Premature ovarian insufficiency diagnosis and management in general practice: A review based on the 2024 international guideline

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Background
Premature ovarian insufficiency (POI), defined as the loss of ovarian function before the age of 40 years, affects approximately 4% of women. POI may occur spontaneously or secondary to medical treatments. POI has significant implications for fertility, psychological wellbeing, and cardiometabolic, cognitive and bone health.

Objective
The aim of this article is to provide general practitioners (GPs) with a concise, evidence-based summary of the 2024 international POI guideline, focusing on diagnosis and management relevant to primary care.

Discussion
GPs play a pivotal part in early recognition and long-term care of women with POI. This review outlines key diagnostic criteria, initial investigations, referral pathways and management options including hormone therapy, chronic disease risk reduction, fertility counselling and psychosocial support. Emphasis is placed on a multidisciplinary patient-centred approach to optimise outcomes and quality of life.

PREMATURE OVARIAN INSUFFICIENCY (POI) is characterised by the cessation of ovarian function before the age of 40 years. POI presents with menstrual irregularities, infertility and/or symptoms of oestrogen deficiency. The 2024 POI guideline,[1–3] developed by an international partnership (European Society of Human Reproduction and Embryology [ESHRE], American Society for Reproductive Medicine, International Menopause Society and Monash University), clinical and topic experts, provides 145 updated, evidence-based recommendations and a healthcare practitioner toolkit for the diagnosis and management of POI, with a strong emphasis on multidisciplinary care.

The hallmark of POI is oligo/amenorrhoea before the age of 40 years, and it is likely that many women with POI will initially present to a general practitioner (GP) with this symptom. Australian women <40 years of age are frequent presenters to general practice, claiming more than 3.5 Medicare services per woman with GPs in a 12-month period between 2021 and 2022.[4] GPs play an important part in identifying and assessing POI. Given the broad impact of POI on physical and psychological health, GPs are central to coordinating care for affected women.

This article aims to summarise the 2024 ESHRE guideline on POI for general practice, focusing on practical aspects of diagnosis, initial assessment and long-term management.

Definition and epidemiology

POI is defined as the loss of ovarian activity before the age of 40 years, characterised by menstrual disturbance and elevated follicle-stimulating hormone (FSH).[1] Early menopause (EM) is menopause occurring between the ages of 40 and 45 years. POI is relatively common, affecting approximately 4% of women, whereas EM affects 12% of women,[1] with increasing prevalence mainly due to POI caused by medical treatments (Tables 1 and 2).[5,6]

Risk factors and causes

Risk factors for POI/EM include: a positive family history, ethnicity, lifestyle, comorbidities, early life and reproductive factors, iatrogenic factors and chemical toxins (Table 1).[1,6,7] POI may occur spontaneously (non-iatrogenic) or following medical treatment such as chemotherapy, radiotherapy or ovarian surgery (Table 2).[1] Newer techniques have identified more single-gene variants, in addition to chromosomal abnormalities, as genetic causes of POI.[8] However, most cases of POI are currently designated 'idiopathic'.

Table 1. Potential risk factors for POI or early menopause

Risk factor	Example
Genetic	Genetic (eg *FMR1* premutation carriers, Turner syndrome) Family history: 2–18-fold increased risk depending on degree of association
Ethnicity	Lower prevalence in Asian women when compared with Hispanic, Black or White women
Early life	Increased risk with maternal smoking during pregnancy, lower childhood socioeconomic status or being part of a multiple birth Decreased risk with longer breastfeeding duration
Reproductive factors	Early menarche Shorter menstrual cycle (<25 days)
Lifestyle	Smoking Low body mass index
Comorbid conditions	Autoimmune disease may occur before or after a diagnosis of POI (eg autoimmune thyroid disease, Addison's disease, polyglandular autoimmune syndromes, systemic lupus erythematosus, rheumatoid arthritis, immune thrombocytopenic purpura, autoimmune haemolytic anaemia, pernicious anaemia, vitiligo, alopecia areata, inflammatory bowel disease, primary biliary cirrhosis, glomerulonephritis, multiple sclerosis and myasthenia gravis) Polycystic ovary syndrome Infections (eg mumps oophoritis)
Iatrogenic	Chemotherapy and radiotherapy depending on type, dose and radiation field Ovarian or pelvic surgery (eg endometriosis, cystectomy)
Environmental	Heavy metals (eg cadmium, thallium, arsenic) Persistent organic pollutants (eg pesticides, industrial chemicals) Plasticizers (eg PFAS, BPA)

BPA, bisphenol A; PFAS, per- and polyfluoroalkyl substances; POI, premature ovarian insufficiency.

