Premature Ovarian Insufficiency (POI)

Patient resource

based on the ESHRE Guideline on Premature Ovarian Insufficiency

asrm American Society for Reproductive Medicine

CREWHiRL Centre for Research Excellence in Women's Health in Reproductive Life

International IMS Menopause Society Promoting education and research on midlife women's health

eshre

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Welcome to the POI Patient Resource!

This resource is for you if:

- You have been diagnosed with premature ovarian insufficiency (POI)
- Are wondering if you have POI.

This resource is intended for patients, but may also be useful for their family members and caregivers.

This resource aims to:

- Increase awareness of premature ovarian insufficiency by sharing up-to-date information.
- Provide you with the latest best practice in healthcare for POI to help you understand and self-manage this condition.
- Encourage you to see your healthcare professional (HCP) regularly.
- Encourage shared decision-making, meaning you and your HCP work together to choose the best treatment options for you.
- Help you make informed decisions about your health.

By using this resource, you can take an active role in your healthcare journey.

Let's work together to achieve the best possible outcomes for your health!

This resource is based on the 2024 updated ESHRE Guideline on the management of women with Premature Ovarian Insufficiency. This new guideline builds on, updates and expands the previous 2016 ESHRE Premature Ovarian Insufficiency Guideline and was developed by a partnership between European Society for Human Embryology and Reproduction (ESHRE), American Society for Reproductive Medicine (ASRM), Monash University Centre for Research Excellence- Women's Health in Reproductive Life (CREWHiRL), and the International Menopause Society (IMS). The final POI Guideline contains 40 key questions with 145 recommendations. All the information and recommendations in the Guideline are based on the best available evidence from research. When there is insufficient evidence from research, a group of experts have formulated recommendations based on their clinical expertise.

We have added the following symbols to explain the strength of the recommendations

👍	Strong recommendation based on research evidence
✓	Recommendation based on considered opinion of the guideline development group

The information in this resource can be used with the co-designed consumer summaries of topics and the Ask Early menopause App. More information is available on page 27 of this resource. The entire Guideline is available on the ESHRE website .

Contents at a Glance

Part A: Introduction

What is Premature Ovarian Insufficiency (POI)?

Premature Ovarian Insufficiency or "POI" was first described in 1942 and since then has been described by different names and definitions. Other names used for premature ovarian insufficiency are primary ovarian insufficiency, premature ovarian failure, gonadal dysgenesis, premature menopause, early menopause and hypergonadotropic hypogonadism.

"Premature ovarian insufficiency" (POI) is recommended as the name for this condition. ✓

POI is a condition where the ovaries stop functioning normally before the age of 40. The ovaries stop releasing eggs and stop producing hormones (estrogen, progesterone, testosterone). This causes your menstrual periods to stop or become irregular and blood tests show high levels of follicle stimulating hormone (FSH) and low estrogen levels. If this happens between ages 40-44 years, it's called **'early menopause'**. POI was previously thought to affect about one in one hundred women before age 40 years (one in one thousand before age 30 years) but recent studies suggest that POI is more common.

POI is defined as a condition where the ovaries stop functioning normally before the age of 40 years. Your periods stop or become irregular AND blood tests show high levels of follicle stimulating hormone (FSH) and low estrogen levels ✓

POI affects about four in one hundred women. ✓

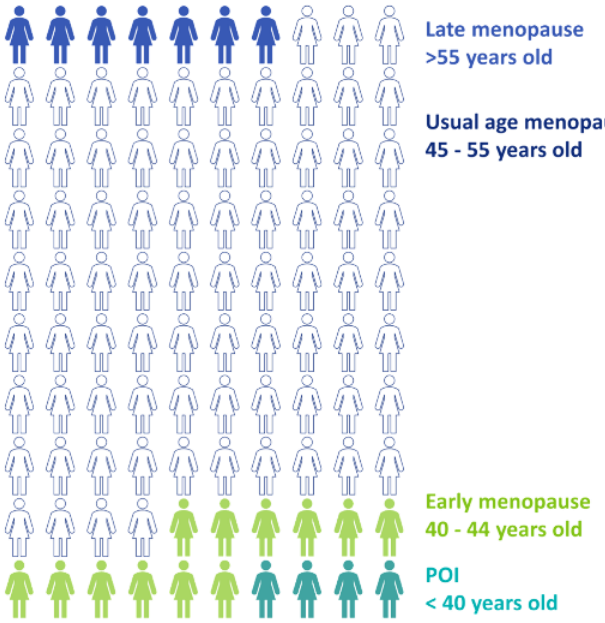
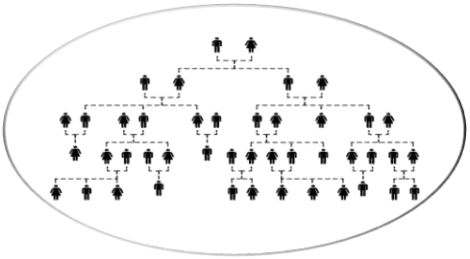


Figure: The usual age of menopause is between 45-55 years but may vary between countries. This figure shows how many women from of a group of 100 will have POI (4%), early (12%) or late menopause (7%) and usual age menopause.

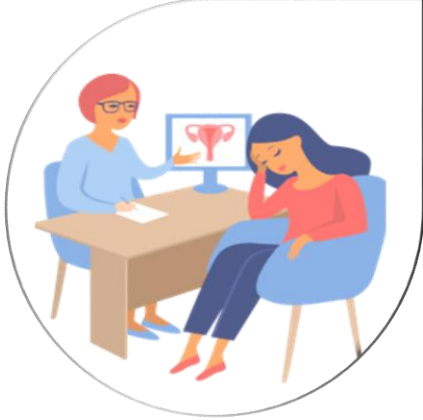
What are the risk factors for POI?



Having a family member (eg. mother, sister, twin) diagnosed with POI increases your risk. Women who smoke have an earlier age at menopause, including POI, compared to non-smokers. Having a known genetic cause of POI (such as a specific gene variant, Fragile X premutation or Turner syndrome) increases your risk. Certain autoimmune conditions (for example, rheumatoid arthritis, polyglandular autoimmune disease, inflammatory bowel disease) are also associated with a higher risk of POI. Medical treatments such as chemotherapy, pelvic radiotherapy or surgery on the ovaries increase your risk. The risk of POI may also vary according to your ethnicity (lower in women of Asian background), reproductive factors (such as earlier age at first menstrual cycle or short menstrual cycle length), social factors (lower education or socioeconomic status, living in a developing country), and exposure to environmental toxins.

