASSESSING FERTILITY**

The anti-Mullerian hormone (AMH) test is most often used along with other hormone tests when IVF treatment is being considered. The level of AMH reflects the number of eggs that can be fertilised for pregnancy. A lower level of AMH suggests fewer eggs.

Although measuring AMH levels can be useful in assessing your egg reserve it cannot predict IVF success. It does not measure the quality of the eggs but only the number of eggs that someone of your age could expect to have.

You can still become pregnant with fewer eggs or have more eggs but not be able to become pregnant. Fertility declines with age, and it is not possible to predict the rate of decline for an individual.

Measuring AMH is most useful in predicting the number of eggs that will be available when your ovaries are stimulated with fertility drugs in IVF treatment.



The total number of healthy, immature eggs stored in the ovaries is called the ovarian reserve. AMH is made by follicles in the ovaries.

PTEx created with Biorender.com

AMH levels and fertility

A woman is born with a lifetime supply of eggs. At birth, she has about one million eggs which decreases naturally during childhood to about 500,000. Only a small number of the remaining eggs go on to mature – usually one at a time as part of the monthly menstrual cycle. AMH is made by follicles in the ovaries. These are little fluid-filled sacs that contain immature eggs and helps the eggs to grow during the menstrual cycle.

Levels of AMH in the blood correspond with the number of eggs. AMH levels gradually decline as a woman ages, and the number of eggs decreases. It drops markedly as menopause approaches, and typically becomes almost undetectable after menopause.

It is known that women with lower AMH levels produce lower numbers of eggs compared with women with higher AMH levels. This impacts on the likely responsiveness to IVF fertility treatment and the chances of becoming pregnant.

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WHAT YOU SHOULD KNOW ABOUT **REPRODUCTIVE CARRIER SCREENING**

If you're thinking of starting a family or are in the early stages of pregnancy, reproductive carrier screening is a way to find out if you and your partner could be carrying a genetic alteration that puts you at risk of having a child with a genetic condition like cystic fibrosis, spina bifida, and more.

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Information about pathology tests to help everyone take control of their health and make the right decisions about their care.

WHAT YOU SHOULD KNOW ABOUT YOUR **NON-INVASIVE PRENATAL TEST (NIPT)**

contains fragments of your baby's DNA. A non-invasive prenatal
NA testing, analyses this DNA in a sample of your blood to assess
e of having a chromosomal disorder such as Down syndrome or

NA -
n most cells

PATHOLOGY TESTS
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Information about pathology tests to help everyone take control of their health and make the right decisions about their care.

WHAT YOU SHOULD KNOW ABOUT **AMH TESTING FOR**

sed along with other hormone tests when IVF
ts the number of eggs that can be fertilised for

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ut only the number of eggs that someone of

e more eggs but not be able to become
ble to predict the rate of decline for an

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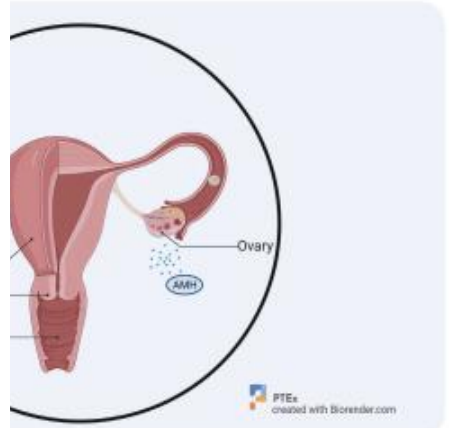

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It is known that women with lower AMH levels produce lower numbers of eggs compared with women with higher AMH levels. This impacts on the likely responsiveness to IVF fertility treatment and the chances of becoming pregnant.

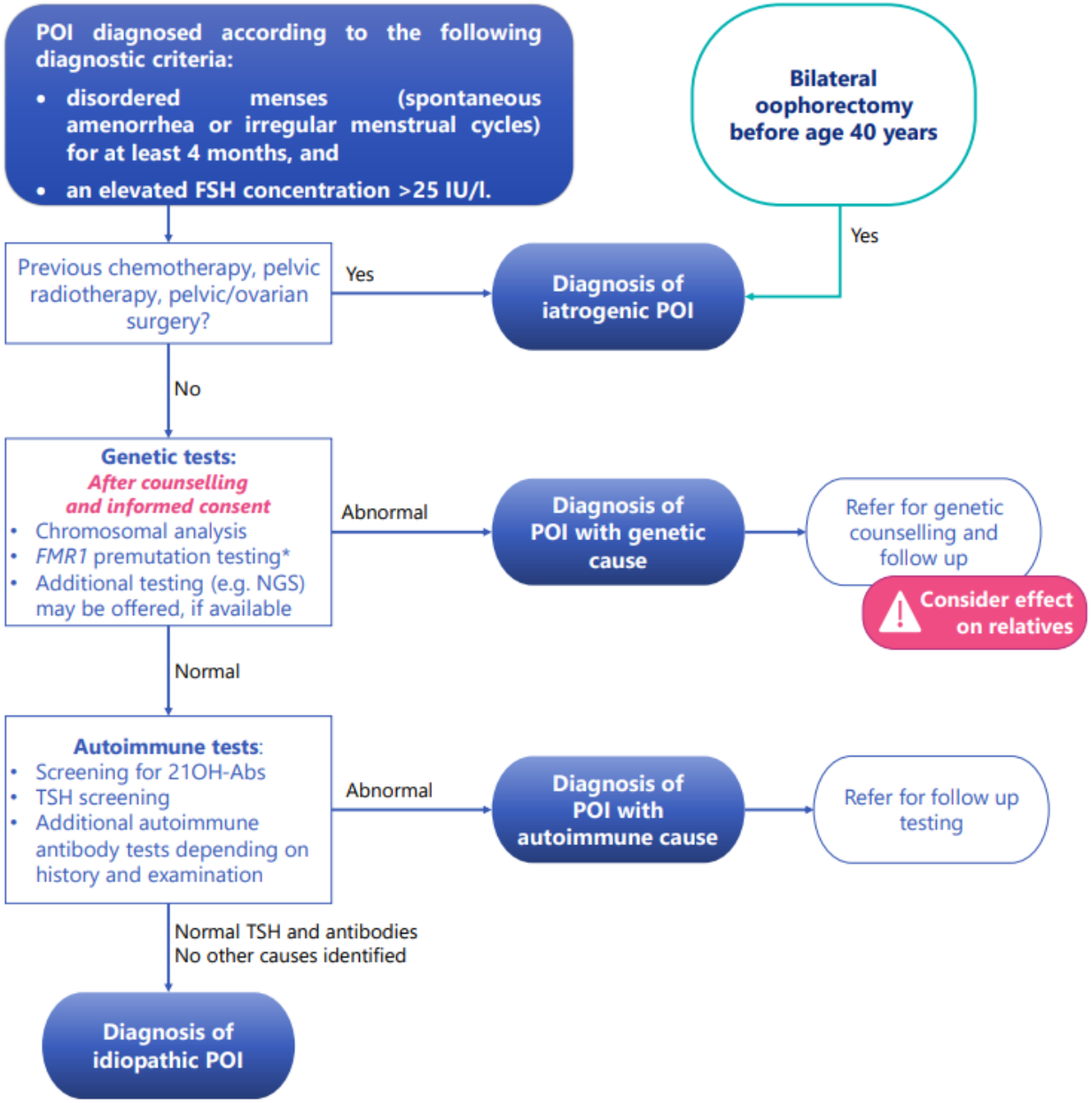
Amy, 37

POI:
Secondary amenorrhoea > 4 months
FSH > 25 IU/L

Primary focus is fertility

- HCG negative
- **FSH 51 IU/L** (follicular: 4–13, mid-cycle: 5–22, luteal: 2–8, menopausal: 26–135)
- LH 35 IU/L (follicular: 2–10, mid-cycle: 10–80, luteal: 2–8, menopausal: 8–59)
- oestradiol <88 pmol/L (follicular: <88–607, mid-cycle: 315–1828, luteal: 161–774, menopausal: <201)
- TSH normal
- prolactin normal
- testosterone low normal, SHBG normal, FAI normal
- Pelvic ultrasound – normal uterine size, ‘inactive ovaries’

