1-Medications for Obesity

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Abstract

Importance Obesity affects approximately 19% of women and 14% of men worldwide and is associated with increased morbidity. Antiobesity medications (AOMs) modify biological processes that affect appetite and significantly improve outcomes, such as type 2 diabetes, hypertension, and dyslipidemia. Observations AOMs should be administered in combination with lifestyle interventions and can be classified according to their mechanisms of action. Orlistat modifies digestive tract absorption and causes gastrointestinal adverse effects, such as oily fecal spotting and urgency, in more than 25% of patients. Centrally acting drugs, such as phentermine-topiramate and naltrexone-bupropion, regulate appetite in the brain and are associated with constipation in approximately 20% of patients, although the incidence of other adverse effects (eg, paresthesia, nausea) varies by medication. Nutrient-stimulated hormone-based medications, such as liraglutide, semaglutide, and tirzepatide, mimic the actions of enteropancreatic hormones that modify central appetite regulation and provide multiple cardiometabolic weight-loss benefits. Adverse effects of these drugs include nausea (28%-44%), diarrhea (21%-30%), and constipation (11%-24%). The relative potency of adult obesity medications has been studied in meta-analyses. Compared with placebo, orlistat was associated with 3.1% greater weight loss (52 randomized clinical trials [RCTs]; 16 964 participants), phentermine-topiramate was associated with 8.0% greater weight loss (5 RCTs; 3407 participants), naltrexone-bupropion was associated with 4.1% greater weight loss (6 RCTs; 9949 participants), liraglutide was associated with 4.7% greater weight loss (18 RCTs; 6321 participants), semaglutide was associated with 11.4% greater weight loss (5 RCTs; 4421 participants), and tirzepatide 15 mg was associated with 12.4% greater weight loss (6 RCTs; 1972 participants). Conclusion and Relevance Obesity is associated with increased morbidity. Antiobesity medications are effective adjunctive therapy to lifestyle changes for improved weight loss and health outcomes.

Keywords

Keywords Plus

SEMAGLUTIDE 2.4 MGCONTROLLED-RELEASE PHENTERMINE/TOPIRAMATEWEIGHT-LOSSDOUBLE-BLINDCONTROLLED-TRIALDOUBLE-DUMMYRISK-FACTORSBODY-WEIGHTADULTSOVERWEIGHT

2-Obesity in adults

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(provided by Clarivate) ,Source LANCET,Volume 404,Issue 10456,Page 972-987,DOI 10.1016/S0140-6736(24)01210-8,Published SEP 7 2024,Early Access SEP 2024,Indexed 2024-09-16,Document Type Review

Abstract

Obesity has increased in prevalence worldwide and WHO has declared it a global epidemic. Population-level preventive interventions have been insufficient to slow down this trajectory. Obesity is a complex, heterogeneous, chronic, and progressive disease, which substantially affects health, quality of life, and mortality. Lifestyle and behavioural interventions are key components of obesity management; however, when used alone, they provide substantial and durable response in a minority of people. Bariatric (metabolic) surgery remains the most effective and durable treatment, with proven benefits beyond weight loss, including for cardiovascular and renal health, and decreased rates of obesity-related cancers and mortality. Considerable progress has been made in the development of pharmacological agents that approach the weight loss efficacy of metabolic surgery, and relevant outcome data related to these agents' use are accumulating. However, all treatment approaches to obesity have been vastly underutilised.

Keywords

Keywords Plus

LIFE-STYLE INTERVENTIONY GASTRIC BYPASSLAPAROSCOPIC SLEEVE GASTRECTOMYSEMAGLUTIDE 2.4 MGBODY-MASS INDEXTERM-FOLLOW-UPBARIATRIC SURGERYWEIGHT-LOSSMETABOLIC SURGERYMEDICAL THERAPY

3-Inflammation and resolution in obesity

Soták, M (Sotak, Matus) [1] ; Clark, M (Clark, Madison) [2] , [3] ; Suur, BE (Suur, Bianca E.) [2] , [3] ; Börgeson, E (Borgeson, Emma) [1] , [2] , [3](provided by Clarivate) ,Source NATURE REVIEWS ENDOCRINOLOGY,Volume 21 ,Issue 1,Page 45-61,DOI 10.1038/s41574-024-01047-y,Published JAN 2025,Early Access OCT 2024,Indexed 2024-11-06,Document Type Review

Abstract

Inflammation is an essential physiological defence mechanism, but prolonged or excessive inflammation can cause disease. Indeed, unresolved systemic and adipose tissue inflammation drives obesity-related cardiovascular disease and type 2 diabetes mellitus. Drugs targeting pro-inflammatory cytokine pathways or inflammasome activation have been approved for clinical use for the past two decades. However, potentially serious adverse effects, such as drug-induced weight gain and increased susceptibility to infections, prevented their wider clinical implementation. Furthermore, these drugs do not modulate the resolution phase of inflammation. This phase is an active process orchestrated by specialized pro-resolving mediators, such as lipoxins, and other endogenous resolution mechanisms. Pro-resolving mediators mitigate inflammation and development of obesity-related disease, for instance, alleviating insulin resistance and atherosclerosis in experimental disease models, so mechanisms to modulate their activity are, therefore, of great therapeutic interest. Here, we review current clinical attempts to either target pro-inflammatory mediators (IL-1 beta, NOD-, LRR- and pyrin domain-containing protein 3 (NLRP3) inflammasome, tumour necrosis factor (TNF) and IL-6) or utilize endogenous resolution pathways to reduce obesity-related inflammation and improve cardiometabolic outcomes. A remaining challenge in the field is to establish more precise biomarkers that can differentiate between acute and chronic inflammation and to assess the functionality of individual leukocyte populations. Such advancements would improve the monitoring of drug effects and support personalized treatment strategies that battle obesity-related inflammation and cardiometabolic disease. This Review discusses translational attempts to mitigate the inflammation that drives obesity-related cardiometabolic diseases. The Review also focuses on mechanisms that control inflammatory cascades, either through traditional anti-inflammatory drugs or via the specialized pro-resolving mediators that actively control the resolution of inflammation.

Chronic unresolved systemic and adipose tissue inflammation drives obesity-related cardiometabolic disease.Drugs targeting pro-inflammatory cytokines, or inflammasome activation, are approved for clinical use but can elicit serious adverse effects (such as weight gain and increased susceptibility to infections), hampering their clinical implementation.The resolution phase of inflammation is an active process regulated by specialized pro-resolving mediators. These mediators mitigate obesity-related inflammation and systemic disease in experimental models and are of therapeutic interest.The field lacks biomarkers that can differentiate between acute and chronic inflammation and assess the functionality

of individual leukocyte populations, which would improve personalized treatment strategies and support drug monitoring.

Keywords

Keywords Plus

PRORESOLVING LIPID MEDIATORSADIPOSE-TISSUE INFLAMMATIONC-REACTIVE PROTEINNF-KAPPA-BLIPOXIN A(4)INSULIN-RESISTANCERESOLVIN D1OMEGA-3 SUPPLEMENTATIONSECONDARY PREVENTIONFATTY-ACIDS

4-Obesity Management in Adults: A Review

Elmaleh-Sachs, A (Elmaleh-Sachs, Arielle) [1] , [2] , [3] ; Schwartz, JL (Schwartz, Jessica L.) [4] ; Bramante, CT (Bramante, Carolyn T.) [5] ; Nicklas, JM (Nicklas, Jacinda M.) [6] ; Gudzune, KA (Gudzune, Kimberly A.) [4] ; Jay, M (Jay, Melanie) [2] , [7] (provided by Clarivate) ,Source JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION,Volume 330,Issue 20,Page 2000-2015,DOI 10.1001/jama.2023.19897,Published NOV 28 2023,Indexed 2024-02-03,Document Type Review

Abstract

IMPORTANCE Obesity affects approximately 42% of US adults and is associated with increased rates of type 2 diabetes, hypertension, cardiovascular disease, sleep disorders, osteoarthritis, and premature death. OBSERVATIONS A body mass index (BMI) of 25 or greater is commonly used to define overweight, and a BMI of 30 or greater to define obesity, with lower thresholds for Asian populations (BMI >= 25-27.5), although use of BMI alone is not recommended to determine individual risk. Individuals with obesity have higher rates of incident cardiovascular disease. In men with a BMI of 30 to 39, cardiovascular event rates are 20.21 per 1000 person-years compared with 13.72 per 1000 person-years in men with a normal BMI. In women with a BMI of 30 to 39.9, cardiovascular event rates are 9.97 per 1000 person-years compared with 6.37 per 1000 person-years in women with a normal BMI. Among people with obesity, 5% to 10% weight loss improves systolic blood pressure by about 3 mm Hg for those with hypertension, and may decrease hemoglobin A(1c) by 0.6% to 1% for those with type 2 diabetes. Evidence-based obesity treatment includes interventions addressing 5 major categories: behavioral interventions, nutrition, physical activity, pharmacotherapy, and metabolic/bariatric procedures. Comprehensive obesity care plans combine appropriate interventions for individual patients. Multicomponent behavioral interventions, ideally consisting of at least 14 sessions in 6 months to promote lifestyle changes, including components such as weight self-monitoring, dietary and physical activity counseling, and problem solving, often produce 5% to 10% weight loss, although weight regain occurs in 25% or more of participants at 2-year follow-up. Effective nutritional approaches focus on reducing total caloric intake and dietary strategies based on patient preferences. Physical activity without calorie reduction typically causes less weight loss (2-3 kg) but is important for weight-loss maintenance. Commonly prescribed medications such as antidepressants (eg, mirtazapine, amitriptyline) and antihyperglycemics such as glyburide or insulin cause weight gain, and clinicians should review and consider alternatives. Antiobesity medications are recommended for nonpregnant patients with obesity or overweight and weight-related comorbidities in conjunction with lifestyle modifications. Six medications are currently approved by the US Food and Drug Administration for long-term use: glucagon-like peptide receptor 1 (GLP-1) agonists (semaglutide and liraglutide only), tirzepatide (a glucose-dependent insulinotropic polypeptide/GLP-1 agonist), phentermine-topiramate, naltrexone-bupropion, and orlistat. Of these, tirzepatide has the greatest effect, with mean weight loss of 21% at 72 weeks. Endoscopic procedures (ie, intragastric balloon and endoscopic sleeve gastroplasty) can attain 10% to 13% weight loss at 6 months. Weight loss from metabolic and bariatric surgeries (ie, laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass) ranges from 25% to 30% at 12 months. Maintaining long-term weight loss is difficult, and clinical guidelines support the use of long-term antiobesity medications when weight maintenance is inadequate with lifestyle interventions alone. CONCLUSION AND RELEVANCE Obesity affects approximately 42% of adults in the US. Behavioral interventions can attain approximately 5% to 10% weight loss, GLP-1 agonists and glucose-dependent insulinotropic polypeptide/GLP-1 receptor agonists can attain approximately 8% to 21% weight loss, and bariatric surgery can attain approximately 25% to 30% weight loss. Comprehensive, evidence-based obesity treatment combines behavioral interventions, nutrition, physical activity, pharmacotherapy, and metabolic/bariatric procedures as appropriate for individual patients.

Keywords **Obesity**

Keywords Plus

LIFE-STYLE INTERVENTIONWEIGHT-LOSS PROGRAMSCONTROLLED-TRIALDOUBLE-BLINDBARIATRIC SURGERYAMERICAN SOCIETYEXTENDED-RELEASEOVERWEIGHTCAREMETAANALYSIS

5-Determinants of childhood obesity in China

Yuan, CZ (Yuan, Changzheng) [1] ; Dong, YH (Dong, Yanhui) [2] , [3] ; Chen, H (Chen, Hui) [1] ; Ma, L (Ma, Le) [4] ; Jia, LH (Jia, Lihong) [5] ; Luo, JY (Luo, Jiayou) [6] ; Liu, Q (Liu, Qin) [7] ; Hu, YF (Hu, Yifei) [8] ; Ma, J (Ma, Jun) [2] , [3] ; Song, Y (Song, Yi) [2] , [3] (provided by Clarivate) **,Source LANCET PUBLIC HEALTH,Volume 9,Issue 12,Page e1105-e1114,DOI 10.1016/S2468-2667(24)00246- Published DEC 2024,Early Access DEC 2024,Indexed 2024-12-18,Document Type Article**

Abstract

Over the past four decades, China has witnessed an important nutritional transition, characterised by a heightened overnutrition burden among children. The country now has the largest population of children with obesity globally. In this paper, we review the epidemiology of childhood obesity in China, its determinants, and risk factors, with a particular focus on school-aged children. Evidence unveils substantial variations across age, gender, and region. We describe multilevel obesogenic determinants, including macro-level social, cultural, and environmental factors; meso-level factors related to schools and communities; and micro-level factors tied to families and individuals from the perinatal-infant stage to childhood and adolescence. The primary drivers of childhood obesity appear to be rooted in the broader macro-level social, economic, and technological environment; obesogenic factors, which have affected school, community, and family environments; and accelerated unhealthy behaviour uptake. Identifying and characterising the catalysts behind the rise in childhood obesity in China is imperative for the development of scalable, effective, and tailored prevention, control, and intervention strategies.

Keywords

Keywords Plus

OVERWEIGHTHEALTHCHILDRENSCHOOLADOLESCENTSRISKASSOCIATIONPREGNANCYWEIGHTCONSEQUENCES

6-Tirzepatidefor Obesity Treatment and Diabetes Prevention

Jastreboff, AM (Jastreboff, Ania M.) [1] , [2] ; le Roux, CW (le Roux, Carel W.) [3] ; Stefanski, A (Stefanski, Adam) [4] ; Aronne, LJ (Aronne, Louis J.) [5] ; Halpern, B (Halpern, Bruno) [6] ; Wharton, S (Wharton, Sean) [7] , [8] ; Wilding, JPH (Wilding, John P. H.) [9] ; Perreault, L (Perreault, Leigh) [10] ; Zhang, SY (Zhang, Shuyu) [4] ; Battula, R (Battula, Ramakrishna) [4] ; Group Author,SURMOUNT-1 Investigators (SURMOUNT-1 Investigators) (provided by Clarivate) ,Source NEW ENGLAND JOURNAL OF MEDICINE,Volume 392,Issue 10,Page 958-971,DOI 10.1056/NEJMoa2410819,Published MAR 6 2025,Indexed 2025-07-27,Document Type Article

Abstract

BACKGROUND

Obesity is a chronic disease and causal precursor to myriad other conditions, including type 2 diabetes. In an earlier analysis of the SURMOUNT-1 trial, tirzepatide was shown to provide substantial and sustained reductions in body weight in persons with obesity over a 72-week period. Here, we report the 3-year safety outcomes with tirzepatide and its efficacy in reducing weight and delaying progression to type 2 diabetes in persons with both obesity and prediabetes.