As POI can affect long term health, it is important that your HCP talk with you about the risk of POI and how to reduce the risk when planning treatments that can affect the ovaries, e.g surgery on the ovaries or uterus (womb), chemotherapy or radiotherapy. ✓

It is recommended that HCPs identify and counsel women who are at risk of POI and talk with them about what they can do about their fertility. ✓



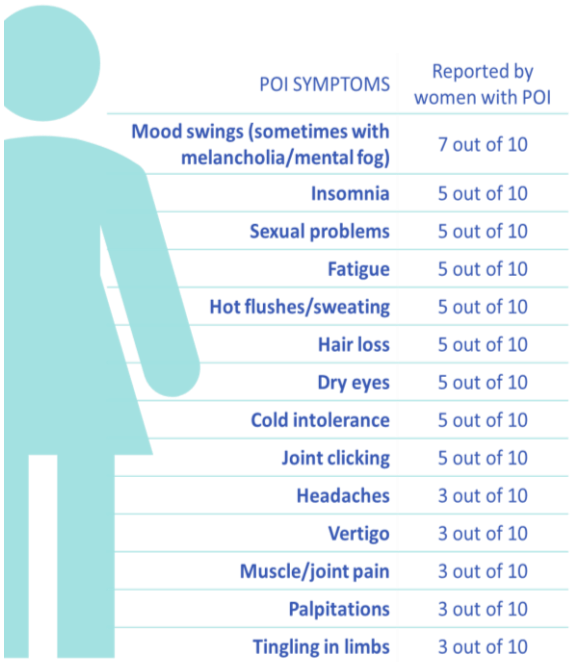
PART B: Diagnosis of POI

Symptoms, Investigations and Cause

What are the symptoms of POI?

Symptoms of POI vary in different women. Women with POI will often stop having periods (called amenorrhoea) or have them less often (called oligomenorrhoea). Some people with POI, often due to genetic causes, may never start having periods (called primary amenorrhoea). You might have symptoms like hot flushes, night sweats, vaginal dryness, itching, discomfort, needing to pass urine more often, or pain during sex. These symptoms are due to low estrogen levels. Problems getting pregnant can be a sign of POI. Symptoms and signs related to the cause of POI (such as Turner syndrome, autoimmune disease, or cancer) or other existing health issues may also be present.

Figure: Symptoms reported by women with POI



POI SYMPTOMS	Reported by women with POI
Mood swings (sometimes with melancholia/mental fog)	7 out of 10
Insomnia	5 out of 10
Sexual problems	5 out of 10
Fatigue	5 out of 10
Hot flushes/sweating	5 out of 10
Hair loss	5 out of 10
Dry eyes	5 out of 10
Cold intolerance	5 out of 10
Joint clicking	5 out of 10
Headaches	3 out of 10
Vertigo	3 out of 10
Muscle/joint pain	3 out of 10
Palpitations	3 out of 10
Tingling in limbs	3 out of 10

Symptoms may change or go away as ovarian activity changes.

The severity of symptoms can vary depending on the cause of POI.

It is recommended that HCPs ask women with no menstrual periods or irregular periods about symptoms of low estrogen such as hot flushes. ✓

It is recommended that HCPs check for POI in women under age 40 with no periods or irregular periods and/ or symptoms of low estrogen. ✓

How is POI diagnosed?

POI is diagnosed by checking how often you have menstrual periods (over 4 months or more) and by testing hormone levels in the blood. When diagnosing POI, HCPs need to first rule out pregnancy and consider if hormonal contraception is masking symptoms.

A person who has both ovaries surgically removed before age 40 years has a diagnosis of POI and no further testing is needed.

What investigations (tests) should be done?

POI is diagnosed in women under 40 years when a woman has irregular periods or no menstrual periods for at least four months and abnormal hormone tests which indicate POI. 

A diagnosis of POI is made when a woman has irregular periods or no periods for at least 4 months AND a high follicle stimulating (FSH) hormone level on a blood test. FSH levels can be tested again in 4-6 weeks if the diagnosis of POI is uncertain after the first FSH test. ✓

A blood test showing a low estrogen level helps to confirm the diagnosis of POI but a low estrogen level alone cannot be used to diagnose POI. ✓

AMH (anti-mullerian hormone) is a hormone produced by the small follicles (immature egg cells and their surrounding supporting cells) in the ovary. An AMH test is often done to check ovarian reserve as part of infertility treatment. AMH has been proposed as a test to diagnose POI but it is no better than FSH testing. AMH tests may not be available in some countries and there are different methods used for AMH testing. For most women, current AMH tests are not accurate enough to predict who will develop POI. Research shows that FSH testing is the recommended test.

A blood test for anti-mullerian hormone (AMH) should not be used as the main test to diagnose POI 

A blood test for AMH can help confirm a diagnosis of POI if the FSH blood test results do not confirm the diagnosis of POI ✓

What causes POI?

POI can be iatrogenic, which means it has been caused by medical treatment, including for cancer or benign (non-cancer) disease. POI may also happen without warning (spontaneous non-iatrogenic POI) and in this case, your doctor will perform several tests to look for for a cause. POI can be due to a genetic or autoimmune cause, but for many women, no cause of POI is found and the term 'idiopathic POI' is used. It is likely that for many women with 'idiopathic POI', there is an underlying genetic cause that can't be detected with current tests.

It is recommended that HCPs tell women with POI about the different causes of POI, the limits of current tests in working out a cause, and that an exact cause may not be found. ✓

Iatrogenic POI (POI due to medical treatments)

Surgical removal of both ovaries (ovariectomy/oophorectomy) before the age of 40 years results in POI and is the most common cause of iatrogenic POI. Surgical removal of the ovaries is performed for many reasons including a high risk of developing ovarian cancer, e.g. in women carrying a mutation in the BRCA gene. Surgery on the uterus or ovaries before the age of 40 years, such as the treatment of endometriosis or ovarian cysts, especially if this is needed to be done more than once, may also lead to POI.

