Clinical guidelines on the management of individuals with overweight/obesity and glucose metabolism disorders – 2026. Position statement of Diabetes Poland

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Abstract

Obesity and glucose metabolism disorders are among the principal public health challenges of the twenty-first century, and their clinical and epidemiological burden continues to grow despite expanding educational and preventive efforts. Although Diabetes Poland (PTD) has issued annual guidelines for the management of diabetes since 2005, no dedicated Polish recommendations had previously addressed the combined issue of overweight/obesity and glucose metabolism disorders. This document presents the first edition of such recommendations, developed by a multidisciplinary expert panel comprising specialists in diabetology, endocrinology, paediatrics, psychiatry, psychotherapy, nephrology, cardiology, hypertensiology, and human nutrition. The recommendations are based on current clinical trial evidence and existing international guidelines, with each recommendation assigned a graded strength of supporting evidence. The statement frames obesity as a complex, chronic disease of genetic, metabolic, behavioural, and environmental origin and addresses its definition, terminology, diagnosis (body mass index, waist circumference, and body composition, with age- and sex-adjusted assessment in children), epidemiology, pathogenesis, and secondary causes. It reviews the main clinical consequences, including cardiovascular-kidney-metabolic complications, hypertension, steatotic liver disease, and sexual dysfunction, and provides detailed guidance on treatment goals and monitoring, therapeutic education, dietary and lifestyle interventions, pharmacotherapy, and bariatric surgery. Separate recommendations are provided for children and adolescents, for adults over 65 years, and for the organisation of care. These recommendations integrate contemporary evidence into a practical framework intended to standardize and improve the care of people with overweight/obesity and glucose metabolism disorders.

Key words: obesity, overweight, glucose metabolism disorders, diabetes.

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List of abbreviations

ABCD – adiposity-based chronic disease
ACT – acceptance and commitment therapy
ACTH – adrenocorticotropic hormone
ADI – acceptable daily intake
AER – albumin excretion rate (24-hour urinary albumin excretion)
AFLP – acute fatty liver of pregnancy
AGEs – advanced glycation end-products
AID – automated insulin delivery
ALD – alcohol-related liver disease
ALT – alanine aminotransferase
anti-TG – anti-thyroglobulin antibodies
anti-TPO – anti-thyroid peroxidase antibodies
APD – antipsychotic drugs
AST – aspartate aminotransferase
Ab – amyloid beta peptide
BDNF – brain-derived neurotrophic factor
BED – binge eating disorder
BMI – body mass index
BMI SDS – body mass index standard deviation score
BWL – behavioural weight loss
Ca – calcium
CBT – cognitive behavioural therapy
CBT-E – enhanced cognitive behavioural therapy
CBT-I – cognitive behavioural therapy for insomnia
CGM – continuous glucose monitoring
CKD – chronic kidney disease
CKD-EPI Cr – Chronic Kidney Disease Epidemiology Collaboration creatinine equation
CKD-EPI Cr-Cys – Chronic Kidney Disease Epidemiology Collaboration creatinine–cystatin C equation
CKM – cardiovascular–kidney–metabolic syndrome
CKS – corticosteroids
CNS – central nervous system
COSI – Childhood Obesity Surveillance Initiative
CRH – corticotropin-releasing hormone
DASH – Dietary Approaches to Stop Hypertension
DXA – dual-energy X-ray absorptiometry
eGFR – estimated glomerular filtration rate
ESC – European Society of Cardiology
Fe – iron
FFA – free fatty acids
FIB-4 – Fibrosis-4 Index
FSGS – focal segmental glomerulosclerosis
FSH – follicle-stimulating hormone
fT3 – free triiodothyronine
fT4 – free thyroxine
FTO – fat mass and obesity-associated (gene)
GH – growth hormone (somatotropin)
GI – glycaemic index
GIP – glucose-dependent insulinotropic polypeptide
GL – glycaemic load
GLP-1 – glucagon-like peptide-1
GLP-1 RA – glucagon-like peptide-1 receptor agonist
GnRH – gonadotropin-releasing hormone
HbA1c – glycated haemoglobin
HCC – hepatocellular carcinoma
HCV – chronic hepatitis C
HDL – high-density lipoprotein
HELLP – haemolysis, elevated liver enzymes, low platelets
HFpEF – heart failure with preserved ejection fraction
HFrEF – heart failure with reduced ejection fraction
HOMA-IR – homeostatic model assessment of insulin resistance
HPA – hypothalamic–pituitary–adrenal axis
HR – heart rate
HTN – arterial hypertension
IFG – impaired fasting glucose
IGF-1 – insulin-like growth factor 1
IGT – impaired glucose tolerance
IPT – interpersonal therapy
LAL – lysosomal acid lipase
LDL – low-density lipoprotein
LH – luteinising hormone
MAPK – mitogen-activated protein kinases
MASH – metabolic dysfunction-associated steatohepatitis
MASLD – metabolic dysfunction-associated steatotic liver disease
MetALD – metabolic dysfunction-associated alcohol-related liver disease
Mg – magnesium
MMSE – Mini-Mental State Examination
MNA-SF – Mini Nutritional Assessment Short Form
MoCA – Montreal Cognitive Assessment
MOSH – male obesity-associated secondary hypogonadism
NCS-R – National Comorbidity Survey Replication
NEAT – non-exercise activity thermogenesis
NES – night eating syndrome
OGTT – oral glucose tolerance test
ORG – obesity-related glomerulopathy
OSA – obstructive sleep apnoea
PAI-1 – plasminogen activator inhibitor 1
PAL – physical activity level
PCOS – polycystic ovary syndrome
PDE-5 – phosphodiesterase type 5
PHC – primary health care
PRAT – peri-renal adipose tissue
PTD – Diabetes Poland
RAA – renin–angiotensin–aldosterone
REE – resting energy expenditure
ROS – reactive oxygen species
SCORE2 – Systemic Coronary Risk Estimation 2
SCORE2-OP – Systemic Coronary Risk Estimation 2 – Older Persons
SDB – sleep-disordered breathing

