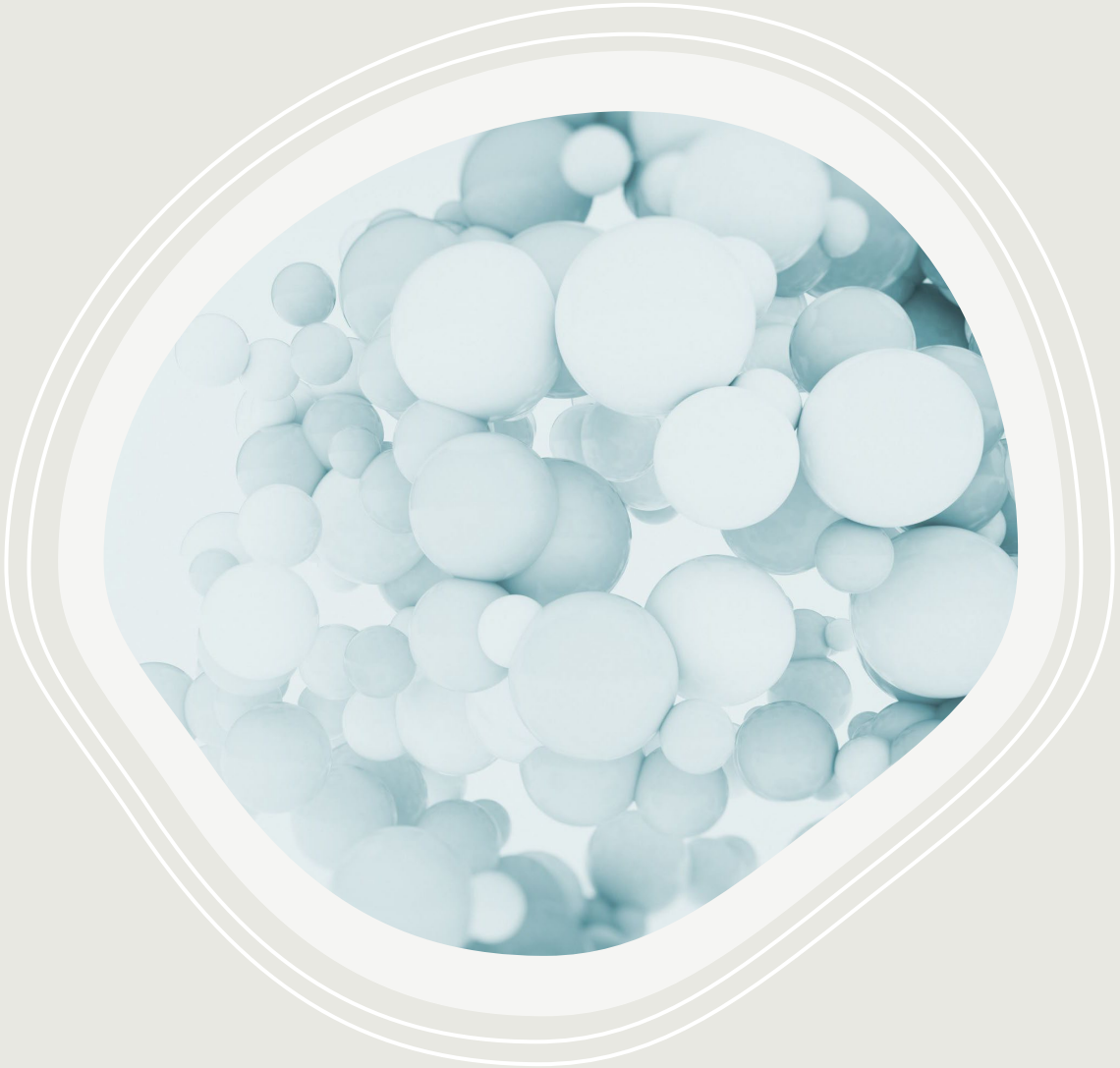


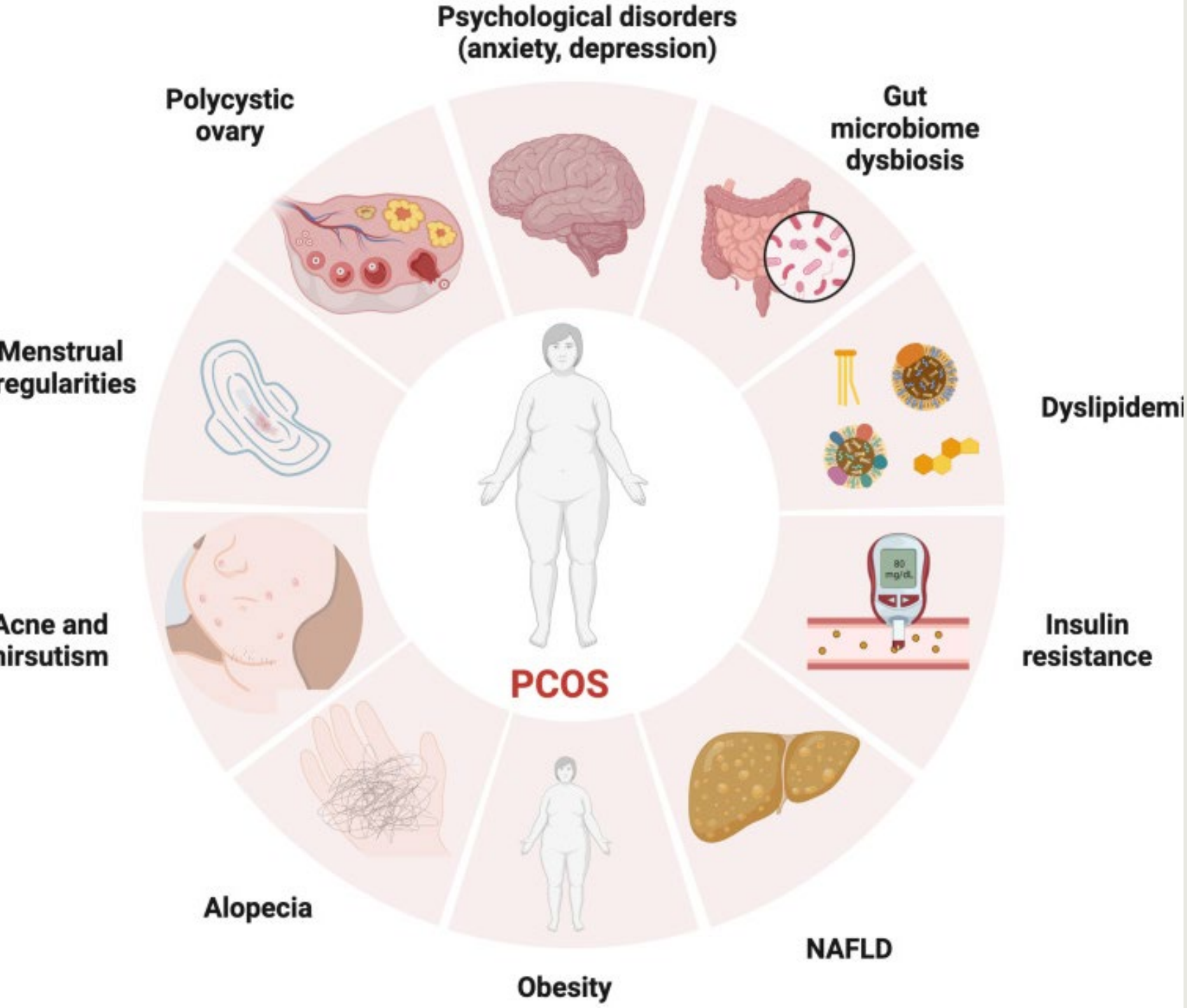
GLP-1 RAs in the Management of PCOS Patients

Significance of the Problem

Polycystic Ovary Syndrome (PCOS) is the most common endocrine disorder in women and a primary cause of female infertility.

