# Study Protocol with SAP and ICF

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Version 1.0

IRB Log No. 2025-44E - H-11-N-140 - Approval Date Dec 04, 2025

## Title:

Evaluating the Efficacy of Various Weekly GLP1receptor Agonist Among Obese Individuals Without Diabetes : a Clinical Trial

## Introduction

Diabetes mellitus is very common health problem affecting "476 million, of which type 2 diabetec patients consider 463 milion , and the number is increasing yearly .(GBD,2017). According to one large randomizedcontrolled trial (RCT) including 11,140 patients , with every 1% increase in glycosylated hemoglobin (HbA1c), risk was increased up to 40% of all-cause and cardiovascular mortality(Zoungas et al; 2012). Now its hard to have good control of blood sugar , and therapeutic achievements are needed to reach glycemic control (UKPDS 34,28). Glucagon-like peptide 1 receptor agonist (GLP-1 RA) is a group of antidiabetic therapy that affect glucose metabolism, increase beta cells performance , and reduce body weight without hypoglycemia (Aroda ,2018). GLP-1 RAs are divided into short- and long-acting types according into mechanism of action (Guja et al;2017) (Chatterjee et al;2018),. Compared with other antihyperglycemic therapies , RCTs have reported better long-term effects, especially in relation with cardiovascular results (Aroda ,2018). GLP-1RAs mediate its action on glucose metabolism by increasing insulin secretion induced by hyperglycemia, reduce glucagon secretion during hyperglycemia, decrease gastric emptying, preventing postprandial hyperglycemia , and decrease appetite and subsequently body weight. ( Baggio, Drucker ;2007)(Maselli,Camilleri;2021) Short acting GLP-1RAs (exenatide and lixisenatide) decrease nocturnal and fasting glucose response but maintain the effect on gastric emptying during long run therapy . Long acting GLP-1Ras (eg, liraglutide, exenatide, and dulaglutide) have greater impact on nocturnal and fasting glucose and Glycosylated haemoglobin (HbA1c), both of them combined with basal insulin. GLP-1RAs significantly decrease the weight of obese type 2 diabetec patients (Garvey et al;2023)(Wharton et al;2023) '" The US Food and Drug Administration has approved various preparation or doses of GLP-1RAs for type 2 diabetes therapy : exenatide, liraglutide, dulaglutide, albiglutide, lixisenatide, semaglutide, and tirzepatide.(USA FDA ). Independent evaluation is needed for different GLP-1RA drugs, regarding : pharmacokinetics, efficacy, side effects rates, and required doses . (Trujillo, Neur ;2014). In addition, its needed for physicians to know each GLP-1RA drug advantages and disadvantages to make the appropriate clinical decisions. A lot of network metaanalyses make comparison of the efficacy of various GLP-1RAs. (Jiang et al;2021)( Xia et al;2021) ,However, there are new GLP-1RAs drugs quickly developing , and more drugs have announced this year, involving orforglipron, retatrutide, and CagriSema (semaglutide with cagrilintide).besides, An updated evidence synthesis considering various large scale trials published currently is urgently needed. (Zaccardi et al;2016)(Dahl et al;2022) Thus, these preceding studies are not any more enough to provide adequate and timely support for patients, physicians, and investigators.

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❖ **Aim of study:** The study is designed to evaluate the efficacy of GLP1 analogues in individuals obese non-diabetic regarding metabolic and lipid profile and weight reduction.

❖ **Objectives:** To prove that, GLP1 receptor agonists can be used effectively as a weight reduction agents among non-diabetec obese population and can influence their lipid and metabolic profile

❖ **Methodology:** Site of study: the study will be conducted in single center (Alzafer) hospital Najran KSA . The sample size: 150 person . Subjects included in the study will be divided into 3 groups: Group 1: include 50 non-diabetic obese subjects receiving Dulaglutide Group 2: include 50 non-diabetic obese subjects receiving Semaglutide Group 3: include 50 non-diabetic obese subjects receiving Tirazepetide The study will be done in November 2025 to April 2026 Subject included lithe study : :criteriaInclusion Subjects (above 18 years old) obese body mass index (BMI) above 30 :Exclusion criteria Subjects with liver disease, renal dysfunction diabetes, pancreatic diseases , thyroid disorder or goiter psychological diseases like depression and pregnant women, and Patients who will refuse to be enrolled in the study or refuse to sign the consent will be also excluded, Method of selection of sample: the sample will be selected by randomized method.