METHODS

We performed a phase 3, double-blind, randomized, controlled trial in which 2539 participants with obesity, of whom 1032 also had prediabetes, were assigned in a 1:1:1:1 ratio to receive tirzepatide at a once-weekly dose of 5 mg, 10 mg, or 15 mg or placebo. The current analysis involved the participants with both obesity and prediabetes, who received their assigned dose of tirzepatide or placebo for a total of 176 weeks, followed by a 17-week off-treatment period. The three key secondary end points, which were controlled for type I error, were the percent change in body weight from baseline to week 176 and onset of type 2 diabetes during the 176-week and 193-week periods.

RESULTS

At 176 weeks, the mean percent change in body weight among the participants who received tirzepatide was -12.3% with the 5-mg dose, -18.7% with the 10-mg dose, and -19.7% with the 15-mg dose, as compared with -1.3% among those who received placebo (P<0.001 for all comparisons with placebo). Fewer participants received a diagnosis of type 2 diabetes in the tirzepatide groups than in the placebo group (1.3% vs. 13.3%; hazard ratio, 0.07; 95% confidence interval [CI], 0.0 to 0.1; P<0.001). After 17 weeks off treatment or placebo, 2.4% of the participants who received tirzepatide and 13.7% of those who received placebo had type 2 diabetes (hazard ratio, 0.12; 95% CI, 0.1 to 0.2; P<0.001). Other than coronavirus disease 2019, the most common adverse events were gastrointestinal, most of which were mild to moderate in severity and occurred primarily during the dose-escalation period in the first 20 weeks of the trial. No new safety signals were identified.

CONCLUSIONS

Three years of treatment with tirzepatide in persons with obesity and prediabetes resulted in substantial and sustained weight reduction and a markedly lower risk of progression to type 2 diabetes than that with placebo.

Keywords

Keywords Plus

LIFE-STYLE INTERVENTIONIMPAIRED GLUCOSE-TOLERANCEBARIATRIC SURGERYDOUBLE-BLINDREDUCTIONPEOPLELIRAGLUTIDEMANAGEMENTOVERWEIGHTMORTALITY

7-Definition and diagnostic criteria of clinical obesity

Rubino, F (Rubino, Francesco) [1] , [2] , [4] ; Cummings, DE (Cummings, David E.) [5] , [6] ; Eckel, RH (Eckel, Robert H.) [7] ; Cohen, R (Cohen, Ricardo, V) [8] ; Wilding, JPH (Wilding, John P. H.) [9] ; Brown, WA (Brown, Wendy A.) [10] ; Stanford, FC (Stanford, Fatima Cody) [11] , [12] , [13] ; Batterham, RL (Batterham, Rachel L.) [14] , [15] ; Farooqi, IS (Farooqi, I. Sadaf) [16] , [17] ; Farpour-Lambert, NJ (Farpour-Lambert, Nathalie J.) [18] ; (provided by Clarivate) ,Source LANCET DIABETES & ENDOCRINOLOGY,Volume 13,Issue 3,Page 221-262,DOI 10.1016/S2213-8587(24)00316-4,Published MAR 2025,Early Access FEB 2025,Indexed 2025-11-21,Document Type ArticleKeywords

Keywords Plus

BODY-MASS INDEXFATTY LIVER-DISEASEADVERSE CHILDHOOD EXPERIENCESAMERICAN ASSOCIATIONRISK-FACTORCARDIOVASCULAR-DISEASECONSENSUS STATEMENTENERGY-EXPENDITUREPOSITION STATEMENTWEIGHT STIGMA

8-Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

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Abstract

BackgroundSemaglutide, a glucagon-like peptide-1 receptor agonist, has been shown to reduce the risk of adverse cardiovascular events in patients with diabetes. Whether semaglutide can reduce cardiovascular risk associated with overweight and obesity in the absence of diabetes is unknown.MethodsIn a multicenter, double-blind, randomized, placebo-controlled, event-driven superiority trial, we enrolled patients 45 years of age or older who had preexisting cardiovascular disease and a body-mass index (the weight in kilograms divided by the square of the height in meters) of 27 or greater but no history of diabetes. Patients were randomly assigned in a 1:1 ratio to receive once-weekly subcutaneous semaglutide at a dose of 2.4 mg or placebo. The primary cardiovascular end point was a composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke in a time-to-first-event analysis. Safety was also assessed.ResultsA total of 17,604 patients were enrolled; 8803 were assigned to receive semaglutide and 8801 to receive placebo. The mean (+/- SD) duration of exposure to semaglutide or placebo was 34.2 +/- 13.7 months, and the mean duration of follow-up was 39.8 +/- 9.4 months. A primary cardiovascular end-point event occurred in 569 of the 8803 patients (6.5%) in the semaglutide group and in 701 of the 8801 patients (8.0%) in the placebo group (hazard ratio, 0.80; 95% confidence interval, 0.72 to 0.90; P<0.001). Adverse events leading to permanent discontinuation of the trial product occurred in 1461 patients (16.6%) in the semaglutide group and 718 patients (8.2%) in the placebo group (P<0.001).ConclusionsIn patients with preexisting cardiovascular disease and overweight or obesity but without diabetes, weekly subcutaneous semaglutide at a dose of 2.4 mg was superior to placebo in reducing the incidence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke at a mean follow-up of 39.8 months.

Keywords

Keywords Plus

Obesity

CORONARY-HEART-DISEASERECEPTOR AGONISTSBLOOD-PRESSURERISK-FACTORSWEIGHT-LOSSOVERWEIGHTMETAANALYSISMANAGEMENTPARTICIPANTSCHOLESTEROL

9-Semaglutide and Cardiovascular Outcomes in Obesity without Diabetes

Koskinas, KC (Koskinas, Konstantinos C.) [1] ; Van Craenenbroeck, EM (Van Craenenbroeck, Emeline M.) [2] , [3] ; Antoniades, C (Antoniades, Charalambos) [4] ; Blüher, M (Blueher, Matthias) [5] , [6] ; Gorter, TM (Gorter, Thomas M.) [7] ; Hanssen, H (Hanssen, Henner) [8] ; Marx, N (Marx, Nikolaus) [9] ; McDonagh, TA (McDonagh, Theresa A.) [10] , [11] ; Mingrone, G (Mingrone, Geltrude) [12] , [13] , [14] ; Rosengren, A (Rosengren, Annika) [15] , [16] ; Group Author ESC Sci Document Grp (ESC Sci Document Grp) (provided by Clarivate) ,Source EUROPEAN HEART JOURNAL,Volume 45,Issue 38,Page 4063-4098,DOI 10.1093/eurheartj/ehae508,Published AUG 30 2024,Early Access AUG 2024,Indexed 2024-10-09,Document Type Review

Abstract

The global prevalence of obesity has more than doubled over the past four decades, currently affecting more than a billion individuals. Beyond its recognition as a high-risk condition that is causally linked to many chronic illnesses, obesity has been declared a disease per se that results in impaired quality of life and reduced life expectancy. Notably, two-thirds of obesity-related excess mortality is attributable to cardiovascular disease. Despite the increasingly appreciated link between obesity and a broad range of cardiovascular disease manifestations including atherosclerotic disease, heart failure, thromboembolic disease, arrhythmias, and sudden cardiac death, obesity has been underrecognized and sub-optimally addressed compared with other modifiable cardiovascular risk factors. In the view of major repercussions of the obesity epidemic on public health, attention has focused on population-based and personalized approaches to prevent excess weight gain and maintain a healthy body weight from early childhood and throughout adult life, as well as on comprehensive weight loss interventions for persons with established obesity. This clinical consensus statement by the European Society of Cardiology discusses current evidence on the epidemiology and aetiology of obesity; the interplay between obesity, cardiovascular risk factors and cardiac conditions; the clinical management of patients with cardiac disease and obesity; and weight loss strategies including lifestyle changes, interventional procedures, and anti-obesity medications with particular focus on their impact on cardiometabolic risk and cardiac outcomes. The document aims to raise awareness on obesity as a major risk factor and provide guidance for implementing evidence-based practices for its prevention and optimal management within the context of primary and secondary cardiovascular disease prevention.

Graphical Abstract Main causal factors and cardiovascular consequences of obesity. CV, cardiovascular; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; SCD, sudden cardiac death.

Keywords

Obesity

Author Keywords

Anti-obesity drugsAdipose tissueArrhythmiaAtherosclerosisBariatric interventionsCardiovascular diseaseLifestyle interventionsHeart failureCardiovascular risk factorsVenous ThromboembolismValvular heart disease

Keywords Plus

BODY-MASS INDEXEPICARDIAL ADIPOSE-TISSUELIFE-STYLE INTERVENTIONPERCUTANEOUS CORONARY INTERVENTIONALL-CAUSE MORTALITYINDUCED WEIGHT-LOSSDOSE-RESPONSE METAANALYSISREDUCED EJECTION FRACTIONOBSTRUCTIVE SLEEP-APNEASUDDEN CARDIAC DEATH

10-Sarcopenia and Sarcopenic Obesity and Mortality Among Older People

Benz, E (Benz, Elizabeth) [1] , [2] , [3] ; Pinel, A (Pinel, Alexandre) [1] ; Guillet, C (Guillet, Christelle) [1] ; Capel, F (Capel, Frederic) [1] ; Pereira, B (Pereira, Bruno) [4] ; De Antonio, M (De Antonio, Marie) [4] ; Pouget, M (Pouget, Melanie) [5] ; Cruz-Jentoft, AJ (Cruz-Jentoft, Alfonso J.) [6] ; Eglseer, D (Eglseer, Doris) [7] ; Topinkova, E (Topinkova, Eva) [8] , [9] ; (provided by Clarivate) ,Source JAMA NETWORK OPEN,Volume 7,Issue 3,DOI 10.1001/jamanetworkopen.2024.3604,Article Number e243604,Published MAR 25 2024,Indexed 2024-04-12,Document Type Article

Abstract

Importance Sarcopenia and obesity are 2 global concerns associated with adverse health outcomes in older people. Evidence on the population-based prevalence of the combination of sarcopenia with obesity (sarcopenic obesity [SO]) and its association with mortality are still limited. Objective To investigate the prevalence of sarcopenia and SO and their association with all-cause mortality. Design, Setting, and ParticipantsThis large-scale, population-based cohort study assessed participants from the Rotterdam Study from March 1, 2009, to June 1, 2014. Associations of sarcopenia and SO with all-cause mortality were studied using Kaplan-Meier curves, Cox proportional hazards regression, and accelerated failure time models fitted for sex, age, and body mass index (BMI). Data analysis was performed from January 1 to April 1, 2023. Exposures The prevalence of sarcopenia and SO, measured based on handgrip strength and body composition (BC) (dual-energy x-ray absorptiometry) as recommended by current consensus criteria, with probable sarcopenia defined as having low handgrip strength and confirmed sarcopenia and SO defined as altered BC (high fat percentage and/or low appendicular skeletal muscle index) in addition to low handgrip strength. Main Outcome and MeasureThe primary outcome was all-cause mortality, collected using linked mortality data from general practitioners and the central municipal records, until October 2022. Results In the total population of 5888 participants (mean [SD] age, 69.5 [9.1] years; mean [SD] BMI, 27.5 [4.3]; 3343 [56.8%] female), 653 (11.1%; 95% CI, 10.3%-11.9%) had probable sarcopenia and 127 (2.2%; 95% CI, 1.8%-2.6%) had confirmed sarcopenia. Sarcopenic obesity with 1 altered component of BC was present in 295 participants (5.0%; 95% CI, 4.4%-5.6%) and with 2 altered components in 44 participants (0.8%; 95% CI, 0.6%-1.0%). An increased risk of all-cause mortality was observed in participants with probable sarcopenia (hazard ratio [HR], 1.29; 95% CI, 1.14-1.47) and confirmed sarcopenia (HR, 1.93; 95% CI, 1.53-2.43). Participants with SO plus 1 altered component of BC (HR, 1.94; 95% CI, 1.60-2.33]) or 2 altered components of BC (HR, 2.84; 95% CI, 1.97-4.11) had a higher risk of mortality than those without SO. Similar results for SO were obtained for participants with a BMI of 27 or greater. Conclusions and RelevanceIn this study, sarcopenia and SO were found to be prevalent

phenotypes in older people and were associated with all-cause mortality. Additional alterations of BC amplified this risk independently of age, sex, and BMI. The use of low muscle strength as a first step of both diagnoses may allow for early identification of individuals at risk for premature mortality.

Keywords

Keywords Plus

NATIONAL-HEALTHNUTRITIONPREVALENCEGUIDELINESADULTSASSOCIATIONOVERWEIGHTCRITERIARISK

11-Tirzepatide for Heart Failure with Preserved Ejection Fraction and Obesity

Packer, M (Packer, Milton) [1] , [2] ; Zile, MR (Zile, Michael R.) [3] , [4] ; Kramer, CM (Kramer, Christopher M.) [5] ; Baum, SJ (Baum, Seth J.) [6] ; Litwin, SE (Litwin, Sheldon E.) [3] , [4] ; Menon, V (Menon, Venu) [7] ; Ge, JB (Ge, Junbo) [8] ; Weerakkody, GJ (Weerakkody, Govinda J.) [9] ; Ou, Y (Ou, Yang) [9] ; Bunck, MC (Bunck, Mathijs C.) [9] ; Group Author SUMMIT Trial Study Grp (SUMMIT Trial Study Grp) (provided by Clarivate) **Source NEW ENGLAND JOURNAL OF MEDICINE Volume 392,Issue 5,Page 427-437,DOI 10.1056/NEJMoa2410027,Published JAN 30 2025 Indexed 2025-04-18 Document Type Article**

Abstract

BACKGROUND

Obesity increases the risk of heart failure with preserved ejection fraction. Tirzep-atide, a long-acting agonist of glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 receptors, causes considerable weight loss, but data are lacking with respect to its effects on cardiovascular outcomes.

