

## Abstract

Polycystic ovarian syndrome (PCOS) is the most common endocrinopathy in reproductive-aged women worldwide; however, treatment modalities often lack cohesion due to its multifactorial pathophysiology. PCOS is suspected of inducing insulin resistance. Research has explored the use of newly developed incretin mimetics as standard therapy for insulin resistance in insulin-dependent tissues associated with PCOS. The aim of this review was to explore the classes of incretin mimetics, such as glucagon-like peptide-1 (GLP-1) receptor agonists or semaglutide, dual agonists of the GLP-1 receptor and gastric inhibitory peptide (GIP) or tirzepatide, and a new triple agonist, or retratrutide (which is currently seeking FDA-approval), and their suggested benefits as a treatment for PCOS.

## Methodology

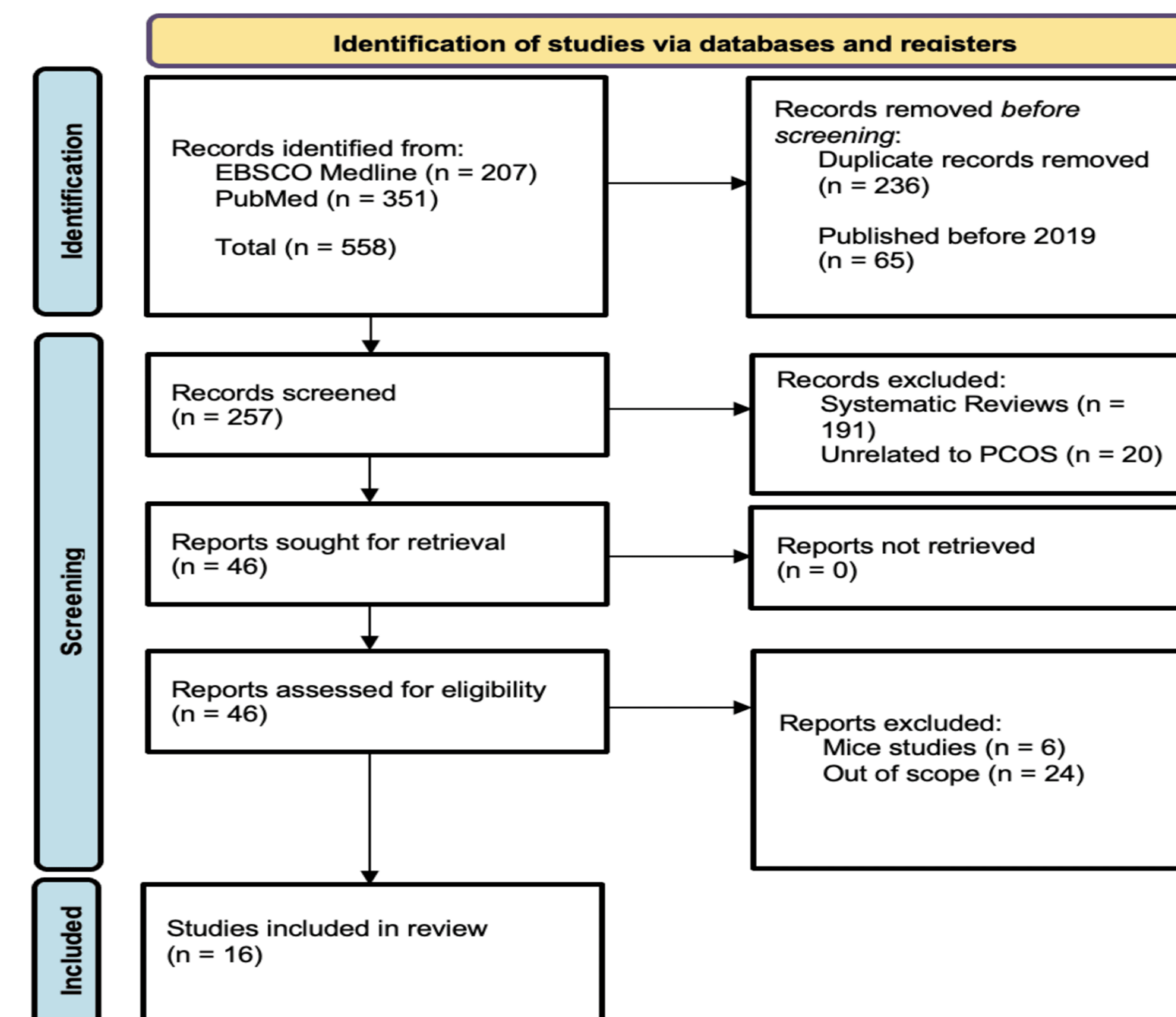


Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram detailing the search strategy utilized for article inclusion