SFA – saturated fatty acids
SGLT-2 – sodium–glucose cotransporter 2
SGLT-2i – sodium–glucose cotransporter 2 inhibitor
SLD – steatotic liver disease
SRED – sleep-related eating disorder
T1DM – type 1 diabetes mellitus
T2DM – type 2 diabetes mellitus
TDD – total daily dose
TEE – total energy expenditure
TRH – thyrotropin-releasing hormone
TSH – thyroid-stimulating hormone (thyrotropin)
UACR – urinary albumin-to-creatinine ratio
UPCR – urinary protein-to-creatinine ratio
VLDL – very-low-density lipoprotein
WHO – World Health Organization
WHR – waist-to-hip ratio
WHtR – waist-to-height ratio
Zn – zinc

Diabetes Poland evidence-grading system

Level of evidence	Description
A	Clear evidence from well-conducted, generalizable randomized controlled trials that are adequately powered, including: • Evidence from a well-conducted multicenter trial • Evidence from a meta-analysis that incorporated quality ratings in the analysis • Supportive evidence from well-conducted randomized controlled trials that are adequately powered, including: – Evidence from a well-conducted multicenter trial – Evidence from a meta-analysis that incorporated quality ratings in the analysis
B	Evidence from randomized controlled trials with an identified flaw that may limit validity of the results Supportive evidence from well-conducted cohort studies, including: • Evidence from a well-conducted prospective cohort study or registry • Evidence from a well-conducted meta-analysis of cohort studies • Supportive evidence from a well-conducted case-control study
C	Supportive evidence from poorly controlled or uncontrolled studies, including: • Evidence from randomized clinical trials with one or more major or three or more minor methodological flaws that could invalidate the results • Evidence from observational studies with high potential for bias (such as case series with comparison with historical controls) • Evidence from case series or case reports • Conflicting evidence with the weight of evidence supporting the recommendation
E	Expert consensus or clinical experience

