SPECIAL REPORT

Management of obesity in the times of climate change and COVID-19: an interdisciplinary expert consensus report

Ewa Płaczkiewicz-Jankowska[1], Leszek Czupryniak[2], Grzegorz Gajos[3,4], Andrzej Lewiński[5], Marek Ruchała[6], Magdalena Stasiak[7], Krzysztof Strojek[8], Ewelina Szczepanek-Parulska[6], Mariusz Wyleżoł[9,10], Lucyna Ostrowska[11], Piotr Jankowski[12,13]

1 Polish Institute for Evidence-Based Medicine, Kraków, Poland
2 Department of Diabetology and Internal Medicine, Medical University of Warsaw, Warsaw, Poland
3 Department of Coronary Artery Disease and Heart Failure, Institute of Cardiology, Jagiellonian University, Medical College, Kraków, Poland
4 Department of Coronary Artery Disease and Heart Failure, John Paul II Hospital, Kraków, Poland
5 Department of Endocrinology and Metabolic Diseases, Medical University of Lodz, Łódź, Poland
6 Department of Endocrinology, Metabolism and Internal Medicine, Poznan University of Medical Sciences, Poznań, Poland
7 Department of Endocrinology and Metabolic Diseases, Polish Mother's Memorial Hospital Research Institute, Łódź, Poland
8 Department of Internal Diseases, Diabetology and Cardiometabolic Diseases, SMDZ in Zabrze, Medical University of Silesia, Katowice, Poland
9 Department of General, Vascular and Oncological Surgery, Medical University of Warsaw, Warsaw, Poland
10 Warsaw Center for Medical and Surgical Treatment of Obesity, Czerniakowski Hospital, Warsaw, Poland
11 Department of Dietetics and Nutrition, Medical University of Bialystok, Białystok, Poland
12 Department of Internal Medicine and Geriatric Cardiology, Center of Postgraduate Medical Education, Warsaw, Poland
13 Department of Epidemiology and Health Promotion, School of Public Health, Center of Postgraduate Medical Education, Warsaw, Poland

KEY WORDS

diabetes, diet, environment, metabolic, obesity

ABSTRACT

Obesity is a chronic disease associated with increased metabolic and cardiovascular risk, excessive morbidity and mortality worldwide. The authors of the present consensus, clinicians representing medical specialties related to the treatment of obesity and its complications, reviewed a number of European and American guidelines, published mostly in 2019–2021, and summarized the principles of obesity management to provide a practical guidance considering the impact that increased adiposity poses to health. From a clinical perspective, the primary goal of obesity treatment is to prevent or slow down the progression of diseases associated with obesity, reduce metabolic and cardiovascular risk, and improve the quality of life by achieving adequate and stable weight reduction. However, obesity should be not only considered a disease requiring treatment in an individual patient, but also a civilization disease requiring preventive measures at the populational level. Despite the evident benefits, obesity management within the health care system—whether through pharmacotherapy or bariatric surgery—is only a symptomatic treatment, with all its limitations, and will not ultimately solve the problem of obesity. The important message is that available treatment options fail to correct the true drivers of the obesity pandemic. To this end, new solutions and efforts to prevent obesity in the populations are needed.

Correspondence to:
Ewa Płaczkiewicz-Jankowska, MD, PhD, Polish Institute for Evidence-Based Medicine, ul. Gazowa 41A, 31-060 Kraków, Poland, phone: +48 12 211 22 54, e-mail: mmplaczk@cyf-kr.edu.pl
Received: January 4, 2022.
Revision accepted: February 9, 2022.
Published online: February 11, 2022.
Pol Arch Intern Med. 2022; 132 (3): 16216
doi:10.20452/pamw.16216

Introduction Obesity is now recognized as a chronic disease associated with increased metabolic and cardiovascular risk, excessive morbidity and mortality over the years. Current definitions of obesity direct attention to health consequences and challenges of excessive body weight, highlighting its chronic nature. The World Health Organization (WHO) defines overweight and obesity as an abnormal and excessive accumulation of body fat in the human body that poses a risk to health,[1] and the American Association of Clinical Endocrinologists describes it as an adiposity-based chronic disease.[2] Obesity has long been recognized as a major risk factor for type 2 diabetes (T2D), hypertension, dyslipidemia, and atherosclerotic cardiovascular disease

(including coronary syndromes and stroke), but also for non alcoholic fatty liver disease, gastroesophageal reflux, obstructive sleep apnea, hypoventilation syndrome, endocrine disruptions, infertility, stress urinary incontinence, osteoarthritis, and depression. Patients with obesity also have a particularly increased risk of endometrial, breast, ovarian, prostate, liver, gallbladder, colon, and kidney cancer. Two studies published in 2016—a meta-analysis involving 10.6 million people,[3] and a systematic review involving 30 million people[4]—clearly demonstrated that both overweight and obesity are associated with an increased risk of death. The higher the body mass index (BMI), the higher the risk of many diseases and mortality.[5] This problem continues to grow despite the existing knowledge and the fact that scientists and physicians have been informing the public and patients about these risks for many years. Since 1975, there has been a more than 3-fold increase in the prevalence of obesity worldwide—in 2016, almost 2 billion adults were overweight, and more than 650 million were obese. In Poland, around 8 million adults suffer from obesity. The results of a survey among European adults from 20 countries showed that overweight and obesity affected more than half of them (53.1%).[6] The unfavorable trend in the prevalence of obesity was detected also among patients with very high cardiovascular risk.[7] Moreover, the ongoing COVID-19 pandemic revealed that obese people infected with SARS-CoV-2 are at a higher risk of developing more severe disease, and have a significant risk of death from the disease.

The authors of the present consensus, who are clinicians representing medical specialties related to the treatment of obesity and its complications: diabetologists, endocrinologists, cardiologists, and a bariatric surgeon, reviewed a number of European and American guidelines published mostly in 2019–2021,[8-17] and summarized the principles of obesity management to provide a practical guidance considering the impact that increased adiposity poses to health. The work was done without commercial support of any kind. In our opinion, obesity should not only be considered a disease requiring treatment in an individual patient, but also a disorder (civilization disease) requiring preventive measures at the population level. As awareness of the risks associated with the climate change grows, attention must be paid to the impact of food overprocessing and its nutritional deprivation on both health and the environment. The actions that need to be taken now to protect human health are consistent with the actions necessary to protect the environment and the climate—and they go beyond the health care systems.

Overnutrition conundrum Obesity results from a long-term energy imbalance between energy consumption and energy expenditure, which creates chronic oversupply of energy resulting in excess body fat storage. In the majority of cases (up to 90%), the obesity is primary, that is, it results from overnutrition, and not from other causes. There are, however, numerous behavioral, biological, genetic, environmental, psychogenic, and social factors known to increase the risk, along with the expansion of global trade and its impact on nutrition, and a prevalent sedentary lifestyle. The human body perfectly stores and saves the energy and obesity develops according to a simple biological rule that every calorie ingested, which is not immediately used for energy production, is rapidly stored in the form of fat to conserve energy. Obesity as a disease should not be viewed as a result of a lack of willpower but as a failure of homeostatic mechanisms regulating appetite, energy intake, and energy expenditure, as they become inefficient with increased adiposity. This homeostatic system depends on the complex interplay of several areas of the brain, neurohormonal function of the gastrointestinal tract, and hormone secretion by adipose tissue, and its failure may explain why spontaneous remission does not occur in obesity. Over the last decades changing environment and industrial food production have greatly increased processed food choices and changed human eating habits, both in terms of food quality and quantity. WHO in its most recent recommendations issued before the 2021 United Nations Climate Change Conference pointed out that current food systems, particularly industrial production methods, are driving global trends toward malnutrition in all its forms, including obesity and climate damaging environmental impacts.[18] The excessive consumption of cheaper processed foods may result from a lower socioeconomic status, including poorer access to knowledge and medical care, and limited financial resources. Stress and sleep deprivation, global increase in shift work demands, psychogenic factors including low self-esteem, self-perception disorders, emotional eating, and mental conditions, that is, atypical depression, anxiety, compulsive eating, and night eating syndromes can contribute to the development of obesity. Multiple causes of obesity must be considered in the efforts of its prevention.

Key messages

- Excessive consumption of high-energy foods and insufficient physical activity are major behavioral risk factors for positive energy balance and subsequent development of obesity, along with other numerous biological, environmental, psychogenic, and social factors known to increase this risk.
- A failure of homeostatic mechanisms regulating appetite, energy intake, and energy expenditure, which become inefficient with increased adiposity, may explain why spontaneous remission does not occur in obesity.