Diagnosis of POI



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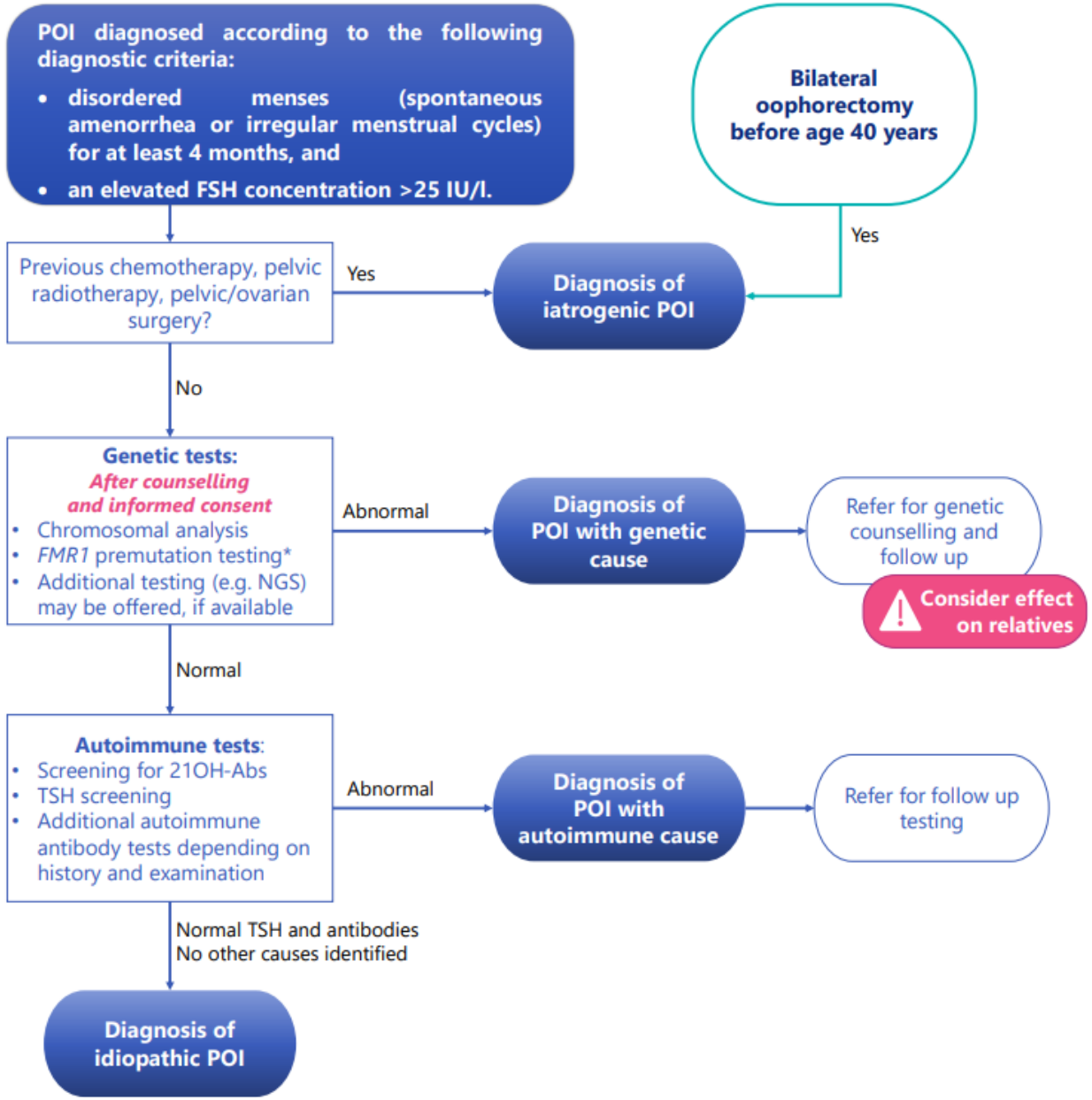
ESHRE Pages

Diagnosis of POI

Karyotype in all women, regardless of age at diagnosis

*Fragile X premutation testing is indicated in all women diagnosed with POI. This needs to be performed as a specific test as multigene panels and NGS are not useful in detecting FMR1 premutation.

Where available and after genetic counselling, additional genetic testing (e.g. next-generation sequencing) can be offered to identify other potential genes that may cause POI



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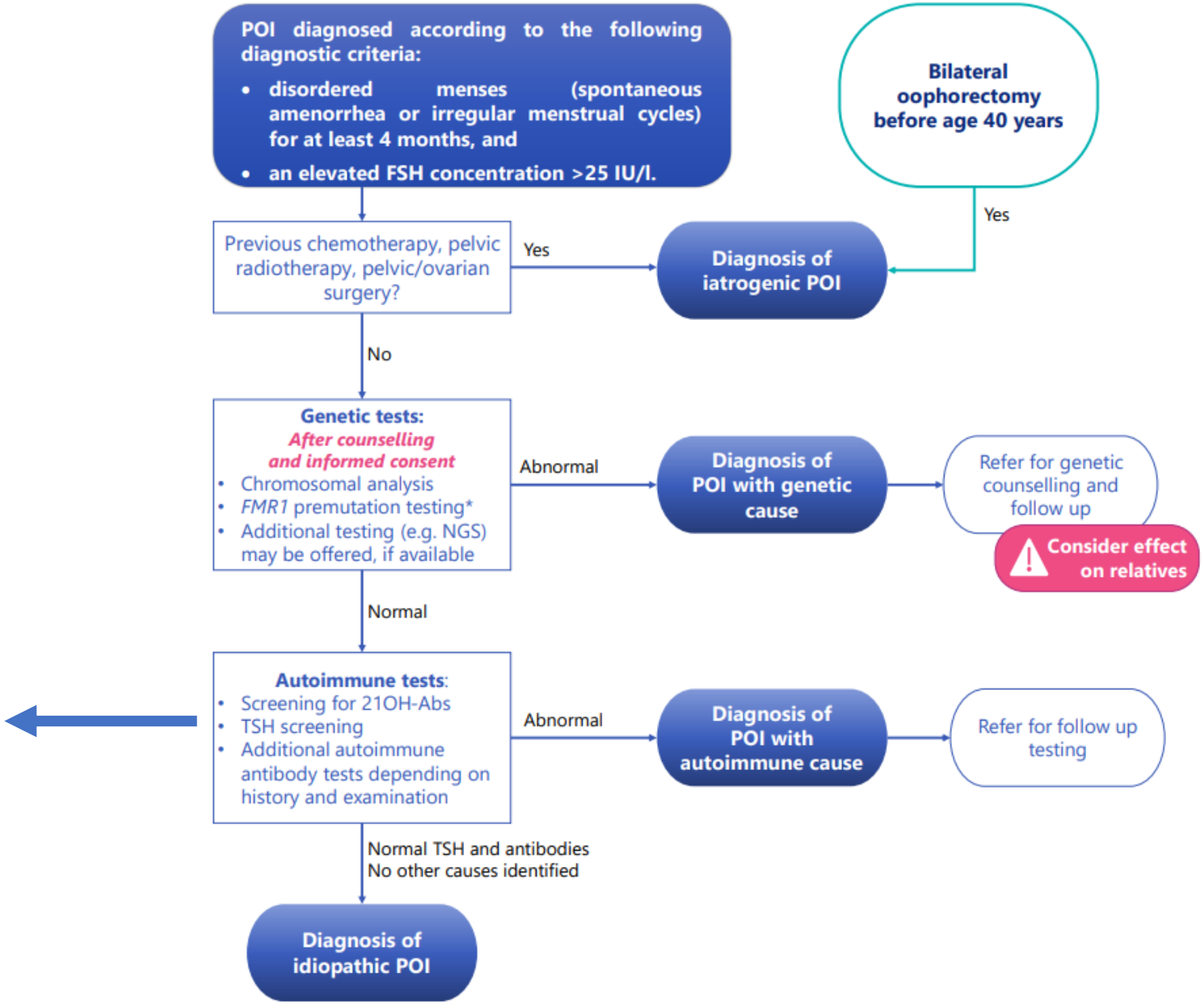
Diagnosis of POI