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1. DEFINITION, TERMINOLOGY, AND DIAGNOSIS OF OBESITY

Key recommendations
• Obesity is a complex, chronic disease arising from the combined effects of genetic, metabolic, behavioural, and environmental factors. [**E**]
• The diagnostic work-up of obesity employs calculation of body mass index (BMI) together with methods designed to characterise the distribution of adipose tissue (e.g., waist circumference, body composition assessment). [**A**]
• In children and adolescents with obesity and glucose metabolism disorders, age- and sex-adjusted BMI assessment, analysis of the growth trajectory, and routine measurement of waist circumference are recommended to identify central obesity and stratify metabolic risk. [**B**]

Obesity is a chronic metabolic disease characterised by excessive and/or abnormal accumulation of adipose tissue, leading to an increased risk of long-term health complications, impaired quality of life, and reduced life expectancy [1].

The contemporary understanding of obesity recognises it as a complex disorder with a genetic, metabolic, environmental, and behavioural background. The drivers of the current rise in the prevalence of overweight and/or obesity are attributed in particular to the increased availability of highly processed, energy-dense foods and sweetened beverages, coupled with a low level of physical activity [1, 2].

1.1. Diagnostic criteria

The fundamental and traditional diagnostic instrument is BMI, defined as the quotient of body mass (kg) and the square of height (m²) [1, 3, 4]:

- overweight: BMI 25.0–29.9 kg/m²;
- obesity: BMI ≥ 30.0 kg/m²:
  – class I: 30.0–34.9 kg/m²;
  – class II: 35.0–39.9 kg/m²;
  – class III: ≥ 40.0 kg/m².

The diagnostic work-up of obesity additionally includes [3, 5]:

- waist circumference measurement (a marker of visceral obesity) – values ≥ 94 cm in men and ≥ 80 cm in women (European population) indicate abdominal obesity;
- the waist-to-hip ratio (WHR) > 0.85 in women and > 0.9 in men;
- the WHtR > 0.5;
- assessment of body composition;
- assessment for metabolic complications (hyperglycaemia, arterial hypertension, dyslipidaemia, metabolic dysfunction-associated steatotic liver disease [MASLD], sleep apnoea).

BMI, although widely used, is not a precise measure of obesity, since it does not distinguish adipose tissue from lean body mass and does not take account of fat distribution [6, 7].

In 2025, an expert panel consensus was published proposing a new approach to the diagnosis of obesity that takes account of indicators of adipose tissue excess in addition to BMI [3].

The concept of *clinical* and *pre-clinical* obesity has likewise been introduced in order to distinguish individuals with organ dysfunction and/or physical limitations attributable to obesity from those without such features (Table 1.1) [3, 7].

The concept of clinical and pre-clinical obesity is contentious, as it implies that obesity may not lead to adverse consequences for prognosis or quality of life in its early stages. However, the changes already present at the cellular, tissue, and organ-structural levels caused by even a modest increase in adipose tissue do produce clinical alterations at this stage and warrant therapeutic intervention [3, 5, 8].

1.2. Distinct features of obesity diagnosis in children and adolescents

The diagnosis of obesity in developmental age differs from the criteria applied in adults owing to dynamic changes in growth, body composition, and physiological differences in the distribution of adipose tissue [9, 10].

In children and adolescents up to 18 years of age, obesity is diagnosed on the basis of age- and sex-adjusted BMI using the Polish percentile charts (OLA/OLAF):

Table 1.1. Clinical and pre-clinical obesity

Feature	Pre-clinical obesity	Clinical obesity
Adipose tissue mass	Excessive (based on BMI and other anthropometric measurements)	Excessive (based on BMI and other anthropometric measurements)
Pathophysiological changes	Cellular- and tissue-level changes leading to alterations in organ structure	Changes in organ function leading to organ failure
Clinical manifestations	Slight or absent; organ function largely preserved	Overt clinical symptoms, limitations in everyday activity, presence of complications
Therapeutic approach	Prevention of progression to clinical obesity and of the development of additional comorbidities	Improvement of the function of damaged organs

- overweight: BMI > 85th percentile for age and sex;
- obesity: BMI > 97th percentile for age and sex.

