abdominal adiposity and circulating glutamate is causal, as well as the direction of this association, is unknown. Here, we aimed to determine whether obesity and abdominal obesity were causally associated with circulating glutamate levels. **Methods:** We used a two-sample bi-directional inverse-variance weighted Mendelian randomization study design (IVW-MR). We derived summary statistics for our exposures and outcomes from published genome-wide association studies from the GIANT consortium (n = 681 275) and blood metabolites (n = 7 804). We identified independent genetic variants ($r^2 < 0.1$) associated with body mass index (BMI) and waist-to-hip ratio adjusted for BMI (WHRadjBMI, $p < 5x10^{-8}$) as well as circulating glutamate ($p < 5x10^{-5}$). **Results:** We found no causal association between circulating glutamate levels and BMI (beta = 0.082, SE = 0.0413, p = 0.0471) or WHRadjBMI (beta = -0.00106, SE = 0.0401, p = 0.979). However, there was a positive effect of BMI (beta = 0.0608, SE = 0.0150, $p = 5.19x10^{-5}$) and WHRadjBMI (beta = 0.0701, SE = 0.0198, $p = 3.98x10^{-4}$) on circulating glutamate level. **Conclusion:** This Mendelian randomization analysis suggests that obesity and abdominal obesity are causally related to elevated circulating glutamate levels. Glutamate levels are not causally related to adiposity. Whether the downregulation of branched-chain amino acid catabolism in adipose tissue reported in obesity underlies this association should be explored.

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

Once-weekly Subcutaneous Semaglutide 2.4 mg Reduces Body Weight in Adults with Overweight or Obesity Regardless of Baseline Characteristics (STEP 1)

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Background: Semaglutide is a long-acting, subcutaneous (s.c.), glucagon-like peptide-1 analogue that is currently being investigated for obesity management in adults with overweight or obesity in the phase 3 STEP clinical trial program. Varying degrees of weight loss were observed with once-weekly s.c. semaglutide 2.4 mg in STEP 1, and a post-hoc analysis was conducted to investigate weight loss in subgroups of participants based on their baseline characteristics.

Methods: STEP 1 was a randomized, double-blind, placebo-controlled, phase 3 trial (NCT03548935). Adults aged ≥18 years with either body mass index (BMI) ≥27 kg/m^2 with ≥1 weight-related comorbidity or BMI ≥30 kg/m^2, without type 2 diabetes, were randomized 2:1 to 68 weeks' treatment with once-weekly s.c. semaglutide 2.4 mg or placebo, as adjunct to lifestyle intervention. A descriptive evaluation of categorical weight loss with semaglutide from baseline to week 68 (≥20%, 15-<20%, 10-<15%, 5-<10%) by baseline characteristics (age, sex, race [White, Asian, Black or African American, other], body weight, BMI, waist circumference, and glycemic status [normo-glycemia, prediabetes]) was conducted. Mean percent weight loss with semaglutide from baseline to week 68 was analyzed separately by sex (male, female) and baseline body weight (≥115 kg, 100-<115 kg, 90-<100 kg, <90 kg) using a mixed model for repeated measurements analysis with treatment, subgroup (of sex or baseline body weight), and the interaction between treatment and subgroup as factors, and baseline body weight as a covariate, all nested within visit (based on the trial product estimand [treatment effect assuming treatment adherence and without use of rescue intervention] for the on-treatment period).

Results: STEP 1 included 1,961 randomized participants (mean age 46 years, body weight 105.3 kg, BMI 37.9 kg/m^2; 74.1% female). For categorical weight loss, the observed proportions of participants with ≥20%, 15-<20%, 10-<15%, and 5-<10% weight loss at week 68 were 34.8%, 19.9%, 20.0%, and 17.5% with semaglutide vs 2.0%, 3.0%, 6.8%, and 21.2% with placebo, respectively. The distribution of participants across weight loss groups did not appear to be affected by any baseline characteristics, except sex and baseline body weight. Mean percent weight loss at week 68 with semaglutide was greater among females than males, and in participants with lower vs higher baseline body weight. Sex and baseline body weight were independently associated with weight loss with semaglutide vs placebo at week 68 ($p<0.001$ for both tests for subgroup interactions).

Conclusion: In STEP 1, weight loss with once-weekly s.c. semaglutide 2.4 mg was seen in all subgroups evaluated, and was generally not influenced by baseline characteristics. The exception was sex and baseline body weight; female sex and a low baseline body weight were associated with a greater response to semaglutide.