Screening for anti-ovarian autoantibodies are non-specific and not diagnostic

Screening for thyroid peroxidase (TPO) antibodies not routinely indicated, as high prevalence in the general population. **Thyroid function should be assessed by measuring thyroid stimulating hormone (TSH) at POI diagnosis. TSH should be repeated every 5 years or with symptoms.**

Screening for adrenal autoantibodies. Requested once.



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Management of POI:
fertility
chronic disease
prevention
psychological health
cause of POI, if identified

Table: Longterm consequences

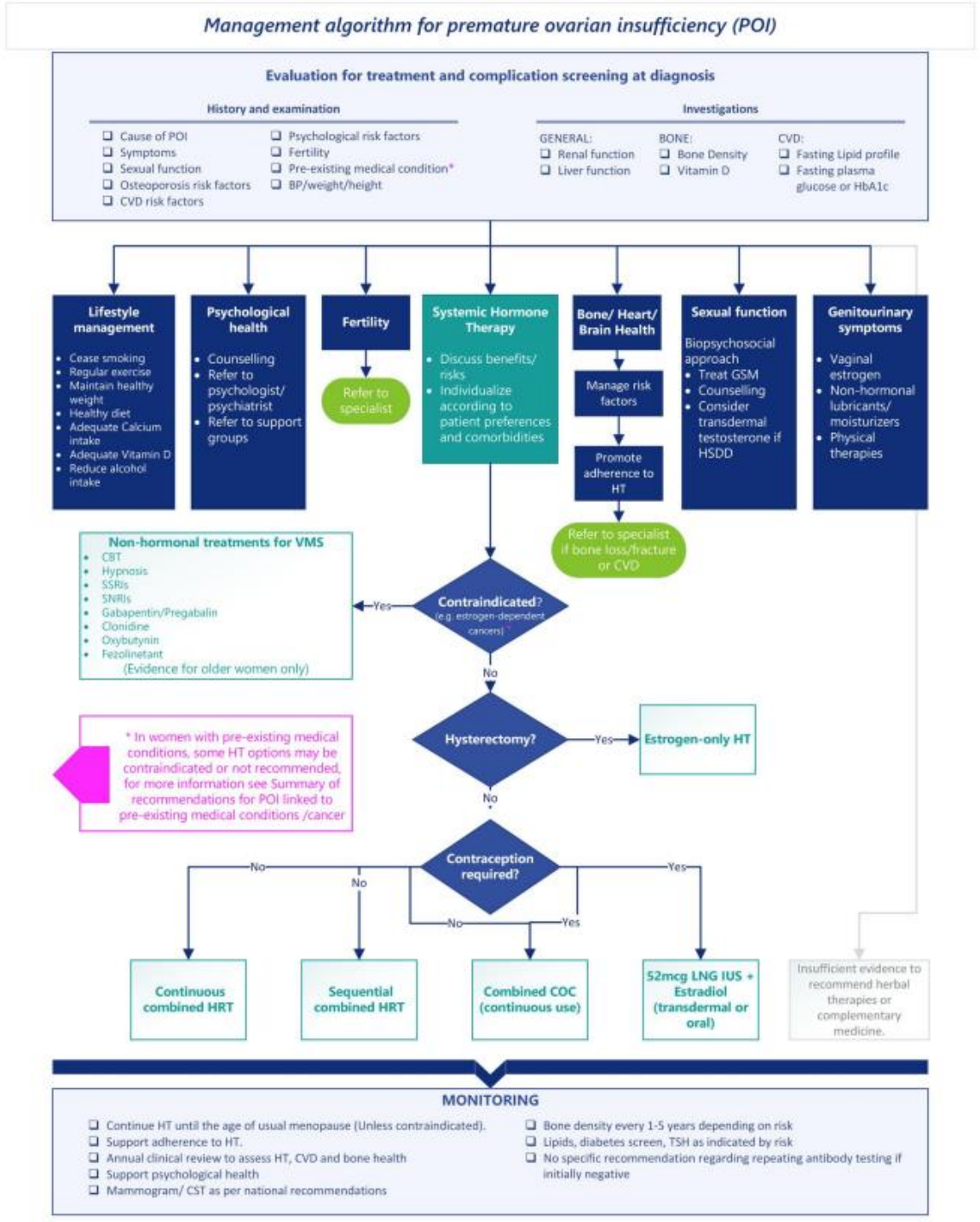
	Increased risk of:	
	**Cardiac**	• Hypertension • Coronary artery disease, heart failure, • Atrial fibrillation • Stroke
	**Metabolic**	• Diabetes mellitus • Dyslipidemia • Metabolic syndrome
	**Musculoskeletal**	• Decreased bone density and osteoporosis • Decreased muscle mass and strength
	**Psychological**	• Anxiety • Depression • Poor self-esteem, body image • Decreased quality of life
	**Brain**	• Cognitive impairment • Dementia • Parkinsonism
	**Infertility**	
	**Life expectancy**	• Reduced life expectancy with untreated POI mainly due to cardiac disease