In children younger than 3 years of age, the assessment of weight-for-length is recommended, in line with the standards of the World Health Organization (WHO):

- overweight: > +2 SD above the median;
- obesity: > +3 SD above the median.

In contrast to adults, a single BMI measurement has limited diagnostic value. Of key importance is analysis of the growth trajectory, including accelerated weight gain, the crossing of successive percentile channels, and the early occurrence of the so-called *adiposity rebound*.

BMI does not reflect adipose tissue distribution and does not allow assessment of the visceral component. In children and adolescents with glucose metabolism disorders, particular importance should be placed on the identification of central obesity by means of waist circumference measurement referenced to age- and sex-specific norms. WHtR may be used as an auxiliary measure; a value ≥ 0.5 may indicate increased metabolic risk. During puberty, the interpretation of results should take account of physiological changes in the proportions of adipose tissue.

Assessment of body composition (e.g. by bioelectrical impedance analysis or dual-energy X-ray absorptiometry [DXA]) may complement diagnostic evaluation, particularly in cases of discrepancy between BMI and the clinical picture, and may also assist in monitoring the effects of treatment.

1.3. Terminology

The use of specific terminology is intended to counteract the still widespread stigmatisation of obesity and to reinforce its perception as a chronic disease requiring treatment, rather than as a cosmetic flaw or a state entirely subject to the patient's volition (Table 1.2).

The term "obesity disease" was introduced to emphasise the disease aspect of excess body weight and its consequences; however, the increasing use of this term should not suggest that "obesity" is not itself a disease or that the term should be avoided. The appropriate medical terms are *treatment of obesity* or *body weight reduction* – not *slimming* – and, in the context of pharmacotherapy, *anti-obesity drugs* are employed, not *slimming drugs*.

The term *person with obesity* is recommended in preference to *obese person*, in accordance with the principle of *person-first language*, which emphasises that the disease does not define the individual. The term *person living with obesity* is also used with increasing frequency [1, 5, 8].

The use of stigmatising terminology towards patients is unacceptable.

2. EPIDEMIOLOGY OF OVERWEIGHT AND OBESITY AND OF ACCOMPANYING GLUCOSE METABOLISM DISORDERS

A consistent increase in the prevalence of obesity has been observed in recent years, particularly among men aged 40–65 years, in populations with lower educational attainment, and in children and adolescents [11–13]. General epidemiological data are summarised in Table 2.1.

2.1. Epidemiology of overweight and obesity

2.1.1. Adults

Worldwide. Obesity currently constitutes one of the most significant public health challenges worldwide. The prevalence of overweight and obesity is rising steadily across all regions. In 2010, BMI ≥ 25 kg/m² was found in 36–37% of adults; by 2015, this figure had reached approximately 40% of the adult population (almost 2 billion people). Projections for 2030 suggest that overweight or obesity will affect approximately 50% of the world's adult population – almost 3 billion people – including obesity in 17% of men and 22% of women. In most countries of the world, the lifetime risk of BMI ≥ 25 kg/m² exceeds 50%, and in many countries it reaches 80% [12, 13].

Europe. The WHO European Region (WHO/Europe) is among the areas with the highest prevalence of overweight and obesity. In 2010, BMI ≥ 25 kg/m² was found in 60% of men and 50% of women; in 2015, in 62% of men and 51% of women; and by 2030 the corresponding figures are projected to reach 65% and 52%. Europe is characterised by a high lifetime risk of obesity – in many countries, the maximum prevalence in the 40–70-year age groups exceeds 70–80% [11, 14, 15].