## Conclusions

Effects demonstrated in studies on PCOS patients with GLP-1 receptor agonist

Reduction in HbA1C, insulin levels with monotherapy and combination therapy

Improvements in hyperandrogenism (improved menstruation and reduction in hirsutism)

Improvements in cystic morphology (reduction in ovarian cysts)

## Introduction

- Worldwide 5-10% of women are diagnosed with PCOS annually, the most common endocrinopathy in reproductive-aged women.
- The 2003 Rotterdam criteria confirms a diagnosis of PCOS with two out of three of the following: 1. oligomenorrhea, 2. hyperandrogenism, and/or 3. polycystic-appearing ovarian morphology on ultrasound. PCOS is often difficult to treat due to its etiology arising in the endocrine system, but clinical manifestation in the ovaries.
- The most recent guidelines for treatment recommend a combination of oral contraceptive pills, such as estradiol-progesterone, and metformin.
- Recent literature has explored incretin mimetics such as GLP-1 receptor agonists as adjunct therapy. GLP-1 receptor agonists act to reduce insulin resistance by increasing glucose transporters, which in turn decreases inflammation, modulates lipid metabolism, and promotes insulin secretion. GLP-1 receptor agonists are recommended because of the relationship between PCOS and other insulin resistant related clinical manifestations.

## Results

Effects demonstrated in studies on PCOS patients with GLP-1 receptor agonist	Tirzepatide efficacy when compared to semaglutide
Reduction in HbA1C, insulin levels with monotherapy and combination therapy	Greater reductions in body weight, BMI, and waist circumference
Improvements in hyperandrogenism (improved menstruation and reduction in hirsutism)	Greater improvements in insulin sensitivity rate compared to semaglutide
Improvements in cystic morphology (reduction in ovarian cysts)	Greater glycemic efficacy than semaglutide injections, with significantly greater decreases in HbA1C

- Effects demonstrated in studies on PCOS patients with GLP-1 receptor agonists
  - Reduction in HbA1C, insulin levels with monotherapy and combination therapy
  - Improvements in hyperandrogenism (improved menstruation and reduction in hirsutism)
  - Improvements in cystic morphology (reduction in ovarian cysts)
- Studies comparing drug efficacies
  - Tirzepatide may be more effective than semaglutide due to greater reductions in body weight, BMI, and waist circumference.
  - Tirzepatide showed greater improvements in insulin sensitivity rate compared to semaglutide.
  - Tirzepatide injections demonstrated greater glycemic efficacy than semaglutide injections, with significantly greater decreases in HbA1C.

## Conclusions/References

- The development of GLP-1 receptor agonists and their proven benefits in improving insulin sensitivity, body weight, and BMI suggest promising therapy for PCOS patients due to the overlapping pathophysiology between the condition and the medications' current approved uses.
- This review found that PCOS patients treated with GLP-1 receptor agonists, both as adjuvant therapy and monotherapy, had significant improvements in their anthropometric measurements as well as biomarkers of insulin resistance.
- While the studies in this review present promising advancements in the management of PCOS patients, the limited literature investigating the use of GLP-1 receptor agonists as specific treatment for PCOS imposes difficulty in determining their utilization as a standardized treatment modality.
- While incretin mimetics all suggest promising improvements in insulin sensitivity, BMI, and body weight for PCOS patients, the exact mechanism behind how these medications affect dysmenorrhea and androgen imbalance associated with PCOS is unclear.
- While some studies show that normal menses returns after semaglutide treatment, it is ambiguous as to whether it is secondary to reductions in body weight or improved insulin sensitivity post-treatment. Further research should be conducted to determine the mechanism behind how the use of incretin mimetics affects the appearance of polycystic ovaries and hyperandrogenism in PCOS patients.
- Despite its complexity, the development of GLP-1 receptor agonists proves to be an exciting new horizon in the management of patients with PCOS and might offer researchers a deeper understanding into its pathophysiology.