Management of POI

1

2

3



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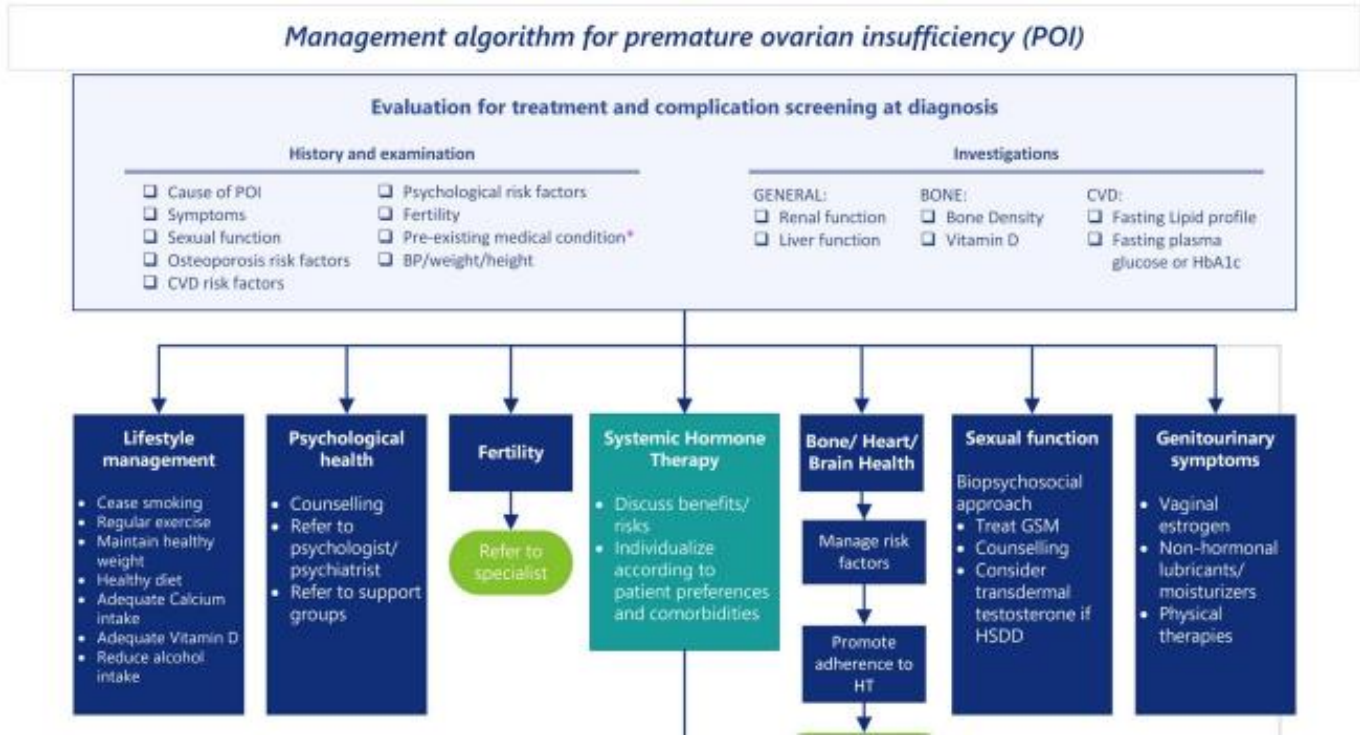
Management of POI



Women with POI should be informed that POI without HT is associated with reduced life expectancy, largely due to cardiovascular disease.	STRONG ⊕⊕◯◯
HT is recommended for women with POI until the usual age of menopause for primary prevention to reduce the risk of morbidity and mortality, whether there are estrogen deficiency symptoms or not.	STRONG ⊕◯◯◯
The guideline group recommends that women with POI should be encouraged to adopt a healthy lifestyle (including avoiding smoking, having a healthy diet and regular physical activity, and maintaining a healthy weight range) to reduce cardiovascular risk.	GPP

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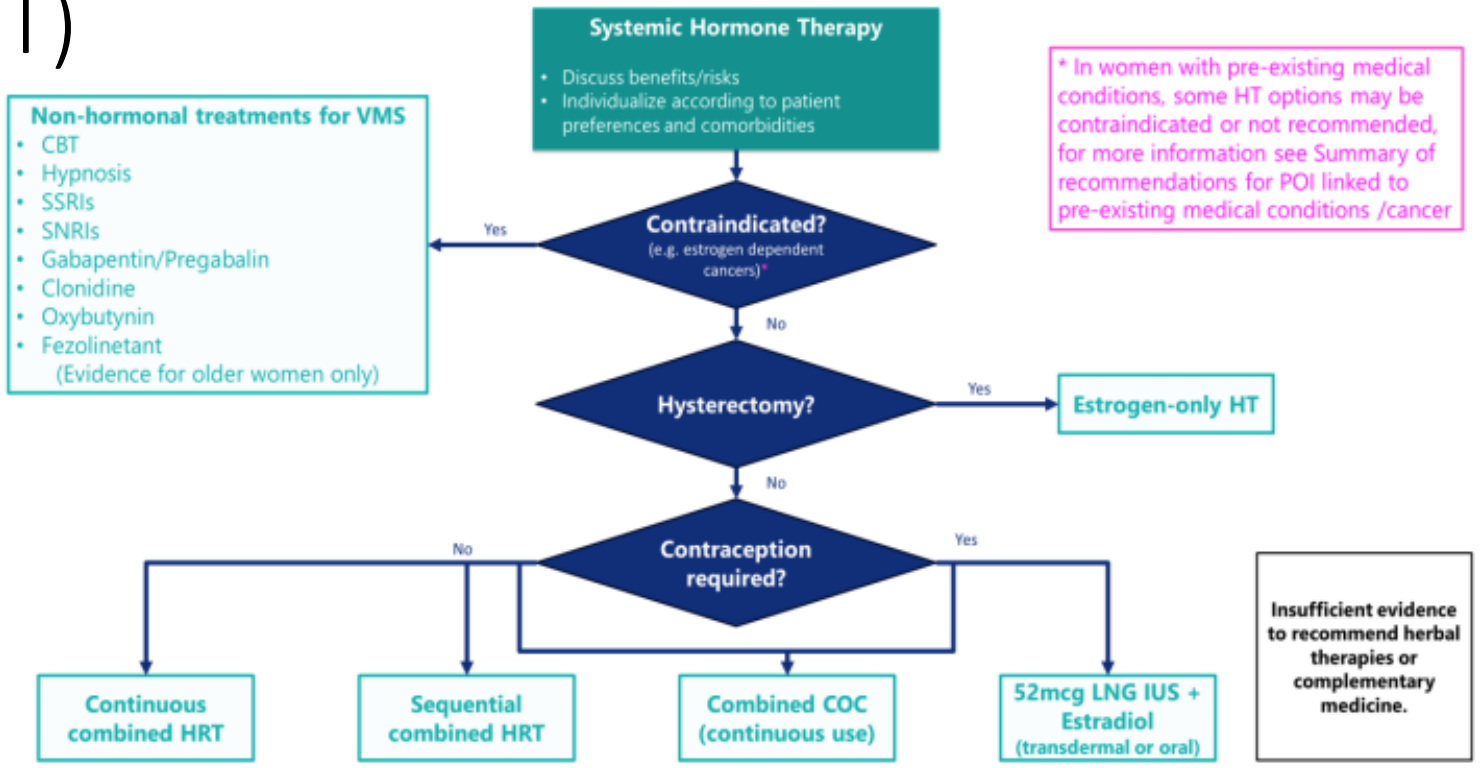
Hormone therapy (HT)

Hormone therapy is recommended for primary prevention in POI irrespective of oestrogen deficiency symptoms and continued until the usual age of menopause

Non-hormonal pharmacological and non-pharmacological therapies that are effective in peri/postmenopausal women can be considered. (NAMS position statement 2023)

Complementary therapies evidence in limited and should not replace HT



Abbreviations: CBT, cognitive behaviour therapy; COC, combined oral contraceptive pill; HRT, Hormone Replacement Therapy; HT, Hormone therapy (HRT+COC); LNG IUS, levonorgestrel intrauterine system; SNRIs, serotonin nor-epinephrine reuptake inhibitors; SSRIs, selective serotonin reuptake inhibitors; VMS, vasomotor symptoms

Hormone therapy

- Hormone therapy encompasses both hormone replacement therapy and the combined oral contraceptive pill