Clinical presentation and diagnosis

A diagnosis of POI should be considered in women aged <40 years presenting with:

- menstrual irregularities or primary/secondary amenorrhoea
- menopausal symptoms such as vasomotor or genitourinary symptoms
- infertility
- symptoms and signs associated with an underlying cause, such as autoimmune disease[9] or Turner syndrome[10] (Tables 1 and 2).

Initial investigations should be directed at assessing the cause of menstrual disturbance, including:

- pregnancy test
- serum FSH (low FSH levels indicate a pituitary/hypothalamic cause of secondary amenorrhoea, whereas normal FSH levels suggest polycystic ovary syndrome)
- serum estradiol (a low estradiol level is consistent with a diagnosis of POI but is not part of diagnostic criteria)
- thyroid-stimulating hormone and prolactin (to exclude other causes of amenorrhoea)
- pelvic ultrasonography (small ovaries with absent follicles helps to confirm diagnosis).

Table 2. Causes of POI

Cause	Example
Genetic	Chromosomal: Turner syndrome (X chromosome) Single-gene variants: Fragile X premutation (*FMR1* gene)
Autoimmune	Autoimmune disease may occur before or after a diagnosis of POI. Conditions include: autoimmune thyroid disease, Addison's disease, polyglandular autoimmune syndromes, systemic lupus erythematosus, rheumatoid arthritis, immune thrombocytopenic purpura, autoimmune haemolytic anaemia, pernicious anaemia, vitiligo, alopecia areata, inflammatory bowel disease, primary biliary cirrhosis, glomerulonephritis, multiple sclerosis and myasthenia gravis
Iatrogenic	Chemotherapy, radiotherapy, bilateral oophorectomy, ovarian surgery
Environmental	Smoking, chemical toxins
Infections	Mumps oophoritis
Idiopathic	Underlying cause not identified but likely to be genetic

POI, premature ovarian insufficiency.