Chemotherapy and radiotherapy for treatment of cancer or benign diseases may cause damage to the ovaries, leading to POI. The amount of damage depends on several factors, including the type and dose of treatment, the part of the body that had radiotherapy and the age of the person. It is often hard to predict whether a woman will develop POI. You may be given treatment during your chemotherapy to try to protect your ovaries and prevent POI

It is recommended that HCPs discuss the risk of POI with the person before any medical or surgical treatment that may cause POI. ✓

Fertility preservation needs to be considered before any medical or surgical treatments that may cause POI. 👍

If you are to have treatment for cancer or benign diseases that could result in POI, your HCP should discuss this with you before starting treatment.
The topics that should be discussed are:

- your risk of developing POI,
- your options for prevention of POI, and
- your options for fertility preservation before medical treatment or surgery

Genetic and chromosomal causes

POI can be caused by a change in your chromosomes or genes. This is the genetic information you received from your parents and which you pass on to your children. Examples of the most frequent chromosomal/genetic causes are Turner Syndrome and Fragile-X syndrome respectively.

To check whether you have a chromosomal or genetic change causing POI, chromosomal and Fragile-X testing are recommended via a blood test. Counselling is important before the test to explain about the potential results and what they may mean for you and your relatives. New genetic tests are available in some countries (e.g France and Norway) which can detect more gene variants which cause POI. If a genetic or chromosomal cause for POI is found, this may have implications for your family members, both male and female. Your HCP should discuss this with you before testing and provide information on how to talk to your relatives.

It is recommended that before genetic testing for POI, HCPs talk about the genetic tests for POI, what they mean and consider a referral for specialist genetic counselling. ✓

Chromosome tests and a test for Fragile X gene premutation are recommended for women with POI when POI is not caused by medical treatments. 👍

Further specific genetic testing can be offered to women if these tests are available and after counselling. 👍

Autoimmune causes of POI

Our body makes antibodies to fight viruses and bacteria. In autoimmune diseases, the body makes antibodies that attack itself, called autoantibodies. Women with POI might have autoantibodies against the thyroid gland in the neck, which can cause thyroid problems. It's not clear if these autoantibodies cause POI. Sometimes, the body makes autoantibodies which attack the adrenal glands near the kidneys which also causes inflammation in the ovaries and destroys eggs.

Your doctor might do a blood test to look for these autoantibodies. If they find any, they may do more tests to check your adrenal and thyroid gland function, and may need to send you to a specialist. Other autoimmune diseases linked to POI include rheumatoid arthritis, lupus, pernicious anemia, inflammatory bowel disease, myasthenia gravis, and coeliac disease. If you have symptoms of these diseases, you might need more tests for other autoantibodies.

A test for 21-hydroxylase adrenal antibodies should be done in women with an unknown cause of POI. If the test shows positive 21-hydroxylase antibodies then referral to an endocrinologist is needed. If the first test is negative then there is no need to retest 21-hydroxylase antibodies unless symptoms of adrenal deficiency appear.

Thyroid function should be checked at POI diagnosis and every 5 years, or if symptoms of thyroid problems appear. Women with POI and abnormal thyroid function tests need to be assessed and thyroid problems treated.