Links between food, obesity and the environment The global food production systems are currently the single largest driver of nature and

biodiversity loss, responsible for about one quarter of global greenhouse gas emissions.[18] Industrial food production and its excessive availability and consumption create obesogenic environment that impacts human health. The other side of excessive food consumption is food waste that significantly affects the environment.[19] According to the United Nations Environment Programme Food Waste Index 2021, around 931 million tons of food waste were generated in 2019. Of those, 61% came from households, and estimates suggest that 8%–10% of global greenhouse gas emissions are associated with food that is not consumed.[20] Wasting food is not only an ethical and economic issue but it also depletes the environment of its limited natural resources.[21] The problem of food waste is also directly related to obesity. The metabolic food waste refers to the resources lost and the unnecessary ecological cost of an excessive consumption of food leading to obesity.[22] The annual global metabolic food waste associated with overweight and obesity was estimated at 140.7 million tons, and it was the highest in developed countries and driven by animal product consumption.[22] The annual amount of metabolic food waste in Sweden was 480–710 kilotons, and the estimated greenhouse gas emissions related to that food waste accounted for approximately 2% of the total and 10% of the food-related climate impact in Sweden.[23] From this broader perspective, there is an unsustainable environmental cost and ecological impact of obesity due to excessive food consumption and metabolic waste.[22] Dietary patterns consistent with individual energy and nutrient requirements along with reduced consumption of animal products could significantly reduce the environmental footprint associated with obesity.

Key messages

- Obesogenic environment, industrial food production, and high consumption followed by food waste significantly impact human health and the planet's natural resources.
- Food, environment, and health are interrelated and should all be considered in the search for solutions to obesity.

Who is there to prevent obesity? Not only the patients and their health choices but also the obesogenic environment must be addressed and modified to improve health. Effective prevention of obesity would reduce the risk of many comorbidities, so it deserves the attention of health care providers, but also of communities, families and the governments, to strive for changes in the living and working environments to make them less conducive to obesity.[24]

WHO recommends promotion of sustainable and resilient food production, more affordable, nutritious diets, sustainable healthy urban designs with improved access to green public space, and priority for walking, cycling, and public transport.[18] To date, only a few countries have developed dietary guidelines that promote environmentally sustainable diets that ensure food security, improve diet quality and human health, and respond to climate change challenges; this may be hindered by the influence of large commercial interests in the public policy development process.[24] Food safety and labelling should be reassessed to better inform consumers. Raising awareness among the general public and engaging people to make healthy choices could become a meaningful factor in obesity prevention.

Key messages

- Preventing obesity is a global issue that should become a priority to governments, communities, and individual consumers.
- There is a need to increase public awareness of the impact that nutrition has on both health and the environment.

How to diagnose obesity and its complications? The primary care physicians to whom patients report most frequently play the greatest role in diagnosing overweight (pre-obesity) and obesity. To assess abnormal body weight in the adult population, the WHO recommends the use of BMI, calculated as a quotient of body weight (in kilograms) and the square of the individual's height (in meters). It is a quick, simple, and reproducible way of diagnosing body mass abnormalities in adults,[1] and its ranges are based on the effect that excessive body fat has on disease and death risk. The interpretation of BMI does not depend on either age (in adults) or sex, but its usefulness as an indicator of metabolic risk is limited, unless the values are very high, because it does not take into account body fat distribution and the ratio of muscle and fat tissue. A simplified method of assessing central obesity is the measurement of waist circumference. Using the results of the WHO report, the cardiometabolic risk can be estimated by taking into account both BMI and waist circumference measurements[25] (TABLE 1). A meta-analysis concluded that both BMI and waist circumference are similarly, strongly, and continuously associated with T2D and cardiovascular diseases.[26] In fact, BMI and waist circumference can be measured by patients themselves on a regular basis, thus allowing for monitoring their progress — or its lack — in obesity treatment. Moreover, waist-to-hip ratio was shown to predict cardiovascular mortality independently of BMI.[16]

Each patient diagnosed with obesity should be evaluated for obesity-related comorbidities and cardiovascular risk. Patient general assessment should include a history of weight changes, motivation level to make lifestyle changes, and the presence of comorbidities. Laboratory tests should be performed at the beginning of the clinical evaluation of each patient with obesity — they are an objective complement to the subjective and physical examination. Blood pressure (BP) measurement, fasting plasma lipid and glucose levels, family history and smoking history are needed to assess metabolic and cardiovascular risk,[9] blood alanine aminotransferase activity as a screening

TABLE 1 WHO classification of body mass index and waist circumference association with metabolic and cardiovascular risk factors and suggested treatment

BMI (kg/m²)[a]	Nutritional status[25]	Association with cardiometabolic risk factors[b25]	Number of comorbidities[c]	Suggested treatments of obesity[11,12]
25.0–29.9	Overweight (pre-obesity)	Increased risk (or high risk if waist ≥102 cm in men or ≥88 cm in women)	0	• Healthy lifestyle is indicated
			≥1	• Healthy lifestyle is indicated • Pharmacotherapy may be considered if BMI ≥27 kg/m²
30.0–34.9	Grade I obesity	High risk (or very high risk if waist ≥102 cm in men or ≥88 cm in women)	0	• Healthy lifestyle is indicated • Pharmacotherapy may be considered
			≥1[d]	• Healthy lifestyle is indicated • Pharmacotherapy should be considered[e]
35.0–39.9	Grade II obesity	Very high risk	0	• Healthy lifestyle is indicated • Pharmacotherapy should be considered[e]
			≥1	• Healthy lifestyle is indicated • Pharmacotherapy should be considered[e] • Bariatric surgery should be considered[e]
≥40.0	Grade III (morbid) obesity	Extremely high risk[f]	NA	• Healthy lifestyle is indicated • Pharmacotherapy should be considered[e] • Bariatric surgery should be considered[e]

a Asians have lower values: normal BMI is 18.0–22.9 kg/m², overweight is defined as BMI 23.0–24.9 kg/m² and obesity as BMI ≥25 kg/m².

b The risk ranks shown above were proposed in the WHO document[25] and refer to the risk of having or developing cardiometabolic risk factors (ie, disease risk, not disease outcome). They reflect scientific evidence that increased waist circumference is independently associated with morbidity but does not refer to the risk of cardiovascular death, which should be calculated using dedicated risk assessment tools such as the SCORE system, Framingham risk score, or Pooled cohort equations, and does not take into account BMI or waist circumference values.

c Associated with overweight or obesity, that is, pre-diabetes or T2D, hypertension, dyslipidemia, hepatic steatosis, obstructive sleep apnea, cardiovascular disease

d According to the US guidelines bariatric surgery may be considered as an option to treat T2D in adults with grade I obesity who do not achieve durable weight loss and improvement in comorbidities (including hyperglycemia) with nonsurgical methods.[12,17]

e Treatment may be indicated for selected motivated patients.

f No waist circumference measurements necessary

Abbreviations: BMI, body mass index; NA, not applicable; T2D, type 2 diabetes, WHO, World Health Organization

test for non alcoholic steatohepatitis,[11] and thyroid stimulating hormone as a screening test for thyroid function are also recommended in all patients with obesity.[15]

Key messages

- BMI should be calculated in all patients presenting to their primary care physician to help effectively diagnose overweight and obesity (TABLE 1), evaluate cardio-metabolic risk, and take care of obesity-related comorbidities.
- Abdominal obesity is associated with higher cardiovascular risk regardless of BMI.
- Waist circumference should be measured in patients with a BMI of 25–35 kg/m², and 2 action levels are indicated: (i) weight reduction should be encouraged in men with waist circumference 102 cm or greater and in women with values equal or above 88 cm, and (ii) if waist circumference values are lower but equal or above 94 cm in men 80 cm in women, weight gain should be prevented.

Patients with specific comorbidities and conditions **Type 2 diabetes** The relationships between excessive adiposity (overweight and obesity), insulin resistance, and finally impaired β-cell function leading to T2D have long been known. Since 2008, with the publication of 3 landmark studies on T2D: ACCORD (the Action to Control Cardiovascular Risk in Diabetes),[27] ADVANCE (the Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation),[28] and VADT (the Veterans Affairs Diabetes Trial),[29] there has been evidence that tight glycemic control alone does not prevent or reverse diabetic macrovascular complications and does not reduce cardiovascular morbidity and the risk of death. Since 2018, following the series of cardiovascular outcomes trials starting with the EMPA-REG OUTCOME (Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients)[30] and the LEADER (Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results),[31] studies on T2D treatment have also primarily focused on cardiovascular and renal outcomes, and not only on glycemic control.[32] Studies demonstrated that some newer glucose-lowering agents (GLP-1 receptor agonists [GLP-1 RAs] and sodium-glucose co-transporter-2 [SGLT2] inhibitors), when added to a standard care, can further lower the risk of

myocardial infarction, heart failure, stroke, kidney failure (slow down progression of chronic kidney disease), and cardiovascular death, and that the effect is not dependent on the level of glycemic control. In T2D and obesity, GLP-1 RA should be used as a preferred glucose-lowering treatment, whereas in patients with T2D, obesity and heart failure in cardiovascular disease SGLT2 inhibitors should be prioritized.[33,34]

However, despite therapeutic advances and increasing costs to the health care systems, T2D remains one of the leading causes of morbidity, disability, and premature death worldwide. Treating obesity to achieve sustained weight loss of 15% or higher was shown to significantly improve T2D progression.[35,36] With the treatments or interventions available to successfully treat obesity and correct pathophysiological pathways to insulin resistance and T2D we could be able to improve the disease outcomes, so there is an interest in changing the approach for newly diagnosed patients to include weight loss recommendation.[37] Optimal future treatment guidelines should include substantial, sustained weight loss as one of the treatment targets for patients with T2D.