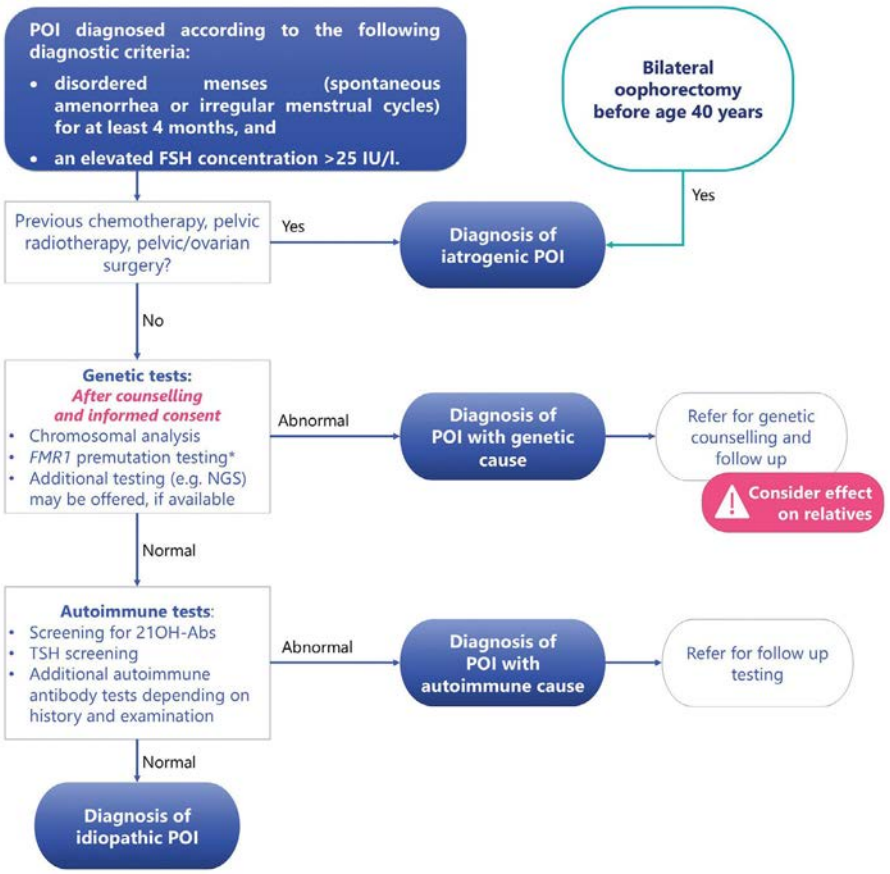

Figure 1. Summary of the recommendations for diagnosis of premature ovarian insufficiency (POI), as well as the recommended further testing to establish a cause of POI.

*Fragile X (*FMR1* gene) 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.

21OH-Abs, 21-hydroxylase autoantibodies; BSO, bilateral salpingo-oophorectomy; NGS, next-generation sequencing; TSH, thyroid stimulating hormone.

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Australian women with POI have reported a diagnostic delay of up to 1.9 years.[11]

Diagnosis of POI can be made if a woman aged <40 years reports oligo/amenorrhoea for ≥4 months and has an FSH level >25 IU/L.[1]

If the diagnosis of POI remains uncertain, then serum FSH testing can be repeated after 4–6 weeks, or anti-Müllerian hormone (AMH) level can be checked.[1] An undetectable AMH level is indicative of POI. The diagnosis of POI can cause significant distress and must be conveyed in a sensitive manner with time for questions and provision of psychological support.[1] Once POI is diagnosed, then investigations are directed at determining the cause, and GPs may consider non-GP specialist referral at this stage (Figure 1 and Table 2).

Consequences of POI

POI is associated with significant negative impacts on psychological and physical functioning (Figure 2).[1] Bilateral oophorectomy is associated with increased menopausal symptoms and chronic disease risk when compared with non-iatrogenic POI.[1] Consequences related to the cause of POI must also be considered, such as cancer, autoimmune disease or Turner syndrome.[10]

Australian women have reported that their greatest fear related to having POI is osteoporosis, followed by loss of sexual desire, weight gain, having no more children and ageing.[11]

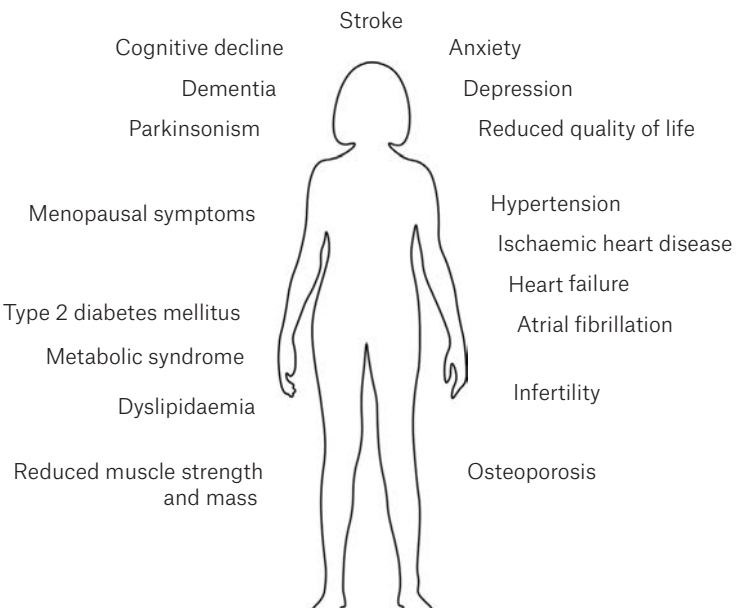

Figure 2. Consequences of premature ovarian insufficiency.