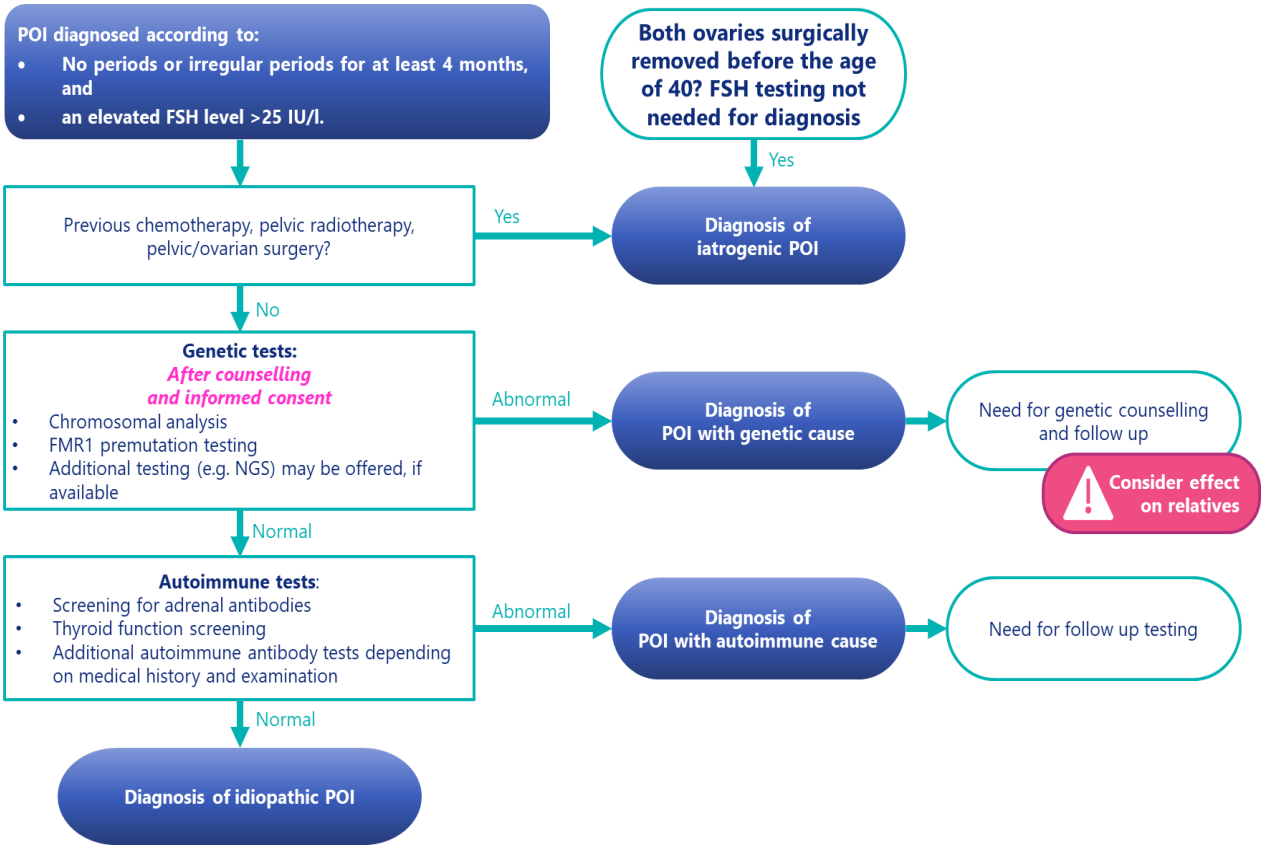
Other causes of POI

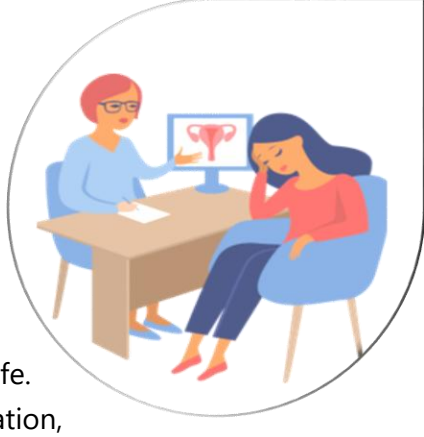
In a few cases, POI has been linked to a previous infection (e.g mumps). This has not been shown in studies of large groups of women, and therefore women with POI do not need to be screened for previous infections.

Idiopathic or unexplained POI

In most women with non-iatrogenic POI, the genetic or autoantibody tests are normal and there is no specific cause of POI identified. This is called "idiopathic POI".

Figure: Flow chart for diagnosis and cause of POI





Care for women with POI at diagnosis

Being diagnosed with POI can be very distressing and you may experience a range of emotions. How quickly the diagnosis is made and how you are told of the diagnosis can impact your emotional wellbeing and quality of life. Getting accurate information about POI that meets your needs and situation, having your questions answered, being able to make decisions together with your healthcare team and referrals to support groups or counselling can be helpful.

It is recommended that HCPs tell women that they have a diagnosis of POI in a caring and sensitive way, give clear accurate personalised information, and allow time for questions. ✓

It is recommended that HCPs and women should make decisions together and preferably the same healthcare team continues care with the person. ✓

It is recommended that women with POI are referred to support groups and support for mental health. ✓

Relatives of women with POI

If you are diagnosed with non-iatrogenic POI then your female relatives are at higher risk of POI. If a genetic cause of POI is identified then this may have implications for both your female and male relatives. Genetic counselling may be helpful to understand what your diagnosis means for you and your relatives. Counselling or a psychologist referral may also be helpful for you and your relatives if the diagnosis of POI is affecting emotional wellbeing or psychological health. There is no way to predict or prevent non-iatrogenic POI. Referral to a specialist to consider ovarian reserve testing or fertility options may be helpful.

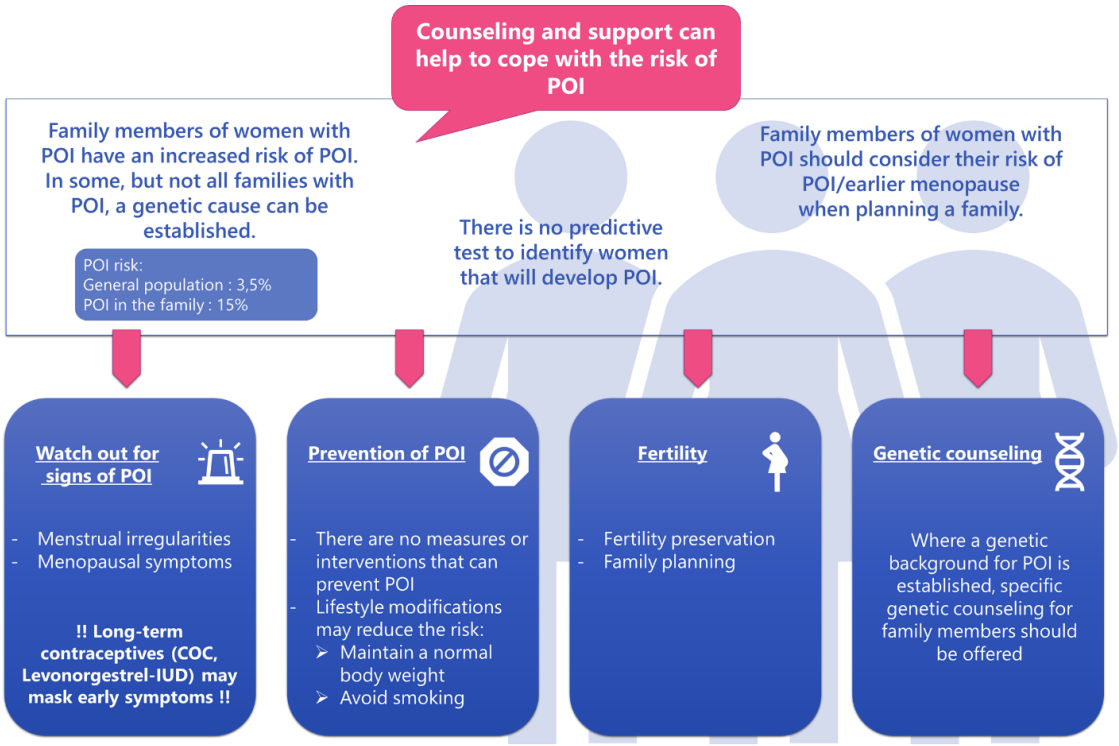
It is recommended that relatives of women with known genetic causes of POI, such as Fragile X premutation, should have genetic counselling and testing. ✓

Female relatives (like sisters or daughters) of women with non-iatrogenic POI should be counselled that they are at higher risk of POI.

It is recommended that female relatives of women with non-iatrogenic POI should be offered support about their increased risk. Relatives should be aware of the symptoms and signs of POI and see a HCP if they notice symptoms. ✓

It is recommended that female relatives of women with non-iatrogenic POI be aware that there is no way to predict or prevent POI. Relatives might consider family planning and fertility options. ✓

Figure: Advice for relatives of women with POI



COC- combined oral contraceptive

Part C: Consequences of POI

What are the effects of POI on my health?

Women with POI have unique needs. Being diagnosed with POI can be a life changing experience and you may feel overwhelmed and isolated. You may not only suffer from symptoms associated with low estrogen levels, but can also experience other issues, with a significant impact on your quality of life and longterm health. POI can have significant effects on fertility, bone health, cardiovascular health, sexual wellbeing, psychological wellbeing and brain function.