PCOS affects up to 20% of women worldwide, and its prevalence has been on the rise over the last decade.

Its development and clinical presentation are characterized by multiple underlying metabolic, hyperandrogenic, reproductive abnormalities, and psychological disorders.



Manifestations of PCOS

It is primarily characterized by ovulation dysfunction (manifesting in the form of menstrual irregularities, such as oligomenorrhea and amenorrhea),

hyperandrogenemia (manifesting as hirsutism, acne, or alopecia),

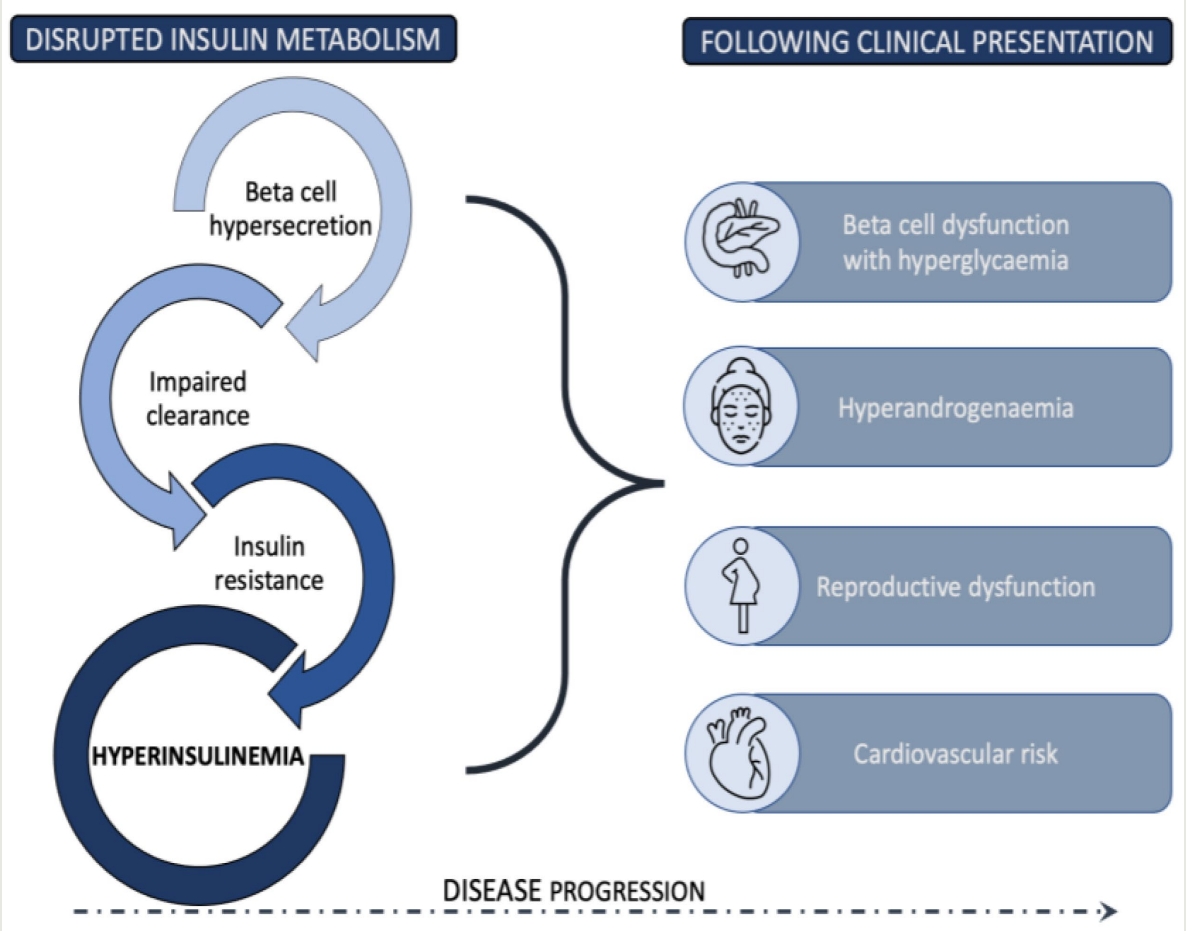
and polycystic ovarian morphology.