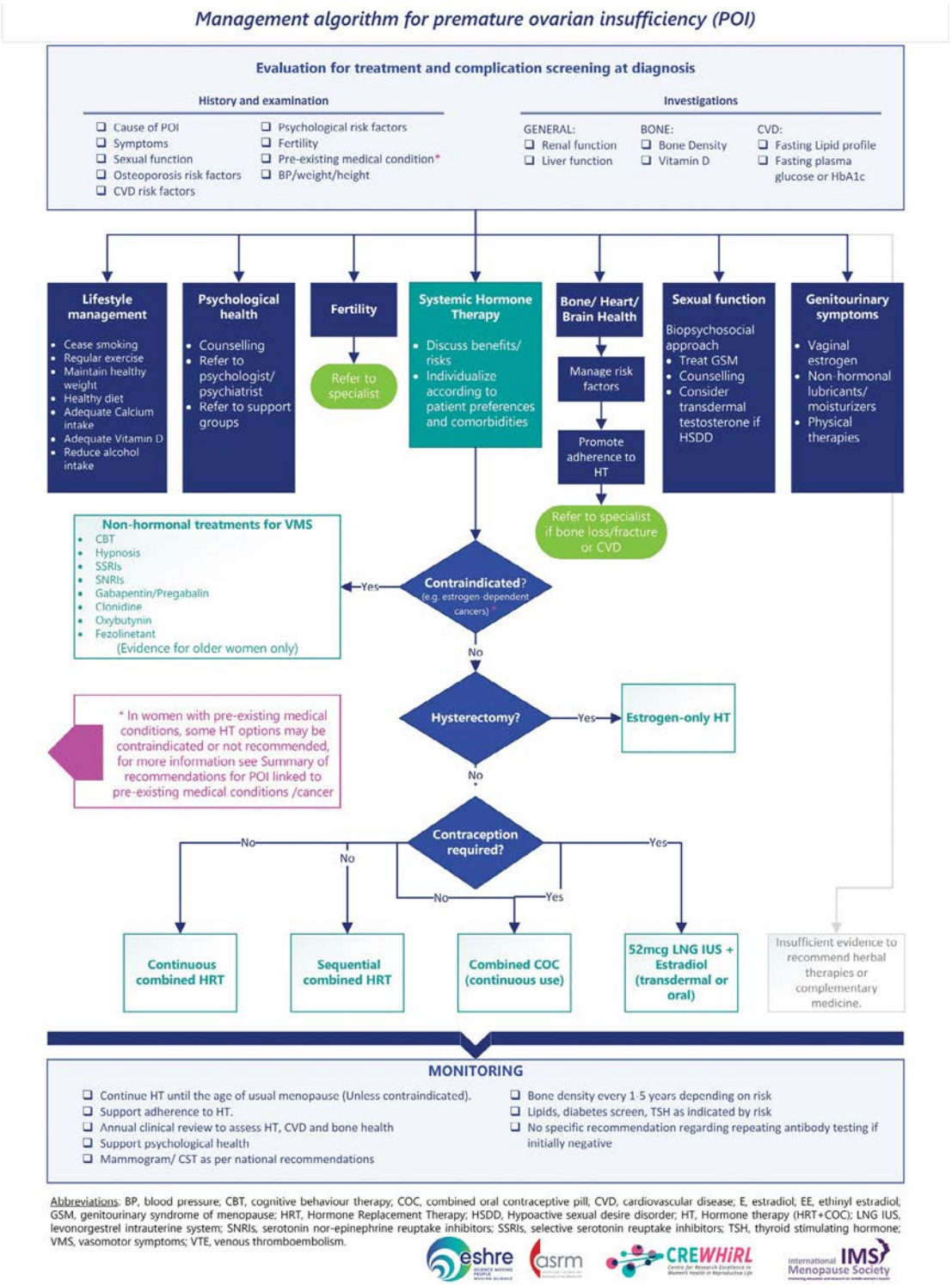

Figure 3. Management algorithm for premature ovarian insufficiency (POI), summarising the recommendations on evaluation and screening, treatment options and monitoring.

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Management

An approach to evaluation and overview of management is shown in Figure 3. GPs play a key part, especially regarding psychological support, ongoing management and follow-up (Table 3). In July 2025, in response to the recommendations from the Senate Community Affairs References Committee Report on Issues related to menopause and perimenopause, a new Medicare Benefits Schedule (MBS) item (695) for GP assessment and management of menopause and perimenopause (including POI) was introduced (www9.health.gov.au/mbs/fullDisplay.cfm?type=item&q=695&qt=item).