- Estradiol containing COCs have not been studied specifically in women with POI

Indications for hormone therapy

Vasomotor symptoms	**YES**	HT is indicated for the treatment of vasomotor symptoms in women with POI.
Genitourinary symptoms	**YES**	Offer vaginal estrogen therapy to improve genital, sexual and urinary symptoms. Women with POI may be offered vaginal estrogen therapy if genitourinary symptoms are not fully relieved by systemic HT.
Life expectancy	**YES**	Women with POI should be offered HT at least until the usual age of menopause as primary prevention to reduce risk of overall morbidity and mortality
Skeletal health	**YES**	HT is recommended to maintain bone health and prevent osteoporosis; it is plausible that it will reduce the risk of fracture.
Muscle health	**Uncertain**	The effect of HRT on muscle parameters in women with POI is uncertain but may be of benefit.
Cardiovascular health	**YES**	Estrogen therapy has beneficial cardiometabolic effects which can influence cardiovascular disease risk. Non-use of HT is associated with an increased risk of cardiovascular events and mortality. HT is therefore recommended until the usual age of menopause.
Quality of life	**Uncertain**	HT has a positive impact on quality of life in women at usual age of menopause. There are minimal data regarding women with POI, but HT may be of benefit
Sexual function	**YES**	Where HT has been prescribed for other indications to women with POI, it may ameliorate sexual function, acknowledging the effect is generally small.
Neurological function	**YES**	HT may be recommended in women with POI to protect neurological function even in the absence of menopausal symptoms.
Fertility treatment	**YES**	HRT in higher doses creates a favourable hormonal environment for fertility intervention such as replacement of embryos in oocyte donation IVF.
Puberty Induction	**YES**	HRT is indicated for normal pubertal development and skeletal maturation

Jane, 24

Iatrogenic POI post treatment for NHL

Hodgkin's Lymphoma 2010. Age 20. Chemotherapy and peripheral stem cell transplant 2011

Premature ovarian insufficiency 2014. Age 24.

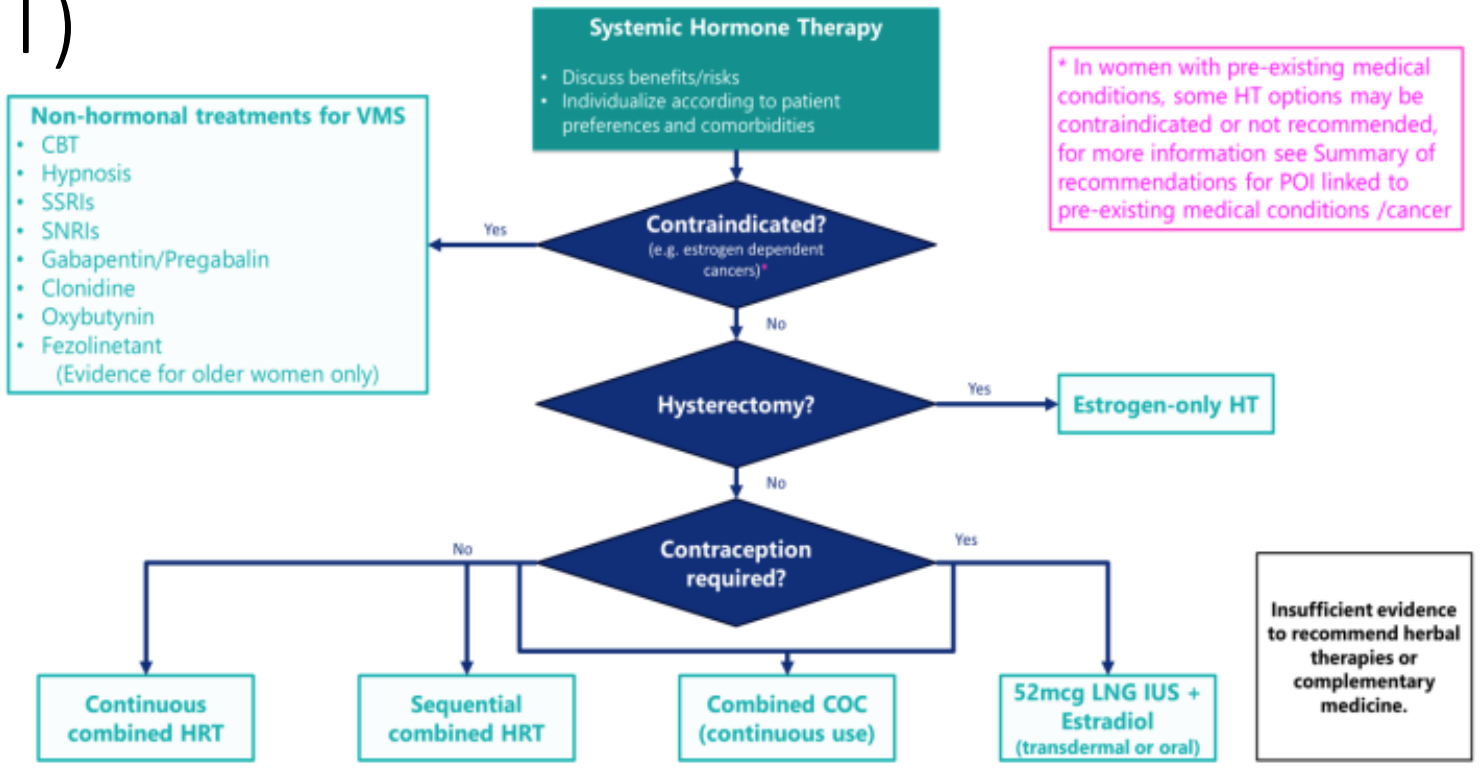
- FSH 102, LH 53, oestradiol <30 with undetectable AMH 2014.
- Levlen ED commenced until pregnancy plans and likely to need egg donor.

Hormone therapy (HT)

Hormone therapy is recommended for primary prevention in POI irrespective of oestrogen deficiency symptoms and continued until the usual age of menopause

Non-hormonal pharmacological and non-pharmacological therapies that are effective in peri/postmenopausal women can be considered. (NAMS position statement 2023)

Complementary therapies evidence in limited and should not replace HT



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Hormone therapy and comorbidities

Cancer/previous diagnosis	HT	Risk of recurrence with HT use	Other considerations
Squamous cell carcinoma	Recommended	Not increased	
Cervical adenocarcinoma	Consider after risk assessment	Low risk	
Early-stage low-risk endometrioid adenocarcinoma	Consider after risk assessment	Low risk	
Epithelial ovarian cancer	Consider after risk assessment	Low to moderate risk	
Non-epithelial ovarian cancer	Consider after risk assessment	Moderate risk	Tumour hormone receptor status.
Hormone dependent ovarian or uterine tumours (uterine sarcoma, endometrioid carcinoma, ovarian clear cell carcinoma, ovarian granulosa cell tumour, sex cord-stromal tumours)	Contra-indicated	High risk	
Breast cancer survivors.	Contra-indicated	High risk	
BRCA1/2 mutation carrier after RRBO, without a personal history of breast cancer	Can be considered	NA	Estrogen-only HRT has lower risk compared to combined estrogen/progestogen
POI following hematopoietic stem cell transplantation	Recommended	Not increased	Individualised HT / pubertal induction