METHODS

In this international, double-blind, randomized, placebo-controlled trial, we randomly assigned, in a 1:1 ratio, 731 patients with heart failure, an ejection fraction of at least 50%, and a body-mass index (the weight in kilograms divided by the square of the height in meters) of at least 30 to receive tirzepatide (up to 15 mg subcutaneously once per week) or placebo for at least 52 weeks. The two primary end points were a composite of adjudicated death from cardiovascular causes or a worsening heart-failure event (assessed in a time-to-first-event analysis) and the change from baseline to 52 weeks in the Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS; scores range from 0 to 100, with higher scores indicating better quality of life).

RESULTS

A total of 364 patients were assigned to the tirzepatide group and 367 to the placebo group; the median duration of follow-up was 104 weeks. Adjudicated death from cardiovascular causes or a worsening heart-failure event occurred in 36 patients (9.9%) in the tirzepatide group and in 56 patients (15.3%) in the placebo group (hazard ratio, 0.62; 95% confidence interval [CI], 0.41 to 0.95; P= 0.026). Worsening heart-failure events occurred in 29 patients (8.0%) in the tirzepatide group and in 52 patients (14.2%) in the placebo group (hazard ratio, 0.54; 95% CI, 0.34 to 0.85), and adjudicated death from cardiovascular causes occurred in 8 patients (2.2%) and 5 patients (1.4%), respectively (hazard ratio, 1.58; 95% CI, 0.52 to 4.83). At 52 weeks, the mean (+/- SD) change in the KCCQ-CSS was 19.5 +/- 1.2 in the tirzepatide group as compared with 12.7 +/- 1.3 in the placebo group (between-group difference, 6.9; 95% CI, 3.3 to 10.6;

P<0.001). Adverse events (mainly gastrointestinal) leading to discontinuation of the trial drug occurred in 23 patients (6.3%) in the tirzepatide group and in 5 patients (1.4%) in the placebo group.

CONCLUSIONS

Treatment with tirzepatide led to a lower risk of a composite of death from cardiovascular causes or worsening heart failure than placebo and improved health status in patients with heart failure with preserved ejection fraction and obesity.

Keywords

Keywords Plus

ADIPOSE-TISSUEINFLAMMATIONSEMAGLUTIDEWEIGHT

12-Once-Weekly Semaglutide in Persons with Obesity and Knee Osteoarthritis

Bliddal, H (Bliddal, Henning) [1] ; Bays, H (Bays, Harold) [3] ; Czernichow, S (Czernichow, Sebastien) [4] ; Hemmingsson, JU (Hemmingsson, Joanna Udden) [5] , [6] ; Hjelmesæth, J (Hjelmesaeth, Joran) [7] , [8] ; Morville, TH (Morville, Thomas Hoffmann) [2] ; Koroleva, A (Koroleva, Anna) [2] ; Neergaard, JS (Neergaard, Jesper Skov) [2] ; Sánchez, PV (Sanchez, Patricia Velez) [9] ; Wharton, S (Wharton, Sean) [10] , [11] , [12] , [13] ;,Group Author,STEP 9 Study Grp (STEP 9 Study Grp) (provided by Clarivate) ,Source NEW ENGLAND JOURNAL OF MEDICINE,Volume 391,Issue 17,Page 1573-1583,DOI 10.1056/NEJMoa2403664,Published OCT 31 2024,Indexed 2024-12-13,Document Type Article

Abstract

Background Weight reduction has been shown to alleviate symptoms of osteoarthritis of the knee, including pain. The effect of glucagon-like peptide-1 receptor agonists on outcomes in knee osteoarthritis among persons with obesity has not been well studied. Methods We conducted a 68-week, double-blind, randomized, placebo-controlled trial at 61 sites in 11 countries. Participants with obesity (a body-mass index [BMI; the weight in kilograms divided by the square of the height in meters] of >= 30) and a clinical and radiologic diagnosis of moderate knee osteoarthritis with at least moderate pain were randomly assigned, in a 2:1 ratio, to receive once-weekly subcutaneous semaglutide (2.4 mg) or placebo, in addition to counseling on physical activity and a reduced-calorie diet. The primary end points were the percentage change in body weight and the change in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain score (on a scale of 0 to 100, with higher scores reflecting worse outcomes) from baseline to week 68. A key confirmatory secondary end point was the physical-function score on the 36-Item Short Form Health Survey (SF-36), version 2 (on a scale of 0 to 100, with higher scores indicating greater well-being). Download a PDF of the Plain Language Summary. Results A total of 407 participants were enrolled. The mean age was 56 years, the mean BMI 40.3, and the mean WOMAC pain score 70.9. A total of 81.6% of the participants were women. The mean change in body weight from baseline to week 68 was -13.7% with semaglutide and -3.2% with placebo (P<0.001). The mean change in the WOMAC pain score at week 68 was -41.7 points with semaglutide and -27.5 points with placebo (P<0.001). Participants in the semaglutide group had a greater improvement in SF-36 physical-function score than those in the placebo group (mean change, 12.0 points vs. 6.5 points; P<0.001). The incidence of serious adverse events was similar in the two groups. Adverse events that led to permanent discontinuation of the trial regimen occurred in 6.7% of the participants in the semaglutide group and in 3.0% in the placebo group, with gastrointestinal disorders being the most common reason for discontinuation. Conclusions Among participants with obesity and knee osteoarthritis with moderate-to-severe pain, treatment with once-weekly injectable semaglutide resulted in significantly greater reductions in body weight and pain related to knee osteoarthritis than placebo. (Funded by Novo Nordisk; STEP 9 ClinicalTrials.gov number, NCT05064735.)

Keywords

Keywords Plus

Obesity

DOUBLE-

DUMMYOVERWEIGHTWEIGHTADULTSHIPCLASSIFICATIONLIRAGLUTIDEMANAGEMENTHANDPAIN

13-Once-Weekly Semaglutide in Persons with Obesity and Knee Osteoarthritis

Bliddal, H (Bliddal, Henning) [1] ; Bays, H (Bays, Harold) [3] ; Czernichow, S (Czernichow, Sebastien) [4] ; Hemmingsson, JU (Hemmingsson, Joanna Udden) [5] , [6] ; Hjelmesæth, J (Hjelmesaeth, Joran) [7] , [8] ; Morville, TH (Morville, Thomas Hoffmann) [2] ; Koroleva, A (Koroleva, Anna) [2] ; Neergaard, JS (Neergaard, Jesper Skov) [2] ; Sánchez, PV (Sanchez, Patricia Velez) [9] ; Wharton, S (Wharton, Sean) [10] , [11] , [12] , [13] ; Group Author STEP 9 Study Grp (STEP 9 Study Grp)(provided by Clarivate) ,Source NEW ENGLAND JOURNAL OF MEDICINE,Volume 391,Issue 17,Page 1573-1583,DOI 10.1056/NEJMoa2403664,Published OCT 31 2024,Indexed 2024-12-13,Document Type Article

Abstract

Background Weight reduction has been shown to alleviate symptoms of osteoarthritis of the knee, including pain. The effect of glucagon-like peptide-1 receptor agonists on outcomes in knee osteoarthritis among persons with obesity has not been well studied. Methods We conducted a 68-week, double-blind, randomized, placebo-controlled trial at 61 sites in 11 countries. Participants with obesity (a body-mass index [BMI; the weight in kilograms divided by the square of the height in meters] of >= 30) and a clinical and radiologic diagnosis of moderate knee osteoarthritis with at least moderate pain were randomly assigned, in a 2:1 ratio, to receive once-weekly subcutaneous semaglutide (2.4 mg) or placebo, in addition to counseling on physical activity and a reduced-calorie diet. The primary end points were the percentage change in body weight and the change in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain score (on a scale of 0 to 100, with higher scores reflecting worse outcomes) from baseline to week 68. A key confirmatory secondary end point was the physical-function score on the 36-Item Short Form Health Survey (SF-36), version 2 (on a scale of 0 to 100, with higher scores indicating greater well-being). Download a PDF of the Plain Language Summary. Results A total of 407 participants were enrolled. The mean age was 56 years, the mean BMI 40.3, and the mean WOMAC pain score 70.9. A total of 81.6% of the participants were women. The mean change in body weight from baseline to week 68 was -13.7% with semaglutide and -3.2% with placebo (P<0.001). The mean change in the WOMAC pain score at week 68 was -41.7 points with semaglutide and -27.5 points with placebo (P<0.001). Participants in the semaglutide group had a greater improvement in SF-36 physical-function score than those in the placebo group (mean change, 12.0 points vs. 6.5 points; P<0.001). The incidence of serious adverse events was similar in the two groups. Adverse events that led to permanent discontinuation of the trial regimen occurred in 6.7% of the participants in the semaglutide group and in 3.0% in the placebo group, with gastrointestinal disorders being the most common reason for discontinuation. Conclusions Among participants with obesity and knee osteoarthritis with moderate-to-severe pain, treatment with once-weekly injectable semaglutide resulted in significantly greater reductions in body weight and pain related

to knee osteoarthritis than placebo. (Funded by Novo Nordisk; STEP 9 ClinicalTrials.gov number, NCT05064735.)

Keywords

Keywords Plus

DOUBLE-DUMMYOVERWEIGHTWEIGHTADULTSHIPCLASSIFICATIONLIRAGLUTIDEMANAGEMENTHANDPAIN

14-Tirzepatide as Compared with Semaglutide for the Treatment of Obesity

Aronne, LJ (Aronne, Louis J.) [1] ; Horn, DB (Horn, Deborah Bade) [2] ; le Roux, CW (le Roux, Carel W.) [3] , [4] ; Ho, W (Ho, Wayne) [5] , [6] ; Falcon, BL (Falcon, Beverly L.) [7] ; Gomez Valderas, E (Gomez Valderas, Elisa) [7] ; Das, S (Das, Sagar) [7] ; Lee, CJ (Lee, Clare J.) [7] ; Glass, LC (Glass, Leonard C.) [7] ; Senyucel, C (Senyucel, Cagri) [7] ; Group Author,Surmount-5 Trial Investigators (Surmount-5 Trial Investigators) (provided by Clarivate) ,Source NEW ENGLAND JOURNAL OF MEDICINE,Volume 393,Issue 1,Page 26-36,DOI 10.1056/NEJMoa2416394,Published JUL 1 2025,Early Access MAY 2025,Indexed 2025-05-15,Document Type Article

Abstract

BACKGROUND

Tirzepatide and semaglutide are highly effective medications for obesity management. The efficacy and safety of tirzepatide as compared with semaglutide in adults with obesity but without type 2 diabetes is unknown.

METHODS

In this phase 3b, open-label, controlled trial, adult participants with obesity but without type 2 diabetes were randomly assigned in a 1:1 ratio to receive the maximum tolerated dose of tirzepatide (10 mg or 15 mg) or the maximum tolerated dose of semaglutide (1.7 mg or 2.4 mg) subcutaneously once weekly for 72 weeks. The primary end point was the percent change in weight from baseline to week 72. Key secondary end points included weight reductions of at least 10%, 15%, 20%, and 25% and a change in waist circumference from baseline to week 72.

RESULTS

A total of 751 participants underwent randomization. The least-squares mean percent change in weight at week 72 was -20.2% (95% confidence interval [CI], -21.4 to -19.1) with tirzepatide and -13.7% (95% CI, -14.9 to -12.6) with semaglutide (P<0.001). The least-squares mean change in waist circumference was -18.4 cm (95% CI, -19.6 to -17.2) with tirzepatide and -13.0 cm (95% CI, -14.3 to -11.7) with semaglutide (P<0.001). Participants in the tirzepatide group were more likely than those in the semaglutide group to have weight reductions of at least 10%, 15%, 20%, and 25%. The most common adverse events in both treatment groups were gastrointestinal, and most were mild to moderate in severity and occurred primarily during dose escalation.

CONCLUSIONS

Among participants with obesity but without diabetes, treatment with tirzepatide was superior to treatment with semaglutide with respect to reduction in body weight and waist circumference at week 72.

Keywords

Obesity

Keywords Plus

WEIGHT-LOSSPEOPLEGIP

15-Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity

Malhotra, A (Malhotra, Atul) [1] ; Grunstein, RR (Grunstein, Ronald R.) [2] , [3] ; Fietze, I (Fietze, Ingo) [4] ; Weaver, TE (Weaver, Terri E.) [5] , [6] ; Redline, S (Redline, Susan) [8] , [9] ; Azarbarzin, A (Azarbarzin, Ali) [8] , [9] ; Sands, SA (Sands, Scott A.) [8] , [9] ; Schwab, RJ (Schwab, Richard J.) [7] ; Dunn, JP (Dunn, Julia P.) [10] ; Chakladar, S (Chakladar, Sujatro) [10] ; Group Author SURMOUNT-OSA Investigators (SURMOUNT-OSA Investigators) (provided by Clarivate) ,Source NEW ENGLAND JOURNAL OF MEDICINE,Volume 391,Issue 13,Page 1193-1205,DOI 10.1056/NEJMoa2404881,Published OCT 3 2024,Early Access JUN 2024,Indexed 2024-08-14,Document Type Article

Abstract

BACKGROUND

Obstructive sleep apnea is characterized by disordered breathing during sleep and is associated with major cardiovascular complications; excess adiposity is an etiologic risk factor. Tirzepatide may be a potential treatment.

METHODS

We conducted two phase 3, double-blind, randomized, controlled trials involving adults with moderate-to-severe obstructive sleep apnea and obesity. Participants who were not receiving treatment with positive airway pressure (PAP) at baseline were enrolled in trial 1, and those who were receiving PAP therapy at baseline were enrolled in trial 2. The participants were assigned in a 1:1 ratio to receive either the maximum tolerated dose of tirzepatide (10 mg or 15 mg) or placebo for 52 weeks. The primary end point was the change in the apnea-hypopnea index (AHI, the number of apneas and hypopneas during an hour of sleep) from baseline. Key multiplicity-controlled secondary end points included the percent change in AHI and body weight and changes in hypoxic burden, patient-reported sleep impairment and disturbance, high-sensitivity C-reactive protein (hsCRP) concentration, and systolic blood pressure.

