

Panay N, Anderson RA, Bennie A, Cedars M, Davies M, Ee C, Gravholt CH, Kalantaridou S, Kallen A, Kim KQ, Misrahi M, Mousa A, Nappi RE, Rocca WA, Ruan X, Teede H, Vermeulen N, Vogt E, Vincent AJ;

ESHRE, ASRM, CREWHIRL, and IMS Guideline Group on POI. Evidence-based guideline: premature ovarian insufficiency. Hum Reprod Open. 2024 Dec 9;2024(4):hoae065. doi: 10.1093/hropen/hoae065. PMID: 39660328; PMCID: PMC11631070.

BACKGROUND

Premature ovarian insufficiency (POI) is a major challenge for women's health, with far-reaching physical and emotional consequences. Potential consequences include negative effects on quality of life, fertility, bone health, cardiovascular health and cognition. Although hormone therapy (HT) can alleviate some of these effects, many questions remain about the optimal treatment of POI. The guideline was developed using the structured methodology for developing ESHRE guidelines.

In the following Part 1, the relevant aspects of POI diagnosis are presented. In a future Part 2, POI management will be discussed in more detail.

SUMMARY

- 1) Definition of POI: Loss of ovarian activity before the age of 40, characterised by oligomenorrhoea, elevated gonadotropins and low serum estradiol (E2) levels
- 2) The prevalence of non-iatrogenic POI in the general population ranges from 1% in older studies to 3.5% in more recent publications.
- 3) Modifiable risk factors for POI: gynaecological surgical practice, lifestyle factors such as smoking, treatment regimens for malignant and chronic diseases.
- 4) Diagnostic criteria for POI: abnormal menstrual cycles (spontaneous amenorrhoea or irregular menstrual cycles) over a period of at least 4 months and an elevated FSH concentration > 25 IU/l. FSH should be repeated in 4-6 weeks if there is diagnostic uncertainty. FSH testing for the diagnosis of POI does not need to be linked to a specific day of the menstrual cycle. POI should not be diagnosed on the basis of serum E2 or AMH concentrations.
- 5) Differential diagnostic considerations Pregnancy should be excluded in women with amenorrhoea. Use of hormonal therapy (including oral, injectable or long-acting contraceptives) may mask or cause amenorrhoea or irregular menstrual cycles and may decrease serum FSH concentrations. Some hormonal therapies (e.g. combined oral contraceptives) may need to be discontinued before a diagnosis of POI can be confirmed. Women who have undergone bilateral salpingo-oophorectomy (BSO) before the age of 40 have a diagnosis of POI and no further diagnostic testing is required.
- 6) Clarification of causes for a non-iatrogenic POI:
 - a. Genetic testing: chromosome analysis, FMR1 premutation testing (fragile X syndrome gene), additional genetic testing (e.g. next-generation DNA testing) as appropriate.

- b. Screening for 21-hydroxylase autoantibodies (21OH-Abs); women with POI and positive 21OH-Abs should be referred to an endocrinologist for adrenal function testing. If 21OH antibodies are negative in women with POI, there is no need to repeat the test later in life unless signs or symptoms of adrenal insufficiency develop.
- c. TSH measurement every 5 years and repeat if symptoms develop. FSH testing for the diagnosis of POI does not need to be linked to a specific day of the menstrual cycle.
- d. Do not screen for anti-ovarian autoantibodies.

7) Advice for relatives of women with POI:

- a. Genetic counselling and testing should be offered to relatives of women with FMR1 premutation or other identified genetic causes of POI.
- b. Female relatives (e.g. sisters or daughters) of women with non-iatrogenic POI should be informed that they are at increased risk of developing POI themselves; ovarian reserve testing may be helpful.
- c. Female relatives (e.g. sisters or daughters) of women with non-iatrogenic POI should be educated about the signs and symptoms of POI and should seek prompt medical attention if they develop them.
- d. Female relatives (e.g. sisters or daughters) of women with non-iatrogenic POI should be informed that there are no established methods for predicting or preventing POI. Some relatives may wish to consider family planning and fertility preservation options.