1

Comorbidity	HT	Type of risk	Probability	Proposed HT
Breast cancer survivor	Contra-indicated	Recurrence	High	n/a
BRCA1/2 mutations after RRSO, without a personal history of breast cancer	Can be considered	Developing BC	Low	TE/MP/DYD [1]
Migraine	Can be considered	Ischaemic stroke	Unclear	Dose/regimen/administration can be adapted in line with migraine symptoms
Migraine with Aura	Can be considered	Ischaemic stroke	Unclear	Transdermal estrogen (COC contraindicated[2])
Hypertension	Can be considered	CVD/VTE	Low	TE/MP/DYD [1]
Diabetes mellitus	Can be considered	CVD/VTE	Low	TE/MP/DYD [1]
Obesity	Can be considered	CVD/VTE	Low	TE/MP/DYD [1]
Endometriosis	Can be considered	Disease reactivation / malignancy	Low	combined estrogen-progestogen
Prior VTE	Can be considered after haematologist review.	VTE/PE	High	TE/MP/DYD [1] (COC contraindicated[2])
Malabsorption	Recommended	Inadequate absorption of oral therapy	Unclear	Non-oral HT
Known CVD	Relatively Contra-indicated	CVD	Unclear	TE/MP/DYD [1]
Abnormal liver function	Can be considered	Worsening of liver function	Unclear	Transdermal estrogen

- [1] TE/MP/DYD: Transdermal estrogen, Micronized progesterone, Dydrogesterone
- [2] See https://www.cdc.gov/reproductivehealth/contraception/mmwr/mec/summary.html

Jane, 25

Iatrogenic POI post treatment for NHL

Hodgkin's Lymphoma 2010. Age 20. Chemotherapy and peripheral stem cell transplant 2011

Premature ovarian insufficiency 2014. Age 24.

DVT and PE October 2015.

- Clexane -> Apixiban
- Levlen ED ceased. Switched to cyclical, topical MHT preparations.

Spontaneous pregnancy 2017 delivered 4/2018. Diet controlled GDM. Clexane for duration.

Second spontaneous pregnancy 2021 - delivered March 2022. Clexane for duration.

- Mirena inserted, continues topical oestrogen - 50mcg/24hrs.

Hormone therapy and comorbidities

Cancer/previous diagnosis	HT	Risk of recurrence with HT use	Other considerations
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2

- [1] TE/MP/DYD: Transdermal estrogen, Micronized progesterone, Dydrogesterone
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Jane, 35

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- Mirena inserted, continues topical oestrogen - 50mcg/24hrs.

Low BMD - Z score -2.9 FN 1/2021. Lowest z score -2.2 femoral neck 2025

Bone health

Emerging evidence that the dose of oestrogen is important for bone health

Doses higher than previous recommended 2mg oestradiol or 100mcg transdermal

Or

Combined oral contraceptive pill (COC) use continuous regimen to limit placebo

Estrogen dose in COCs containing 1.5mg estradiol or 20mcg ethinyl estradiol may be inadequate for bone health.

