

Efficacy of myoinositol vs myoinositol with metformin in people with Polycystic Ovary Syndrome: a systematic review and meta-analysis

INPLASY202640076

doi: 10.37766/inplasy2026.4.0076

Received: 22 April 2026

Published: 23 April 2026

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ADMINISTRATIVE INFORMATION**Support** - None.**Review Stage at time of this submission** - Data analysis.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202640076**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 April 2026 and was last updated on 23 April 2026.**INTRODUCTION**

Review question / Objective A systematic review and meta-analysis to evaluate the efficacy of myoinositol in combination with metformin compared to myoinositol monotherapy in women with polycystic ovary syndrome, in terms of clinical, metabolic, and hormonal parameters.

Rationale Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age and is associated with various metabolic, hormonal, and reproductive complications that significantly affect quality of life. Although metformin has demonstrated efficacy in the management of insulin resistance and other clinical parameters, its use is limited by gastrointestinal side effects and poor treatment adherence. In contrast, myoinositol has emerged as a therapeutic alternative with a favorable safety profile and comparable effects. In this context, the combination of both has been proposed as a potentially more effective strategy; however, the available evidence is limited and inconsistent.

Furthermore, no systematic review has directly compared the combination of myoinositol and metformin with myoinositol monotherapy. Therefore, it is necessary to conduct a systematic review with meta-analysis to synthesize the available evidence and provide objective information to support clinical decision-making, optimize treatment, and improve the quality of life of patients with PCOS.

Condition being studied Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women of reproductive age. It is primarily characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology, and is commonly associated with metabolic abnormalities such as insulin resistance, obesity, infertility, and hormonal imbalances, including alterations in the LH/FSH ratio. Due to its heterogeneous nature and its impact on reproductive and metabolic health, as well as quality of life, PCOS represents a clinically relevant condition for the evaluation of various therapeutic strategies.

METHODS

Search strategy The search strategy was designed to identify studies comparing the combination of myoinositol and metformin versus myoinositol monotherapy in women with Polycystic Ovary Syndrome (PCOS). It was structured around three core concepts: condition (PCOS), intervention/comparator (myo-inositol and metformin), and outcome (efficacy). No restrictions were applied based on language, publication year, or document type in any of the sources consulted, except in Springer Nature Link, where the "article" filter was applied.

The initial strategy was constructed using controlled terms when available (such as MeSH terms in PubMed) and free-text keywords, including synonyms and recognized spelling variations in the literature. The main terms were: "Polycystic Ovary Syndrome," "Stein-Leventhal Syndrome," and "PCOS" for the condition; "inositol," "myo-inositol," and "myoinositol" for the intervention/comparator; and "metformin" for the combined intervention. The term "efficacy" was added to focus the search on studies that evaluated therapeutic effects.

Participant or population People diagnosed with Polycystic Ovary Syndrome (PCOS), of any age and with any of the Rotterdam criteria phenotypes, due to the limited number of studies available.

Intervention Combination of metformin and myoinositol, with no restriction as to the dose administered or the formulation used.

Comparator Myoinositol monotherapy.

Study designs to be included Controlled clinical trials and quasi-experimental studies.

Eligibility criteria Inclusion criteria:

- Women diagnosed with Polycystic Ovary Syndrome (PCOS) were included, regardless of age, encompassing all phenotypes defined by the Rotterdam criteria, given the limited availability of data.
- The intervention consisted of a combination of metformin and myoinositol, with no restrictions on dosage or formulation.
- The combination therapy was compared with myoinositol monotherapy.
- Adequate clinical, metabolic, and hormonal data were required for comprehensive evaluation, including outcomes related to anthropometric measures (e.g., body mass index and infertility), metabolic parameters associated with glucose and

insulin regulation (e.g., fasting blood glucose, fasting blood insulin, and HOMA-IR), and relevant hormonal indicators of Polycystic Ovary Syndrome (e.g., LH/FSH ratio).

Exclusion criteria:

Individuals diagnosed with Polycystic Ovary Syndrome (PCOS) were excluded if, despite receiving combined treatment with metformin and myoinositol, they also underwent ovulation induction using agents other than metformin, such as letrozole, clomiphene citrate, tamoxifen, or similar medications.

Information sources Web of Science, Scopus, EBSCOhost CINAHL, Springer Nature Link, PubMed, Scielo and LILACS.

Main outcome(s) No statistically significant differences were observed between the combination of myo-inositol and metformin and myoinositol monotherapy in the evaluated clinical, metabolic, and hormonal outcomes, including body mass index (BMI), infertility, fasting blood glucose (FBG), fasting blood insulin (FBI), HOMA-IR, and the LH/FSH ratio.

Quality assessment / Risk of bias analysis The risk of bias of the included studies was assessed using the Risk of Bias 2 (RoB 2) tool. For the non-randomized study, the ROBINS-I tool was used.

Strategy of data synthesis The following information was extracted from the selected full-text articles: first author and year of publication; study population characteristics; details of the intervention, including dosage and frequency; as well as the mean values, standard deviations, and sample sizes for both the intervention and control groups for each of the evaluated outcomes.

For the meta-analysis, the number of participants in each group, along with the corresponding means and standard deviations, were extracted in order to calculate mean differences and their associated standard deviations. The results were synthesized according to the predefined clinical, metabolic, and hormonal outcomes.

Subgroup analysis Subgroup analyses were not performed due to the limited number of included studies and the insufficient availability of comparable data across studies.

Sensitivity analysis Statistical heterogeneity across studies was assessed using Cochran's Q test (statistical significance: $p < 0.10$) and quantified using the I^2 statistic, interpreted according to the following Cochrane Handbook

thresholds: 0-40% (heterogeneity not important), 30-60% (moderate), 50-90% (substantial), and 75-100% (considerable).

For dichotomous outcomes, specifically infertility, the relative risk (RR) with 95% confidence intervals was used. For continuous outcomes including body mass index (BMI), fasting blood insulin (FBI), fasting blood glucose (FBG), HOMA-IR, and LH/FSH ratio, the mean difference (MD) was applied when studies reported results in the same units of measurement. When scales or units were not comparable across studies, the standardized mean difference (SMD) was used instead. All outcomes were reported with their corresponding 95% confidence intervals.

Language restriction No.

Country(ies) involved Mexico.

Keywords Polycystic Ovary Syndrome (PCOS), myoinositol, metformin, combination therapy, effect.

Contributions of each author

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