1. Fertility

As POI is a condition where the ovaries stop functioning normally before the age of 40, the chances of becoming pregnant naturally is greatly reduced. For a few women with POI, the ovaries still have some egg cells and they may become pregnant. This happens rarely, and is usually soon after POI diagnosis, when women may still have periods and when FSH levels are closer to the normal range. The cause of POI may also affect pregancy risks after natural conception and specialist advice may be needed. For many women with POI, infertility is a main concern and it can have a signficiant impact on emotional wellbeing and quality of life.

If you have POI, you usually have difficulties getting pregnant naturally. However, if you have not had both ovaries surgically removed, then there may be a small chance of spontaneous pregnancy, so your HCP should discuss the need for contraception with you.

If you had both ovaries removed during surgery, you are no longer able to get pregnant naturally.

Currently there are no treatments or procedures that can reverse POI or increase your chances of getting pregnant naturally.

Your risk of POI and how to preserve your fertility needs to be discussed before treatments that can affect the ovaries, such as surgery on the ovaries or uterus (womb), chemotherapy or radiotherapy.

Assisted reproduction techniques using egg donation (oocyte, egg-cell) or embryo donation are potential options for women with POI wanting to become pregnant. In vitro fertilization (IVF) is an option to get pregnant after POI if you were able to freeze your oocytes (egg cells) or ovarian tissue before having chemotherapy, radiotherapy or surgery.

Oocyte (egg-cell) donation can be an option to get pregnant.

If you consider oocyte donation from your sister you should be aware that this can have a higher risk of an insufficient number of eggs maturing in your sister's ovaries

For some women with POI, pregnancy can have higher risks which may be due to using oocyte donation or the cause of POI, such as Turner syndrome or some cancer treatments. You may need pre-pregnancy assessment and counselling with heart and pregnancy specialists. You may also need closer monitoring during your pregnancy with a specialist care team.

If you get pregnant through oocyte donation, you may be at increased risk for complications during pregnancy. To prevent these complications, you need to tell your HCP that your pregnancy is due to oocyte donation. You may need some additional tests before pregnancy, and close monitoring during pregnancy.

Natural pregnancy in women with idiopathic POI or POI after chemotherapy usually does not have higher risks than normal pregnancies.

If you have had radiation to the uterus (womb) then pregnancy is high risk and you need special care.

A heart specialist should be part of the care team if you had certain cancer treatments that can affect the heart and you want to get pregnant.

If you have Turner Syndrome, you need to have your heart checked and counselling from heart and pregnancy specialists before planning a pregnancy, especially if thinking about oocyte or embryo donation.

If you have Turner syndrome, pregnancy is high risk and you need special care with a heart specialist as part of the care team

For some women with POI, pregnancy is very high risk and may be life threatening, and therefore HCPs may advise you against pregnancy using oocyte donation

2. Bone, muscle, heart and brain

Estrogen helps keep your bones, muscles, heart, brain, and metabolism healthy. Low estrogen levels can cause menopausal symptoms and also affect your bones, muscles, heart, and brain. If POI is not treated, it can lead to a shorter lifespan, mainly because of heart disease. There may also be other health problems depending on what caused your POI such as cancer treatment or Turner syndrome.

POI is associated with reduced bone density; you may be at increased risk of bone fractures later in life.

POI may be associated with reduced muscle bulk (mass) and strength

POI is associated with an increased risk of developing heart disease including coronary heart disease, heart failure and stroke.

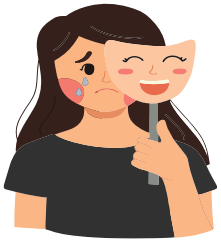
POI is linked to a higher risk of cognitive problems (thinking and memory) and dementia.

Untreated POI is associated with a reduced lifespan mainly due to heart disease

A healthy lifestyle (e.g. regular physical activity, stop smoking, healthy diet, maintaining a healthy weight and limited alcohol intake) can help reduce the impact of POI on your bones, muscle, heart and brain. ✓

3. Emotional Wellbeing

POI can significantly impact your psychological wellbeing and quality of life.

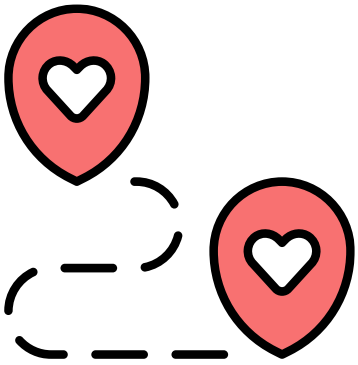


POI can affect your mental and emotional health and your quality of life. You might feel sad, anxious, depressed, have mood swings, low self-esteem, guilt, shame, or feel alone. Infertility, menopausal symptoms, and other health issues can also affect how you feel. But not all feelings are bad; some women feel relieved to finally have answers about their body.

It's important to talk to someone and get help if you're struggling with your mental or emotional health. Your HCP can give you the support and care you need. Learning more about POI and joining a support group can also help. Living a healthy lifestyle can improve your emotional health too.

4. Sexual Wellbeing

POI can have a significant impact on your sexual wellbeing and sex life. You may experience vaginal dryness, reduced libido (sexual desire), and pain during intercourse.



Infertility, menopausal symptoms, low energy, mental health issues, social problems, and other health concerns can affect your sexual wellbeing and your relationship with your partner. Sexual problems are different for each woman. A personal approach is needed to manage these concerns, looking at your body, psychological, and social factors ("biopsychosocial model"). Treatments can include medications, physical therapy, and counselling. Talking about your feelings and concerns with your partner can also help.

It is recommended that your HCP sensitively talk with you about the impact of POI on your sex wellbeing or sex life. They can recommend the right treatment for your needs including hormone replacement therapy, local vaginal therapy, testosterone therapy, vaginal moisturisers, physical therapy, vaginal lubricants and counselling.

Part D: Managing POI

6 Tips to manage POI

1

Aim for a healthy lifestyle, including:

- **A balanced diet and maintain a healthy weight**
- **Regular exercise for at least 150 minutes/week (aerobic, weight-bearing and resistance)**
- **Stop smoking**
- **Limit alcohol**

Living a healthy lifestyle is good for everyone, even though there's not much specific evidence for POI. A healthy lifestyle can help your overall health, emotional wellbeing, and prevent chronic diseases. It can also reduce the impact of POI on your bones, muscles, heart, and brain. There are no studies that show that quitting smoking helps POI symptoms, but stopping smoking is good for your general health, especially for your bones and heart.