Hypertension Overweight and obesity are among the main causes of hypertension. In addition, obesity is one of the leading causes of treatment-resistant hypertension. Weight loss not only reduces the risk of hypertension, but it also enables target BP values to be achieved in hypertensive individuals. In people with mild hypertension, who achieve considerable weight reduction, antihypertensive treatment is no longer necessary, and in people with more severe forms of hypertension, the dosage or number of hypotensive drugs may be reduced. Weight loss achieved through lifestyle modification translates into a significant reduction in systolic BP of 1.05 mm Hg (95% CI, 0.66–1.43) and diastolic BP of 0.92 mm Hg (95% CI, 0.55–1.28) for each kilogram lost.[38] Moreover, weight loss achieved after bariatric surgery in hypertensive patients results in a significant reduction in BP.[39] Additionally, a meta-analysis of 18 studies showed that liraglutide reduced systolic BP by 3.18 mm Hg (95% CI, 2.05–4.32), with no significant effect on diastolic BP, however, with concomitant increase in heart rate by 2 to 3 beats per minute.[40] Similar results were obtained for oral semaglutide, which produced a 3.16 mm Hg (95% CI, 1.77–4.56) reduction in systolic BP, with no significant effect on diastolic pressure.[41] The results of a meta-analysis of 27 studies indicated that orlistat in comparison with placebo is associated with a 1.15 mm Hg (95% CI, 0.19–2.11) reduction in systolic blood pressure and a 1.07 mm Hg (95% CI, 0.45–1.69) reduction in diastolic blood pressure.[42] In contrast, the use of a combination of naltrexone and bupropion did not reduce BP (meta-analysis of 4 studies),[43] and in fact this drug combination is contraindicated in patients with uncontrolled hypertension.

Dyslipidemia Treatment of obesity, regardless of the method used, is associated with improvements in the lipid profile. A recently published systematic review and meta-analysis of 73 randomized trials evaluating obesity treatment methods found that in adults with overweight or obesity, weight reduction through lifestyle changes, pharmacological or surgical therapy was associated with significant improvements in total cholesterol (TC), triglycerides, high-density lipoprotein cholesterol and, to a moderate extent, low-density lipoprotein cholesterol (LDL-C) concentrations.[44] Of note, pharmacological treatment of obesity compared with lifestyle resulted in over 30% greater reductions in LDL-C concentrations per kg of weight loss, respectively: –1.67 mg/dl (95% CI, –2.28 to –1.06) vs –1.28 mg/dl (95% CI, –2.19 to –0.37 mg/dl).[43] GLP-1 RAs used for obesity treatment not only affect plasma lipid concentrations but also beneficially modify their metabolism within the vessel wall and atherosclerotic plaque. GLP-1 RAs (including liraglutide) were shown to reduce the production of oxygen free radicals in the vessel wall, which prevents the oxidation of LDL-C and reduces the activation of inflammatory cells in the atherosclerotic plaque. This direct anti atherosclerotic effect appears to contribute to a reduction in the incidence of macrovascular complications (primarily stroke) in patients with T2D.[45] Another systematic review with meta-analysis including 121 randomized trials on the effects of 14 the most popular dietary programs on lipid profile revealed that the most pronounced and longest lasting reductions in LDL-C were achieved by the individuals following the Mediterranean diet.[46]

COVID-19 The course of COVID-19 varies from asymptomatic infection to a critical condition leading to death. Since the COVID-19 pandemic began, numerous studies have shown that many of the sickest patients were those with obesity. Another meta-analysis demonstrated that individuals with obesity were at a higher risk of testing positive for COVID-19 (>46% higher), for hospitalization (113% higher), for intensive care unit admission (74% higher), and for mortality (48% increase in deaths).[47] More recent studies and systematic reviews proved that the higher the degree of obesity, the higher the risk of almost all of the above events, including the risk for admission to an intensive care unit, invasive mechanical ventilation, and increased in-hospital mortality.[48,49]

Urinary incontinence Central and general obesity are key factors associated with urinary incontinence in both men and women, and with overactive bladder syndrome in women but not in men.[50] Overweight and obesity are strong predictors of the occurrence of stress urinary incontinence in women, who are more likely to suffer from other conditions resulting in pelvic floor

weakening. However, while these patients should be offered treatment options to reduce excess weight, this should not deter general practitioners from referring them to secondary care and providing with a full choice of treatment for urinary incontinence.[51]

Infertility and pregnancy in obesity Women with obesity show poorer reproductive outcomes regardless of the mode of conception, and higher BMI is associated with poorer fertility prognosis.[52] Polycystic ovary syndrome (PCOS) is one of the leading causes of infertility, being the most common endocrine disorder in women of reproductive age, commonly associated with overweight or obesity.[53]

In pregnant women with obesity, a systematic review demonstrated an increased risk of gestational diabetes, preeclampsia, gestational hypertension, depression, instrumental and caesarean birth, and surgical site infection than in women of healthy weight. Maternal obesity was also linked to greater risk of preterm birth, large-for-gestational-age infants, fetal defects, congenital anomalies, and perinatal death.[54]

While most studies compare pregnancy complications and neonatal outcomes in bariatric patients with obese control groups matched for preoperational BMI, they usually show the positive influence of bariatric procedures, as obesity is an independent risk factor of many comorbidities. A comparison of women after bariatric procedures with a group of controls matched for BMI at the beginning of pregnancy showed that bariatric patients have a decreased risk of pregnancy comorbidities and large-for-gestational-age infants even when compared with the non obese population.[55] Nevertheless, pregnancy in a woman after bariatric surgery should be considered a high-risk pregnancy and should be cared for by a multidisciplinary team with appropriate micronutrient and vitamin supplementation.[56]

Key messages

- Excessive adiposity is the main pathophysiological cause of the leading cardiovascular risk factors: T2D, hypertension, and dyslipidemia.
- Despite the therapeutic progress and growing costs to health care systems, T2D and hypertension remain the leading causes of cardiovascular morbidity, disability, and premature death worldwide.
- With the treatments or interventions available to successfully reduce excessive adiposity, we could be able to improve metabolic and cardiovascular outcomes.
- Obesity is recognized as a significant risk factor for COVID-19 severity and poor outcomes in hospitalized patients.
- Women with obesity have an increased risk of infertility, and pregnancy can be associated with numerous metabolic and obstetric complications.

Why should obesity be treated and what are the treatment goals Numerous studies have demonstrated health improvements with weight reduction (TABLE 2). A recent statement of the American Heart Association points out that obesity leads to the development of cardiovascular disease and cardiovascular disease mortality independently of other cardiovascular risk factors.[16] Obesity present at the time of diagnosis of atherosclerotic cardiovascular disease, heart failure, arrhythmias, and atrial fibrillation clearly impacts clinical outcomes and increases the risk for sudden cardiac death.[16] The primary goal of obesity treatment from a clinical perspective is to prevent or slow down the progression of the diseases associated with obesity, with T2D among them, reduce metabolic and cardiovascular risk, and improve the quality of life by achieving adequate and stable weight reduction.[12]

Weight loss goals should be set individually according to patient's health needs and in consultation with the patient to make them realistic. Important determinants of the outcome are the level of weight loss achieved, its sustainability, and the stage of the disease at which the intervention was delivered.

Key messages

- The goal of obesity treatment should be individually determined weight loss to reduce metabolic and cardiovascular risk and obesity–related comorbidities (TABLE 2), as well as to improve the quality of life and extend disability-free life.
- In patients with high cardiovascular risk, including patients with T2D, a minimal loss of 5%–15% of bodyweight should be encouraged.
- Greater weight loss (≥15%) can have a favorable effect on metabolic and cardiovascular risk and is desirable, but usually requires additional (pharmacological or surgical) treatment.

How can obesity be treated: general remarks All patients with obesity should be counselled on the importance and principles of a diet, the benefits of regular exercise, and should agree on a realistic weight loss goal that initially should be at least 5% of a baseline to improve the course of comorbidities (TABLE 2). Restricted food intake, increased physical activity, and weight self-monitoring should be encouraged. Where possible, psychosocial or emotional factors contributing to the development of obesity should be recognized and properly addressed, along with lifestyle modifications. Medications known to promote weight gain (eg, sulfonylureas, corticosteroids, tricyclic antidepressants, lithium, antipsychotics, anticonvulsants, some β-blockers, and others) should be avoided, discontinued or replaced if possible. Antipsychotics with a low potential for causing metabolic disorders should be preferred in patients with increased metabolic risk (a comparative meta-analysis of 32 antipsychotics found that drugs with the lowest risk of weight gain are ziprasidone, lurasidone, aripiprazole, haloperidol, brexpiprazole, and cariprazine).[62] One study showed that metformin was effective and contributed to weight loss, when started earlier in the course of antipsychotic treatment.[63] In the case of secondary obesity (eg, hypothyroidism, Cushing's syndrome, hypogonadism, hypothalamic obesity, rare

TABLE 2 Expected health benefits associated with weight loss (expressed as a percentage of baseline) in patients with obesity

Expected improvement of obesity-related disorders and diseases	Percentage of body weight loss needed for health improvement[a]			References
	5%–10%	10%–15%	>15%	
Prevention of T2D	Yes	Yes	Yes	35,36,59,61
Remission of T2D	No	?	Yes	59,61
Significant improvement of atherogenic dyslipidemia	?	Yes	Yes	58,59,61
Significant improvement or remission of hypertension	?	Yes	Yes	58,59
Reduction of steatosis in NAFLD	Yes	Yes	Yes	57,58,61
Reduction of inflammation and inhibition of fibrosis in NASH	No	?	?	57,58,61
Improved fertility and reduction of symptoms in PCOS	?	Yes	Yes	58,61
Improvement or resolution of hypogonadism in men	?	Yes	Yes	58,61
Reduction in the severity of musculoskeletal complaints	?	Yes	Yes	58,61
Significant improvement in symptoms of obstructive sleep apnea	?	Yes	Yes	58,61
Significant improvement in symptoms of gastroesophageal reflux	No	Yes	Yes	58
Significant improvement in symptoms of stress urinary incontinence	?	Yes	Yes	58,61
Reduction in the risk of heart failure with reduced ejection fraction	No	No	Yes	59,60
Reduction in cardiovascular mortality	No	No	Yes	59,61

a The final result also depends on additional factors, such as duration and severity of disease (eg, T2D, hypertension), age, genetics, etc.