❖ **Type of study**: randomized controlled clinical trials The subjects will be followed up every month in internal medicine outpatient clinics at Al-Zafer hospital Najran and make sure they take the medications regularly and population will not continue medicine intake will be removed from the study and measuring the parameters at pretreatment time , 3 months post treatment and 6 months post treatment we will follow in every subject parameters like weight, body mass index, lipid profile, liver functions and presence or absence of GIT upsets

❖ Steps of performance and techniques used: ❖ Full history tacking: with special consideration to age, sex, and location of residence. ❖ General examination: with special consideration to weight, height, body mass index was calculated by dividing weight (in kilograms) by the square of the height (in meters) and blood pressure and waist circumference ❖ Laboratory investigation: include fasting blood glucose , lipid profile (total cholesterol ,triglycerides, LDL,HDL) , liver enzymes ❖ Ethical consideration: Approvals obtained performing the study 1- from official or governmental department. 2-"IRB Approval Obtained: Dec 04, 2025 - H-11-N-140 - Log 2025-44E - Exempt in Najran health cluster in Najran .

## Statistical Analysis Plan:

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STATISTICAL ANALYSIS PLAN (SAP) - Document Date: Dec 04, 2025
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Primary Endpoint: Percent change in body weight from baseline to Week 12 and Week 24.

Analysis:
- Descriptive statistics: Mean ± SD for continuous variables (weight, BMI, lipid, liver enzymes), n (%) for categorical.
- Primary analysis: One-way ANOVA to compare mean percent weight change among three groups. Normality tested by Shapiro-Wilk. If non-normal, Kruskal-Wallis test. If ANOVA significant ($p<0.05$), post-hoc Tukey test for pairwise comparisons.
- Secondary endpoints:
  * Change in BMI, waist circumference: ANOVA
  * Lipid profile (TC, TG, LDL, HDL): ANOVA / ANCOVA adjusted for baseline
  * Liver functions: ANOVA
  * Proportion achieving >=5% weight loss: Chi-square test
  * Presence of GIT upsets (nausea, vomiting etc): Chi-square / Fisher exact
- Software: IBM-SPSS for Windows version 27, 2020
- Significance: $p<0.05$ two-sided
- Missing data: Last observation carried forward (LOCF), per-protocol analysis for compliant subjects
- Sample size: 150 total, 50 per group, randomized
- Type of study: Randomized controlled clinical trial

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INFORMED CONSENT FORM (ICF)
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Study Title: Evaluating the Efficacy of Various Weekly GLP1 Receptor Agonists Among Obese Individuals Without Diabetes: A Clinical Trial

IRB: New Najran General Hospital - H-11-N-140 - Log 2025-44E
Approval Date: Dec 04, 2025 - Site: Al-Zafer Hospital, Najran
Contact: eam-nngh-research@moh.gov.sa | +966175227736
PI: Dr. Hany Mostafa Omar Mohamed

1. PURPOSE: Compare 3 weekly GLP1 drugs (Dulaglutide, Semaglutide, Tirzepatide) for weight reduction in 150 non-diabetic obese subjects (BMI>30, age>18).

2. PROCEDURES: Randomized into 3 groups (50 each). 3 visits: Baseline, Week 12 (3 months), Week 24 (6 months). At each visit: weight (kg, calibrated digital scale), height, BMI, waist, BP, labs: FBG, lipid profile (TC,TG,LDL,HDL), liver enzymes. Follow-up monthly in internal medicine OPD.

3. RISKS: Nausea, vomiting, diarrhea, abdominal pain, constipation, decreased appetite. Rare: pancreatitis, gallbladder problems.

4. BENEFITS: Possible weight loss, improved lipids, free follow-up. No guarantee. Helps future obesity treatment.

5. CONFIDENTIALITY: Coded data, SPSS v27, no name in publications.

6. VOLUNTARY: Voluntary, can withdraw anytime without affecting care. If not compliant with medication, will be removed.

7. CONTACTS: PI Dr. Hany / IRB H-11-N-140

CONSENT:
I have read this form, understand purpose/procedures/risks/benefits, voluntary.

Participant Name: _____ Signature: _____ Date: _____
Person Obtaining Consent: _____ Signature: _____ Date: _____
Investigator: Dr. Hany Mostafa Omar Mohamed Signature: _____ Date: _____

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