Australian women have reported that their GP was expected to be the third best source of information, after their gynaecologist and the internet,[11] and young women with early-onset cancer report that it is crucial for them to have support from their GPs to manage issues such as menopause after cancer.[12] Key considerations are summarised below, and a detailed healthcare professional toolkit is available online (www.eshre.eu/-/media/sitecore-files/Guidelines/POI/2024/POI-GUIDELINE_HCP-Toolkit-2024.pdf).

Providing information

Providing information is considered important by women with POI; it assists self-management and promotes quality of life.[1,13] Accompanying the POI guideline are free resources for women (www.eshre.eu/Guidelines-and-Legal/Guidelines/Premature-ovarian-insufficiency) including the AskEarlyMenopause app (https://mchri.org.au/guidelines-resources/community/ask-early-menopause-resources).

Hormone therapy

Hormone therapy (HT) has benefits for vasomotor symptoms, genitourinary symptoms, sexual function, reducing chronic disease risk (cardiovascular disease [CVD], osteoporosis) and raising life expectancy.[1] HT is indicated for all women with POI unless contraindicated and needs to be instituted promptly and continued until at least the usual age of menopause (~51 years). HT should be personalised with shared decision making. HT prescribing follows principles as for women with usual-age menopause. However, doses of at least 2 mg oral estradiol or 100 mcg estradiol transdermal patch or equivalent estradiol gel are suggested, especially for bone health and symptom relief.[1] Oestrogen should be combined with a progestogen if the patient has an intact uterus, and the dose of progestogen should be increased with higher oestrogen doses. Transdermal HT is preferred in the setting of malabsorption, increased thrombotic risk, liver disease and migraine. The oral contraceptive pill can be prescribed but should be used continuously to maintain bone density and prevent symptoms. However, studies investigating bone health outcomes have used the 30 mcg ethinyl estradiol dose, and data are lacking regarding the use of 20 mcg ethinyl estradiol- or estetrol-containing (eg Nextstellis [Mayne Pharma International, Salisbury South, South Australia]) contraceptive pills. Consider referral to an endocrinologist or gynaecologist if HT is contraindicated or complex comorbidities exist. Gradually increasing doses of transdermal oestrogen, not the contraceptive pill, is recommended for individuals requiring pubertal induction,[1] and referral to the appropriate non-GP specialist, such as paediatric endocrinologist or gynaecologist, is advised.

Table 3. Summary of the role of the GP in the diagnosis and management of POI

Role	Actions
Early identification	Recognise symptoms, initiate investigations.
Diagnosis	Confirm with FSH and clinical history. Repeat FSH after 4–6 weeks or check AMH if diagnosis uncertain. Convey diagnosis in a sensitive manner with time for questions. Refer for identification of cause as needed.
Initial management	Assess for consequences of POI such as chronic disease risk (BP, weight/height, bone density, vitamin D level, fasting lipid profile, fasting plasma glucose or HbA1c). Assess fertility, psychosocial and sexual/genitourinary health needs. Assess and support healthy lifestyle behaviours. Assess risk factors for and prescribe personalised HT if there are no contraindications or refer to non-GP specialist as needed. Provide education and psychological support. Coordinate referrals as needed.
Referral	Genetic counselling, gynaecology, endocrinology, fertility, psychology, physiotherapy/exercise physiology, sexual counselling, dietitian as needed.
Long-term follow-up	Monitor and address ongoing lifestyle, HT adherence, bone, cardiovascular, sexual, fertility and psychological health needs.

AMH, anti-Müllerian hormone; BP, blood pressure; FSH, follicle-stimulating hormone; GP, general practitioner; HT, hormone therapy; POI, premature ovarian insufficiency.

Other therapies

Other therapies, such as non-HTs, may be considered for the management of symptoms in those with contraindications to HT; however, most studies have been conducted in the non-POI population.[1] Non-hormonal treatments for vasomotor symptoms include cognitive behaviour therapy, hypnosis, fezolinetant, selective serotonin reuptake inhibitors, serotonin–noradrenaline reuptake inhibitors, gabapentin and oxybutynin. The benefits of complementary therapies are unproven, and these should not replace HT.[1]

Musculoskeletal health

In addition to HT, all women should be advised to do weight-bearing and resistance exercise, avoid smoking, maintain a normal body weight, avoid excess alcohol and maintain adequate calcium and vitamin D intake. Other risk factors for osteoporosis should be identified and addressed.