RESULTS

At baseline, the mean AHI was 51.5 events per hour in trial 1 and 49.5 events per hour in trial 2, and the mean body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) was 39.1 and 38.7, respectively. In trial 1, the mean change in AHI at week 52 was -25.3 events per hour (95% confidence interval [CI], -29.3 to -21.2) with tirzepatide and -5.3 events per hour (95% CI, -9.4 to -1.1) with placebo, for an estimated treatment difference of -20.0 events per hour (95% CI, -25.8 to -14.2) ($P<0.001$). In trial 2, the mean change in AHI at week 52 was -29.3 events per hour (95% CI, -33.2 to -25.4) with tirzepatide and -5.5 events per hour (95% CI, -9.9 to -1.2) with placebo, for an estimated treatment difference of -23.8 events per hour (95% CI, -29.6 to -17.9) ($P<0.001$). Significant improvements in the

measurements for all prespecified key secondary end points were observed with tirzepatide as compared with placebo. The most frequently reported adverse events with tirzepatide were gastrointestinal in nature and mostly mild to moderate in severity.

CONCLUSIONS

Among persons with moderate-to-severe obstructive sleep apnea and obesity, tirzepatide reduced the AHI, body weight, hypoxic burden, hsCRP concentration, and systolic blood pressure and improved sleep-related patient-reported outcomes.

Keywords

Keywords Plus

POSITIVE AIRWAY PRESSURETHERAPYMANAGEMENTGUIDELINEADULTSCPAPCARE

16-The Role of Obesity in Type 2 Diabetes Mellitus-An Overview

Chandrasekaran, P (Chandrasekaran, Preethi) [1] ; Weiskirchen, R (Weiskirchen, Ralf) [2](provided by Clarivate) **,Source INTERNATIONAL JOURNAL OF MOLECULAR SCIENCES,Volume 25,Issue 3,DOI 10.3390/ijms25031882,Article Number 1882,Published FEB 2024,Indexed 2024-02-19,Document Type Review**

Abstract

Obesity or excessive weight gain is identified as the most important and significant risk factor in the development and progression of type 2 diabetes mellitus (DM) in all age groups. It has reached pandemic dimensions, making the treatment of obesity crucial in the prevention and management of type 2 DM worldwide. Multiple clinical studies have demonstrated that moderate and sustained weight loss can improve blood glucose levels, insulin action and reduce the need for diabetic medications. A combined approach of diet, exercise and lifestyle modifications can successfully reduce obesity and subsequently ameliorate the ill effects and deadly complications of DM. This approach also helps largely in the prevention, control and remission of DM. Obesity and DM are chronic diseases that are increasing globally, requiring new approaches to manage and prevent diabetes in obese individuals. Therefore, it is essential to understand the mechanistic link between the two and design a comprehensive approach to increase life expectancy and improve the quality of life in patients with type 2 DM and obesity. This literature review provides explicit information on the clinical definitions of obesity and type 2 DM, the incidence and prevalence of type 2 DM in obese individuals, the indispensable role of obesity in the pathophysiology of type 2 DM and their mechanistic link. It also discusses clinical studies and outlines the recent management approaches for the treatment of these associated conditions. Additionally, in vivo studies on obesity and type 2 DM are discussed here as they pave the way for more rigorous development of therapeutic approaches.

Keywords

Author Keywords

obesitytype 2 diabetespathophysiologyincidenceprevalencemanagementtherapeutic approachin vivo studiesclinical trials

Keywords Plus

IMPROVES INSULIN-RESISTANCEADIPOSE-TISSUEOXIDATIVE STRESSMETABOLIC SYNDROMEWEIGHT MANAGEMENTPEPTIDE-1 ANALOGFAT ACCUMULATIONMOUSE MODELWHITEOVERWEIGHT

Obesity

17-Semaglutide in Patients with Heart Failure with Preserved Ejection Fraction and Obesity

Kosiborod, MN (Kosiborod, Mikhail N.) [1] ; Abildstrom, SZ (Abildstrom, Steen Z.) [2] ; Borlaug, BA (Borlaug, Barry A.) [4] ; Butler, J (Butler, Javed) [5] , [6] ; Rasmussen, S (Rasmussen, Soren) [2] ; Davies, M (Davies, Melanie) [7] , [8] ; Hovingh, GK (Hovingh, G. Kees) [2] ; Kitzman, DW (Kitzman, Dalane W.) [11] , [12] ; Lindegaard, ML (Lindegaard, Marie L.) [2] ; Moller, DV (Moller, Daniel V.) [2] ; Group Author STEP-HFpEF Trial Comm Invest (STEP-HFpEF Trial Comm Invest) (provided by Clarivate) ,Source NEW ENGLAND JOURNAL OF MEDICINE,Volume 389,Issue 12,Page 1069-1084,DOI 10.1056/NEJMoa2306963,Published SEP 21 2023,Indexed 2024-02-16,Document TypeArticle

Abstract

Background Heart failure with preserved ejection fraction is increasing in prevalence and is associated with a high symptom burden and functional impairment, especially in persons with obesity. No therapies have been approved to target obesity-related heart failure with preserved ejection fraction. Methods We randomly assigned 529 patients who had heart failure with preserved ejection fraction and a body-mass index (the weight in kilograms divided by the square of the height in meters) of 30 or higher to receive once-weekly semaglutide (2.4 mg) or placebo for 52 weeks. The dual primary end points were the change from baseline in the Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS; scores range from 0 to 100, with higher scores indicating fewer symptoms and physical limitations) and the change in body weight. Confirmatory secondary end points included the change in the 6-minute walk distance; a hierarchical composite end point that included death, heart failure events, and differences in the change in the KCCQ-CSS and 6-minute walk distance; and the change in the C-reactive protein (CRP) level. Results The mean change in the KCCQ-CSS was 16.6 points with semaglutide and 8.7 points with placebo (estimated difference, 7.8 points; 95% confidence interval [CI], 4.8 to 10.9; P<0.001), and the mean percentage change in body weight was -13.3% with semaglutide and -2.6% with placebo (estimated difference, -10.7 percentage points; 95% CI, -11.9 to -9.4; P<0.001). The mean change in the 6-minute walk distance was 21.5 m with semaglutide and 1.2 m with placebo (estimated difference, 20.3 m; 95% CI, 8.6 to 32.1; P<0.001). In the analysis of the hierarchical composite end point, semaglutide produced more wins than placebo (win ratio, 1.72; 95% CI, 1.37 to 2.15; P<0.001). The mean percentage change in the CRP level was -43.5% with semaglutide and -7.3% with placebo (estimated treatment ratio, 0.61; 95% CI, 0.51 to 0.72; P<0.001). Serious adverse events were reported in 35 participants (13.3%) in the semaglutide group and 71 (26.7%) in the placebo group. Conclusions In patients with heart failure with preserved ejection fraction and obesity, treatment with semaglutide (2.4 mg) led to larger reductions in symptoms and physical limitations, greater improvements in exercise function, and greater weight loss than placebo. (Funded by Novo Nordisk; STEP-HFpEF ClinicalTrials.gov number, NCT04788511.)

Obesity

Keywords

Keywords Plus

CITY CARDIOMYOPATHY QUESTIONNAIRENATRIURETIC PEPTIDESHEALTHPHENOTYPEADULTS

18-Semaglutide in Patients with Obesity-Related Heart Failure and Type 2 Diabetes

Kosiborod, MN (Kosiborod, M. N.) [1] ; Petrie, MC (Petrie, M. C.) [2] ; Borlaug, BA (Borlaug, B. A.) [6] ; Butler, J (Butler, J.) [7] , [8] ; Davies, MJ (Davies, M. J.) [3] , [4] ; Hovingh, GK (Hovingh, G. K.) [9] ; Kitzman, DW (Kitzman, D. W.) [11] , [12] ; Moller, DV (Moller, D. V.) [9] ; Treppendahl, MB (Treppendahl, M. B.) [9] ; Verma, S (Verma, S.) [13] ; Group Author STEP-HFpEF DM Trial Comm Investigators (STEP-HFpEF DM Trial Comm Investigators) (provided by Clarivate) ,Source NEW ENGLAND JOURNAL OF MEDICINE,Volume 390,Issue 15,Page 1394-1407,DOI 10.1056/NEJMoa2313917,Published APR 6 2024,Indexed 2025-02-12,Document Type Article,

Abstract

BACKGROUND

Obesity and type 2 diabetes are prevalent in patients with heart failure with preserved ejection fraction and are characterized by a high symptom burden. No approved therapies specifically target obesity-related heart failure with preserved ejection fraction in persons with type 2 diabetes.

METHODS

We randomly assigned patients who had heart failure with preserved ejection fraction, a body-mass index (the weight in kilograms divided by the square of the height in meters) of 30 or more, and type 2 diabetes to receive once-weekly semaglutide (2.4 mg) or placebo for 52 weeks. The primary end points were the change from baseline in the Kansas City Cardiomyopathy Questionnaire clinical summary score (KCCQ-CSS; scores range from 0 to 100, with higher scores indicating fewer symptoms and physical limitations) and the change in body weight. Confirmatory secondary end points included the change in 6-minute walk distance; a hierarchical composite end point that included death, heart failure events, and differences in the change in the KCCQ-CSS and 6-minute walk distance; and the change in the C-reactive protein (CRP) level.

RESULTS

A total of 616 participants underwent randomization. The mean change in the KCCQ-CSS was 13.7 points with semaglutide and 6.4 points with placebo (estimated difference, 7.3 points; 95% confidence interval [CI], 4.1 to 10.4; P<0.001), and the mean percentage change in body weight was -9.8% with semaglutide and -3.4% with placebo (estimated difference, - 6.4 percentage points; 95% CI, -7.6 to -5.2; P<0.001). The results for the confirmatory secondary end points favored semaglutide over placebo (estimated between-group difference in change in 6-minute walk distance, 14.3 m [95% CI, 3.7 to 24.9; P = 0.008]; win ratio for hierarchical composite end point, 1.58 [95% CI, 1.29 to 1.94; P<0.001]; and estimated treatment ratio for change in CRP level, 0.67 [95% CI, 0.55 to 0.80; P<0.001]). Serious adverse events were reported in 55 participants (17.7%) in the semaglutide group and 88 (28.8%) in the placebo group.

CONCLUSIONS

Obesity

Among patients with obesity-related heart failure with preserved ejection fraction and type 2 diabetes, semaglutide led to larger reductions in heart failurerelated symptoms and physical limitations and greater weight loss than placebo at 1 year.

Keywords

Keywords Plus

CITY CARDIOMYOPATHY QUESTIONNAIREPRESERVED EJECTION FRACTION

19-The association between sleep timing, eating behavior, and obesity in young adults

Borisenkov, M (Borisenkov, Mikhail) [1] ; Tserne, T (Tserne, Tatyana) [1] ; Bakutova, L (Bakutova, Larisa) [1] ; Smirnov, V (Smirnov, Vasily) ; Popov, S (Popov, Sergey) [1] (provided by Clarivate) **Source CHRONOBIOLOGY INTERNATIONAL,Volume 42,Issue 10,Page 1417-1426,DOI 10.1080/07420528.2025.2551025,Published OCT 3 2025,Early Access AUG 2025,Indexed 2025-09-03,Document Type Article**

Abstract

The aim of this study was to analyse the association between sleep timing, eating behavior, and risk of obesity. The study included 1577 participants with an average age of 19.5 +/- 4.8 (range: 13-40) y, women: 76%. Each participant provided personal information and filled out five questionnaires: the Munich Chronotype Questionnaire, the Pittsburgh Sleep Quality Index, the Zung Self-Rating Depression Scale, the Yale Food Addiction Scale, and the Dutch Eating Behavior Questionnaire. Restrained (OR 1.54, 95% CI 1.24-1.92), external (OR 1.67, 95% CI 1.34-2.10), and emotional (OR 2.31, 95% CI 1.79-2.98) eating behaviors, were found to be independently associated with food addiction. Obesity was positively associated with restrained (beta = 0.41), and emotional (beta = 0.12) eating behaviours in 13-40-y-olds and with food addiction (beta = 0.12) in 13-20-y-olds. Poor sleep quality was positively associated with all three types of eating behavior (beta = 0.10-0.15). Restrained eating behavior was negatively associated with chronotype (beta = -0.08). Emotional eating behavior was more often observed in females (beta = -0.18) and in persons with depression (beta = 0.16). Social jetlag was associated with the external eating behavior (beta = 0.09) in 13-20-y-olds. Promising direction for further research in the field of chrononutrition is to study the relationship between chronotype, restrained eating behavior, and obesity.

Keywords

Author Keywords

Chronotypesocial jetlagsleep qualityeating behaviorobesityyoung adults

Keywords Plus

SOCIAL JETLAGFOOD ADDICTIONPRELIMINARY VALIDATIONDEPRESSIONCHRONOTYPECHILDRENSCALEINDEX

20-Efficacy and Safety of GLP-1 Medicines for Type 2 Diabetes and Obesity

Drucker, DJ (Drucker, Daniel J.) [1] (provided by Clarivate) ,Source DIABETES CARE,Volume 47,Issue 11,DOI 10.2337/dci24-0003,Published NOV 2024,Indexed 2024-11-09,Document Type Review

Abstract

The development of glucagon-like peptide 1 receptor agonists (GLP-1RA) for type 2 diabetes and obesity was followed by data establishing the cardiorenal benefits of GLP-1RA in select patient populations. In ongoing trials investigators are interrogating the efficacy of these agents for new indications, including metabolic liver disease, peripheral artery disease, Parkinson disease, and Alzheimer disease. The success of GLP-1-based medicines has spurred the development of new molecular entities and combinations with unique pharmacokinetic and pharmacodynamic profiles, exemplified by tirzepatide, a GIP-GLP-1 receptor coagonist. Simultaneously, investigational molecules such as maritide block the GIP and activate the GLP-1 receptor, whereas retatrutide and survodutide enable simultaneous activation of the glucagon and GLP-1 receptors. Here I highlight evidence establishing the efficacy of GLP-1-based medicines, while discussing data that inform safety, focusing on muscle strength, bone density and fractures, exercise capacity, gastrointestinal motility, retained gastric contents and anesthesia, pancreatic and biliary tract disorders, and the risk of cancer. Rapid progress in development of highly efficacious GLP-1 medicines, and anticipated differentiation of newer agents in subsets of metabolic disorders, will provide greater opportunities for use of personalized medicine approaches to improve the health of people living with cardiometabolic disorders.