No - no effect proven

Yes - improvement, remission, or resolution

? - possible but uncertain improvement

Abbreviations: NAFLD, non alcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis, PCOS, polycystic ovary syndrome, other see **TABLE 1**

genetic syndromes, and others) appropriate management is necessary.[15]

Important elements to provide appropriate care for patients with obesity include:

1) measuring body weight (calculating BMI) and waist circumference (if BMI <35 kg/m^2) at each visit;
2) proper communication with the person suffering from obesity and avoiding stigma or discrimination;
3) tests to rule out the secondary obesity;
4) avoiding medications that promote weight gain;
5) screening for obesity-related disorders and diseases;
6) interventions for health-promoting lifestyle changes, motivation, and monitoring of the treatment outcomes;
7) offering pharmacological treatment options for obesity to individuals who meet the eligibility criteria and are likely to benefit from it;
8) offering bariatric surgery option to patients who meet the eligibility criteria for such a therapy and referral to metabolic surgery centers;
9) preventing of weight regain in patients in whom obesity treatment was successful;
10) treating of comorbidities or disorders that are cardiovascular risk factors, including hypertension, dyslipidemia and hyperglycemia (prediabetes and T2D), and obstructive sleep apnea. These treatments should be prioritized and prescribed at the time of diagnosis; they should be continued independently of the efforts to reduce body weight.

Nutrition The energy-restricted diet recommended in obese patients should on average result in a deficit of 500–800 kcal/day. This usually does not require elimination of any nutrients. An individual approach to each patient is important, taking into account that 1 kg of body fat = 8000 kcal. A loss of 0.5–1 kg/week for the first 3–6 months of a diet is considered a safe rate of weight loss, although the anticipated rate should depend on age, gender, initial body weight, and individual response. It is important to discuss with the patient the desired and realistic weight loss goals and agree on health promoting lifestyle changes. Optimally, patients could be assisted by a dietician who could develop a diet plan tailored to their needs. Patients with pre-diabetes or T2D need training in assessing dietary carbohydrates and recognizing low glycemic index foods.

Many diets have been developed for weight reduction but not all are safe, and the long-term effectiveness of some has not been established. It is not so much the choice of a specific calorie-restricted diet but one that the patient will fully accept and follow with a few simple principles (**TABLE 3**). Diets and behavioral changes that create an energy deficit, regardless of macronutrient composition, will result in weight loss. There is sufficient scientific evidence to recommend for example the Mediterranean, Dietary

TABLE 3 Basic principles of a healthy diet

Reduced intake of	• sugar-containing products (no sweetened beverages) • saturated fat • sodium • refined grains • starchy vegetables
Increased intake of	• vegetables • legumes • whole grains • beneficial fats (omega-3 fatty acids)
Predefined number and size of meals per day	• 3 meals and 2 low energy snacks • or 3 meals and no snacks

Approaches to Stop Hypertension, and Nordic (Baltic) diets.[13] Of note, diets richer in plant foods and with lower amounts of animal foods are associated with a lower risk of cardiovascular morbidity and mortality in the general population.[64] Food is the most powerful factor in optimizing human health and environmental sustainability.[65] According to the EAT-Lancet Commission, healthy diets have an optimal caloric intake and consist largely of a diversity of plant-based foods, low amounts of animal foods, contain unsaturated rather than saturated fats, and limited amounts of refined grains, highly processed foods, and added sugars. The new term "planetary health diet" refers to a flexitarian diet proposed by the EAT-Lancet commission to highlight the critical role that diets play in linking human health and environmental sustainability.[65]

Key messages

• The energy-restricted diet to treat obesity should lead to a deficit of 500–800 kcal/day.

• The aims of dietary management are to reduce body weight, waist circumference, improve or normalize BP and blood glucose, and lipid levels.

• In patients at increased cardiovascular risk diets with proven beneficial effects on cardiovascular risk are recommended.

Physical activity At least 150–420 minutes of physical activity per week on at least 3 days (equivalent to 30–60 min of activity per day),[11] or if tolerable from 75 to 150 min a week of vigorous intensity aerobic physical activity is recommended. The frequency, intensity, and duration of the activity should be tailored to the individual's abilities, and should gradually increase over time, if possible. In fact, the WHO guidelines (2020) provide detailed information for different age groups and specific populational groups on how much physical activity is needed to maintain health.[66] Physical activity recommendations for people with obesity should be individualized for better effect and include preferred activities (such as sports, active recreation, or dance), and therefore both quantitative and qualitative aspects of physical activity should be considered. A combination of aerobic and resistance (strength) training was shown to have a greater impact on overall health than aerobic or resistance training alone, but any form of physical activity is beneficial and should be encouraged. Using mobile apps that offer assistance in maintaining a healthy lifestyle was confirmed to improve fitness and weight loss outcomes. Moderate physical activity, implemented together with an appropriate diet, allows for better results in terms of weight loss, improved metabolic variables (reducing insulin resistance), and functioning of the cardiovascular, respiratory and musculoskeletal systems, as well as of mental and sexual health. There is evidence that physical activity is associated with lower risk of all-cause mortality and cardiovascular disease mortality.[66] In older people, physical activity improves mobility and coordination, reduces the risk of falls, and prevents a loss of muscle mass.

Key messages

• Daily physical activity and reduced sedentary time are recommended to every patient with obesity. Seating should be interrupted after 30 min and a short period of time (even a few minutes) should be spent walking or standing.

• Optimally 150–420 min per week (≥30–60 min/day) or more of moderate-intensity physical activity, either aerobic or resistance, is recommended, and physical activity guidance for people with obesity should be individualized.

Therapeutic education and psychological counselling

Behavioral intervention to maintain control over the quantity and quality of food consumed and to establish healthy habits facilitates adherence to dietary recommendations and a physical activity plan. All intervention strategies in obesity management depend on and begin with behavioral changes—it is psychological and behavioral intervention that provides information on how to effectively implement and maintain the desired changes.[67] Complex psychological interventions combining behavioral modifications (goal setting, self-monitoring, problem solving) could be used.[13] Psychotherapy is needed in the treatment of emotional eating, compulsive eating syndrome, and night eating syndrome. Proper communication with the patient and avoidance of stigma are helpful in therapeutic education. Clear information about possible treatment options and shared decision-making can increase patients' motivation and contribute to conscientious adherence to treatment. An effective strategy of lifestyle modification is to involve family or friends or colleagues from work. Otherwise, without changes in the immediate environment, patients find it very difficult to sustainably modify their behavior.

Key messages

• The effectiveness of all lifestyle intervention strategies, including healthy eating and physical activity, depends on behavioral changes.

• Lifestyle modification can be difficult and is only moderately effective, but even small changes are important and can improve health outcomes.

Pharmacological treatments for obesity Generally, the medications approved by the European Medicines Agency (EMA) for the management of obesity (listed below) are intended for individuals with BMI of 30 kg/m^2 or over or 27 to 30 kg/m^2, if additionally at least 1 obesity-related disease or risk factor (eg, T2D, dyslipidemia, hypertension) is present. The choice of pharmacological treatment that is initially proposed to patients is determined mainly by the severity of obesity, its complications, and the patient's willingness to make healthy lifestyle changes. Safety and efficacy of the therapy should be considered in the context of the patient's comorbidities.

The aim of pharmacological treatment of obesity is to help patients adhere more effectively to dietary recommendations and develop health-promoting lifestyle changes that should result in substantial weight loss and reduction of metabolic and cardiovascular risk. A meta-analysis showed that pharmacological treatment of obesity significantly reduced weight, BP, glycated hemoglobin (HbA_{1c}) (improved glycemic control), and cardiovascular mortality.[68]

There are no uniform criteria for how long to treat obesity with lifestyle changes alone and when to start pharmacological treatment, but the presence of metabolic and cardiovascular risk, expected health benefits and economic considerations should be taken into account. Typically, treatment should be considered if more than 5% weight reduction is not achieved despite 3–6 months of intensive lifestyle efforts.