Underlying PCOS Pathogenesis

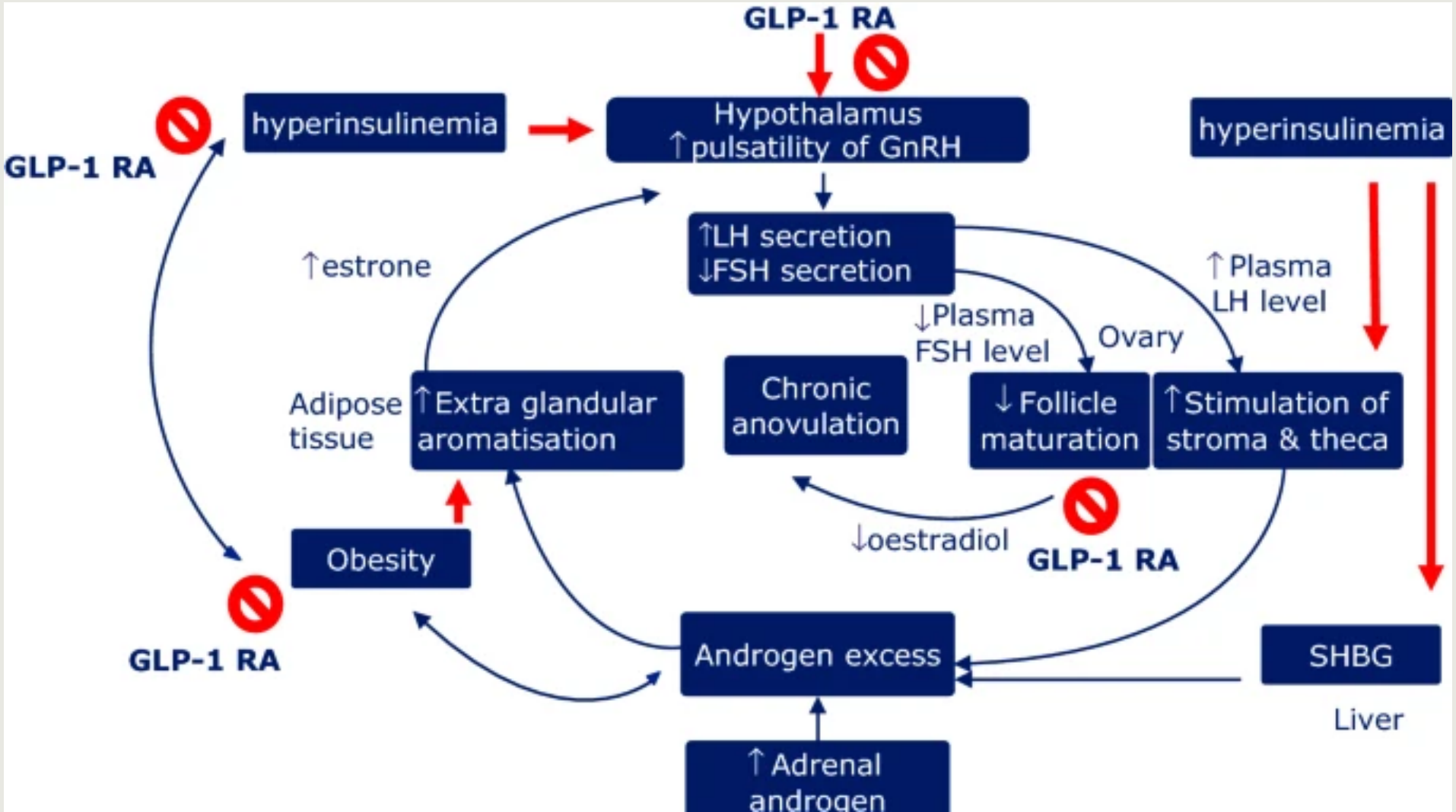
The pathogenesis of PCOS is multifactorial, with insulin resistance (IR) playing a central role.