Keywords

Keywords Plus

PEPTIDE-1 RECEPTOR AGONISTSSEMAGLUTIDE 2.4 MGONCE-WEEKLY CAGRILINTIDEDOUBLE-BLINDCALCITONIN CONCENTRATIONSGLUCAGON RECEPTORWEIGHT MANAGEMENTPARALLEL-GROUPENERGY-INTAKE

21-Tirzepatide Reduces LV Mass and Paracardiac Adipose Tissue in Obesity-Related Heart Failure

Kramer, CM (Kramer, Christopher M.) [1] ; Borlaug, BA (Borlaug, Barry A.) [2] ; Zile, MR (Zile, Michael R.) [3] ; Ruff, D (Ruff, Dustin) [4] ; Dimaria, JM (Dimaria, Joseph M.) ; Menon, V (Menon, Venu) [5] ; Ou, Y (Ou, Yang) [4] ; Zarante, AM (Zarante, Angela M.) [6] ; Hurt, KC (Hurt, Karla C.) [4] ; Murakami, M (Murakami, Masahiro) [4] ; Group Author SUMMIT Trial Study Grp (SUMMIT Trial Study Grp) (provided by Clarivate) **,Source JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY,Volume 85,Issue 7,Page 699-706,DOI 10.1016/j.jacc.2024.11.001,Published FEB 2025,Early Access FEB 2025,Indexed 2025-03-01,Document Type Article**

Abstract

BACKGROUND Obesity is a known risk factor for heart failure with preserved ejection fraction (HFpEF) and is considered a distinct phenotype with more concentric remodeling. Epicardial adipose tissue (EAT) is also increased in obesity-related HFpEF and is associated with adverse events. OBJECTIVES The cardiac magnetic resonance (CMR) substudy of the SUMMIT trial aimed to examine the effects of tirzepatide on cardiac structure and function with the underlying hypothesis that it would reduce left ventricular (LV) mass and EAT in obesity-related HFpEF. METHODS A total of 175 patients with obesity-related HFpEF from the parent study of tirzepatide (2.5 mg subcutaneously weekly, increasing to a maximum of 15 mg weekly) or matching placebo underwent CMR at baseline, which consisted of multiplanar cine imaging. A total of 106 patients completed the CMR and had adequate image quality for analysis of LV and left atrial structure and function and paracardiac (epicardial plus pericardial) adipose tissue at both baseline and 52 weeks. The prespecified primary endpoint of this substudy was between-group changes in LV mass. RESULTS LV mass decreased by 11 g (95% CI:-19 to-4 g) in the treated group (n = 50) when corrected for placebo (n = 56) (P = 0.004). Paracardiac adipose tissue decreased in the treated group by 45 mL (95% CI:-69 to-22 mL) when corrected for placebo (P < 0.001). The change in LV mass in the treated group correlated with changes in body weight (P < 0.02) and tended to correlate with changes in waist circumference and blood pressure (P = 0.06 for both). The LV mass change also correlated with changes in LV end-diastolic volume and left atrial end-diastolic and end-systolic volumes (P < 0.03 for all). CONCLUSIONS The CMR substudy of the SUMMIT trial demonstrated that tirzepatide therapy in obesity-related HFpEF led to reduced LV mass and paracardiac adipose tissue as compared with placebo, and the change in LV mass paralleled weight loss. These physiologic changes may contribute to the reduction in heart failure events seen in the main SUMMIT trial. (A Study of Tirzepatide [LY3298176] in Participants With Heart Failure With Preserved Ejection Fraction [HFpEF] and Obesity: The SUMMIT Trial; NCT04847557) (JACC. 2025;85:699-706) (c) 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation.

Keywords

Obesity

Author Keywords

cardiac MRIGLP1 agonistHFpEFLV massobesity

Keywords Plus

CARDIOVASCULAR MAGNETIC-RESONANCESEMAGLUTIDE

22-Continued Treatment With Tirzepatide for Maintenance of Weight Reduction in Adults With Obesity

Aronne, LJ (Aronne, Louis J.) [1] , [2] ; Sattar, N (Sattar, Naveed) [3] ; Horn, DB (Horn, Deborah B.) [4] ; Bays, HE (Bays, Harold E.) [5] ; Wharton, S (Wharton, Sean) [6] , [7] ; Lin, WY (Lin, Wen-Yuan) [8] ; Ahmad, NN (Ahmad, Nadia N.) [9] ; Zhang, SY (Zhang, Shuyu) [9] ; Liao, R (Liao, Ran) [9] ; Bunck, MC (Bunck, Mathijs C.) [9] ; Group Author SURMOUNT-4 Investigators (SURMOUNT-4 Investigators) (provided by Clarivate),**Source JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION,Volume 331,Issue 1,Page 38-48,DOI 10.1001/jama.2023.24945,Published JAN 2 2024,Early Access DEC 2023,Indexed 2023-12-30,Document Type Article**

Abstract

Importance The effect of continued treatment with tirzepatide on maintaining initial weight reduction is unknown.Objective To assess the effect of tirzepatide, with diet and physical activity, on the maintenance of weight reduction.Design, Setting, and Participants This phase 3, randomized withdrawal clinical trial conducted at 70 sites in 4 countries with a 36-week, open-label tirzepatide lead-in period followed by a 52-week, double-blind, placebo-controlled period included adults with a body mass index greater than or equal to 30 or greater than or equal to 27 and a weight-related complication, excluding diabetes.Interventions Participants (n = 783) enrolled in an open-label lead-in period received once-weekly subcutaneous maximum tolerated dose (10 or 15 mg) of tirzepatide for 36 weeks. At week 36, a total of 670 participants were randomized (1:1) to continue receiving tirzepatide (n = 335) or switch to placebo (n = 335) for 52 weeks.Main Outcomes and MeasuresThe primary end point was the mean percent change in weight from week 36 (randomization) to week 88. Key secondary end points included the proportion of participants at week 88 who maintained at least 80% of the weight loss during the lead-in period.Results Participants (n = 670; mean age, 48 years; 473 [71%] women; mean weight, 107.3 kg) who completed the 36-week lead-in period experienced a mean weight reduction of 20.9%. The mean percent weight change from week 36 to week 88 was -5.5% with tirzepatide vs 14.0% with placebo (difference, -19.4% [95% CI, -21.2% to -17.7%]; P < .001). Overall, 300 participants (89.5%) receiving tirzepatide at 88 weeks maintained at least 80% of the weight loss during the lead-in period compared with 16.6% receiving placebo (P < .001). The overall mean weight reduction from week 0 to 88 was 25.3% for tirzepatide and 9.9% for placebo. The most common adverse events were mostly mild to moderate gastrointestinal events, which occurred more commonly with tirzepatide vs placebo.Conclusions and Relevance In participants with obesity or overweight, withdrawing tirzepatide led to substantial regain of lost weight, whereas continued treatment maintained and augmented initial weight reduction.Trial RegistrationClinicalTrials.gov Identifier: NCT04660643

Keywords

Obesity

Keywords Plus

PLACEBO-CONTROLLED TRIALGLP-1 RECEPTOR AGONISTDOUBLE-BLINDDUAL GIPLIRAGLUTIDEMULTICENTERORLISTATEFFICACYPEOPLE

23-Strengths and Limitations of BMI in the Diagnosis of Obesity: What is the Path Forward?

Sweatt, K (Sweatt, Katherine) [1] ; Garvey, WT (Garvey, W. Timothy) [1] ; Martins, C (Martins, Catia) [1](provided by Clarivate) **Source CURRENT OBESITY REPORTS,Volume 13,Issue 3,Page 584-595,DOI 10.1007/s13679-024-00580-1,Published SEP 2024,Early Access JUL 2024,Indexed 2024-07-16,Document Type Review**

Abstract

Purpose of ReviewThis review aims to discuss strengths and limitations of body mass index (BMI) in diagnosing obesity, the use of alternative anthropometric measurements, and potential new technology that may change the future of obesity diagnosis and management.Recent FindingsThe diagnosis of obesity requires the anthropometric assessment of adiposity. In clinical settings, this should include BMI with confirmation that elevated BMI represents excess adiposity and a measure of fat distribution (i.e., waist circumference (WC), waist to height ratio (WHtR), or WC divided by height0.5 (WHR.5R). Digital anthropometry and bioelectric impedance (BIA) can estimate fat distribution and be feasibly employed in the clinic. In addition, the diagnosis should include a clinical component assessing the presence and severity of weight-related complications.SummaryAs anthropometric measures used in the diagnosis of obesity, BMI is generally sufficient if confirmed to represent excess adiposity, and there are advantages to the use of WHtR over WC to assess fat distribution. BIA and digital anthropometry have the potential to provide accurate measures of fat mass and distribution in clinical settings. There should also be a clinical evaluation for the presence and severity of obesity complications that can be used to stage the disease.

Keywords

Author Keywords

ObesityBMIDiagnosticScreeningAdiposityAnthropometrics

Keywords Plus

BODY-MASS INDEXBIOELECTRICAL-IMPEDANCE ANALYSISOBSTRUCTIVE SLEEP-APNEAALL-CAUSE MORTALITYTO-HEIGHT RATIOCARDIOVASCULAR-DISEASE RISKCORONARY-HEART-DISEASEWAIST CIRCUMFERENCEABDOMINAL OBESITYFAT DISTRIBUTION

24-IFSO Consensus on Definitions and Clinical Practice Guidelines for Obesity Management-an International Delphi Study

Salminen, P (Salminen, Paulina) [1] , [2] ; Kow, L (Kow, Lilian) [3] ; Aminian, A (Aminian, Ali) [4] ; Kaplan, LM (Kaplan, Lee M.) [5] ; Nimeri, A (Nimeri, Abdelrahman) [6] ; Prager, G (Prager, Gerhard) [7] ; Behrens, E (Behrens, Estuardo) [8] ; White, KP (White, Kevin P.) [9] ; Shikora, S (Shikora, Scott) [6] Group Author IFSO Experts Pane (IFSO Experts Pane)(provided by Clarivate) ,Source OBESITY SURGERY,Volume 34,Issue 1,Page 30-42,DOI 10.1007/s11695-023-06913-8,Published JAN 2024,Early Access NOV 2023,Indexed 2023-12-17,Document Type Article

Abstract

IntroductionThis survey of international experts in obesity management was conducted to achieve consensus on standardized definitions and to identify areas of consensus and non-consensus in metabolic bariatric surgery (MBS) to assist in an algorithm of clinical practice guidelines for the management of obesity.MethodsA three-round Delphi survey with 136 statements was conducted by 43 experts in obesity management comprising 26 bariatric surgeons, 4 endoscopists, 8 endocrinologists, 2 nutritionists, 2 counsellors, an internist, and a pediatrician spanning six continents over a 2-day meeting in Hamburg, Germany. To reduce bias, voting was unanimous, and the statements were neither favorable nor unfavorable to the issue voted or evenly balanced between favorable and unfavorable. Consensus was defined as >= 70% inter-voter agreement.ResultsConsensus was reached on all 15 essential definitional and reporting statements, including initial suboptimal clinical response, baseline weight, recurrent weight gain, conversion, and revision surgery. Consensus was reached on 95/121 statements on the type of surgical procedures favoring Roux-en-Y gastric bypass, sleeve gastrectomy, and endoscopic sleeve gastroplasty. Moderate consensus was reached for sleeve gastrectomy single-anastomosis duodenoileostomy and none on the role of intra-gastric balloons. Consensus was reached for MBS in patients > 65 and < 18 years old, with a BMI > 50 kg/m(2), and with various obesity-related complications such as type 2 diabetes, liver, and kidney disease.ConclusionsIn this survey of 43 multi-disciplinary experts, consensus was reached on standardized definitions and reporting standards applicable to the whole medical community. An algorithm for treating patients with obesity was explored utilizing a thoughtful multimodal approach.

Keywords

Author Keywords

Obesity, Severe obesityMetabolic bariatric surgeryBariatric surgeryBariatric endoscopyAnti-obesity medicationsMedical treatmentDefinitionsOutcomesConsensusIFSODelphi survey

25-Regular Consumption of Black Tea Kombucha Modulates the Gut Microbiota in Individuals with and without Obesity

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Abstract

Background: Kombucha, a fermented beverage obtained from a Symbiotic Culture of Bacteria and Yeast, has shown potential in modulating gut microbiota, although no clinical trials have been done. Objectives: We aimed to evaluate the effects of regular black tea kombucha consumption on intestinal health in individuals with and without obesity. Methods: A pre-post clinical intervention study was conducted lasting 8 wk. Forty-six participants were allocated into 2 groups: normal weight + black tea kombucha (n = 23); and obese + black tea kombucha (n = 23). Blood, urine, and stool samples were collected at baseline (T0) and after 8 wk of intervention (T8). Results: A total of 145 phenolic compounds were identified in the kombucha, primarily flavonoids (81%) and phenolic acids (19%). Kombucha favored commensal bacteria such as Bacteroidota and Akkermanciaceae, especially in the obese group. Subdoligranulum, a butyrate producer, also increased in the obese group after kombucha consumption ($P = 0.031$). Obesity-associated genera Ruminococcus and Dorea were elevated in the obese group at baseline ($P < 0.05$) and reduced after kombucha consumption, becoming similar to the normal weight group (Ruminococcus: obese T8 x normal weight T8: $P = 0.27$; Dorea: obese T8 x normal weight T0: $P = 0.57$; obese T8 x normal weight T8: $P = 0.32$). Fungal diversity increased, with a greater abundance of Saccharomyces in both groups and reductions in Exophiala and Rhodotorula, particularly in the obese group. Pichia and Dekkera, key microorganisms in kombucha, were identified as biomarkers after the intervention. Conclusions: Regular kombucha consumption positively influenced gut microbiota in both normal and obese groups, with more pronounced effects in the obese group, suggesting that it may be especially beneficial for those individuals.

Keywords

Author Keywords

Obesity

bioactive compoundsCamellia sinensisintestinal permeabilitypolyphenolszonulin

Keywords Plus

AKKERMANSIA-MUCINIPHILADIETARY POLYPHENOLSCYSTIC-FIBROSISGREEN TEAFERMENTATIONDERMATITIDISMETABOLISMPREBIOTICSABUNDANCEGLUCOSE

26-Update on the Obesity Epidemic: Is the Sharp Rise of the Evil Empire Truly Levelling Off?