A fixed dose formulation of naltrexone and bupropion A therapy with naltrexone and bupropion combines 2 centrally acting medicines approved for use in other indications. Bupropion is recommended for the treatment of nicotine dependence and in patients with depression. It is a non selective dopamine and noradrenaline reuptake inhibitor and an acetylcholinergic nicotinic receptor antagonist, while naltrexone is an opioid receptor antagonist used in the treatment of alcohol and opiate dependence. The combination of naltrexone and bupropion may regulate the activity in the dopamine reward system in the brain and therefore help control food cravings and also overeating behaviors. There are many possible drug interactions that should be ruled out, and this drug combination is contraindicated in patients with uncontrolled hypertension, history of seizures, bulimia or anorexia nervosa in the past, chronic opioid use, severe hepatic impairment, end-stage renal disease, and pregnancy.

In a meta-analysis of 2 randomized trials (n = 2264), bupropion combined with naltrexone decreased weight by 5.0 (95% CI, 4.4–5.5) kg as compared with placebo.[69] In a more recent meta-analysis of 4 randomized trials (n = 4536), naltrexone and bupropion combination was related to a 2.53 (95% CI, 1.85–3.21) kg reduction of baseline body weight as compared with placebo.[70] Another meta-analysis of 4 trials (n = 3239) provided weight reduction by 4.4 (95% CI, 3.7–5.1) kg.[71]

Glucagon-like peptide-1 receptor agonists Liraglutide (daily 3.0 mg subcutaneous injections) is the first GLP-1 RA registered for obesity treatment. The drug was developed and is used to treat T2D, but at a lower registered dose of 1.8 mg/day. GLP-1 is an incretin hormone secreted by the ileum in response to a meal. It increases the secretion of insulin from pancreatic β-cells in response to glucose and stimulates the satiety center. Liraglutide at a dose of 3 mg daily was associated with weight loss and also reduced waist circumference, systolic and diastolic BP, and improvement in lipid panel among overweight and obese patients with and without T2D. Classic adverse effects include nausea and vomiting, especially at the beginning of treatment, but there are no significant drug interactions. Main contraindications are a history of pancreatitis, severe hepatic impairment, end-stage renal disease, and pregnancy.

In a meta-analysis of 4 randomized trials (n = 4978), liraglutide (3 mg daily) decreased weight by 5.2 (95% CI, 4.3–6.2) kg as compared with placebo.[71] Another meta-analysis of 9 randomized trials showed a reduction in weight of 4.49 (95% CI, 3.72–5.26) kg,[72] whereas the most recent and the biggest meta-analysis so far (31 randomized studies, 8060 participants) showed the difference of 4.2 (95% CI, 3.6–4.8) kg.[73]

In June 2021, the Food and Drug Administration (FDA) approved another GLP-1 RA—semaglutide as weekly 2.4 mg subcutaneous injections—for the treatment of obesity based on the STEP (Effect and Safety of Semaglutide 2.4 mg Once-weekly in Subjects With Overweight or Obesity and Type 2 Diabetes) trial results. Obesity treatment with semaglutide after 68 weeks was associated with placebo-subtracted weight loss of 6.2% and significant HbA_{1c} reduction of 1.6%, reaching goal HbA_{1c} equal or below 6.5% (≤48 mmol/mol) in 68% of participants of baseline 8.1% (65 mmol/mol), thus confirming that greater weight loss improves glycemic control.[74] In people with obesity but no T2D, weight loss at week 68 was even greater with placebo-subtracted mean weight loss of 12.4% (95% CI, −13.4 to −11.5; $P < 0.001$), and of note much more patients in the semaglutide group than in the placebo group achieved a significant therapeutic goal (TABLE 2) of body weight reduction of at least 15% (50.5% vs 4.9%).[75]

Although there is evidence of some weight loss in patients treated with other GLP-1 RAs,[76] new concepts of drug combinations for obesity that are already under investigation and include combinations of 2 [GIP and GLP-1 RA] or 3 [glucagon + GIP + GLP-1 RA] incretin hormones are awaited with interest. While other pathways of feeding regulation control are also investigated, as of today, incretin family hormones offer the greatest hope for effective pharmacotherapy of obesity.

Orlistat Orlistat is a potent and selective inhibitor of gastrointestinal and pancreatic lipase, and therefore it reduces fat absorption in the intestine, which results in weight loss. Absorption of fat-soluble vitamins may be impaired during treatment and requires supplementation, and absorption of other medications may also be affected. Orlistat is the oldest of the currently used drugs registered for the treatment of obesity and it is generally considered a third-line drug in the treatment of obesity. It is not preferred by patients and its long-term adherence is very low due to unpleasant malabsorption-related gastrointestinal side effects, such as flatulence, oily stool, diarrhea, and stool incontinence.[10,11]

In a meta-analysis of 14 randomized trials (n = 3391), orlistat decreased weight by 2.6 kg (95% CI, 2.3–2.9), as compared with placebo.[69] Another meta-analysis of 33 randomized studies (n = 9732) showed a reduction in weight of 2.1 kg (95% CI, 1.7–2.5), while a more recent analysis of 17 trials showed a difference of 3.1 kg (95% CI, 2.4–3.8).[40,71]

Choosing a medication and monitoring the treatment course In patients with obesity-related cardiovascular or metabolic risk factors, drugs that effectively reduce the risk of cardiovascular events should always be preferred. In patients with T2D, coexisting cardiovascular disease or chronic kidney disease, as indicated in the guidelines for the management of these disorders, priority should be given to medications with proven risk-reducing effects on cardiovascular events and life extension.[77]

When choosing a medication for the treatment of obesity, it is important to consider the expected weight loss effect, but at the same time to aim for a therapeutic effect (TABLE 2)—a reduction in metabolic and cardiovascular risk. A recent systematic review with network meta-analysis summarized the evidence for the benefits and harms of weight lowering drugs and found that in adults with overweight and obesity phentermine-topiramate (registered by the FDA but not EMA) and GLP-1 RAs (registered by both FDA and EMA) proved to be the most successful in reducing weight; of the GLP-1 RAs, semaglutide might be the most effective. In a post-hoc analysis, semaglutide showed substantially larger benefits than other drugs for both likelihood of weight loss of 5% or more (odds ratio [OR], 9.82; 95% CI, 7.09–13.61), and percentage bodyweight change (mean difference, –11.41; 95% CI, –12.54 to –10.27), with a similar risk of adverse events as other drugs.[78] Increased adverse events leading to drug discontinuation occurred for treatments with naltrexone-bupropion (OR, 2.69; 95% CI, 2.11–3.43), phentermine-topiramate (OR, 2.40; 95% CI, 1.69–3.42), GLP-1 RAs (OR, 2.17; 95% CI, 1.71–2.77), and orlistat (OR, 1.72; 95% CI, 1.44–2.05).[78]

In making a shared decision with the patient, individual patient's safety considerations and the cost of therapy must also be taken into account.

Indications for specific drugs:

- in patients with pre-diabetes, T2D, hypertension, cardiovascular disease, obstructive sleep apnea or PCOS[10,11] consider a GLP-1 RA (liraglutide 3 mg daily) as a first-line drug, naltrexone and bupropion combination as second-line drugs, and orlistat as a third-line treatment;
- in patients with psychogenic background of obesity (cravings) or depression and patients smoking tobacco products[10] consider naltrexone and bupropion combination as first-line drugs, a GLP-1 RA (liraglutide 3 mg daily) as a second-line drug, and orlistat as a third-line treatment.

The efficacy and safety of the treatment should be assessed at least monthly for the first 3 months. The decision on continuation or discontinuation of a drug should be made after at least 3 months of treatment based on the achieved weight loss that should exceed 5% of the initial value. In patients with no contraindications to treatment and good tolerability, greater weight loss and health benefits are achieved with therapy lasting 6 months or longer. In addition, maintenance of previously achieved weight loss may also be an indication for treatment if behavioral management is insufficient—with longer pharmacological treatment there is a better chance to consolidate new health-promoting habits. An important goal of the therapy is the long-term improvement in health status as a result of weight reduction. For this reason, more clinical evidence from long-term, appropriately designed studies is needed to determine the optimal duration of pharmacotherapy and distant benefits. Results from the recently published STEP 4 study of semaglutide indicated that high efficacy of the therapy ends when the drug is discontinued.[79]

Key messages

- Pharmacological treatment of obesity should be considered in patients with BMI of 30 kg/m^2 or higher or BMI of 27 kg/m^2 or higher who have obesity-related comorbidities, and it should be used in combination with diet and physical activity modification and behavioral intervention. Individual patients' safety considerations and the costs of the therapy should also be considered.
- In patients with obesity-related cardiovascular or metabolic risk factors, drugs that effectively reduce the risk of cardiovascular events should be prioritized.
- Pharmacotherapy may be also considered to maintain the weight loss achieved with behavioral intervention to prevent weight regain.
- Failure to achieve weight loss of at least 5% of baseline after 3 months of therapy is an indication for drug discontinuation.
- Obesity treatment does not end when the desired weight is achieved.

