

# INPLASY PROTOCOL

To cite: Tian et al. Premature ovarian insufficiency is associated with increased risk of depression, anxiety and poor life quality: a meta-analysis. Inplasy protocol 202310020. doi: 10.37766/inplasy2023.1.0020

Received: 09 January 2023

Published: 10 January 2023

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**Support:** National Natural Science Foundation of China (81871133 and 82271660).

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

## Conflicts of interest:

None declared.

## Premature ovarian insufficiency is associated with increased risk of depression, anxiety and poor life quality: a meta-analysis

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**Review question / Objective:** A meta-analysis of cross-sectional, case-control and cohort studies (S) was conducted to explore whether women with POI/POF (P) could increase risk of depression, anxiety, and poor quality of life (O). Intervention studies (I) are eligible only if pre-intervention data were available(I) and the comparator(C) of this meta-analysis was people who do not suffer from POI (age-matched).

**Condition being studied:** Several studies have been conducted to show that POI affects the quality of life of patients, of which psychological and psychosocial factors cannot be ignored as a part. Most studies have shown that POI patients are more prone to negative emotions such as depression and anxiety than normal people, but some studies have also shown that normal POI patients are psychologically indistinguishable from normal people. Therefore, meta-analysis is needed to determine the effect of POI on psychological factors and to better guide the clinical treatment plan.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 January 2023 and was last updated on 10 January 2023 (registration number INPLASY202310020).

## INTRODUCTION

**Review question / Objective:** A meta-analysis of cross-sectional, case-control

and cohort studies (S) was conducted to explore whether women with POI/POF (P) could increase risk of depression, anxiety, and poor quality of life (O). Intervention

studies (I) are eligible only if pre-intervention data were available(I) and the comparator(C) of this meta-analysis was people who do not suffer from POI (age-matched).

**Rationale:** Premature ovarian insufficiency (POI) has had a significant adverse impact on reproductive health of women around the world. Recent data indicate that POI has been associated with psychological and psychosocial factors including the depression and anxiety. However, little meta-analysis that POI increased the risk of psychological aspect has ever been done. Here, we conducted a meta-analysis to systematically delineate the impact profile of POI on psychological and psychosocial factors.

**Condition being studied:** Several studies have been conducted to show that POI affects the quality of life of patients, of which psychological and psychosocial factors cannot be ignored as a part. Most studies have shown that POI patients are more prone to negative emotions such as depression and anxiety than normal people, but some studies have also shown that normal POI patients are psychologically indistinguishable from normal people. Therefore, meta-analysis is needed to determine the effect of POI on psychological factors and to better guide the clinical treatment plan.

## METHODS

**Search strategy:** The strategies used to search studies were as follows: “psychology” or “psychological” or “mental” or “psychosocial” or “psychologically” or “mood” or “depression” or “anxiety” or “pressure” or “stress” or “insomnia” or “sleeplessness” or “poor sleep” or “positive mindset” or “fatigue” or “well-being” or “quality of life” and “premature ovarian insufficiency” or “premature ovarian failure” or “diminished ovarian reserve” or “premature menopause”. In addition, references cited in the related articles were also screened for identifying relevant studies.

**Participant or population:** Patients reported the clinical psychological and psychosocial symptoms including the depression, anxiety and sleep quality with clear diagnosis of biochemical POI/POI/POF.

**Intervention:** Biochemical POI/POI/POF.

**Comparator:** People who do not suffer from POI (age-matched).

**Study designs to be included:** Cohort study, case-control study, and cross-sectional study.

**Eligibility criteria:** (1)Studies reported the clinical psychological and psychosocial symptoms including the depression, anxiety and sleep quality; (2) We considered randomized clinical trials or intervention studies for eligibility if they provided related data at the preintervention phase. (3) Included studies must be clearly record odds ratios (ORs) or relative risk (RR) values and 95% confident intervals (CIs) or have raw data from which ORs and 95% CI could be calculated.

**Information sources:** Major electronic databases including PubMed, Web of Science, Embase, China National Knowledge Infrastructure (CNKI) and Wanfang Database.

**Main outcome(s):** Data extraction were performed independently by two researchers. First author’s name, year of publication, nation, research type, sample size, mean age, source of subjects, clinical characteristics, as well as ORs and 95% CIs of psychological and psychosocial symptoms were recorded. If the study did not present the Odds ratio (OR) values, we computed as OR value = odds of case exposure / odds of control exposure with the raw data. Pooled ORs and 95% confident intervals (CIs) of patients in the experimental group suffering from depression, anxiety or poor quality of life compared to control patients. Odds ratios (ORs) prevalence and 95% confident intervals (CIs) of patients in the experimental group suffering from

depression, anxiety or poor quality of life compared to control patients.

**Additional outcome(s):** None.

**Data management:** Calculated ORs and 95% CI from raw data were applied by SPSS 26.0. All statistical analyses in the present study were conducted with Comprehensive Meta-Analysis software (CMA 3.0).

**Quality assessment / Risk of bias analysis:** All data extraction were performed independently by two researchers. The first author names, publication year, nation, research type, sample size, mean ages, source of subject, and basic clinical characteristics. ORs and 95% CIs of psychological and psychosocial symptoms were extracted from those articles. ORs and 95% CIs were calculated with the raw data if the study did not present the OR value, The quality of eligible studies was evaluated by the Newcastle-Ottawa Scale (NOS). The NOS has a score range of zero to nine, and studies with a score of more than five were eligible. Between-study heterogeneities were evaluated by Q test and I<sup>2</sup> statistic. If I<sup>2</sup> was greater than 50%, between study heterogeneities were considered to be obvious and the random-effects model was applied. We then conducted subgroup analysis and meta-regression analyses to explore heterogeneities in effect sizes. The publication bias was assessed by Egger's test and funnel plot. If publication bias was shown, we used the trim and fill method to evaluate the influence of bias on the obtained results.

**Strategy of data synthesis:** Pooled ORs value and 95% CIs as the main indices were used to assess potential impact of POI on various psychological factors, and a p-value less than 0.05 was considered to be statistically significant. Between-study heterogeneities were evaluated by Q test and I<sup>2</sup> statistic. If I<sup>2</sup> was greater than 50%, between study heterogeneities were considered to be obvious and the random-effects model was applied. We then conducted subgroup analysis and meta-

regression analyses to explore heterogeneities in effect sizes. The publication bias was assessed by Egger's test and funnel plot. If publication bias was shown, we used the trim and fill method to evaluate the influence of bias on the obtained results.

**Subgroup analysis:** Subgroup analysis of research type, survey method and country-type were conducted. Also, meta regression analysis of publication year and mean age were performed.

**Sensitivity analysis:** A sensitivity analysis using the leave-one-out method was carried out to assess the stability of meta-analysis.

**Language restriction:** Studies published in either English or Chinese were considered in this review. Language limits would not be imposed on the search.

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

**Other relevant information:** None.

**Keywords:** Premature ovarian insufficiency; Depression; Anxiety; Poor life quality; Systematic review.

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