Koliaki, C (Koliaki, Chrysi) [1] ; Dalamaga, M (Dalamaga, Maria) [2] ; Liatis, S (Liatis, Stavros) [1] (provided by Clarivate) ,Source CURRENT OBESITY REPORTS,DOI 10.1007/s13679-023-00527-y,Early Access OCT 2023,Indexed 2024-02-24,Document Type Review; Early Access

Abstract

Purpose of ReviewTo provide an update on current obesity prevalence trends and summarize the available evidence suggesting a possible plateau or stabilization in obesity rates after the previous sudden global rise.Recent FindingsThe escalating global obesity epidemic represents one of the most serious public health challenges. There have been some indications that in high-income populations, the rate of obesity increase in adults has been stabilized after the decade 2000-2010, suggesting a possible plateau. Current evidence also suggests that obesity rates have been stabilized in children and adolescents of most economically advanced countries since 2000, which is possibly related to healthier dietary habits and increased levels of physical activity. On the other hand, there is a steady uninterrupted rise in low-income nations, and the universal trend is obesity escalation rather than slowdown, mainly driven by sharp increases in the obesity prevalence of low-income populations. Furthermore, an increasing number of high- and middle-income countries are currently experiencing an epidemic of severe obesity. In high-income populations, severe obesity is expected to double its prevalence from 10 to 20% between 2020 and 2035, posing an enormous threat for healthcare systems. Even if transiently stabilized, the obesity prevalence remains globally at unacceptably high levels, and there is no guarantee that the current stability (if any) will be maintained for long.SummaryIn this review, we explore the underlying drivers of the global obesity epidemic; we provide possible explanations for the reported slowdown of the obesity rates in some countries; and we overall take a critical perspective on the obesity plateau hypothesis, emphasizing the urgent need for immediate effective actions at population and regional level in order to halt the alarming obesity escalation and its serious health risks.

Keywords

Author Keywords

AdiposityBody mass indexEpidemiologyObesityOverweightPrevalencePlateauStabilizationTrend

Keywords Plus

BODY-MASS INDEXPHYSICAL-ACTIVITYCHILDHOOD OVERWEIGHTDECREASING PREVALENCENUTRITION TRANSITIONADOLESCENT OBESITYTRENDSCHILDRENEVOLUTIONSCHOOLCHILDREN

27-Glucagon-Like Peptide 1 Receptor Agonists and 13 Obesity-Associated Cancers in Patients with Type 2 Diabetes

Wang, LS (Wang, Lindsey) [1] ; Xu, R (Xu, Rong) [2] , [3] ; Kaelber, DC (Kaelber, David C.) [4] , [5] , [6] , [7] ; Berger, NA (Berger, Nathan A.) [1] , [3] **Source JAMA NETWORK OPEN,Volume 7,Issue 7,DOI 10.1001/jamanetworkopen.2024.21305,Article Number e2421305,Published JUL 5 2024,Indexed 2024-07-18,Document Type Article**

Abstract

Importance Thirteen human malignant neoplasms have been identified as obesity-associated cancers (OACs), ie, the presence of excess body fat is associated with increased risk of developing cancer and worse prognosis in patients with these specific tumors. The glucagon-like peptide receptor agonist (GLP-1RA) class of pharmaceuticals are effective agents for the treatment of type 2 diabetes (T2D) and for achieving weight loss, but the association of GLP-1RAs with the incident risk of 13 OACs is unclear. Objective To compare the incident risk of each of the 13 OACs in patients with T2D who were prescribed GLP-1RAs vs insulins or metformin. Design, Setting, and Participants This retrospective cohort study was based on a nationwide multicenter database of electronic health records (EHRs) of 113 million US patients. The study population included 1 651 452 patients with T2D who had no prior diagnosis of OACs and were prescribed GLP-1RAs, insulins, or metformin during March 2005 to November 2018. Data analysis was conducted on April 26, 2024. Exposures Prescription of GLP-1RAs, insulins, or metformin. Main Outcomes and Measures Incident (first-time) diagnosis of each of the 13 OACs occurring during a 15-year follow-up after the exposure was examined using Cox proportional hazard and Kaplan-Meier survival analyses with censoring applied. Hazard ratios (HRs), cumulative incidences, and 95% CIs were calculated. All models were adjusted for confounders at baseline by propensity-score matching baseline covariates. Results In the study population of 1 651 452 patients with T2D (mean [SD] age, 59.8 [15.1] years; 827 873 [50.1%] male and 775 687 [47.0%] female participants; 5780 [0.4%] American Indian or Alaska Native, 65 893 [4.0%] Asian, 281 242 [17.0%] Black, 13 707 [0.8%] Native Hawaiian or Other Pacific Islander, and 1 000 780 [60.6%] White participants), GLP-1RAs compared with insulin were associated with a significant risk reduction in 10 of 13 OACs, including in gallbladder cancer (HR, 0.35; 95% CI, 0.15-0.83), meningioma (HR, 0.37; 95% CI, 0.18-0.74), pancreatic cancer (HR, 0.41; 95% CI, 0.33-0.50), hepatocellular carcinoma (HR, 0.47; 95% CI, 0.36-0.61), ovarian cancer (HR, 0.52; 95% CI, 0.03-0.74), colorectal cancer (HR, 0.54; 95% CI, 0.46-0.64), multiple myeloma (HR, 0.59; 95% CI, 0.44-0.77), esophageal cancer (HR, 0.60; 95% CI, 0.42-0.86), endometrial cancer (HR, 0.74; 95% CI, 0.60-0.91), and kidney cancer (HR, 0.76; 95% CI, 0.64-0.91). Although not statistically significant, the HR for stomach cancer was less than 1 among patients who took GLP-1RAs compared with those who took insulin (HR, 0.73; 95% CI, 0.51-1.03). GLP-1RAs were not associated with a reduced risk of postmenopausal breast cancer or thyroid cancer. Of those cancers that

showed a decreased risk among patients taking GLP-1RAs compared with those taking insulin, HRs for patients taking GLP-1RAs vs those taking metformin for colorectal and gallbladder cancer were less than 1, but the risk reduction was not statistically significant. Compared with metformin, GLP-1RAs were not associated with a decreased risk of any cancers, but were associated with an increased risk of kidney cancer (HR, 1.54; 95% CI, 1.27-1.87). Conclusions and Relevance In this study, GLP-1RAs were associated with lower risks of specific types of OACs compared with insulins or metformin in patients with T2D.

These findings provide preliminary evidence of the potential benefit of GLP-1RAs for cancer prevention in high-risk populations and support further preclinical and clinical studies for the prevention of certain OACs.

Keywords

Keywords Plus

BREAST-CANCER

28-Discontinuation and Reinitiation of Dual-Labeled GLP-1 Receptor Agonists Among US Adults With Overweight or Obesity

Rodriguez, PJ (Rodriguez, Patricia J.) [1] ; Zhang, V (Zhang, Vincent) [2] ; Gratzl, S (Gratzl, Samuel) [1] ; Do, D (Do, Duy) [1] ; Cartwright, BG (Goodwin Cartwright, Brianna) [1] ; Baker, C (Baker, Charlotte) [1] ; Gluckman, TJ (Gluckman, Ty J.) [3] ; Stucky, N (Stucky, Nicholas) [1] ; Emanuel, EJ (Emanuel, Ezekiel J.) [2] (provided by Clarivate) ,Source JAMA NETWORK OPEN,Volume 8 ,Issue 1,DOI 10.1001/jamanetworkopen.2024.57349,Article Number e2457349,Published JAN 31 2025,Indexed 2025-02-09,Document Type Article

Abstract

Importance Adherence to glucagon-like peptide-1 receptor agonists (GLP-1 RAs) is important for their effectiveness. Discontinuation and reinitiation patterns are not well understood. Objective To describe rates of and factors associated with discontinuation and subsequent reinitiation of GLP-1 RAs among adults with overweight or obesity. Design, Setting, and Participants In this retrospective cohort study, 125 474 adults with overweight or obesity newly initiated treatment with a dual-labeled GLP-1 RA (liraglutide, semaglutide, or tirzepatide) between January 1, 2018, and December 31, 2023, with a baseline body mass index of 27 or more, an available weight measurement within 60 days before initiation, and regular care in the year before initiation were identified using electronic health record data from a collective of US health care systems. Patients were followed up for up to 2 years to assess discontinuation and for 2 additional years to assess reinitiation. Exposure Patients were stratified by presence of type 2 diabetes at baseline. Main Outcomes and MeasuresProportions of patients discontinuing and reinitiating GLP-1 RA were estimated from Kaplan-Meier models. Associations of sociodemographic characteristics, health factors, weight changes, and gastrointestinal adverse events with discontinuation and reinitiation outcomes were modeled using time-varying Cox proportional hazards regression models. All analyses were conducted separately for patients with and patients without type 2 diabetes. Results In this cohort study of 125 474 adults (mean [SD] age, 54.4 [13.1] years; 82 063 women [65.4%]), 76 524 (61.0%) had type 2 diabetes. One-year discontinuation was significantly higher for patients without type 2 diabetes (64.8% [95% CI, 64.4%-65.2%]) compared with those with type 2 diabetes (46.5% [95% CI, 46.2%-46.9%]). Higher weight loss (1% reduction in weight from baseline was associated with a 3.1% [95% CI, 2.9%-3.2%] lower hazard of discontinuation for patients with type 2 diabetes and a 3.3% [95% CI, 3.2%-3.5%] lower hazard of discontinuation for patients without type 2 diabetes) and higher income (type 2 diabetes only; >$80 000: hazard ratio [HR], 0.72 [95% CI, 0.69-0.76]) were significantly associated with lower rates of discontinuation, while moderate or severe incident gastrointestinal adverse events were associated with a higher hazard of discontinuation (with type 2 diabetes: HR, 1.38 [95% CI, 1.31-1.45]; without type 2

diabetes: HR, 1.19 [95% CI, 1.12-1.27]). Of 41 792 patients who discontinued and had a discontinuation weight measurement available, 1-year reinitiation was lower for those without type 2 diabetes (36.3% [95% CI, 35.6%-37.0%]) compared with those with type 2 diabetes (47.3% [95% CI, 46.6%-48.0%]). Weight regain of 1% from discontinuation was significantly associated with increased hazards of reinitiation of 2.3% (95% CI, 1.9%-2.8%) for patients with type 2 diabetes and 2.8% (95% CI, 2.4%-3.2%) for patients without type 2 diabetes. Conclusions and Relevance In this cohort study, most patients with overweight or obesity discontinued GLP-1 RA therapy within 1 year, but those without type 2 diabetes had higher discontinuation rates and lower reinitiation rates. Inequities in access and adherence to effective treatments have the potential to exacerbate disparities in obesity.

29-The spleen-liver axis supports obesity-induced systemic and fatty liver inflammation via MDSC and NKT cell enrichment

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Abstract

Obesity promotes adipose tissue inflammation and leads to impaired local but also systemic immune cell homeostasis. This chronic low-grade inflammation plays a significant role in the development of obesity-associated secondary diseases such as metabolic associated fatty liver disease or cancer. The spleen as the central organ of immune cell regulation is anatomically directly connected to the visceral adipose tissue and the liver via the portal vein circulation. However, the inter-organ crosstalk and linkage between obesity-induced systemic, hepatic and splenic immune cell dysregulation is not clearly outlined. In this study blood, spleen, and liver immune cells of non-obese wildtype vs. leptin deficient obese BTBR mice were isolated and analyzed in terms of leukocyte composition by flow cytometry. Significant differences between circulating, spleen- and liver-resident immune cell distribution revealed, that obesity-induced hepatic and systemic immune cell dysregulation is distinct from splenic immune cell reprogramming. Fatty liver inflammation was associated with splenic myeloid derived suppressor cell (MDSC) and natural killer T cell (NKT) enrichment whereas loss of hepatic T and B cells was not reflected by the splenic lymphocyte landscape. Correlation analysis confirmed a selective strong positive correlation between spleen and liver MDSC and NKT cell distribution indicating that the spleen-liver axis modulates obesity-induced immune dysregulation in a cell-specific manner. Similar results were observed in a diet-induced obesity mouse model. These data provide novel insights into the role of the spleen-liver axis in obesity-induced inflammation and foster the understanding of obesity-associated complications such as fatty liver disease and cancer.

Keywords

Author Keywords

ObesityT cell dysregulationSpleen-liver-axisMyeloid-derived suppressor cellsNatural killer cells

Keywords Plus

MYELOID-DERIVED SUPPRESSORKILLER T-CELLSADIPOSE-TISSUEINSULIN-RESISTANCENONALCOHOLIC STEATOHEPATITISDIETCANCERMICEACCUMULATIONPROGRESSION

30-The association between triglyceride-glucose index and its combination with obesity indicators and cardiovascular disease: NHANES 2003-2018

Dang, KK (Dang, Keke) [1] ; Wang, XY (Wang, Xuanyang) [1] ; Hu, JX (Hu, Jinxia) [1] ; Zhang, YT (Zhang, Yuntao) [2] ; Cheng, LC (Cheng, Licheng) [1] ; Qi, X (Qi, Xiang) [1] ; Liu, L (Liu, Lin) [1] ; Ming, Z (Ming, Zhu) [1] ; Tao, XM (Tao, Xinmiao) [1] ; Li, Y (Li, Ying) [1] (provided by Clarivate) ,Source CARDIOVASCULAR DIABETOLOGY,Volume 23,Issue 1,DOI 10.1186/s12933-023-02115-9,Article Number 8,Published JAN 6 2024,Indexed 2024-01-29,Document Type Article

Abstract

Background In the American population, the relationship between the triglyceride-glucose (TyG) index and TYG combined with indicators of obesity and cardiovascular disease (CVD) and its mortality has been less well studied.Methods This cross-sectional study included 11,937 adults from the National Health and Nutrition Examination Survey (NHANES) 2003-2018. Cox proportional hazards model, binary logistic regression analyses, restricted cubic spline (RCS), and receiver operating characteristic (ROC) were used to analyze the relationship between TyG and its combined obesity-related indicators and CVD and its mortality. Mediation analysis explored the mediating role of glycated hemoglobin and insulin in the above relationships.Results In this study, except for no significant association between TyG and CVD mortality, TyG, TyG-WC, TyG-WHtR, and TyG-BMI were significantly and positively associated with CVD and CVD mortality. TyG-WHtR is the strongest predictor of CVD mortality (HR 1.66, 95% CI 1.21-2.29). The TyG index correlated better with the risk of coronary heart disease (OR 2.52, 95% CI 1.66-3.83). TyG-WC correlated best with total CVD (OR 2.37, 95% CI 1.77-3.17), congestive heart failure (OR 2.14, 95% CI 1.31-3.51), and angina pectoris (OR 2.38, 95% CI 1.43-3.97). TyG-WHtR correlated best with myocardial infarction (OR 2.24, 95% CI 1.45-3.44). RCS analyses showed that most of the above relationships were linear (P-overall < 0.0001, P-nonlinear > 0.05). Otherwise, ROC curves showed that TyG-WHtR and TyG-WC had more robust diagnostic efficacy than TyG. In mediation analyses, glycated hemoglobin mediated in all the above relationships and insulin-mediated in partial relationships.Conclusions TyG-WC and TyG-WtHR enhance CVD mortality prediction, diagnostic efficacy of CVD and its mortality, and correlation with some CVD over and above the current hottest TyG. TyG-WC and TyG-WtHR are expected to become more effective metrics for identifying populations at early risk of cardiovascular disease and improve risk stratification.