Table 1.2. Definitions of selected terms used in the diagnosis of obesity

Term	Meaning
Adiposity-based chronic disease (ABCD)	A chronic disease caused by excessive accumulation of adipose tissue (a term encompassing the full spectrum of the consequences of obesity)
Complicated obesity	The presence of clinically significant health consequences of obesity
Obesity without metabolic complications	The absence of overt metabolic disturbances attributable to obesity – but still warranting treatment

Table 2.1. General data on the prevalence of obesity and overweight and on glucose metabolism disorders in the population of individuals with obesity, in Poland and worldwide

Category	Poland	Worldwide
Overweight and obesity in adults	M 60%; F 45–50%	40%
Obesity in adults	25%	25%
Overweight and obesity in children and adolescents	30% (aged 7–9 years)	20%
Obesity in children and adolescents	4.3%	5–10%
T2DM in adults with obesity	15–25%	10–20%
IGT in adults with obesity	25–35%	15–30%
T2DM in children and adolescents with obesity	2%	4% (aged 11–18 years)
Glucose tolerance disorders in children and adolescents with obesity	16% (IGT, 9–18 years); 3% (IFG, 9–18 years)	25% (IGT, 4–10 years); 21% (IGT, 11–18 years)

F – females; IFG – impaired fasting glucose; IGT – impaired glucose tolerance; M – males, T2DM – type 2 diabetes.

Poland. Poland lies within a European region with a high prevalence of overweight and obesity. Overweight and obesity affect more than 60% of adult men and approximately 45–50% of women, while obesity (BMI ≥ 30 kg/m²) affects approximately 25% of the adult population. Over the past two decades, a systematic increase in the prevalence of obesity has been observed, particularly [13, 16–18]:

- in men aged 40–65 years;
- in populations with lower educational attainment;
- in children and adolescents.

2.1.2. Children and adolescents

Worldwide. Globally, the magnitude of excess body weight in young people is rising rapidly. The WHO reports that in 2022 more than 390 million people aged 5–19 years had overweight, including 160 million with obesity; over the same period, the prevalence of excess body weight (including obesity) in this age group rose from 8% (1990) to 20% (2022) [19–21].

Europe. Within the European COSI (Childhood Obesity Surveillance Initiative) surveillance programme (sixth round, 2022–2024; approximately 470,000 children aged 6–9 years across 37 countries), WHO/Europe reports that 25% of children aged 7–9 years are living with overweight (including obesity), and 11% with obesity, with substantial inter-country variation [14, 15, 21].

Poland. Data from the COSI programme and analyses thereof in Poland indicate that the proportion of children with obesity is 4.32% (3.55–5.15%). More detailed data show that one in three children aged 7–9 years has overweight or obesity, and that, among 8-year-olds, one in five boys and one in ten girls meets the criteria for obesity [22–24].

2.2. Epidemiology of glucose metabolism disorders and diabetes in individuals with obesity

2.2.1. Adults

Worldwide. Obesity is one of the strongest risk factors for the development of glucose metabolism disorders: 70–80% of cases of type 2 diabetes (T2DM) worldwide are associated with excess body weight. Among individuals with obesity, the prevalence of T2DM is 10–20% (depending on the region), and impaired glucose tolerance (IGT) occurs in 15–30%. In 2021, 0.7 million premature deaths were attributed to T2DM, and 55% of these were attributable to elevated BMI [12, 13].

Europe. In Europe, the prevalence of T2DM in the adult population is 6–10%, rising to 15–25% in individuals with obesity. IGT occurs in 20–30% of individuals with obesity, particularly often in the 45–70-year age group [13, 14].

Poland. In Poland, diabetes affects approximately 9–10% of the adult population, and a further 20–25% have prediabetes. Among individuals with obesity, T2DM occurs in 15–25% and IGT in 25–35%. At a BMI of 30–34.9 kg/m², the risk of developing diabetes increases 3- to 5-fold; at a BMI ≥ 35 kg/m², it increases up to 6- to 10-fold [16–18].

2.2.2. Children and adolescents

Worldwide. Glucose tolerance disorders in children and adolescents with obesity are common, particularly in severe obesity. IGT occurs in 25% of children with obesity aged 4–10 years and in 21% of adolescents (aged 11–18 years) with obesity, while T2DM is found in 4% of adolescents with obesity. The prevalence of prediabetes in children and adolescents is estimated at approximately 8–9%. T2DM in the developmental age is rarer than prediabetes, but its incidence is rising – in 2021, an estimated 41,600 new cases of T2DM were diagnosed annually worldwide in individuals under 20 years of age [19, 23, 25].

