

PRESS RELEASE

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Large-scale Finnish study discovers link between premature menopause and mortality risk

Women who enter menopause before the age of 40 are more likely to die young, but may lower their risk with hormone therapy, according to research presented at the 26th European Congress of Endocrinology in Stockholm. This long-term Finnish study is the largest carried out on the association between premature menopause and mortality, which highlights the importance of regular medical checkups and appropriate hormone therapy use in these women.

Most women experience menopause between the ages of 45 and 55. However, about 1% of women go through menopause before the age of 40 years, known as premature menopause or premature ovarian insufficiency (POI), and are at a higher risk of long-term health problems such as heart disease. The cause is largely unknown but can be brought on spontaneously or by some medical treatments such as chemotherapy or by surgically removing the ovaries. Hormone replacement therapy (HRT) is the most common treatment but the majority of women with premature menopause do not take these drugs in accordance with the recommendations.

In this study, researchers from the University of Oulu and Oulu University Hospital examined 5,817 women who were diagnosed with spontaneous or surgical premature ovarian insufficiency in Finland, between 1988 and 2017. They compared these women with 22,859 women without POI and found that women with spontaneous premature ovarian insufficiency were more than twice as likely to die of any cause or of heart disease, and more than four times as likely to die of cancer. However, the risk of all-cause and cancer mortality about halved in women who used hormone replacement therapy for more than six months. Women with premature menopause from surgery did not have any added mortality risk.

Previous studies have also shown that women with premature menopause have a higher risk of early death. However, this association has never been studied in women on such a large scale before and followed for up to 30 years. "To our knowledge, this is the largest study performed on the linkage between premature ovarian insufficiency and mortality risk," said Ms Hilla Haapakoski, a PhD student at the University of Oulu, who led the study.

She added: "Our study is one of the first to explore both surgical and spontaneous premature ovarian insufficiency in women's all-cause, cardiovascular and cancer-related mortality, and examine whether hormone replacement therapy for over six months may reduce mortality risk. Our findings suggest specific attention should be paid to the health of women with spontaneous premature ovarian insufficiency to decrease excess mortality."

The team will next assess whether women with premature menopause are more likely to have other illnesses or conditions, such as cancer or heart disease, and whether long-term use of hormone therapy affects these conditions. "Various health risks of women with premature ovarian insufficiency have not been well recognized and the use of HRT is often neglected. We hope to improve the health of these women by increasing awareness of the risks among healthcare professionals and the women themselves", said Ms Haapakoski.

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Abstract

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Mortality among women with POI, nationwide register based case-control study

Introduction/Purpose

Despite some evidence that women with premature ovarian insufficiency (POI, loss of ovarian activity <40 years of age) are at risk for diminished life expectancy, large scale population-based studies are still scarce. The evidence on whether hormone replacement therapy (HRT) use decreases the mortality risk among women with POI are lacking. The aim of our study was to explore mortality among women with spontaneous POI and their controls in a large national cohort and whether HRT use modifies the mortality risk among them.

Methods

All spontaneous POI cases diagnosed in Finland between 1988-2017 were identified by their reimbursement right for HRT, from Social Insurance Institution medicine reimbursement registry. We explored mortality among women with spontaneous POI, compared to age and municipality matched controls (four/each POI case, n=22859). Cox regression analysis was used to compare mortality hazard ratio (HR) between women with POI and their controls in different causes of death. Women with cancer or cardiovascular morbidity before the index day were excluded from the analysis. Women with POI were classified as HRT users if they had purchased systemic HRT for ≥ 6 months. The data on mortality, causes of death and death ages were collected from Cause of Death Registry.

Results

The mean follow-up time for all groups was 17.5 years (standard deviation 8.5). At the end of the follow-up, 9.8% of women with spontaneous POI and 2.9% of controls were deceased. Compared to control women, age-standardized all-cause mortality was increased among women with spontaneous POI, among those without HRT (HR 1.60 95% Confidence Interval, CI 1.07 - 2.37) and those with HRT (HR 2.27 95% CI 1.46 - 3.5). Cancer mortality was also increased among spontaneous POI cases without HRT use, (HR 4.04 95 % CI 3.04 - 5.37) and with HRT (HR 1.78 95 %CI 1.27 - 2.48), as well as cardiovascular mortality (HR 2.30 95% CI 1.34 - 3.97) and (2.53 95% CI 1.58 - 4.06), respectively.

Conclusions

Women with spontaneous POI are at increased risk for all-cause, cardiovascular and cancer mortality, and HRT use of ≥ 6 months did not eliminate the risk. Future studies should focus on whether longer use of HRT associates with diminished mortality risk among women with POI. Specific attention should be paid to health of women with spontaneous POI to decrease excess mortality.

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Notes for Editors

1. For further information about the study, and to arrange an interview with the authors, please contact the ECE 2024 press office:

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2. The study “**Mortality among women with POI, nationwide register based case-control study**” will be presented at 14:50 CET on Sunday 12 May 2024 at the European Congress of Endocrinology at the Stockholm International Fairs (Stockholmsmässan) in Stockholm, Sweden.

3. **About the European Congress of Endocrinology**

The European Congress of Endocrinology (ECE) is the flagship event of the European Society of Endocrinology (ESE). Each year, the Congress attracts around 3,500 international delegates across the spectrum of endocrinology. The 26th ECE will be held at the Stockholm International Fairs (Stockholmsmässan) in Stockholm, Sweden, on 11–14 May 2024. See the full scientific programme here: <https://ese-hormonesapps.m-anage.com/ece2024/en-GB/pag>

4. **About the European Society of Endocrinology**

The [European Society of Endocrinology](#) (ESE) provides a platform to develop and share leading research and best knowledge in endocrine science and medicine. By uniting and representing every part of the endocrine community, we are best placed to improve the lives of patients. With over 5,000 individual members and through the 47 National Societies involved with the ESE Council of Affiliated Societies (ECAS), ESE represents a community of over 20,000 European endocrinologists. We inform policy makers on health decisions at the highest level through advocacy efforts across Europe.