Keywords

Author Keywords

Obesity

Triglyceride glucose (TyG)Triglyceride glucose-waist circumference (TyG-WC)Triglyceride glucose-waist height ratio (TyG-WHtR)Triglyceride glucose-body mass index (TyG-BMI)Cardiovascular disease (CVD) mortalityCardiovascular diseaseNational Health and Nutrition Examination Survey (NHANES)

Keywords Plus

INSULIN-RESISTANCEABDOMINAL ADIPOSITYGLOBAL BURDENNITRIC-OXIDERISK-FACTORSHYPERGLYCEMIAPRODUCTWEIGHTHEALTH

31-Semaglutide and cardiovascular outcomes in patients with obesity and prevalent heart failure: a prespecified analysis of the SELECT trial

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Abstract

Background Semaglutide, a GLP-1 receptor agonist, reduces the risk of major adverse cardiovascular events (MACE) in people with overweight or obesity, but the effects of this drug on outcomes in patients with atherosclerotic cardiovascular disease and heart failure are unknown. We report a prespecified analysis of the effect of once-weekly subcutaneous semaglutide 24 mg on ischaemic and heart failure cardiovascular outcomes. We aimed to investigate if semaglutide was beneficial in patients with atherosclerotic cardiovascular disease with a history of heart failure compared with placebo; if there was a difference in outcome in patients designated as having heart failure with preserved ejection fraction compared with heart failure with reduced ejection fraction; and if the efficacy and safety of semaglutide in patients with heart failure was related to baseline characteristics or subtype of heart failure. Methods The SELECT trial was a randomised, double-blind, multicentre, placebo-controlled, event-driven phase 3 trial in 41 countries. Adults aged 45 years and older, with a BMI of 27 kg/m(2) or greater and established cardiovascular disease were eligible for the study. Patients were randomly assigned (1:1) with a block size of four using an interactive web response system in a double-blind manner to escalating doses of once-weekly subcutaneous semaglutide over 16 weeks to a target dose of 24 mg, or placebo. In a prespecified analysis, we examined the effect of semaglutide compared with placebo in patients with and without a history of heart failure at enrolment, subclassified as heart failure with preserved ejection fraction, heart failure with reduced ejection fraction, or unclassified heart failure. Endpoints comprised MACE (a composite of non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death); a composite heart failure outcome (cardiovascular death or hospitalisation or urgent hospital visit for heart failure); cardiovascular death; and all-cause death. The study is registered with ClinicalTrials.gov, NCT03574597. Findings Between Oct 31, 2018, and March 31, 2021, 17 604 patients with a mean age of 616 years (SD 89) and a mean BMI of 334 kg/m(2) 2 (50) were randomly assigned to receive semaglutide (8803 [500%] patients) or placebo (8801 [500%] patients). 4286 (243%) of 17 604 patients had a history of investigator-defined heart failure at enrolment: 2273 (530%) of 4286 patients had heart failure with preserved ejection fraction, 1347 (314%) had heart failure with reduced ejection fraction, and 666 (155%) had unclassified

heart failure. Baseline characteristics were similar between patients with and without heart failure. Patients with heart failure had a higher incidence of clinical events. Semaglutide improved all outcome measures in patients with heart failure at random assignment compared with those without heart failure (hazard ratio [HR] 072, 95% CI 060-087 for MACE; 079, 064-098 for the heart failure composite endpoint; 076, 059-097 for cardiovascular death; and 081, 066-100 for all-cause death; all p interaction > 0 19). Treatment with semaglutide resulted in improved outcomes in both the heart failure with reduced ejection fraction (HR 065, 95% CI 049-087 for MACE; 079, 058-108 for the composite heart failure endpoint) and heart failure with preserved ejection fraction groups (069, 051-091 for MACE; 075, 052-107 for the composite heart failure endpoint), although patients with heart failure with reduced ejection fraction had higher absolute event rates than those with heart failure with preserved ejection fraction. For MACE and the heart failure composite, there were no significant differences in benefits across baseline age, sex, BMI, New York Heart Association status, and diuretic use. Serious adverse events were less frequent with semaglutide versus placebo, regardless of heart failure subtype. Interpretation In patients with atherosclerotic cardiovascular diease and overweight or obesity, treatment with semaglutide 24 mg reduced MACE and composite heart failure endpoints compared with placebo in those with and without clinical heart failure, regardless of heart failure subtype. Our findings could facilitate prescribing and result in improved clinical outcomes for this patient group. Funding Novo Nordisk.

Keywords

Keywords Plus

REDUCED EJECTION FRACTIONRECEPTOR AGONISTSSGLT2 INHIBITORSLIRAGLUTIDEOVERWEIGHTPEOPLE

32-Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: Standards of Care in Diabetes-2025

AmerDiabetAssocProfessionalPractice (Amer Diabet Assoc Professional Practice Comm) (provided by Clarivate) ,Source DIABETES CARE,Volume 48,Page S167-S180,Supplement 1,DOI 10.2337/dc25-S008,Published JAN 2025,Indexed 2025-01-27,Document Type Review

Abstract

The American Diabetes Association (ADA) "Standards of Care in Diabetes" includes the ADA's current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee, an interprofessional expert committee, are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA's clinical practice recommendations and a full list of Professional Practice Committee members, please refer to Introduction and Methodology. Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes.org/SOC.

Keywords

Keywords Plus

LIFE-STYLE INTERVENTIONY GASTRIC BYPASSLOW-CALORIE DIETLAPAROSCOPIC-SLEEVE-GASTRECTOMYLONG-TERM REMISSIONPOST-HOC ANALYSISBARIATRIC SURGERYDOUBLE-BLINDMETABOLIC SURGERYCOMPLICATION RATES

33-national-level and state-level prevalence of overweight and obesity among children, adolescents, and adults in the USA, 1990-2021, and forecasts up to 2050

By Ng, M (Ng, Marie) ; Dai, XC (Dai, Xiaochen) ; Cogen, RM (Cogen, Rebecca M.) ; Abdelmasseh, M (Abdelmasseh, Michael) ; Abdollahi, A (Abdollahi, Arash) ; Abdullahi, A (Abdullahi, Auwal) ; Aboagye, RG (Aboagye, Richard Gyan) ; Abukhadijah, HJ (Abukhadijah, Hana J.) ; Adeyeoluwa, TE (Adeyeoluwa, Temitayo Esther) ; Afolabi, AA (Afolabi, Aanuoluwapo Adeyimika) ; Group Author GBD 2021 US Obesity Forecasting Collaborators (GBD 2021 US Obesity Forecasting Collaborators) (provided by Clarivate) SourceLANCET,Volume 404,Issue 10469,Page 2278-2298,DOI 10.1016/S0140-6736(24)01548-4,Published DEC 7 2024,Early Access DEC 2024,Indexed 2025 01-25,Document Type Article

Abstract

Background Over the past several decades, the overweight and obesity epidemic in the USA has resulted in a significant health and economic burden. Understanding current trends and future trajectories at both national and state levels is crucial for assessing the success of existing interventions and informing future health policy changes. We estimated the prevalence of overweight and obesity from 1990 to 2021 with forecasts to 2050 for children and adolescents (aged 5-24 years) and adults (aged >= 25 years) at the national level. Additionally, we derived state-specific estimates and projections for older adolescents (aged 15-24 years) and adults for all 50 states and Washington, DC.

Methods In this analysis, self-reported and measured anthropometric data were extracted from 134 unique sources, which included all major national surveillance survey data. Adjustments were made to correct for self-reporting bias. For individuals older than 18 years, overweight was defined as having a BMI of 25 kg/m(2) to less than 30 kg/m(2) and obesity was defined as a BMI of 30 kg/m(2) or higher, and for individuals younger than 18 years definitions were based on International Obesity Task Force criteria. Historical trends of overweight and obesity prevalence from 1990 to 2021 were estimated using spatiotemporal Gaussian process regression models. A generalised ensemble modelling approach was then used to derive projected estimates up to 2050, assuming continuation of past trends and patterns. All estimates were calculated by age and sex at the national level, with estimates for older adolescents (aged 15-24 years) and adults aged (>= 25 years) also calculated for 50 states and Washington, DC. 95% uncertainty intervals (UIs) were derived from the 2 center dot 5th and 97 center dot 5th percentiles of the posterior distributions of the respective estimates.

Findings In 2021, an estimated 15 center dot 1 million (95% UI 13 center dot 5-16 center dot 8) children and young adolescents (aged 5-14 years), 21 center dot 4 million (20 center dot 2-22 center dot 6) older adolescents (aged 15-24 years), and 172 million (169-174) adults (aged >= 25 years) had overweight or obesity in the USA. Texas had the highest age-standardised prevalence of overweight or obesity for male

adolescents (aged 15-24 years), at 52 center dot 4% (47 center dot 4-57 center dot 6), whereas Mississippi had the highest for female adolescents (aged 15-24 years), at 63 center dot 0% (57 center dot 0-68 center dot 5). Among adults, the prevalence of overweight or obesity was highest in North Dakota for males, estimated at 80 center dot 6% (78 center dot 5-82 center dot 6), and in Mississippi for females at 79 center dot 9% (77 center dot 8-81 center dot 8). The prevalence of obesity has outpaced the increase in overweight over time, especially among adolescents. Between 1990 and 2021, the percentage change in the age-standardised prevalence of obesity increased by 158 center dot 4% (123 center dot 9-197 center dot 4) among male adolescents and 185 center dot 9% (139 center dot 4-237 center dot 1) among female adolescents (15-24 years). For adults, the percentage change in prevalence of obesity was 123 center dot 6% (112 center dot 4-136 center dot 4) in males and 99 center dot 9% (88 center dot 8-111 center dot 1) in females. Forecast results suggest that if past trends and patterns continue, an additional 3 center dot 33 million children and young adolescents (aged 5-14 years), 3 center dot 41 million older adolescents (aged 15-24 years), and 41 center dot 4 million adults (aged >= 25 years) will have overweight or obesity by 2050. By 2050, the total number of children and adolescents with overweight and obesity will reach 43 center dot 1 million (37 center dot 2-47 center dot 4) and the total number of adults with overweight and obesity will reach 213 million (202-221). In 2050, in most states, a projected one in three adolescents (aged 15-24 years) and two in three adults (>= 25 years) will have obesity. Although southern states, such as Oklahoma, Mississippi, Alabama, Arkansas, West Virginia, and Kentucky, are forecast to continue to have a high prevalence of obesity, the highest percentage changes from 2021 are projected in states such as Utah for adolescents and Colorado for adults.

Interpretation Existing policies have failed to address overweight and obesity. Without major reform, the forecasted trends will be devastating at the individual and population level, and the associated disease burden and economic costs will continue to escalate. Stronger governance is needed to support and implement a multifaceted whole-system approach to disrupt the structural drivers of overweight and obesity at both national and local levels. Although clinical innovations should be leveraged to treat and manage existing obesity equitably, population-level prevention remains central to any intervention strategies, particularly for children and adolescents.

Keywords

Keywords Plus

BODY-MASS INDEXUNITED-STATESCHILDHOOD OBESITYWAIST CIRCUMFERENCEMATERNAL OBESITYYOUNG ADULTHOODRISK-FACTORSFOOD POLICYTRENDSHEALTH

34-National-level and state-level prevalence of overweight and obesity among children, adolescents, and adults in the USA, 1990-2021, and forecasts up to 2050

Ng, M (Ng, Marie) ; Dai, XC (Dai, Xiaochen) ; Cogen, RM (Cogen, Rebecca M.) ; Abdelmasseh, M (Abdelmasseh, Michael) ; Abdollahi, A (Abdollahi, Arash) ; Abdullahi, A (Abdullahi, Auwal) ; Aboagye, RG (Aboagye, Richard Gyan) ; Abukhadijah, HJ (Abukhadijah, Hana J.) ; Adeyeoluwa, TE (Adeyeoluwa, Temitayo Esther) ; Afolabi, AA (Afolabi, Aanuoluwapo Adeyimika) ; Group Author,GBD 2021 US Obesity Forecasting Collaborators (GBD 2021 US Obesity Forecasting Collaborators)(provided by Clarivate) **,Source LANCET,Volume 404,Issue 10469,Page 2278-2298,DOI 10.1016/S0140-6736(24)01548-4,Published DEC 7 2024,Early Access DEC 2024,Indexed 2025-01-25,Document Type Article**

Abstract

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Interpretation Existing policies have failed to address overweight and obesity. Without major reform, the forecasted trends will be devastating at the individual and population level, and the associated disease burden and economic costs will continue to escalate. Stronger governance is needed to support and implement a multifaceted whole-system approach to disrupt the structural drivers of overweight and obesity at both national and local levels. Although clinical innovations should be leveraged to treat and manage existing obesity equitably, population-level prevention remains central to any intervention strategies, particularly for children and adolescents.