IR was found to be present in 75% of non-obese PCOS patients and 95% of obese patients (Herman et al., 2023).

The degree of IR amid PCOS women correlates with the amount of abdominal adipose tissue

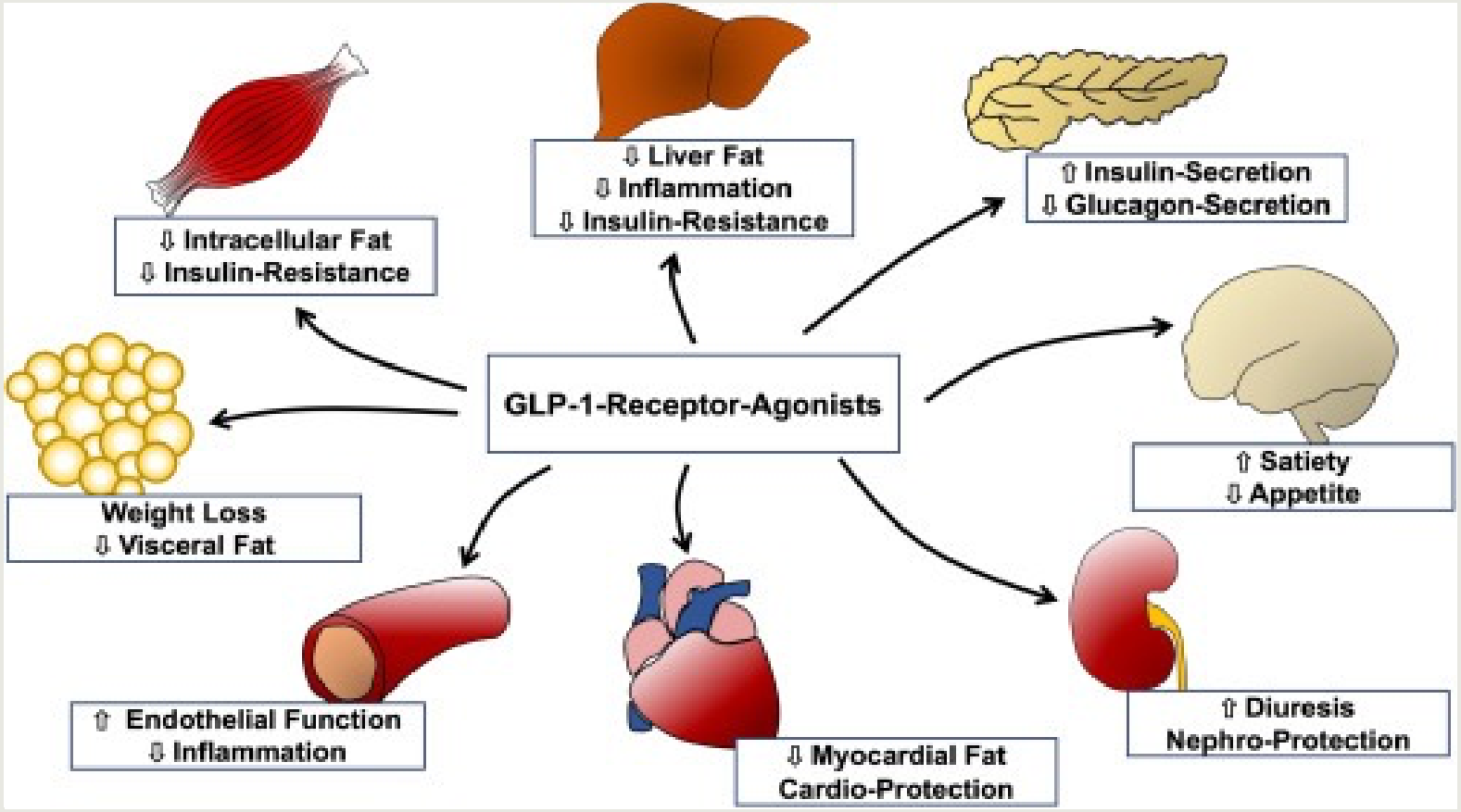


Underlying PCOS Pathogenesis



GLP-1 RAs

Mechanism of Actions



Comparative Therapeutic Effects of GLP-1 RAs and Metformin

- GLP-1 RAs are superior to Metformin in terms of weight loss, the reduction of waist circumference, and BMI. According to Srinivasan and Lofton (2022), following six months of treatment, mean weight loss was 4.9 kg (4.8%) and 9.1 kg (9.8%) in the metformin and GLP-1 (Liraglutide or Semaglutide) cohorts respectively. Similar trends were seen in BMI with reductions of 1.8 kg/m^2 (4.7%) and 3.5 kg/m^2(9.7%).
- GLP-1 RAs surpass Metformin in enhancing insulin sensitivity.
- GLP-1 RAs exhibit similar beneficial effects on menstrual frequency, serum total testosterone, Sexual Hormone Binding Globulin (SHBG), Dehydroepiandrosterone Sulfate (DHEA-S), LH, FBG, triglycerides, total cholesterol, systolic and diastolic blood pressure when compared with Metformin.
- The incidence rates of nausea and headaches with GLP-1 RAs use are higher compared to Metformin, but there are no significant differences in the rates of stomachache, vomiting, bloating, diarrhea, and constipation.

Level I Evidence

A systematic Review and Meta-Analysis conducted by Lyu et al. (2021) demonstrated that GLP-1RAs alone or combined with MET was associated with a **greater weight loss** (N = 318, WMD = −2.61, 95% CI: −3.51 to −1.72, $P \leq 0.001$, I^2 = 77.5%), **more obvious reduction of waist circumference** (N = 276, WMD = −3.46, 95% CI: −4.36 to −2.56, $P \leq 0.001$, I^2 = 0.0%), **and body mass index (BMI)** (N = 318, WMD = −0.93, 95% CI: −1.60 to −0.26, P=0.007, I^2 = 84.9%) in overweight/obese PCOS patients when compared with MET alone.