Surgical treatment of obesity Surgical treatment of obesity (bariatric surgery) is the most effective method for permanent weight loss. It allows

for achieving the desired and lasting results in the shortest time, but it is also the most burdensome method of obesity treatment. It effectively reduces the severity of obesity complications, including hyperlipidemia and T2D, and may even lead to their remission.[43]

Bariatric surgery is indicated when other methods of obesity treatment failed or when it is justified by coexisting diseases. It should be considered as a treatment option in patients with BMI of 40 kg/m^2 or higher and in patients with BMI of 35 kg/m^2 or higher who have obesity-related comorbidities, especially if T2D, hypertension and/or hyperlipidemia coexist, when sufficient weight reduction cannot be achieved with behavioral and pharmacological treatment. According to the US guidelines, bariatric surgery may also be considered as an option to treat T2D in adults with grade I obesity who do not achieve durable weight loss and improvement in comorbidities (including hyperglycemia) with nonsurgical methods.[12,17]

The evidence from observational studies suggests that surgical treatment of obesity is associated with a substantial decrease in fat mass in 1 month (–8.17 kg; 95% CI, –9.07 to –7.27), 3 months (–15.75 kg; 95% CI, –17.49 to –14.0), 6 months (–22.51 kg; 95% CI, –23.93 to –21.09), and 12 months (–29.69 kg; 95% CI, –31.3 to –28.09) after the surgery.[80] Unfortunately, considerable weight regain is observed in about 20%–25% of patients after reaching their nadir weight. Insufficient weight loss is considered the most common indication for revisional bariatric surgery.[81]

Numerous studies have demonstrated long-term sustainability of weight loss and successful remission and prevention of T2D, hypertension, and dyslipidemia for 10 years after bariatric surgery or even longer[35,82]; health improvements that can be expected with weight loss are presented in TABLE 2. In a large systematic review, bariatric surgery was associated with a reduced rate of all-cause mortality and cardiovascular mortality, and it was strongly associated with reduced incidence of T2D, hypertension, dyslipidemia, and ischemic heart disease.[83]

A recent meta-analysis of 5 observational studies including 49 211 participants showed a significantly lower risk of macrovascular complications in patients with T2D, who underwent bariatric surgery, as compared with those with nonsurgical interventions (0.50; 95% CI, 0.35–0.73).[84] These results were confirmed by a meta-analysis of 17 nonrandomized studies showing that patients with T2D, who underwent bariatric surgery, lived 9 years longer than patients not treated with bariatric surgery, and those without diabetes lived 5 years longer than untreated patients without diabetes. Different surgical techniques affected prognosis to a similar degree.[85] Patients undergoing bariatric surgery achieve decreased long-term mortality relative to weight-matched controls.[86] The lack of evidence from randomized clinical trials should be, however, underlined.

The most common current bariatric surgical procedures performed laparoscopically include sleeve gastrectomy (SG), Roux-en-Y gastric bypass, and omega-loop gastric bypass. Other procedures like bilio-pancreatic diversion, bilio-pancreatic diversion with duodenal switch, single anastomosis duodeno-ileal bypass, or gastric banding are performed rarely. The restrictive and/or malabsorptive nature of bariatric surgery may increase the risk for micronutrient deficiencies, including the risk of iron, vitamin B_{12}, folate, and copper deficiency, which can cause anemia, vitamin D deficiency (already exacerbated by obesity), and other problems.[87,88] Patients must be aware of dietary restrictions after the procedure and the need for long-term dietary supplementation. There are also possible complications related to the surgical treatment itself, including rare staple line leaks that lead to infection and gastroesophageal reflux disease that can become a substantial problem after SG.[89]

Bariatric surgery appears to be associated with a reduction in cancer incidence at a populational level,[90] and has the potential to decrease the risk for certain types of cancers (eg, demonstrated in postmenopausal breast and endometrial cancers), but it should not be routinely recommended as a cancer prevention strategy.[91] The controversial association between bariatric surgery and increased colon cancer is of concern. In a large cohort from 5 Nordic countries, the authors found a higher risk of colon cancer in bariatric surgery patients than in the general population that increased over time and exceeded the already elevated risk of obese individuals without surgery. The causes of this surprising increase are unknown but the authors speculate that changes in the gut microbiome and increased exposure to bile acids are responsible.[92] Another matter of concern is the finding of increased risk for cancer development in the esophagus and stomach after SG, which may be linked to chronic reflux, and further studies are needed to investigate the risk.[93]

Because of the potential for early and late complications after bariatric surgery and the chronic nature of obesity, long-term medical follow-up is necessary to improve treatment outcomes. Patients should receive long-term care, preferably in a metabolic surgery center or in a close collaboration with such a unit.

Key messages

- Bariatric surgery should be offered to patients with BMI of 40 kg/m^2 or higher or 35 kg/m^2 or higher with at least 1 obesity-related comorbid condition to reduce distant total mortality, achieve significantly greater weight reduction as compared with pharmacological treatment alone, desired control or remission of T2D, significantly improve patients' quality of life and enable long-term remission of obesity-related disorders, including hypertension, dyslipidemia, hepatic steatosis, and non alcoholic steatohepatitis.

• Bariatric patients require lifelong healthy lifestyle support and dietary supplementation, and monitoring for nutritional status according to appropriate guidelines.
• Bariatric surgery should be performed at experienced centers for gastrointestinal surgery, with multidisciplinary teams involved in long-term patient care.

Summary The prevalence of obesity and the burden of obesity-related comorbidities are significantly increasing worldwide. Excessive adiposity severely impacts health and is associated with increased metabolic and cardiovascular risk, and therefore it deserves more clinical attention. The assessment of patient's body weight should be a fundamental part of the care. Recognizing obesity as a disease being a starting point for the development of serious chronic noncommunicable diseases seems warranted in the light of research data.[37]

Health-promoting lifestyle changes are the primary treatment for obesity. The management of obesity is a logical first-line treatment of obesity-related chronic diseases, as the higher the adiposity and metabolic and cardiovascular risk, the stronger the indications for pharmacological and/or surgical treatment of obesity. With the growing evidence of treatment effectiveness, it should become a standard of care in the future, especially in T2D,[37] although further studies are needed to assess the durability of weight loss effects.

Despite the evident benefits, obesity management within the health care system—whether through pharmacotherapy or bariatric surgery—is only a symptomatic treatment, with all its limitations, and will not ultimately solve the problem of obesity. The important message, above all, is that available treatment options fail to correct the true drivers of the obesity pandemic. To this end, new solutions and efforts to prevent obesity in the populations are needed. Urban environment, widespread physical inactivity, access to processed foods, cultural and social conditions, stress and the association of a healthy diet with sacrifices are not conducive to weight loss. Industrial food production, high processed food consumption and food waste, have significant impacts on human health and on the environment, adding to the real threat of food insecurity due to the climate change.[94] One of the greatest challenges of modern civilization is parallel development and implementation of solutions to prevent obesity in populations on a global scale, while also protecting the climate and the environment.[20]

ARTICLE INFORMATION

CONFLICT OF INTEREST E.P.J. none declared; L.C. *grant/research support:* Bioton, Medicover Foundation, TEVA Pharmaceuticals, *lecture honoraria:* Abbott, Ascensia, Bayer, Boehringer Ingelheim, Eli Lilly, Krka, Medtronic, Merck, MSD, Mundipharma, Neuca, Novo Nordisk, Pfizer, Sanofi, Servier, *consultant/advisor:* Abbott, Ascensia, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Medtronic, Merck, MSD, Mundipharma, Neuca, Novo Nordisk, Polpharma; G.G. *lecture honoraria:* Astra Zeneca, Boehringer Ingelheim, Eli Lilly, Novo Nordisk, *clinical trials:* Astra Zeneca, Boehringer Ingelheim, Eli Lilly, Novo Nordisk; A.L. none declared; M.R. *lecture honoraria:* Bausch Health and Novo Nordisk; M.S. none declared; K.S. *lecture honoraria:* Eli Lilly, Novo Nordisk, Sanofi-Aventis, Servier, Boehringer-Ingelheim, Merck, Astra Zeneca; *clinical trials:* Novo Nordisk, Sanofi Aventis; E.SP. *lecture honoraria:* Bausch Health; M.W. *lecture honoraria:* Medtronic, Ethicon, Novo-Nordisk, Bausch, Pro.med; L.O. *lecture honoraria:* Novo Nordisk, Bausch Health Poland, Celon Pharma; P.J. *consultant/advisor*: Amgen, Boehringer Ingelheim, Novartis, Sanofi, Servier, *grant/research support*: Boehringer Ingelheim, Sanofi, *lecture honoraria*: Boehringer Ingelheim, Novartis, Servier, Teva, Zentiva.

HOW TO CITE Płaczkiewicz-Jankowska E, Czupryniak L, Gajos G, et al. Management of obesity in the times of climate change and COVID-19: an interdisciplinary expert consensus report. Pol Arch Intern Med. 2022; 132: 16216. doi:10.20452/pamw.16216

REFERENCES

1 World Health Organization. Obesity and overweight: fact sheet. 09.06.2021. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight. Accessed September 22, 2021.

2 Mechanick JI, Hurley DL, Garvey WT. Adiposity-based chronic disease as a new diagnostic term: the American Association of Clinical Endocrinologists and American College Of Endocrinology Position Statement. Endocr Pract. 2017; 23: 372-378.

3 Di Angelantonio E, Bhupathiraju ShN, Wormser D, et al; Global BMI Mortality Collaboration. Body-mass index and all-cause mortality: individual--participant-data meta-analysis of 239 prospective studies in four continents. Lancet. 2016; 388: 776-786.

4 Aune D, Sen A, Prasad M, et al. BMI and all cause mortality: systematic review and non-linear dose-response meta-analysis of 230 cohort studies with 3.74 million deaths among 30.3 million participants. BMJ. 2016; 353: i2156.