2 **Your emotional wellbeing is important**

If you feel that POI is affecting your wellbeing, it's okay to ask for help. Your HCP can give you psychological support and refer you to counselling if needed. Joining a support group, managing stress, and living a healthy lifestyle can also help.

3 **Discuss any symptoms you have with your HCP. They can talk with you about treatment options, and together you can work out a plan that is right for you. It is always good to ask questions or talk about your concerns.**

There are treatments to help with the impact of POI on emotional and sexual wellbeing. You can use hormonal and non-hormonal treatments for symptoms like hot flushes and vaginal dryness caused by low estrogen.

4 Keep taking your hormone therapy

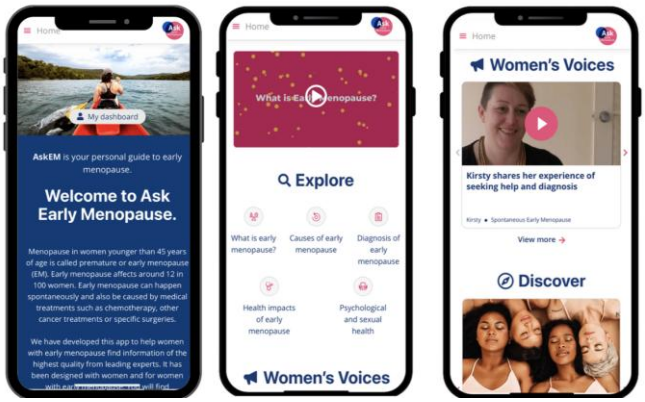
If you don't have a history of breast cancer, hormone therapy is generally safe and can help symptoms and prevent future problems with your bones, heart, and brain. It's important to keep taking your treatment as prescribed. Stopping hormone therapy too soon or not using it regularly can lead to bone loss and increase your risk of heart disease.

5 Have a check-up with your HCP at least once a year

A yearly check-up is helpful to check your heart, bone, and brain health, menopause symptoms, emotional wellbeing, and current treatment needs, including hormone therapy.

6 Learn about POI

Knowing more about POI can help with emotional wellbeing, quality of life, and self-managing POI. The co-designed Ask Early Menopause App is freely available on the Google and Apple stores or at www.askearlymenopause.org.



The Ask Early Menopause App contains evidence-based information about POI and early menopause, women's stories, a personalised dashboard and discussion forum.

What are my options for treatment?

POI cannot be cured, but treatment can help your symptoms and reduce the longterm effects on your health.

1 HORMONE THERAPY (HT)

In women with POI, the ovaries stop making hormones like estrogen, progesterone, and testosterone, which are important for a healthy body. Here we use the term 'HT' to include both hormone replacement therapy (HRT) and the combined oral contraceptive (COC). HT contains estrogen with or without a progestogen. HT can improve symptoms of low estrogen, like hot flushes and night sweats. HT also has other benefits and is recommended even if you don't have symptoms of low estrogen. HRT in women with POI does not prevent natural conception. In general, HRT is preferred but some women may need the COC for contraception.

Hormone therapy is recommended for treatment of symptoms of low estrogen in women with POI.

Hormone therapy is recommended until the usual age of menopause to reduce the risk of chronic disease such as heart disease, osteoporosis (weak bones) and dementia even if you do not have symptoms of low estrogen.

When you reach the age of usual menopause then you can decide whether to continue HRT based on your needs and personal risk-benefit assessment.

Table: Benefits of hormone therapy

Hot flushes and night sweats	☑
Vaginal and urinary symptoms such as vaginal dryness or frequent urination	☑
Life expectancy	☑
Bone health	☑
Muscle health	**Uncertain**
Cardiovascular (Heart) health	☑
Brain health	☑
Quality of life	**Uncertain**
Sexual wellbeing	☑
Fertility treatment	☑
Starting puberty (pubertal induction)	☑

There is no evidence that HRT increases your risk of breast cancer compared to women of the same age without POI.

There are different HRT options. Estrogen is given all the time (continuously). If you have a uterus, you should use combined HRT (estrogen + progestogen) to prevent the lining of the uterus from thickening. Progestogen can be given either sequentially (10-14 days per month, causing regular bleeding) or continuously to avoid bleeding. If you have abnormal vaginal bleeding, you should get it checked by your HCP.

Different types of hormone therapy have different benefits and risks. For example, oral estrogen in HRT tablets or the COC increase the risk of blood clots more than estrogen patches or gels. Women with POI need a higher dose of estrogen (at least 2mg oral estradiol or 100mcg/day estradiol patch) compared to women who go through menopause at the usual age, especially for bone health.

For those needing contraception, the COC is an option. The COC should be taken continuously (skipping the monthly inactive pills) to avoid bone loss. Usual precautions for using the COC apply to women with POI (e.g. older women who smoke should not take the COC). The 52mg levonorgestrel intrauterine system (Mirena®) is another option for contraception or as part of HRT.

It's important to make decisions together with your HCP to find the best option for you. The availability of different estrogen and progestogen preparations varies between countries, and your HCP will know what is available locally.

The choice of hormone therapy depends on your preferences, contraception needs and other existing health issues. Shared decision making between you and your HCP is important to help you decide which option is best for you. ✓

The combined oral contraceptive may be appropriate for some women but should be used continuously (skip the inactive tablets). 

Compounded bioidentical hormone therapy is not recommended due to a lack of information about safety and effectiveness. ✓

Your underlying condition and general health impacts whether or not you can take HRT and which HRT is best for you. Your HCP may perform some tests before prescribing HRT. Shared decision making adressing your individual risks and benefits is needed.