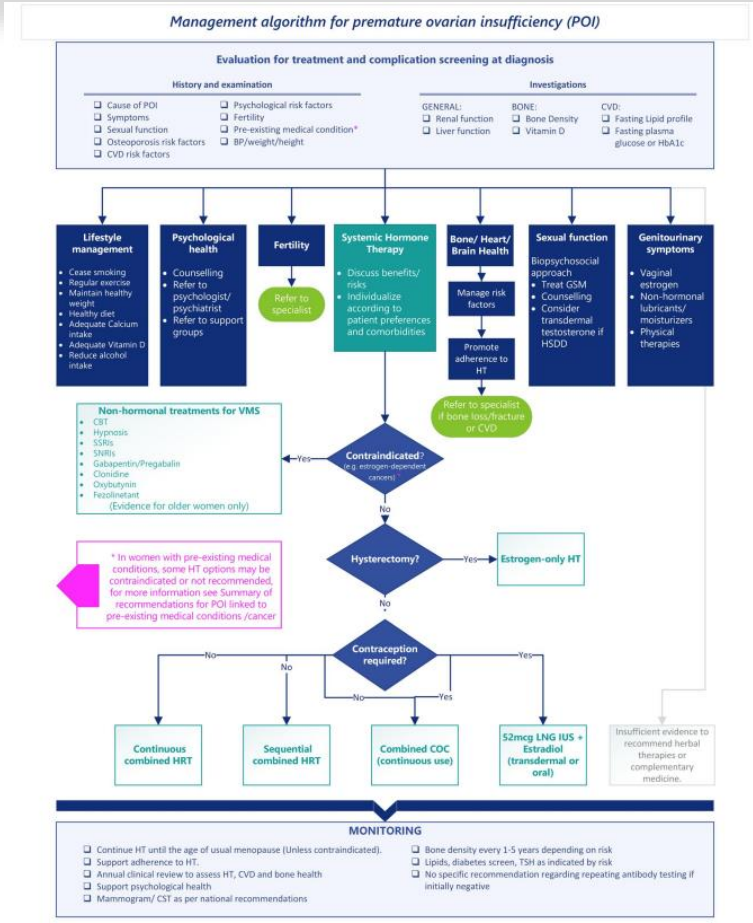
Usual precautions regarding COCs apply

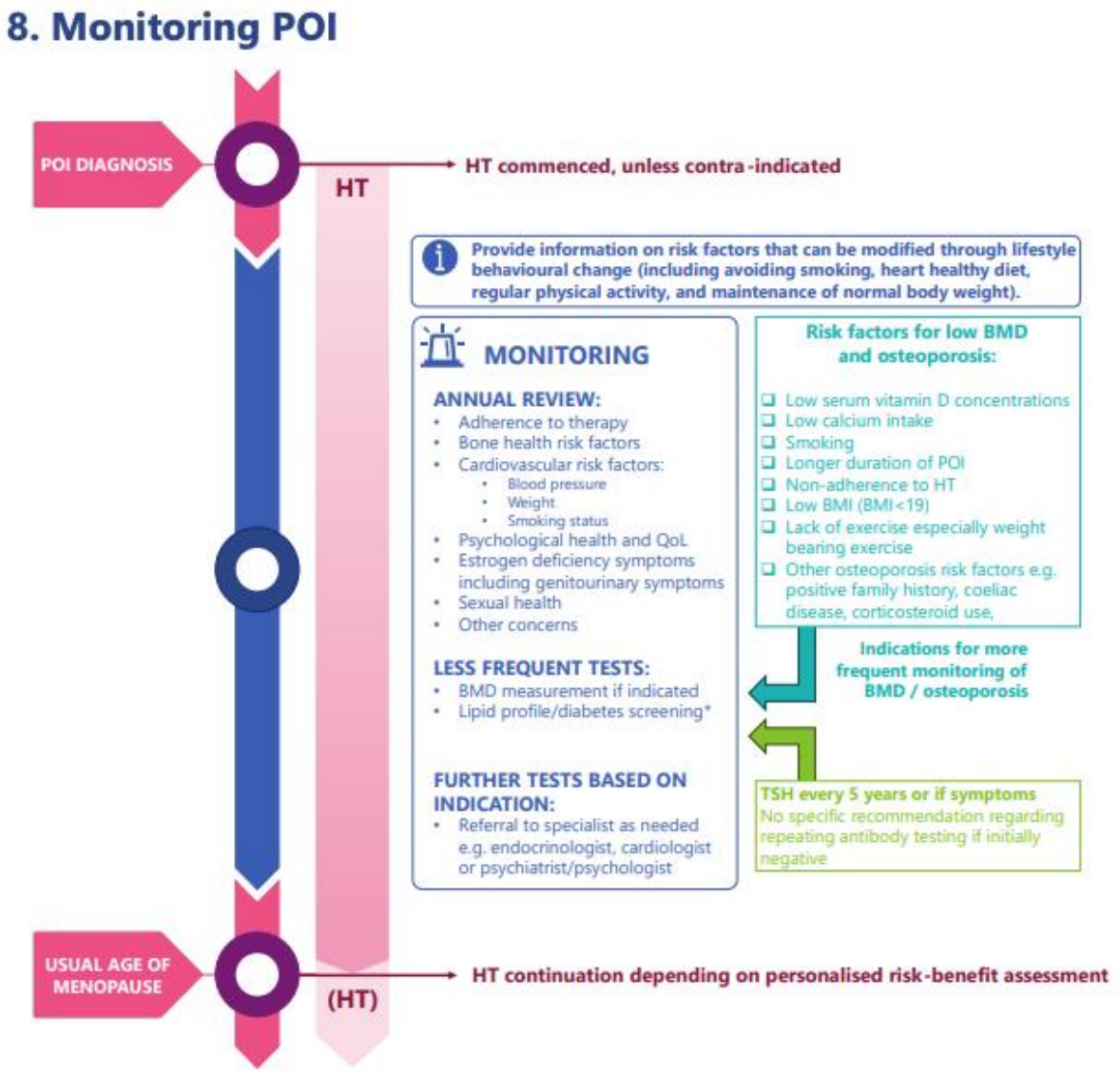
HRT type	***Sequential combined HRT***		***Continuous combined HRT***	
Per 24 hours or day	*Low/standard doses*	*'POI' doses*	*Low/standard dos*	*'POI' doses*
Estradiol type				
Patch (transdermal, µg/24h	**25–50**	**75–100**	**25–50**	**75–100**
Gel sachet (transdermal, mg)	**0.5–1.0**	**1.5–2.0**	**0.5–1.0**	**1.5–2.0**
Gel pump (1 metered dose = 0.75 mg)	**1–2**	**3–4**	**1–2**	**3–4**
Spray (1.53mg per spray)	**1-2**	**3-4**	**1-2**	**3-4**
Oral (mg)	**1.0–2.0**	**2.0–4.0**	**1.0–2.0**	**2.0–4.0**
Progestogen				
Micronized progesterone (oral/per vagina, mg)	**100–200**	**≥ 200 (e.g. 300–400)**	**100**	**≥ 200**
Dydrogesterone (oral, mg)	**10**	**20**	**5.0**	**10**
Medroxyprogesterone acetate (oral, mg)	**5.0**	**10**	**2.5**	**5.0**
Norethisterone acetate (oral, mg)	**2.5–5.0**	**2.5–10**	**1.25–2.5***	**2.5-5.0**
Levonorgestrel intrauterine system (LNG IUS)	**20 µg/day suf**	**ent for low/stand**	**and POI doses**	**mg LNG IUS)**
17 beta-estradiol (E2)/progestogen fi		**l dose combine**	**preparations**	
E2/micronized progesterone (oral, mg)	**1.0–2.0/100–200**	**≥ 2.0/≥ 200**	**1.0–2.0/100–20**	**3.0–4.0/300–40**
E2/norethisterone acetate (transdermal) (µg)	**25–50/85–170**	**75–100/255–340**	**25–50/85–170**	**75–100/255–34**
E2/dydrogesterone (oral, mg)	**1.0–2.0/10**	**2.0/10**	**0.5–1.0/2.5–5.**	**3.0–4.0/7.5–10**
E2/norethisterone acetate (oral, mg)	**1.0–2.0/1.0**	**3.0–4.0/2.0–4.0**	**0.1–2.0/0.5–1.**	**3.0–4.0/1.5–2.0**

Bone health

- Assess baseline risk at diagnosis
  - Risk factors – smoking, alcohol, low BMI, family history of osteoporosis, steroid use
  - **Baseline bone density recommended – Z scores (within 2 SD of the mean is considered normal)**
  - Biochemistry – calcium, vitamin D, renal function
- Lifestyle advice – weight bearing exercise including strength training, limit alcohol, dietary calcium and vit D ***healthybonesaustralia.org.au***
- ***Hormone therapy- unless contraindicated , refer for specialist review***
- Serial bone density
  - Normal at baseline and on HT can repeat 5 years
  - Earlier if lower bone density at baseline ie repeat 1-3 years
- **If falling BMD – review HT preparation, dose and compliance, calcium/D, ? Low BMI, ? Strength training other factors and specialist review**