5 Whitlock G, Lewington S, Sherliker P, et al. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. Lancet. 2009; 373: 1083-1096.

6 Marques A, Peralta M, Naia A, et al. Prevalence of adult overweight and obesity in 20 European countries. Eur. J. Public Health. 2018; 28: 295-300.

7 Kozieł P, Jankowski P, Mirek-Bryniarska E, et al. Obesity in patients with established coronary artery disease over a 20-year period (1997-2017). Pol Arch Intern Med. 2021;131: 26-32.

8 Durrer Schutz D, Busetto L, Dicker D, et al. European practical and patient-centred guidelines for adult obesity management in primary care. Obes Facts. 2019; 12: 40-66.

9 Rosenzweig JL, Bakris GL, Berglund LF, et al. Primary prevention of ASCVD and T2DM in patients at metabolic risk: an Endocrine Society Clinical practice guideline. J Clin Endocrinol Metab. 2019; 104: 3939-3985.

10 Pedersen SD, Manjoo P, Wharton S. Canadian adult obesity clinical practice guidelines: pharmacotherapy in obesity management. https://obesitycanada.ca/guidelines/pharmacotherapy. Accessed September 10, 2021.

11 Wharton S, Lau DCW, Vallis M, et al. Obesity in adults: a clinical practice guideline. CMAJ. 2020; 192: E875-E891.

12 American Diabetes Association. Obesity management for the treatment of type 2 diabetes: standards of medical care in diabetes. Diab Care. 2021; 44 (suppl 1): S100-S110.

13 Krist AH, Davidson KW, Mangione CM; US Preventive Services Task Force. Behavioral counseling interventions to promote a healthy diet and physical activity for cardiovascular disease prevention in adults with cardiovascular risk factors US Preventive Services Task Force recommendation statement. JAMA. 2020; 324: 2069-2075.

14 Cosentino F, Grant PJ, Aboyans V, et al; ESC Scientific Document Group. 2019 ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD. Eur Heart J. 2020; 41: 255-323.

15 Pasquali R, Casanueva F, Haluzik M, et al. European Society of Endocrinology Clinical Practice Guideline: endocrine work-up in obesity. Eur J Endocrinol. 2020; 182: G1-G32.

16 Powell-Wiley TM, Poirier P, Burke LE, et al. Obesity and cardiovascular disease a scientific statement from the American Heart Association. Circulation. 2021; 143: e984-e1010.

17 Mechanick JI, Apovian C, Brethauer S, et al. Clinical practice guidelines for the perioperative nutrition, metabolic, and nonsurgical support of patients undergoing bariatric procedures - 2019 update. Endocr Pract. 2019; 25: 1346-1359.

18 COP26 special report on climate change and health: the health argument for climate action. Geneva: World Health Organization. 2021.

19 Atwoli L, Baqui AH, Benfield T. Call for emergency action to limit global temperature increases, restore biodiversity, and protect health. BMJ. 2021; 385: 1134-1137.

20 UN environment programme. UNEP Food Waste Index Report 2021. https://www.unep.org/resources/report/unep-food-waste-index-report-2021. Accessed September 20, 2021.

21 European Commision on Food Safety: food waste. https://ec.europa.eu/food/safety/food-waste_en. Accessed September 20, 2021.

22 Toti E, Di Mattia C, Serafini M. Metabolic food waste and ecological impact of obesity in FAO World's Region. Front Nutr. 2019; 6: 126.

23 Sundin N, Rosell M, Eriksson M, et al. The climate impact of excess food intake - an avoidable environmental burden. Resour Conserv Recycl. 2021; 174: 105777.

24 Swinburn B, Sacks G, Hall K, et al. The global obesity pandemic: shaped by global drivers and local environments. Lancet. 2011; 378: 804-814.

25 World Health Organization. Waist circumference and waist-hip ratio report of a WHO expert consultation. 08.11.2008. www.who.int/publications/i/item/9789241501491. Accessed September 22, 2021.

26 Wormser D, Kaptoge S, Di Angelantonio E, et al. Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. Lancet. 2011; 377: 1085-1095.

27 Gerstein HC, Miller ME, Byington RP, et al; Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med. 2008; 358: 2545-2559.

28 Patel A, MacMahon S, Chalmers J, et al; ADVANCE Collaborative Group. Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. N Engl J Med. 2008; 358: 2560-2572.

29 Duckworth W, Abraira C, Moritz T, et al; VADT Investigators. Glucose control and vascular complications in veterans with type 2 diabetes. N Engl J Med. 2009; 360: 129-139.

30 Zinman B, Wanner C, Lachin JM, et al; EMPA-REG OUTCOME Investigators. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med. 2015; 373: 2117-2128.

31 Marso SP, Daniels GH, Brown-Frandsen K et al; LEADER Steering Committee; LEADER Trial Investigators. Liraglutide and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2016; 375: 311-322.

32 Davies MJ, D'Alessio DA, Fradkin J, et al. Management of hyperglycemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2018; 41: 2669-2701.

33 Kristensen SL, Rørth R, Jhund PS, et al. Cardiovascular, mortality, and kidney outcomes with GLP-1 receptor agonists in patients with type 2 diabetes: a systematic review and meta-analysis of cardiovascular outcome trials. Lancet Diabetes Endocrinol. 2019; 7: 776-785.

34 McGuire DK, Shih WJ, Cosentino F, et al. Association of SGLT2 inhibitors with cardiovascular and kidney outcomes in patients with type 2 diabetes: a meta-analysis. JAMA Cardiol. 2021; 6: 148-158.

35 Sjöholm K, Sjöström E, Carlsson LM, Peltonen M. Weight change-adjusted effects of gastric bypass surgery on glucose metabolism: 2- and 10-year results from the Swedish Obese Subjects (SOS) Study. Diabetes Care. 2016; 39: 625-631.

36 Lean ME, Leslie WS, Barnes AC, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. Lancet. 2018; 391: 541-551.

37 Lingvay I, Sumithran P, Cohen RV, le Roux CW. Obesity management as a primary treatment goal for type 2 diabetes: time to reframe the conversation. Lancet. 2022; 399: 394-405.

38 Neter JE, Stam BE, Kok FJ, et al. Influence of weight reduction on blood pressure a meta-analysis of randomized controlled trials. Hypertension. 2003; 42: 878-884.

39 Yan Y, Sha Y, Yao G, et al. Roux-en-Y gastric bypass versus medical treatment for type 2 diabetes mellitus in obese patients: a systematic review and meta-analysis of randomized controlled trials. Medicine (Baltimore). 2016; 95: e3462.

40 Zhao X, Huang K, Zheng M, Duan J. Effect of liraglutide on blood pressure: a meta-analysis of liraglutide randomized controlled trials. BMC Endocr Disord. 2019; 19: 4-16.

41 Avgerinos I, Michailidis T, Liakos A, et al. Oral semaglutide for type 2 diabetes: a systematic review and meta-analysis. Diabetes Obes Metab. 2020; 22: 335-345.

42 Sahebkar A, Simental-Mendía LE, Kovanen PT, et al. Effects of orlistat on blood pressure: a systematic review and meta-analysis of 27 randomized controlled clinical trials. J Am Soc Hypertens. 2018; 12: 80-96.

43 Khera R, Pandey A, Chandar AK, et al. Effects of weight-loss medications on cardiometabolic risk profiles: a systematic review and network meta-analysis. Gastroenterology. 2018; 154: 1309-1319.

44 Hasan B, Nayfeh T, Alzuabi M, et al. Weight loss and serum lipids in overweight and obese adults: a systematic review and meta-analysis. J Clin Endocrinol Metab. 2020; 1: 105-117.

45 Nauck MA, Quast DR, Wefers J, Meier JJ. GLP-1 receptor agonists in the treatment of type 2 diabetes - state-of-the-art. Mol Metab. 2020; 46: 101-102.

46 Ge L, Sadeghirad B, Ball GDC, et al. Comparison of dietary macronutrient patterns of 14 popular named dietary programmes for weight and cardiovascular risk factor reduction in adults: systematic review and network meta-analysis of randomised trials. BMJ. 2020; 369: m696.

47 Popkin BM, Du S, Green WD, et al. Individuals with obesity and COVID-19: a global perspective on the epidemiology and biological relationships. Obesity Rev. 2020; 21: e13128.

48 Yang J, Tian C, Chen Y, et al. Obesity aggravates COVID-19: an updated systematic review and meta-analysis. J Med Virol. 2021; 93: 2662-2674.

49 Malik P, Patel U, Patel K, et al. Obesity a predictor of outcomes of COVID-19 hospitalized patients - a systematic review and meta-analysis. Med Virol. 2021; 93: 1188-1193.

50 Lai HH, Helmuth ME, Smith AR, et al. Symptoms of lower urinary tract dysfunction research network (LURN). Relationship between central obesity, general obesity, overactive bladder syndrome and urinary incontinence among male and female patients seeking care for their lower urinary tract symptoms. Urology. 2019; 123: 34-43.

51 Yazdany T, Jakus-Waldman S, Jeppson P, et al. American Urogynecologic Society systematic review: the impact of weight loss intervention on lower urinary tract symptoms and urinary incontinence in overweight and obese women. Female Pelvic Med Reconstr Surg. 2020; 26: 16-29.