A Meta-Analysis of seven RCTs, comprising 464 overweight/obese women with PCOS, conducted by Ma et al. (2021) demonstrated that GLP-1 RAs showed **better effects** relative to metformin **on the reduction of body mass index** (mean difference - 1.72; 95% confidence interval -2.46 to -0.99, P < .001) and **homeostatic model assessment of insulin resistance** (standard mean difference -0.37; 95% confidence interval - 0.60,- 0.15, P = .001). GLP-1 RAs were also found to be associated with **lower abdominal girth** compared to metformin.

Contraindications to GLP-1 RAs Therapy

- Hypersensitivity to the product
- Medullary thyroid carcinoma (personal or family history)
- Multiple endocrine neoplasia syndrome type 2 (MEN 2) (personal or family history)
- Pancreatitis (personal history)
- Pregnancy. Stop taking the drug a minimum of two months prior to trying to conceive

Side Effects of GLP-1 RAs

SIDE EFFECTS:

- Nausea, vomiting
- Diarrhea, constipation
- Heartburn, dyspepsia
- Flatulence, abdominal pain
- Dizziness, headache
- Fatigue
- Dehydration
- Hypoglycemia

PROVIDER to MONITOR for SIGNS of:

- Pancreatitis
- Cholecystitis
- Cholelithiasis
- Retinopathy
- Kidney problems
- Depression or thoughts of suicide

Semaglutide Dosage for Weight Management

OZEMPIC

1st Month – 0.25 mg SQ weekly

2nd Month – 0.5 mg SQ weekly

3rd Month – 1 mg SQ weekly

4th Month – 1.5 mg SQ weekly

5th Month – 2 mg SQ weekly (maximum recommended dosage)

WEGOVY

1st Month – 0.25 mg SQ weekly

2nd Month – 0.5 mg SQ weekly

3rd Month – 1 mg SQ weekly

4th Month – 1.7 mg SQ weekly

5th Month – 2.4 mg SQ weekly (maximum recommended dosage)

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