Women need to have bone mineral density (BMD) assessed at diagnosis, and a repeat bone density measurement in 1–3 years if low bone mass is identified. Dual energy X-ray absorptiometry (DXA) is listed on the MBS (item 12312) for 'female hypogonadism lasting more than 6 months before age 45 years'. Endocrinologist referral for consideration of bone-specific therapies is needed if: (1) HT is contraindicated; (2) fragility fractures occur while on HT; or (3) there is a decrease in BMD on subsequent scans of >5% and/or >0.05 g/cm^2. If BMD is normal and adequate (≥2 mg oral/100 mcg transdermal estradiol) systemic oestrogen replacement is maintained, the value of repeated DXA within 5 years is low.

Cardiovascular health

Women with POI need to be advised that they are at increased risk of CVD including coronary artery disease, heart failure and stroke. HT reduces CVD risk. All women need to have risk factors – including dyslipidaemia and type 2 diabetes – assessed at diagnosis, and at least annual monitoring of blood pressure, weight, waist circumference and smoking status.

Fertility considerations

Fertility considerations are important, as infertility is a major cause of distress. Spontaneous pregnancy may occur in <10% of those with spontaneous POI; this usually occurs soon after diagnosis and with lower FSH levels.[1] HT that provides contraception (eg contraceptive pill or Mirena used with concurrent oral or transdermal oestrogen therapy) should be prescribed to those who do not desire pregnancy. Choice of contraceptive pill needs to be personalised, as noted above, and used continuously. When combined with oestrogen therapy, the Mirena (not the Kyleena) is used and needs to be changed every 5 years. There are no established methods to restore fertility currently, and options for parenthood include oocyte donation, embryo donation or adoption. Referral to a non-GP fertility specialist is necessary. Fertility preservation (eg oocyte cryopreservation) may be considered in at-risk women.

Psychosocial support

Psychosocial support is essential as women with POI experience high rates of anxiety, depression and grief, which contribute to impaired quality of life.[1,13,14] Counselling and peer support and referral should be offered as needed.

Sexual health

Sexual health problems are common and multifactorial and cause distress and impaired quality of life.[1] A biopsychosocial approach[15] is preferred, with counselling and referral (eg sexual therapist, pelvic floor physiotherapist) as needed. Transdermal testosterone therapy can be considered for hypoactive sexual desire disorder.[16]

Genitourinary symptoms

Vaginal oestrogen therapy may be needed in addition to systemic HT for genitourinary symptoms. Non-hormonal vaginal moisturisers and lubricants and pelvic floor physiotherapy may also assist and can be combined with HT.

Healthy lifestyle behaviours

Healthy lifestyle behaviours are important to reduce chronic disease risk, promote emotional wellbeing and potentially assist with symptom management. These include smoking cessation, regular exercise, maintenance of a healthy weight and diet, adequate calcium and vitamin D intake and reduction of alcohol intake. GPs play a pivotal part in supporting women to achieve their goals.

Conclusion

POI is a multifaceted condition with significant implications for women's health and wellbeing. GPs are central to early recognition, diagnosis and long-term care. The 2024 international POI guideline provides a robust framework for evidence-based management, including hormone therapy, chronic disease risk reduction and psychosocial support. A proactive, multidisciplinary approach can significantly improve outcomes and quality of life for women with POI.

Key points

- POI is defined as oligo/amenorrhoea for at least 4 months with an FSH level >25 IU/L occurring before the age of 40 years.
- Early diagnosis is critical to prevent long-term sequelae; thus, POI needs to be considered in any women aged <40 years presenting with oligo/amenorrhoea, infertility or menopausal symptoms.
- HT is the first-line treatment unless contraindicated.
- Provision of information and psychological support, and consideration of fertility needs are also essential care components.
- GPs are central to early diagnosis, ongoing management and coordination of care.

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