# INPLASY PROTOCOL

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**Review Stage at time of this submission:** **Preliminary searches.**

**Conflicts of interest:**
**None declared.**

# Efficacy of progestin-primed ovarian stimulation (PPOS) in patients with polycystic ovary syndrome during IVF/ICSI treatments: A systematic review and meta-analysis

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**Review question / Objective:** **This systematic review aims to evaluate the efficacy of progestin-primed ovarian stimulation (PPOS) on reproductive outcomes in patients with polycystic ovary syndrome (PCOS) undergoing assisted reproductive techniques.**
**Condition being studied:** **PCOS is a common endocrine disorder that can cause infertility in women of childbearing age. The PPOS protocol, which involves oral progestins with gonadotropin (Gn), has been shown to be effective and safe in treating patients with PCOS. However, the question of whether PPOS provides a significant benefit over conventional GnRH analogue protocols in PCOS patients is still controversial.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 April 2023 and was last updated on 18 April 2023 (registration number INPLASY202340059).

## INTRODUCTION

**Review question / Objective:** **This systematic review aims to evaluate the efficacy of progestin-primed ovarian stimulation (PPOS) on reproductive outcomes in patients with polycystic ovary**

syndrome (PCOS) undergoing assisted reproductive techniques.

**Condition being studied:** PCOS is a common endocrine disorder that can cause infertility in women of childbearing age. The PPOS protocol, which involves oral progestins with gonadotropin (Gn), has been shown to be effective and safe in treating patients with PCOS. However, the question of whether PPOS provides a significant benefit over conventional GnRH analogue protocols in PCOS patients is still controversial.

## METHODS

**Search strategy:** A comprehensive search of the following databases from inception until April 2023 will be conducted: MEDLINE(via Pubmed), Embase, and Cochrane Central Register of Controlled Trials (CENTRAL). Keywords included "progestin-primed ovarian stimulation", "PPOS", "polycystic ovary syndrome" , "PCOS", "IVF" , "ICSI", "progest*", "medroxyprogesterone*", “utrogestan” and "dydrogesterone*". Only English publications are included.

**Participant or population:** Patients diagnosed with polycystic ovary syndrome (PCOS) and infertility undergoing in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) are included.

**Intervention:** Controlled ovarian stimulation protocols of PPOS.

**Comparator:** Controlled ovarian stimulation protocol of GnRH analogues.

**Study designs to be included:** We consider randomised controlled trials (RCTs) and observational studies as eligible for inclusion.

**Eligibility criteria:** Studies were excluded if one of the following conditions is met: (1) severe male factors; (2) endometriosis or systemic diseases; (3) unpublished articles and conferences; (4) duplicated, incomplete, or missing data.

**Information sources:** In addition to the electronic databases, as described in the Search strategy, reference lists of included studies and relevant reviews, conference proceedings, and websites of the clinical trial registry were hand-searched to identify additional studies.

**Main outcome(s):** 1. Live birth rate (LBR); 2. the incidence of moderate/severe ovarian hyperstimulation syndrome (OHSS); 3. the number of metaphase II (MII) oocytes.

**Additional outcome(s):** 1. Total dose of gonadotropin (Gn) stimulation; 2. incidence of premature LH surge; 3. number of oocytes retrieved; 4. number of good-quality embryos; 5. cycle cancellation rate; 6. implantation rate (IR); 7. clinical pregnancy rate (CPR) per transfer; 8. ongoing pregnancy rate (OPR) per transfer.

**Quality assessment / Risk of bias analysis:** Two authors independently assess the risk of bias of the included RCTs according to the Cochrane Risk of Bias Tool, considering the following characteristics: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective data reporting, and other sources of bias. Using Newcastle-Ottawa Scale (NOS) to evaluate the quality of observational studies. Disagreements will be resolved by discussed with a third reviewer.

**Strategy of data synthesis:** We calculate odds ratio (OR) with 95% confidence intervals (CIs) for dichotomous outcomes and mean differences (MD) with 95% CIs for continuous outcomes. We use a random-effects model to produce overall estimates in RevMan software. We measure heterogeneity using the I2 statistic, considering an I2 > 50% to be substantial heterogeneity. We aim to assess the publication bias using a funnel plot if at least ten studies are included in the meta-analysis. The GRADE approach will be performed to evaluate each outcome’s certainty of evidence.

**Subgroup analysis:** Subgroup analyses will be conducted to find potential factors influencing the outcomes. The main factors for subgroup analyses are the COS protocols of the control group and oral progestins.

**Sensitivity analysis:** Studies with only RCTs will be calculated for sensitivity analysis.

**Language restriction:** English.

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

**Keywords:** Progestin-primed ovarian stimulation, Polycystic ovary syndrome, PCOS, PPOS, IVF, ICSI.

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