

# Metformin versus GLP-1 Receptor Agonists in Women with Polycystic Ovary Syndrome: A Systematic Review

Sharma, S

PCOS affects 8–13% of reproductive-aged women worldwide

Obesity and insulin resistance drive metabolic and reproductive complications

PCOS is a leading cause of anovulatory infertility

PCOS has lifelong cardiometabolic implications, with increased risk of impaired glucose, type 2 diabetes, dyslipidemia, and hypertension

PCOS is underdiagnosed and diagnosis is often delayed

PCOS affects quality of life beyond reproduction, including higher burdens of psychological symptoms and body-image distress

## Background

Polycystic ovary syndrome (PCOS) is characterised by hyperandrogenism, ovulatory dysfunction and polycystic ovarian morphology.

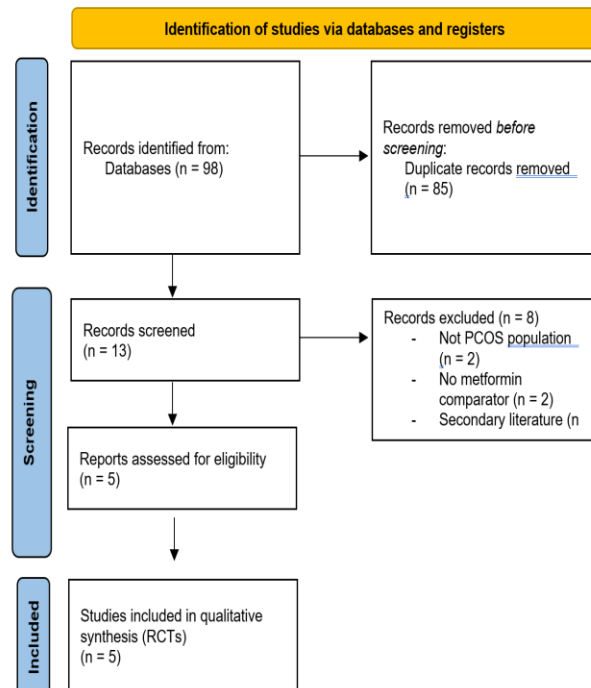
It is strongly associated with insulin resistance and obesity, increasing risk of:

- Type 2 diabetes
- Cardiovascular disease
- Infertility

Metformin is widely used to improve insulin sensitivity and menstrual irregularity.

GLP-1 receptor agonists (GLP-1RAs) produce significant weight loss and may provide superior metabolic and reproductive benefits.

## Results



### 4.1 Characteristics of Included Studies

**Included RCTs: 5**  
**Total randomised participants: 312**  
**Duration range: 12–24 weeks**

#### 4.1.1 Study Design

- Two-arm RCTs (n=3)
- Three-arm RCTs (n=2)
- Open-label trials (n=2)

#### 4.1.2 Country of Origin

- China (n=3)
- Slovenia (n=1)
- USA (n=1)

## Methodology

- Registered in PROSPERO
- PRISMA 2020 guidelines followed
- Systematic database search
- Inclusion: Randomised controlled trials only

## Research Questions

- Are GLP-1 receptor agonists more effective than metformin for weight loss?
- Do GLP-1RAs improve insulin resistance outcomes more than metformin?
- Does combination therapy outperform metformin alone?
- What are the effects on menstrual regularity and ovulation?
- What are the comparative adverse event rates?

## Conclusion

- GLP-1RA-based therapies achieve greater short-term weight loss than metformin alone in women with PCOS
- Combination therapy appears to provide the greatest metabolic benefit
- Evidence for fertility outcomes remains limited
- Treatment choice should balance metabolic benefit, tolerability and cost
- Future trials should prioritise fertility endpoints and longer follow-up

## Outcomes

### Weight / BMI (Primary Finding)

- GLP-1RA strategies consistently produced greater weight loss than metformin
- Combination therapy demonstrated the largest reductions (up to ~6.5 kg at 12 weeks)
- Effects consistent across exenatide, liraglutide, and semaglutide

### Insulin Resistance

- Fasting and post-OGTT glucose improvements favoured GLP-1RA strategies
- Insulin sensitivity indices showed favourable trends
- Combination therapy produced the most consistent metabolic benefit

### Reproductive Outcomes

- One longer-duration RCT demonstrated improved menstrual cyclicity and ovulation
- Shorter trials showed variable reproductive findings
- Pregnancy endpoints underpowered and inconsistently reported

### Adverse Events

- Gastrointestinal symptoms more common with GLP-1RAs
- Injection-site reactions with weekly formulations
- Overall discontinuation rates low

## References

1. Teede HJ, Tay CT, Laven JJE, Dokras A, Moran LJ, Piltonen TT, et al. 2023 International evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Hum Reprod.* 2023;38(9):1749–1765.
2. Jensterle M, Kravos NA, Pfeifer M, Kocjan T, Janež A. A 12-week treatment with the combination of liraglutide and metformin leads to significant weight loss in obese women with polycystic ovary syndrome. *Eur J Endocrinol.* 2014;170(3):451–459.
3. Elkind-Hirsch KE, Marrioneaux O, Bhushan M, Vernor D, Bhushan R. Comparison of single and combined treatment with exenatide and metformin on menstrual cyclicity in overweight women with polycystic ovary syndrome. *J Clin Endocrinol Metab.* 2008;93(7):2670–2678.
4. Zheng X, Lin D, Zhang Y, Lin Y, Song J, Li S, et al. Exenatide versus metformin for overweight/obese women with polycystic ovary syndrome: a randomized controlled trial. *Clin Endocrinol (Oxf).* 2017;86(1):89–96.
5. Ma R, Chen Y, Li X, Zhou Y, Zhang X, Zhang Y, et al. Exenatide combined with metformin improves insulin resistance and weight in overweight/obese women with polycystic ovary syndrome: a randomized controlled trial. *Front Endocrinol (Lausanne).* 2021;12:734799.