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Prevalence of Childhood Obesity in the United States 1999 - 2018: A 20-Year Analysis

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Introduction: Obesity is a public health crisis in the US. Childhood obesity is associated with multiple comorbidities in the adulthood, including metabolic syndrome, cardiovascular diseases, and premature death. A recent study found that the prevalence of childhood obesity varied according to age and ethnicity. This study aims to evaluate the long-term trends and the underexplored socioeconomic factors associated with childhood obesity.
Method: From the US National Health and Nutrition Examination Survey from 1999 to 2018, 35 907 children aged 2–19 with body mass index (BMI) data were included. Prevalence of obesity and severe obesity, defined as BMI ≥95th percentile and ≥120% of 95th percentile of US Centers for Disease Control and Prevention growth charts, respectively. Trends in prevalence of obesity and subgroup analyses according to age group, sex, ethnicity, language used in interview, household education level, and household income level, were analyzed. Data analysis was performed using the R statistical package "survey" (version 3.6.3).
Results: The prevalence of obesity and severe obesity increased from 14.7 [95% CI: 12.9–17.0] % to 19.2 [17.2–21.0] % and 3.9 [2.9–5.0] % to 6.1 [4.8–8.0] % in 1999–2018, respectively (p=0.001 and p=0.014 for obesity and severe obesity, respectively). In 2017–8, the prevalence of obesity among children from Spanish-speaking households was 24.4 [22.4–27.0] %, higher than children from English-speaking households (p=0.027). Children from households with high education level and high income level had a lower prevalence of obesity compared to those with low education level and low income level (p=0.003 and p=0.002 for education level and income level, respectively). Compared to girls, boys had higher prevalence of obesity (p=0.002) and severe obesity (p=0.004).
Conclusion: The prevalence of childhood obesity in America kept increasing during the period 1999–2018 despite various public health initiatives. The problem is worse in children with lower socioeconomic status, and in children from Spanish-speaking households. Public health interventions are urgently needed to halt the rising trend of childhood obesity, and measures specifically catering to children from Spanish-speaking families should be put in place.

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Profile of Intestinal Microbiota and Anxiety Level in Overweight Children and Adolescents

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Justification: Obesity is considered a worldwide epidemic, with a significant increase in its prevalence in the last 30 years in both children and adolescents. Anxiety disorders can be considered both a cause and a consequence of obesity. The intestinal microbiota has been identified as a participant in the inflammatory process of both obesity and depression / anxiety disorders. **Objective:** Describe and compare the intestinal microbiota profile of overweight/obese children/teenagers with and without signs of anxiety. METHODOLOGICAL PROCEDURES: descriptive, observational, cross-sectional study with an analytical character (comparison of groups), carried out during the months of January to October of the year 2019. 30 overweight/obesity children/teenagers (BMI greater than P85 – WHO 2007), between seven and 17 years old, convenience sampling. None of the participants had taken antibiotics during the past eight weeks of participation on the study or had chronic or endocrine disease that was not being adequately treated. The participants were divided into two groups: the first group consists of children/adolescents with excess weight without signs of anxiety (n 16) and the second group consists of children/adolescents with excess weight with signs of anxiety (n 14), assessed by a Screen for Child Anxiety Related Emotional Disorders (SCARED) screening questionnaire. **Results:** The group with signs of anxiety showing higher HOMA IR compared to the group without signs of anxiety with values of 5.05 ± 2.08 and 3.47 ± 1.6 (p = 0.041), respectively. There was a statistically significant difference for beta diversity of the intestinal microbiota profile using the CHAO method (p = 0.025) and the Jackknife method (p = 0.01) between the groups with signs of anxiety and without signs of anxiety. **Conclusion:** difference was found between the intestinal microbiota diversity of obese children / adolescents with signs of anxiety in relation to the intestinal microbiota diversity of obese children / adolescents without signs of anxiety. This finding suggests a possible involvement of the imbalance of the intestinal microbiota with anxiety disorders and depression in children/adolescents with weight excess.

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Relationship Between Metabolic Syndrome Components and Proinflammatory Molecules

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We aimed to study the associations of 5 adipocytokines, two endothelial damage markers, and hs-CRP with the MetS components to distinguish the most significant cytokines likely related to distinct metabolic profiles. **Methods:** Cross-sectional study with 202 Chilean subjects (18–65 years old), categorized by MetS, and No-MetS according to Harmonizing ATP III. Adipocytokines profiling included adiponectin, leptin, hs-CRP, CTRP-1, PAI-1, FABP4, and metalloproteinase (MMP)-9 and MMP-2 activity. **Results:** Subjects with MetS showed higher levels of the most proinflammatories molecules but significantly lower adiponectin than subjects with No-MetS. Among the studied adipocytokines, PAI-1 and adiponectin showed the strongest associations with most of MetS components. PAI-1 was associate with MetS OR 1.107 [1.065–1.151], p< 0.0001, and adiponectin inversely associated with MetS OR 0.710 [0.610 -0.825], p< 0.0001). Following adjustment by