52 Talmor A, Dunphy B. Female obesity and infertility. Best Pract Res Clin Obstet Gynaecol. 2015; 29: 498-506.

53 Yildiz BO, Bozdag G, Yapici Z, et al. Prevalence, phenotype and cardiometabolic risk of polycystic ovary syndrome under different diagnostic criteria. Hum Reprod. 2012; 27: 3067-3073.

54 Marchi J, Berg M, Dencker A, et al. Risks associated with obesity in pregnancy, for the mother and baby: a systematic review of reviews. Obes Rev. 2015; 16: 621-638.

55 Rozanska-Waledziak A, Waledziak M, Bartnik P, et al. The influence of bariatric surgery on pregnancy and perinatal outcomes - a case-control study. J Clin Med. 2020; 9: 1324-1333.

56 Rozanska-Waledziak A, Bartnik P, Kacperczyk-Bartnik J, et al. Pregnancy after bariatric surgery - a narrative literature review. Wideochir Inne Tech Maloinwazyjne. 2021; 16: 30-37.

57 Glass LM, Dickson RC, Anderson JC, et al. Total body weight loss of ≥ 10 % is associated with improved hepatic fibrosis in patients with nonalcoholic steatohepatitis. Dig Dis Sci. 2015; 60: 1024-1030.

58 Garvey WT, Mechanick JI, Brett EM, et al. American Association of Clinical Endocrinologists and American College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. Endocr Pract. 2016; 22: S1-S20.

59 Look AHEAD Research Group. Association of the magnitude of weight loss and changes in physical fitness with long-term cardiovascular disease outcomes in overweight or obese people with type 2 diabetes: a post-hoc analysis of the Look AHEAD randomised clinical trial. Lancet Diabetes Endocrinol. 2016; 4: 913-921.

60 Sundström J, Bruze G, Ottosson J, et al. Weight loss and heart failure: a national study of gastric bypass surgery versus intensive lifestyle treatment. Circulation. 2017; 135: 1577-1585.

61 Ryan DH, Yockey SR. Weight loss and improvement in comorbidity: differences at 5%, 10%, 15%, and over. Curr Obes Rep. 2017; 6: 187-194.

62 Wichniak A, Dudek D, Heitzman J, et al. Metabolic risk reduction in patients with schizophrenia treated with antipsychotics: recommendations of the Polish Psychiatric Association. Psychiatr Pol. 2019; 53: 1191-1218.

63 De Silva VA, Suraweera C, Ratnatunga SS, Dayabandara M. Metformin in prevention and treatment of antipsychotic induced weight gain: a systematic review and meta-analysis. BMC Psychiatry. 2016; 16: 341-351.

64 Hyunju Kim H, Laura E, Caulfield LE, et al. Plant-based diets are associated with a lower risk of incident cardiovascular disease, cardiovascular disease mortality, and all-cause mortality in a general population of middle-aged adults. J Am Heart Assoc. 2019; 8: e012865.

65 Willett W, Rockström J, Loken B, et al. Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. Lancet. 2019; 393: 447-492.

66 World Health Organization. WHO guidelines on physical activity and sedentary behaviour. Geneva; 2020. https://www.who.int/publications/i/item/9789240015128. Accessed October 4, 2021.

67 Look AHEAD Research Group. Eight-year weight losses with an intensive lifestyle intervention: the look AHEAD study. Obesity. 2014; 22: 5-13.

68 Kane JA, Mehmood T, Munir I, et al. Cardiovascular risk reduction associated with pharmacological weight loss: a meta-analysis. Int J Clin Res Trials. 2019; 4: 131-138.

69 Khera R, Murad MH, Chandar AK, et al. Association of pharmacological treatments for obesity with weight loss and adverse events: a systematic review and meta-analysis. JAMA. 2016; 315: 2424-2434.

70 Onakpoya IJ, Lee JJ, Mahtani KR, et al. Naltrexone-bupropion (Mysimba) in management of obesity: a systematic review and meta-analysis of unpublished clinical study reports. Br J Clin Pharmacol. 2020; 86: 646-667.

71 Singh AK, Singh R. Pharmacotherapy in obesity: a systematic review and meta-analysis of randomized controlled trials of anti-obesity drugs. Expert Rev Clin Pharmacol. 2020; 13: 53-64.

72 Vosoughi K, Atieh J, Khanna L et al. Association of glucagon-like peptide 1 analogs and agonists administered for obesity with weight loss and adverse events: a systematic review and network meta-analysis. EClinicalMedicine. 2021; 42: 101213

73 Moon S, Lee J, Chung HS, Kim YJ, et al. Efficacy and safety of the new appetite suppressant, liraglutide: a meta-analysis of randomized controlled trials. Endocrinol Metab (Seoul). 2021; 36: 647-660.

74 Davies M, Færch L, Jeppesen OK, et al. Semaglutide 2·4 mg once a week in adults with overweight or obesity, and type 2 diabetes (STEP 2): a randomised, double-blind, double-dummy, placebo-controlled, phase 3 trial. Lancet. 2021; 397: 971-984.

75 Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med. 2021; 384: 989-1002.

76 Tsapas A, Karagiannis T, Kakotrichi P, et al. Comparative efficacy of glucose-lowering medications on body weight and blood pressure in patients with type 2 diabetes: a systematic review and network meta-analysis. Diabetes Obes Metab. 2021; 23: 2116-2124.

77 Palmer SC, Tendal B, Mustafa RA, et al. Sodium-glucose cotransporter protein-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists for T2D: systematic review and network meta-analysis of randomised controlled trials. BMJ. 2021; 372: 4573.

78 Shi Q, Wang Y, Hao Q, et al. Pharmacotherapy for adults with overweight and obesity: a systematic review and network meta-analysis of randomized controlled trials. Lancet. 2022; 399: 259-269.

79 Rubino D, Abrahamsson N, Davies M, et al. Effect of continued weekly subcutaneous semaglutide vs placebo on weight loss maintenance in adults with overweight or obesity: the STEP 4 randomized clinical trial. JAMA. 2021; 325: 1414-1425.

80 Haghighat N, Ashtari-Larky D, Aghakhani L, et al. How does fat mass change in the first year after bariatric surgery? A Systemic review and meta-analysis. Obes Surg. 2021; 31: 3799-3821.

81 El Ansari W, Elhag W. Weight regain and insufficient weight loss after bariatric surgery: definitions, prevalence, mechanisms, predictors, prevention and management strategies, and knowledge gaps - a scoping review. Obes Surg. 2021; 31: 1755-1766.

82 Adams TD, Davidson, LE, Litwin SE, et al. Weight and metabolic outcomes 12 years after gastric bypass. N Engl J Med. 2017; 377: 1143-1155.

83 Wiggins T, Guidozzi N, Welbourn R, et al. Association of bariatric surgery with all-cause mortality and incidence of obesity-related disease at a population level: a systematic review and meta-analysis. PLoS Med. 2020; 17: e1003206.

84 Hussain S, Khan MS, Jamali MC, et al. Impact of bariatric surgery in reducing macrovascular complications in severely obese T2DM patients. Obes Surg. 2021; 31: 1929-1936.

85 Syn NL, Cummings DE, Wang LZ, et al. Association of metabolic-bariatric surgery with long-term survival in adults with and without diabetes: a one-stage meta-analysis of matched cohort and prospective controlled studies with 174 772 participants. Lancet. 2021; 397: 1830-1841.

86 Julie Kim J, Eisenberg D, Azagury D, et al. American Society for Metabolic and Bariatric Surgery position statement on long-term survival benefit after metabolic and bariatric surgery. Surg Obes Relat Dis. 2016; 12: 453-459.

87 Lewis CA, de Jersey S, Seymour M, et al. Iron, vitamin B(12), folate and copper deficiency after bariatric surgery and the impact on anaemia: a systematic review. Obes Surg. 2020; 30: 4542-4591.

88 Himbert C, Ose J, Delphan M, Ulrich CM. A systematic review of the interrelation between diet- and surgery-induced weight loss and vitamin D status. Nutr Res. 2017; 38: 13-26.

89 Ashrafi D, Osland E, Memon MA. Bariatric surgery and gastroesophageal reflux disease. Ann Transl Med. 2020; 8 (Suppl 1): S11.

90 Wiggins T, Antonowicz SS, Markar SR. Cancer risk following bariatric surgery - systematic review and meta-analysis of national population-based cohort studies. Obes Surg. 2019; 29: 1031-1039.

91 Bruno DS, Berger NA. Impact of bariatric surgery on cancer risk reduction. Ann Transl Med. 2020; 8 (Suppl 1): S13.

92 Tao W, Artama M, von Euler-Chelpin M, et al. Colon and rectal cancer risk after bariatric surgery in a multicountry Nordic cohort study. Int J Cancer. 2020; 147: 728-735.

93 Chen W, Wang Y, Zhu J, et al. Esophagogastric cancer after sleeve gastrectomy: a systematic review of case reports. Cancer Manag Res. 2021; 13: 3327-3334.

94 Romanello M, McGushin A, Di Napoli C, et al. The 2021 report of the Lancet Countdown on health and climate change: code red for a healthy future. Lancet. 2021; 398: 1619-1662.