Use of HRT in different settings is shown below:

Migraine	HRT may be used – estrogen patches or gel preferred	👍
High blood pressure	HRT can be used – estrogen or gel patches preferred	👍
History of previous blood clot (VTE or DVT) or clotting disorder	HRT may be used but referral to a haematologist is recommended - – estrogen patches or gel preferred	👍
Obesity or overweight	HRT can be used– estrogen patches or gel preferred	👍
Gastrointestinal malabsorption	HRT can be used- estrogen patches or gel preferred	
Fibroids	HRT can be used	👍
Endometriosis	HRT may be used- combined estrogen+ progestogen is preferred even after hysterectomy to decrease the risk if reactivation of endometriosis	✓
Breast cancer	HRT/ COC is not recommended	👍
BRCA gene positive	HRT can be used if no history of breast cancer	👍
Gynaecological cancer (ovary, uterus or cervix)	Use of HRT depends on the type of cancer and cancer stage	👍
Blood (haematological) cancer	HRT can be used	👍

2 TESTOSTERONE THERAPY

Testosterone therapy can help with low sexual desire that causes distress. There's not much evidence on using testosterone for other reasons like bone or muscle health, thinking skills, or body composition, and the long-term effects are unknown. It's best to use testosterone therapy through the skin (gel or cream) to reach normal blood levels. If you start testosterone therapy, your blood levels should be monitored, and the treatment's effect should be assessed after 6 months. The long-term safety of testosterone therapy is unknown.

Testosterone therapy can help to manage low sexual desire causing distress in women with POI, but the long-term health effects are unknown.

3 TREATMENTS FOR GENITO-URINARY SYMPTOMS

Local vaginal treatments include estrogen creams or pessaries, vaginal DHEA (prasterone), non-hormonal moisturizers, and lubricants. An oral medication called ospemifene is available in some countries but hasn't been studied in women with POI. Vaginal estrogen is safe for most women to use. Women with estrogen-sensitive breast cancer, especially those taking aromatase inhibitors, should discuss the risks and benefits of vaginal estrogen with their cancer care team. Physical therapy might also help. Many women are reluctant to talk about genitourinary symptoms with their HCP and "suffer in silence."

Local vaginal estrogens are effective in treatment of genito-urinary symptoms.

Vaginal estrogens may be given in addition to systemic HRT if genito-urinary symptoms persist.

Non-hormonal vaginal moisturisers and lubricants can be used for treatment of vaginal discomfort and painful sex due to vaginal dryness whether or not HRT is being used.

Laser and other thermal therapies are not recommended at this time due to limited evidence of effectiveness and safety.

4 NON-HORMONAL TREATMENTS (medications, cognitive behavioural therapy, hypnosis)

Studies mainly in older peri- and postmenopausal women have shown that certain medications, including some antidepressants, gabapentin, fezolinetant, clonidine, and oxybutynin, can help with hot flushes and night sweats. They may also help with sleep problems. Only fezolinetant and clonidine are approved in some countries for treatment of hot flushes and night sweats. The other medications are prescribed "off label" for hot flushes and night sweats (which means prescribed for a reason which differs to the government approved use). Cognitive behavioral therapy can help with hot flushes, night sweats, mood, and sleep. Hypnosis has also been shown to reduce hot flushes and night sweats.

Non-hormonal therapies can help menopausal symptoms in peri- and postmenopausal women. Women with POI may consider using them, but there is little information specific to POI.

5 COMPLEMENTARY THERAPIES

Complementary or natural therapies suggested for low estrogen symptoms include phytoestrogens (soy and red clover), black cohosh, evening primrose oil, dong quai, panax ginseng, wild yam, Chinese herbal medicine, vitamin E, and acupuncture. Most of these therapies have been studied in older peri- and postmenopausal women, with few studies in women with POI. Some studies show a small reduction in symptoms, but these studies are small and not very reliable. They also don't provide information on whether the treatments are safe.

For most complementary therapies, evidence of benefit is limited and data on safety are lacking.

Complementary therapies should not replace hormone therapy due to a lack of information about them being able to prevent long term health issues.

The usefulness of acupuncture for menopause symptoms in POI is uncertain but there does not seem to be any benefit in adding acupuncture to hormone therapy.

Women considering Chinese herbal medicine for menopause symptoms should know that benefits are limited but it does not seem to be harmful in the short-term.

Women should know that there is not enough evidence for the use of other nutrient supplements and herbal medicines.

6 PUBERTAL INDUCTION

Sometimes puberty doesn't develop normally, and periods don't start (called primary amenorrhea). This can happen because of genetic reasons or childhood cancer treatment. When this happens, puberty is started using hormone replacement therapy (HRT) to mimic natural hormone changes (called pubertal induction). Estradiol, usually as a patch or gel, is the preferred type of HRT to start puberty. After about two years, a progestogen is added for 12-14 days per month to start regular bleeding, like periods. The progress of puberty can be monitored through physical examinations, blood tests, pelvic ultrasounds to check uterus growth, and bone density tests.

Puberty should be induced or progressed with estradiol, starting with low dose at the age of 11 with a gradual increase over 2 to 3 years.

The combined oral contraceptive should not be used to start puberty.

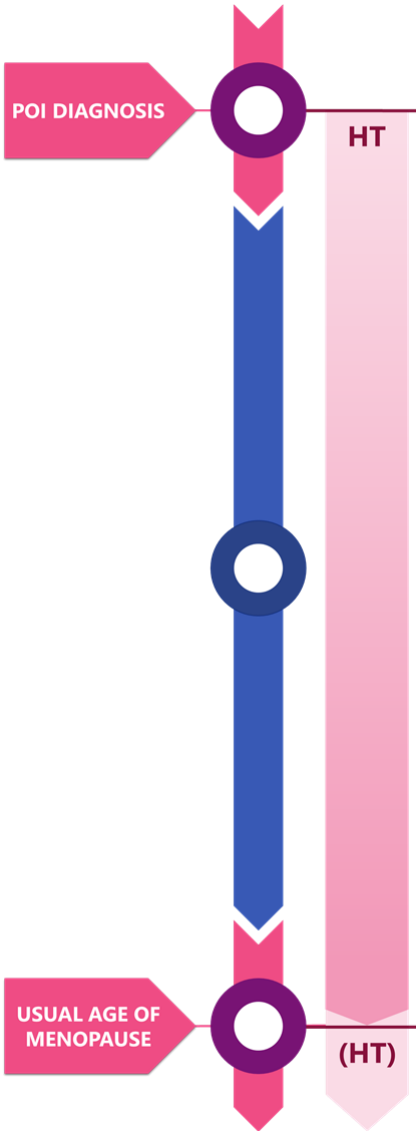
PART E: Monitoring POI

Once POI is diagnosed, a thorough assessment is recommended.

