Methods: In STEP 1, 1961 adults aged ≥18 years with body mass index (BMI) ≥27 kg/m^2 with ≥1 weight-related comorbidity or BMI ≥30 kg/m^2, without diabetes, were randomized to s.c. semaglutide 2.4 mg once-weekly or matched placebo (2:1) for 68 weeks, plus lifestyle intervention. Participants with BMI ≤40 kg/m^2 from 9 sites were eligible for the substudy. Total fat mass, total lean body mass and regional visceral fat mass were measured using DEXA at screening and week 68; visceral fat mass was calculated in the L4 region (both males/females), android region (males), or gynoid region (females), depending on site scanner methodology. Proportions of total fat and lean body mass are shown relative to total body mass; proportion of visceral fat mass is expressed relative to region assessed.
Results: This analysis included 140 participants (semaglutide n=95; placebo n=45) (mean weight 98.4 kg, BMI 34.8 kg/m^2; 76% female). Baseline body composition was similar in those receiving semaglutide and placebo (total fat mass proportion: 43.4% vs 44.6%; regional visceral fat mass proportion: 33.8% vs 36.3%; total lean body mass proportion: 53.9% vs 52.7%; respectively). Percentage change in body weight from baseline to week 68 was -15.0% with semaglutide vs -3.6% with placebo. This resulted in reductions from baseline with semaglutide in total fat mass (-19.3%) and regional visceral fat mass (-27.4%), leading to 3.5%-point and 2.0%-point reductions in the proportions of total fat mass and visceral fat mass, respectively. Total lean body mass decreased from baseline (-9.7%); however, the proportion relative to total body mass increased by 3.0%-points. An increasing improvement in lean body mass:fat mass ratio was seen with semaglutide with increasing weight loss from baseline to week 68 (continuous data). Overall, the ratio increased from baseline (1.34 [95% CI: 1.22, 1.47]) to week 68 by 0.23 [0.14, 0.32], with greater improvement in those with ≥15% weight loss (n=44; 0.41 [0.28, 0.53]) vs <15% weight loss (n=39; 0.03 [-0.05, 0.12]) (observed, dichotomized data; no imputation for missing data). There were no major changes in body composition with placebo from baseline to week 68.
Conclusion: In adults with overweight/obesity, semaglutide 2.4 mg was associated with reduced total fat mass and regional visceral fat mass, and an increased proportion of lean body mass. Greater weight loss was associated with greater improvement in body composition (lean body mass:fat mass ratio).

Adipose Tissue, Appetite, and Obesity
INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Incidence of Insulin Resistance in Obese Adolescent of Type-2 Diabetes Mellitus Patients

Farrukh Javaid, PGR Endocrinology[1], Rukhshan Khurshid, Assitant Professor Biochemistry[1], Huma Ashraf, Associate Professor Biochemistry[2], Abeera Mazhar, PGR Pediatrics[3], Lubna Amir, Associate Professor Pharmacology[4].
[1]Services Hospital / Shalamar Hospital, Lahore, Pakistan, [2]CMH, Lahore, Pakistan, [3]Mayo Hospital, Lahore, Pakistan, [4]FMH, Lahore, Pakistan.

Background: Insulin resistance is a reduced response of tissue to insulin-mediated action on cells. It may be due to many reasons, including the surplus of adipose tissue, which cause a resistance of insulin. Aims and **Objectives:** To find the incidence of insulin resistance in obese adolescent of type-2 diabetes mellitus patients.
Material and **Methods:** The study involved 50 adolescents aged 14–20 years old. Adolescents with BMI > 26.0 Kg/m2 were included in the study. Levels of fasting blood sugar, Hb A1c and serum insulin were estimated. The index of Homeostatic model assessment for insulin resistance or HOMA-IR was calculated. The cut-off value of HOMA-IR was > 3.16 for both genders.
Results: It was observed that the values of BMI and level of fasting blood sugar of first degree relatives of diabetics was significantly higher as compared to their controls. Levels of both blood HbA1c and serum insulin were increased but significant difference was observed only in case of serum insulin when compared with their controls.
Conclusion: Obesity in adolescents of first degree relatives of diabetics shows a major reason of insulin resistance. The incidence of insulin resistance in obese adolescents signals a perturbing trend for the burden of type 2 diabetes in our country.

Adipose Tissue, Appetite, and Obesity
INTEGRATED PHYSIOLOGY OF OBESITY AND METABOLIC DISEASE

Insulin Resistance Moderates the Association Between BMI and Metabolic Syndrome Severity in Women 4–10 Years After Pregnancy, Independent of Gestational Diabetes Status

Makenzie Callahan, MS[1], Samantha Martin, PhD[1], Jessica Bahorski, PhD[2], Gregory Pavela, PhD[1], W Timothy Garvey, MD[1], Paula C. Chandler-Laney, PhD[1].
[1]University of Alabama at Birmingham, Birmingham, AL, USA, [2]Florida State University, Tallahassee, FL, USA.

Objective: Obesity and gestational diabetes mellitus (GDM) increase the risk for metabolic syndrome (MetS). Insulin resistance (IR) is associated with obesity, contributes to risk for GDM, and persists after pregnancy even when glucose tolerance returns. Further, IR may enhance the risk of MetS associated with obesity and GDM. The purpose of this study was to test the hypothesis that IR moderates the relationship between BMI and MetS severity 4–10 years after pregnancy, independent of prior GDM, such that the positive association between BMI and MetS severity is stronger among women with greater IR. **Methods:** This hypothesis was tested in a secondary analysis of data collected from women enrolled in a study of the intergenerational transmission of obesity, 4–10 years after the index pregnancy. Recruitment in the parent study was stratified to include women with normal weight without GDM (NW), overweight or obesity without GDM (OwOB), and women with GDM during the index pregnancy. Standard clinical procedures were used to measure height, weight, waist circumference and blood pressure, and a fasting blood draw was obtained with which to measure glucose, insulin, triglycerides, and HDL-cholesterol. MetS was evaluated as