Keywords

Keywords Plus

BODY-MASS INDEXUNITED-STATESCHILDHOOD OBESITYWAIST CIRCUMFERENCEMATERNAL OBESITYYOUNG ADULTHOODRISK-FACTORSFOOD POLICYTRENDSHEALTH

35-Semaglutide versus placebo in people with obesity-related heart failure with preserved ejection fraction: a pooled analysis of the STEP-HFpEF and STEP-HFpEF DM randomised trials

Butler, J (Butler, Javed) [1] , [2] ; Shah, SJ (Shah, Sanjiv J.) [3] ; Petrie, MC (Petrie, Mark C.) [4] ; Borlaug, BA (Borlaug, Barry A.) [5] ; Abildstrem, SZ (Abildstrem, Steen Z.) [6] ; Davies, MJ (Davies, Melanie J.) [7] ; Hovingh, GK (Hovingh, G. Kees) [6] ; Kitzman, DW (Kitzman, Dalane W.) [6] , [8] ; Verma, S (Verma, Subodh) [9] ; Einfeldt, MN (Einfeldt, Mette Nygaard) [6] ; (provided by Clarivate) ,Source LANCET,Volume 403,Issue 10437,Page 1635-1648,DOI 10.1016/S0140-6736(24)00469-0,Published APR 27 2024,Early Access APR 2024,Indexed 2024-06-06,Document Type Article

Abstract

Background: In the STEP-HFpEF (NCT04788511) and STEP-HFpEF DM (NCT04916470) trials, the GLP-1 receptor agonist semaglutide improved symptoms, physical limitations, bodyweight, and exercise function in people with obesity-related heart failure with preserved ejection fraction. In this prespecified pooled analysis of the STEP-HFpEF and STEP-HFpEF DM trials, we aimed to provide a more definitive assessment of the effects of semaglutide across a range of outcomes and to test whether these effects were consistent across key patient subgroups. Methods: We conducted a prespecified pooled analysis of individual patient data from STEP-HFpEF and STEP-HFpEF DM, randomised, double-blind, placebo-controlled trials at 129 clinical research sites in 18 countries. In both trials, eligible participants were aged 18 years or older, had heart failure with a left ventricular ejection fraction of at least 45%, a BMI of at least 30 kg/m(2), New York Heart Association class II-IV symptoms, and a Kansas City Cardiomyopathy Questionnaire Clinical Summary Score (KCCQ-CSS; a measure of heart failure-related symptoms and physical limitations) of less than 90 points. In STEP-HFpEF, people with diabetes or glycated haemoglobin A(1c) concentrations of at least 65% were excluded, whereas for inclusion in STEP-HFpEF DM participants had to have been diagnosed with type 2 diabetes at least 90 days before screening and to have an HbA(1c) of 10% or lower. In both trials, participants were randomly assigned to either 24 mg semaglutide once weekly or matched placebo for 52 weeks. The dual primary endpoints were change from baseline to week 52 in KCCQ-CSS and bodyweight in all randomly assigned participants. Confirmatory secondary endpoints included change from baseline to week 52 in 6-min walk distance, a hierarchical composite endpoint (all-cause death, heart failure events, and differences in changes in KCCQ-CSS and 6-min walk distance); and C-reactive protein (CRP) concentrations. Heterogeneity in treatment effects was assessed across subgroups of interest. We assessed safety in all participants who received at least one dose of study drug. Findings: Between March 19, 2021 and March 9, 2022, 529 people were randomly assigned in STEP-HFpEF, and between June 27, 2021 and Sept 2, 2022, 616 were randomly assigned in STEP-HFpEF DM. Overall,

1145 were included in our pooled analysis, 573 in the semaglutide group and 572 in the placebo group. Improvements in KCCQ-CSS and reductions in bodyweight between baseline and week 52 were significantly greater in the semaglutide group than in the placebo group (mean between-group difference for the change from baseline to week 52 in KCCQ-CSS 75 points [95% CI 53 to 98]; p<00001; mean between-group difference in bodyweight at week 52 -84% [-92 to -75]; p<00001). For the confirmatory secondary endpoints, 6-min walk distance (mean between-group difference at week 52 171 metres [92 to 250]) and the hierarchical composite endpoint (win ratio 165 [142 to 191]) were significantly improved, and CRP concentrations (treatment ratio 064 [056 to 072]) were significantly reduced, in the semaglutide group compared with the placebo group (p<00001 for all comparisons).

For the dual primary endpoints, the efficacy of semaglutide was largely consistent across multiple subgroups, including those defined by age, race, sex, BMI, systolic blood pressure, baseline CRP, and left ventricular ejection fraction. 161 serious adverse events were reported in the semaglutide group compared with 301 in the placebo group. Interpretation: In this prespecified pooled analysis of the STEP-HFpEF and STEP-HFpEF DM trials, semaglutide was superior to placebo in improving heart failure-related symptoms and physical limitations, and reducing bodyweight in participants with obesity-related heart failure with preserved ejection fraction. These effects were largely consistent across patient demographic and clinical characteristics. Semaglutide was well tolerated.

36-Elucidating the role of diet in maintaining gut health to reduce the risk of obesity, cardiovascular and other age-related inflammatory diseases: recent challenges and future recommendations

Aziz, T (Aziz, Tariq) [1] ; Hussain, N (Hussain, Nageen) [2] ; Hameed, Z (Hameed, Zunaira) [2] ; Lin, L (Lin, Lin) [1] , [3] (provided by Clarivate) ,Source GUT MICROBES,Volume 16,Issue 1,DOI 10.1080/19490976.2023.2297864,Article Number 2297864,PublishedDEC 31 2024,Indexed 2024-01-20,Document Type Review

Abstract

A healthy balanced diet is crucial in protecting the immune system against infections and diseases. Poor diets, such as the Western diet, contribute to the development of metabolic diseases, hypertension, and obesity. Microbiota, primarily composed of different microorganisms and residing in the gastrointestinal tract (GIT), also play a significant role in maintaining gut health. Polyphenols and probiotics found in fruits, vegetables, whole grains, legumes, nuts, and seeds promote gut health and support the growth of beneficial bacteria. Different types of diets, their categories, and their impact on health are also mentioned. The relationship between diet, gut health, and the risk of developing obesity, cardiovascular diseases, and inflammatory diseases is discussed in this review article. The rationale behind the review concludes future recommendations for maintaining gut health and reducing the occurrence of obesity, cardiometabolic diseases, and other inflammatory diseases. There is also the need for standardized research methods, long-term studies, and translating scientific knowledge into practical dietary recommendations.

Keywords

Author Keywords

Inflammatory diseasesmicrobiotaobesityprobioticspolyphenols

Keywords Plus

IN-SILICO CHARACTERIZATIONSPINAL MUSCULAR-ATROPHYMEDITERRANEAN DIETRHEUMATOID-ARTHRITISMETABOLIC SYNDROMECROHNS-DISEASELINOLEIC-ACIDMICROBIOTAMARKERSOVERWEIGHT

37-The triglyceride-glucose index and its obesity-related derivatives as predictors of all-cause and cardiovascular mortality in hypertensive patients: insights from NHANES data with machine learning analysis

Li, CY (Li, Chenyang) [1] ; Zhang, ZX (Zhang, Zixi) [2] ; Luo, XQ (Luo, Xiaoqin) [3] ; Xiao, YC (Xiao, Yichao) [2] ; Tu, T (Tu, Tao) [2] ; Liu, C (Liu, Chan) [4] ; Liu, QM (Liu, Qiming) [2] ; Wang, CC (Wang, Cancan) [5] ; Dai, YG (Dai, Yongguo) [6] ; Zhang, ZY (Zhang, Zeying) [7] ; **(provided by Clarivate) ,Source CARDIOVASCULAR DIABETOLOGY,Volume 24,Issue 1,DOI 10.1186/s12933-025-02591-1,Article Number 47,Published JAN 29 2025,Indexed 2025-02-07,Document Type Article**

Abstract

BackgroundHypertension (HTN) is a global public health concern and a major risk factor for cardiovascular disease (CVD) and mortality. Insulin resistance (IR) plays a crucial role in HTN-related metabolic dysfunction, but its assessment remains challenging. The triglyceride-glucose (TyG) index and its derivatives (TyG-BMI, TyG-WC, and TyG-WHtR) have emerged as reliable IR markers. In this study, we evaluated their associations with all-cause and cardiovascular mortality in hypertensive patients using machine learning techniques.MethodsData from 9432 hypertensive participants in the National Health and Nutrition Examination Survey (NHANES) 1999-2018 were analysed. Cox proportional hazards models and restricted cubic splines were employed to explore mortality risk and potential nonlinear relationships. Machine learning models were utilized to assess the predictive value of the TyG index and its derivatives for mortality outcomes.ResultsThe TyG index and its derivatives were independent predictors of both all-cause and cardiovascular mortality in hypertensive patients. The TyG-WHtR exhibited the strongest association, with each 1-unit increase linked to a 41.7% and 48.1% higher risk of all-cause and cardiovascular mortality, respectively. L-shaped relationships were observed between TyG-related indices and mortality. The incorporation of the TyG index or its derivatives into predictive models modestly improved the prediction performance for mortality outcomes.Conclusions The TyG index and its derivatives are significant predictors of mortality in hypertensive patients. Their inclusion in predictive models enhances risk stratification and may aid in the early identification of high-risk individuals in this population. Further studies are needed to validate these findings in external hypertensive cohorts.

Keywords

Author Keywords

Obesity

Triglyceride-glucose (TyG) indexHypertensionMortalityMachine learningNational Health and Nutrition Examination Survey (NHANES)

Keywords Plus

INSULIN-RESISTANCEASSOCIATIONPRODUCT

38-Global, regional, and national prevalence of child and adolescent overweight and obesity, 1990-2021, with forecasts to 2050: a forecasting study for the Global Burden of Disease Study 2021

Kerr, JA (Kerr, Jessica A.) ; Patton, GC (Patton, George C.) ; Cini, KI (Cini, Karly I.) ; Abate, YH (Abate, Yohannes Habtegiorgis) ; Abbas, N (Abbas, Nasir) ; Abd Al Magied, AHA (Abd Al Magied, Abdallah H. A.) ; Abd ElHafeez, S (Abd ElHafeez, Samar) ; Abd-Elsalam, S (Abd-Elsalam, Sherief) ; Abdollahi, A (Abdollahi, Arash) ; Abdoun, M (Abdoun, Meriem) ; Group Author GBD 2021 Adolescent BMI Collaborators (GBD 2021 Adolescent BMI Collaborators) (provided by Clarivate) ,Source LANCET,Volume 405,Issue 10481,Page 785-812,DOI 10.1016/S0140-6736(25)00397-6,Published MAR 8 2025,Indexed 2025-06-06,Document Type Article

Abstract

Background Despite the well documented consequences of obesity during childhood and adolescence and future risks of excess body mass on non-communicable diseases in adulthood, coordinated global action on excess body mass in early life is still insufficient. Inconsistent measurement and reporting are a barrier to specific targets, resource allocation, and interventions. In this Article we report current estimates of overweight and obesity across childhood and adolescence, progress over time, and forecasts to inform specific actions.

Methods Using established methodology from the Global Burden of Diseases, Injuries, and Risk Factors Study 2021, we modelled overweight and obesity across childhood and adolescence from 1990 to 2021, and then forecasted to 2050. Primary data for our models included 1321 unique measured and self-reported anthropometric data sources from 180 countries and territories from survey microdata, reports, and published literature. These data were used to estimate age-standardised global, regional, and national overweight prevalence and obesity prevalence (separately) for children and young adolescents (aged 5-14 years, typically in school and cared for by child health services) and older adolescents (aged 15-24 years, increasingly out of school and cared for by adult services) by sex for 204 countries and territories from 1990 to 2021. Prevalence estimates from 1990 to 2021 were generated using spatiotemporal Gaussian process regression models, which leveraged temporal and spatial correlation in epidemiological trends to ensure comparability of results across time and geography. Prevalence forecasts from 2022 to 2050 were generated using a generalised ensemble modelling approach assuming continuation of current trends. For every age-sex-location population across time (1990-2050), we estimated obesity (vs overweight) predominance using the log ratio of obesity percentage to overweight percentage.

Findings Between 1990 and 2021, the combined prevalence of overweight and obesity in children and adolescents doubled, and that of obesity alone tripled. By 2021, 931 million (95% uncertainty interval 896-966) individuals aged 5-14 years and 806 million (782-833) aged 15-24 years had obesity. At the super-region level in 2021, the prevalence of overweight and of obesity was highest in north Africa and the

Middle East (eg, United Arab Emirates and Kuwait), and the greatest increase from 1990 to 2021 was seen in southeast Asia, east Asia, and Oceania (eg, Taiwan [province of China], Maldives, and China). By 2021, for females in both age groups, many countries in Australasia (eg, Australia) and in high-income North America (eg, Canada) had already transitioned to obesity predominance, as had males and females in a number of countries in north Africa and the Middle East (eg, United Arab Emirates and Qatar) and Oceania (eg, Cook Islands and American Samoa). From 2022 to 2050, global increases in overweight (not obesity) prevalence are forecasted to stabilise, yet the increase in the absolute proportion of the global population with obesity is forecasted to be greater than between 1990 and 2021, with substantial increases forecast between 2022 and 2030, which continue between 2031 and 2050. By 2050, super-region obesity prevalence is forecasted to remain highest in north Africa and the Middle East (eg, United Arab Emirates and Kuwait), and forecasted increases in obesity are still expected to be largest across southeast Asia, east Asia, and Oceania (eg, Timor-Leste and North Korea), but also in south Asia (eg, Nepal and Bangladesh). Compared with those aged 15-24 years, in most super-regions (except Latin America and the Caribbean and the high-income super-region) a greater proportion of those aged 5-14 years are forecasted to have obesity than overweight by 2050. Globally, 156% (127-172) of those aged 5-14 years are forecasted to have obesity by 2050 (186 million [141-221]), compared with 142% (114-157) of those aged 15-24 years (175 million [136-203]). We forecasted that by 2050, there will be more young males (aged 5-14 years) living with obesity (165% [133-183]) than overweight (129% [122-136]); while for females (aged 5-24 years) and older males (aged 15-24 years), overweight will remain more prevalent than obesity. At a regional level, the following populations are forecast to have transitioned to obesity (vs overweight) predominance before 2041-50: children and adolescents (males and females aged 5-24 years) in north Africa and the Middle East and Tropical Latin America; males aged 5-14 years in east Asia, central and southern sub-Saharan Africa, and central Latin America; females aged 5-14 years in Australasia; females aged 15-24 years in Australasia, high-income North America, and southern sub-Saharan Africa; and males aged 15-24 years in high-income North America.

Interpretation Both overweight and obesity increased substantially in every world region between 1990 and 2021, suggesting that current approaches to curbing increases in overweight and obesity have failed a generation of children and adolescents. Beyond 2021, overweight during childhood and adolescence is forecast to stabilise due to further increases in the population who have obesity. Increases in obesity are expected to continue for all populations in all world regions. Because substantial change is forecasted to occur between 2022 and 2030, immediate actions are needed to address this public health crisis.

Keywords

Obesity

Keywords Plus BODY-MASS INDEXCARDIOVASCULAR RISK-FACTORSADULT ADIPOSITYWEIGHTHEALTHINTERVENTIONHEIGHTFOODBMICOMORBIDITIESI