This includes looking at:	This involves:
• symptoms • emotional wellbeing • sexual wellbeing • lifestyle • risk of longterm health problems like heart disease and osteoporosis • the best type of hormone therapy for you • fertility concerns	• a physical examination • blood tests • a bone density scan if available • other tests based on your specific health issues and the cause of POI.

You and your HCP will work together to create a management plan tailored to your needs. POI is a lifelong condition that requires ongoing treatment, and regular check-ups at least once a year are suggested, but they may be more frequent depending on your health needs. Hormone therapy is recommended until at least the usual age of menopause to reduce long-term health risks, unless it is not safe for you (contra-indicated).

Table: Recommendations for health screening for POI



HT commenced, unless contra-indicated

At Diagnosis	Regular monitoring/ Review*
Symptoms	Yearly
Psychosocial wellbeing	Yearly
Sexual wellbeing	Yearly
Hormone therapy benefits/risks/ adherence	Yearly
Other health issues	Yearly
Lifestyle behaviours eg smoking, exercise, diet	Yearly
Weight, height,	Yearly
Blood pressure	Yearly
Thyroid function	If normal at diagnosis then repeat at five years or if symptoms develop
Kidney and Liver function	Yearly
Cholesterol (blood fats) screen	Yearly or depending on result and overall heart disease risk
Diabetes screen	Yearly or depending on result and overall heart disease risk
Vitamin D level	Yearly or depending on result and overall osteoporosis risk
Bone density	If normal then repeat every 5 years. If low bone density or bone loss then repeat every 1-3 years
Fertility/ contraception counselling	As needed
Pelvic US (pubertal induction or if needed)	As needed
Preconception counselling	As needed but especially important for Turner syndrome
Need for pubertal induction	Frequent review to assess progress
*More frequent review may be required according to individual needs. US: ultrasound	

HT continuation depending on personalised risk-benefit assessment

Where can I find more information or support?

More information on each topic in this resource can be found in the health professional's edition of the guideline on the **ESHRE website**.

Fact sheets on topics related to POI, co-created with women with lived experience are available **here**

The Ask Early menopause App is freely available at the Apple or Google stores or at **www.askearlymenopause.org** and has information, women's stories, a dashboard and discussion forum for women with POI and early menopause. It has 9,000 users worldwide.

For more information or support, contact your HCP or a patient organisation.

In some countries, there are patient support organisations specifically for women with POI. In other countries, information and support are available through national patient organisations for infertility or related to the cause of POI such as Turner Syndrome, Fragile X or cancer support groups.

The **Daisy Network** is a support group specifically for women suffering with POI. They are a registered charity in the UK but have members from all over the world. They provide support, information and a friendly network of people for their members. You can find more information at their website **https://www.daisynetwork.org.uk/**

For contact details of national patient organisations for infertility, you can ask your HCP, or contact **Fertility Europe (www.fertilityeurope.eu)** or **Resolve USA (https://resolve.org/get-help/find-a-support-group/)**

About this resource

How this resource was developed

This resource was written by Dr Nathalie Vermeulen (methodological expert) and Associate Professor Amanda Vincent (Co-chair of the Guideline Development Group) and revised by the Guideline Development Group members including consumer representatives. All the information provided is based on the recommendations in the **2024 ESHRE guideline: management of women with Premature Ovarian Insufficiency (POI)**.

Who developed the ESHRE guideline?

The 2024 ESHRE guideline: management of women with Premature Ovarian Insufficiency (POI) was developed by a multidisciplinary guideline development group including gynaecologists and endocrinologists, but also experts in bone health, cardiology, psychology, neurology, genetics, primary care, a literature methodology expert and patient representatives.

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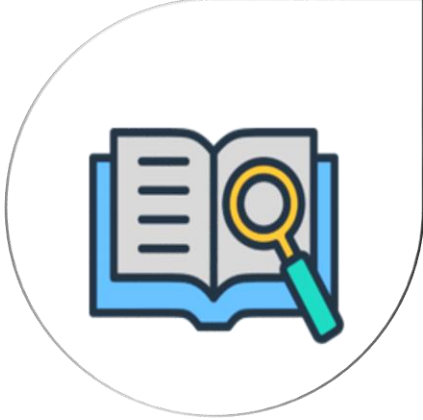

Dictionary

Assisted reproductive technology (ART): Treatments that help people get pregnant. These include intra-uterine insemination (IUI), in vitro fertilisation (IVF), intracytoplasmic sperm injection (ICSI), donor insemination, and egg donation.

Dyspareunia: Recurrent or persistent genital pain directly before, during, or shortly after sex.

Embryo: A fertilised egg.

Estrogen/Oestrogen: A female sex hormone made by developing eggs in the ovaries.

Fertility problem: When a couple doesn't get pregnant after 2 years of regular unprotected sex (at least every 2 to 3 days).

Hormone: A molecule made by one part of the body and carried in the blood to another part to cause an effect.

In vitro fertilization (IVF): A technique where eggs are taken from a woman and fertilised with a man's sperm outside the body. Usually, one or two embryos are then put into the womb. If one attaches successfully, it results in a pregnancy.

Infertility: Not being able to get pregnant. Clinically, it's defined as not achieving a pregnancy after 12 months or more of regular unprotected sex.

Menstruation: The monthly period or bloody discharge from the uterus; it consists of blood and tissue from the uterine lining.

Off-label use: Prescription of an approved drug for a different reason to that approved by the government.

Ovary: An organ in the pelvis of women that contains eggs and makes female sex hormones.

Progesterone: A hormone made by the ovary after ovulation (when the egg is released). It prepares the uterine lining for the embryo.

Progestogen: A term for compounds that bind to the progesterone receptor and affect the uterine lining. It includes progesterone and synthetic compounds used in hormone therapy. Some progestogens also bind to other receptors in the body and have additional effects.

Disclaimer

The European Society of Human Reproduction and Embryology (ESHRE) developed the current information resource for patients based on the clinical practice guideline. The aim of clinical practice guidelines is to aid healthcare professionals in everyday clinical decision about appropriate and effective care of their patients.

This resource is in no way intended to replace, dictate or fully define evaluation and treatment by a qualified physician. It is intended solely as an aid for patients seeking general information on issues in reproductive medicine.

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