

# INPLASY PROTOCOL

To cite: Cai et al. Metabolic differences in women with premature ovarian insufficiency: a systematic review and meta-analysis. Inplasy protocol 2021100091. doi: 10.37766/inplasy2021.10.0091

Received: 24 October 2021

Published: 24 October 2021

**Corresponding author:**  
Jian Xu

xuj@zju.edu.cn

**Author Affiliation:**  
Zhejiang University School of Medicine.

**Support:** None.

**Review Stage at time of this submission:** Data analysis - Completed but not published.

**Conflicts of interest:**  
None declared.

## Metabolic differences in women with premature ovarian insufficiency: a systematic review and meta-analysis

Cai, WY<sup>1</sup>; Luo, X<sup>2</sup>; Wu, W<sup>3</sup>; Song, J<sup>4</sup>; Xie, N<sup>5</sup>; Duan, C<sup>6</sup>; Wu, XK<sup>7</sup>; Xu, J<sup>8</sup>.

**Review question / Objective:** This review aimed to investigate the metabolic profile of women with premature ovarian insufficiency (POI) compared relative to women with normal ovarian functioning.

**Condition being studied:** Premature ovarian insufficiency (POI) is defined as amenorrhea due to the loss of normal ovarian function before the age of 40 years. Additionally, it is characterized by abnormally increased levels of gonadotrophins and decreased levels of estrogen. Although the cause of POI is unclear, it is hypothesized that hormonal and metabolic abnormalities, infections, environmental exposures, medical treatments, endocrinology disorders, and autoimmune diseases may all contribute to this condition. Most women with POI develop symptoms of estrogen deficiency, including vasomotor flushes, vaginal dryness, sexual dysfunction, osteoporosis, and long-term cardiovascular disease. Additionally, POI is associated with lower health-related quality of life compared to normal ovarian controls. Further, these patients require additional support from clinicians.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 October 2021 and was last updated on 24 October 2021 (registration number INPLASY2021100091).

### INTRODUCTION

**Review question / Objective:** This review aimed to investigate the metabolic profile of women with premature ovarian insufficiency (POI) compared relative to women with normal ovarian functioning.

**Condition being studied:** Premature ovarian insufficiency (POI) is defined as amenorrhea due to the loss of normal ovarian function before the age of 40 years. Additionally, it is characterized by abnormally increased levels of gonadotrophins and decreased levels of estrogen. Although the cause of POI is

unclear, it is hypothesized that hormonal and metabolic abnormalities, infections, environmental exposures, medical treatments, endocrinology disorders, and autoimmune diseases may all contribute to this condition. Most women with POI develop symptoms of estrogen deficiency, including vasomotor flushes, vaginal dryness, sexual dysfunction, osteoporosis, and long-term cardiovascular disease. Additionally, POI is associated with lower health-related quality of life compared to normal ovarian controls. Further, these patients require additional support from clinicians.

## METHODS

**Participant or population:** Women with POI.

**Intervention:** None.

**Comparator:** Women with normal ovarian function.

**Study designs to be included:** Observational studies.

**Eligibility criteria:** Observational studies that compared at least one of the metabolic outcomes of interest in patients with POI to control women with normal ovarian function were included. Metabolic parameters included waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting glucose (FG), insulin (INS), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides (TG). Review articles, opinions, book chapters, letters, published abstracts, animal studies, case reports and studies with no suitable control group were excluded.

**Information sources:** PubMed, Embase, and Web of Science. References from all included studies were also assessed to identify relevant articles not captured by the electronic searches.

**Main outcome(s):** Waist circumference (WC), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting

glucose (FG), insulin (INS), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides (TG).

**Quality assessment / Risk of bias analysis:** Newcastle-Ottawa scale (NOS).

**Strategy of data synthesis:** Review Manager version 5.4.1 and Stata version 8.0 were used to analyze the extracted data. Mean difference (MD) with 95% confidence interval (CI) was pooled to measure effect size. The heterogeneity of studies was measured using the I<sup>2</sup> index: below 40% indicated no heterogeneity; more than 40% indicated heterogeneity existed. The fixed-effects model was used when no heterogeneity was observed, and the random-effects model was used when heterogeneity existed. Publication bias was assessed using funnel plot asymmetry and Egger's line regression test.

**Subgroup analysis:** To measure the effect of confounders on the effect size of potential moderators, subgroup analysis and meta-regression were performed.

**Sensitivity analysis:** To confirm the robustness of the results, sensitivity analysis was performed by excluding each one included study.

**Country(ies) involved:** China.

**Keywords:** Premature ovarian insufficiency; metabolic; lipid; glucose; systematic review.

### Contributions of each author:

Author 1 - Wang-Yu Cai.  
Email: 1585322398@qq.com  
Author 2 - Xi Luo.  
Author 3 - Wei Wu.  
Author 4 - Jianyuan Song.  
Author 5 - Ningning Xie.  
Author 6 - Cuicui Duan.  
Author 7 - Xiaoke Wu.  
Author 8 - Jian Xu.  
Email: xuj@zju.edu.cn