Monitoring

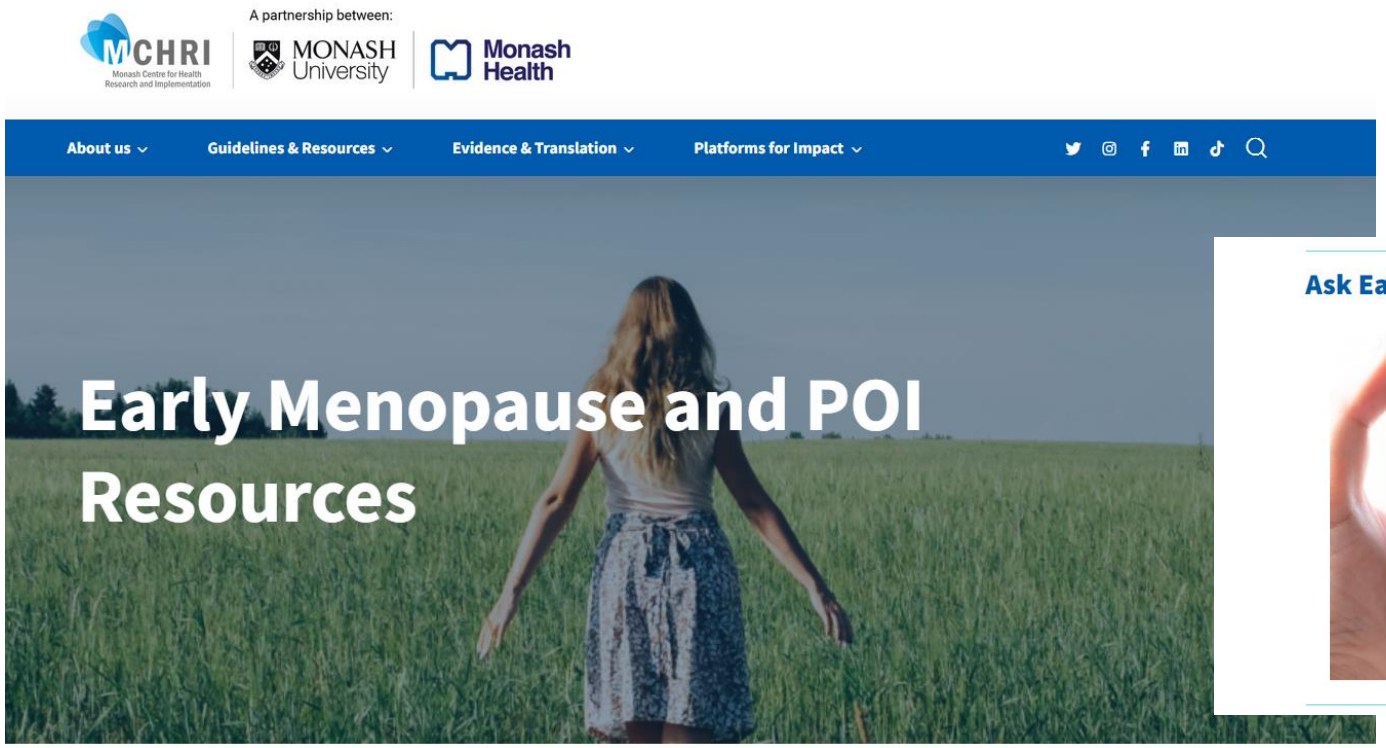


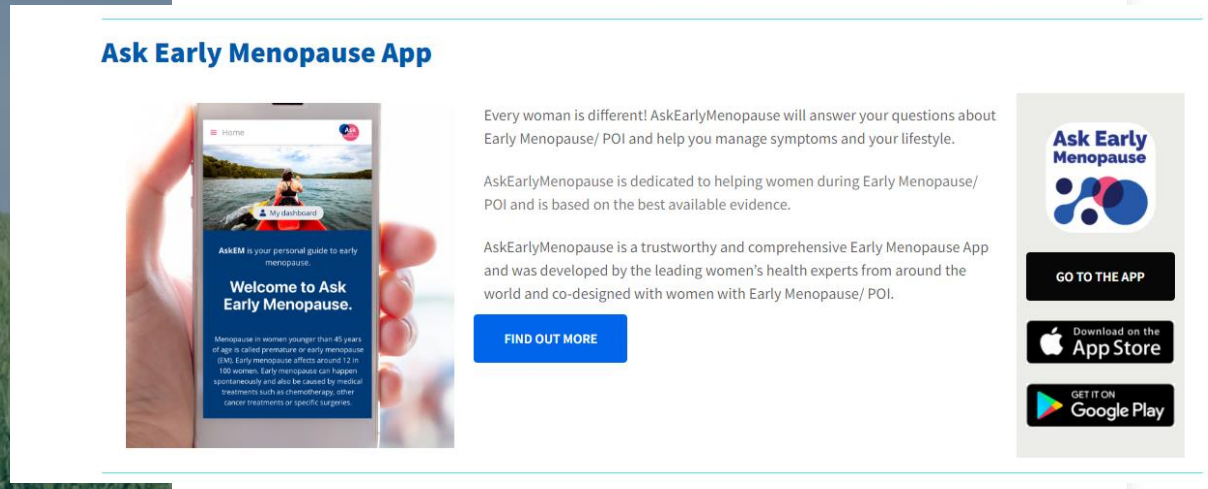


frequency of measurement after screening at diagnosis should be based on the presence of hyperlipidaemia, hyperglycaemia and additional risk factors or global cardiovascular risk.

- Cervical cancer screening and mammography as per national guidelines

Resources


A partnership between:
MCHRI
Monash Centre for Health Research and Implementation
MONASH University
Monash Health
About us
Guidelines & Resources
Evidence & Translation
Platforms for Impact
Early Menopause and POI Resources
What is POI?
What is Early Menopause?


Ask Early Menopause App
Every woman is different! AskEarlyMenopause will answer your questions about Early Menopause/ POI and help you manage symptoms and your lifestyle.
AskEarlyMenopause is dedicated to helping women during Early Menopause/ POI and is based on the best available evidence.
AskEarlyMenopause is a trustworthy and comprehensive Early Menopause App and was developed by the leading women's health experts from around the world and co-designed with women with Early Menopause/ POI.
FIND OUT MORE
Ask Early Menopause
GO TO THE APP
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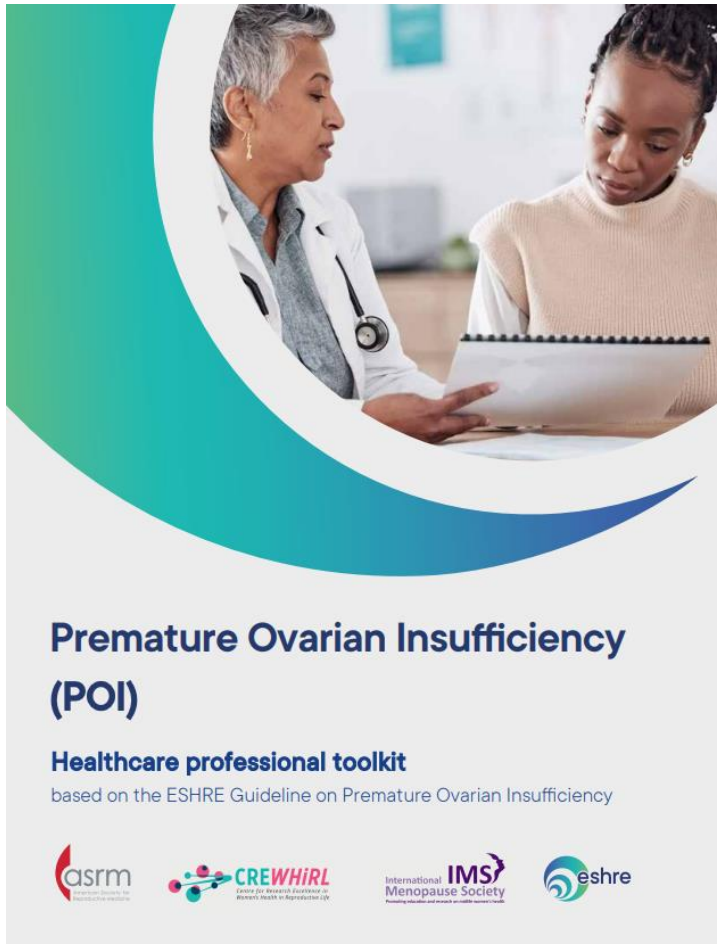
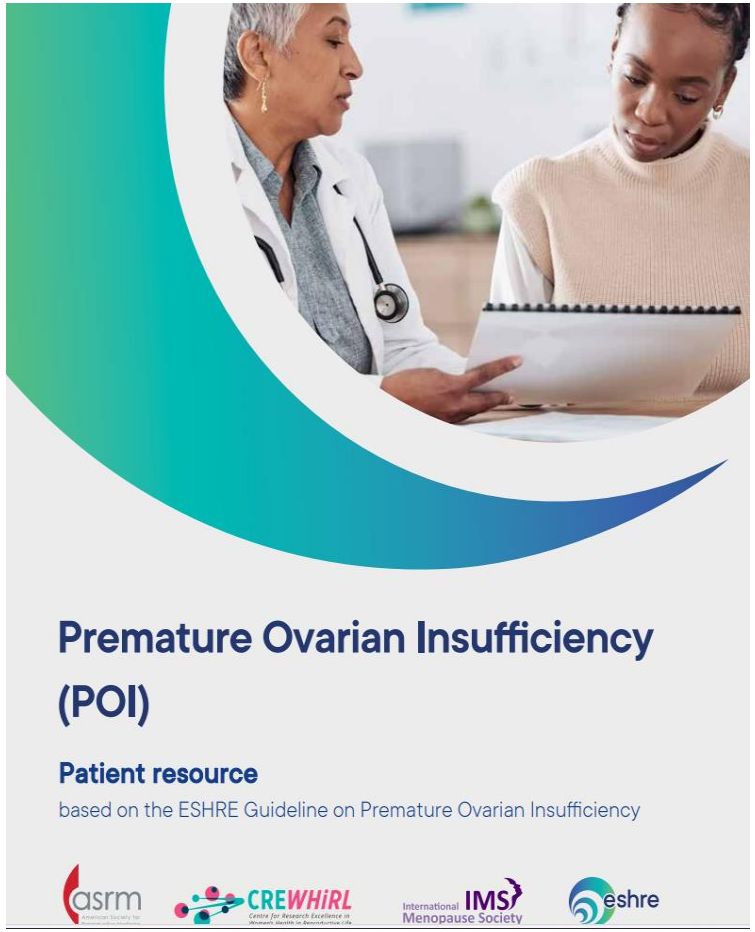
Thankyou


Premature Ovarian Insufficiency (POI)
Healthcare professional toolkit
based on the ESHRE Guideline on Premature Ovarian Insufficiency
asrm
CREWHiRL
International IMS Menopause Society
eshre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