Europe. In Europe, the prevalence of T2DM in children remains low (0.6–2.7 cases per 100,000 children and adolescents), but the trend is upward. In practice, most paediatric obesity-related glycaemic disorders take the form of impaired fasting glucose (IFG)/IGT. The risk of developing diabetes increases with the severity of obesity, with age, with sexual maturation, and in the presence of hepatic steatosis [15, 23, 25].

Poland. In Poland – as in most European countries – hyperglycaemic states are detected in nearly 20% of children with obesity aged 9–18 years: IGT (16%), IFG (~3%), and hemoglobin A_{1c} (HbA_{1c}) values of 5.7–6.4%. T2DM in childhood remains a rare diagnosis (~2% in children with obesity), although both data and clinical observations suggest a rising trend. From a public-health perspective, the key issue is that the high prevalence of overweight/obesity among early-school-age children in Poland (i.e. one in three children) creates a large pool of individuals at high risk of developing prediabetes and diabetes in the future [23–25].

3. PATHOPHYSIOLOGY OF OBESITY

Key recommendations
• Obesity has a complex, multifactorial pathogenesis.
• Biological and genetic factors play an important role in the development of obesity, alongside behavioural, psychological, social, and economic factors.
• The identification of these factors enables a better understanding of the individual mechanisms leading to the development of obesity and increases the effectiveness of its treatment.
• In children and adolescents, the developmental stage, perinatal parameters, and the period of puberty should be taken into account as factors modifying the risk of overweight/obesity.

Obesity is a chronic disease characterised by the excessive accumulation of adipose tissue. Of pivotal importance in its pathogenesis is a sustained positive energy balance, in which energy intake exceeds energy expenditure. An equally important role is played by disturbances in the mechanisms regulating body weight, often described as a change in the body weight "set point" [26].

The body-weight set point is defined as the range of body weight physiologically maintained by neurohormonal mechanisms involved in the regulation of food intake and energy expenditure [26]. Chronic energy excess and the action of environmental factors may lead to a shift of the set point to a higher value, as a result of which the increased body weight becomes the new state of equilibrium. In such circumstances, attempts to reduce body weight trigger compensatory mechanisms – increased hunger and reduced energy expenditure – that favour the perpetuation of obesity.

At present, obesity is regarded as a chronic disorder of the body's energy homeostasis whose development is fostered by the consumption of energy-dense, processed foods and a sedentary lifestyle [26].

3.1. Disturbances in the regulation of fat storage in the development of obesity

3.1.1. Regulation of food intake

Homeostatic regulation of food intake is intended to maintain the energy balance of the organism and is based principally on mechanisms operating at the level of the hypothalamus and the brainstem [26]. The key structure is the arcuate nucleus of the hypothalamus, which contains two antagonistically acting neuronal populations.

In the arcuate nucleus of the hypothalamus there are neurons expressing **neuropeptide Y (NPY)** and **the agouti-related peptide (AgRP)**. Activation of these neurons increases hunger and intensifies food intake. In their vicinity are neurons expressing **proopiomelanocortin (POMC)**, which secrete α-melanocyte-stimulating hormone (α-MSH); the latter exerts an anorectic effect through stimulation of the MC4R and MC3R melanocortin receptors located on neurons of the paraventricular nucleus of the hypothalamus. POMC neurons also secrete another anorexigenic peptide – **cocaine- and amphetamine-regulated transcript (CART)** [26–28].

Under conditions of negative energy balance and weight reduction, AgRP neurons are activated and POMC neuronal activity is inhibited, leading to increased hunger and intensified food intake [27, 28]. The activity of these neurons is regulated by peripheral signals conveying information about the energy-homeostatic state of the organism.

Leptin is a hormone secreted by adipose tissue which, through activation of POMC neurons and inhibition of NPY/AgRP neurons, reduces food intake. The absence or severe deficiency of leptin caused by mutations of its gene leads to substantially increased food intake and the development of obesity. In primary obesity, however, blood leptin concentrations are increased and positively correlated with the amount of adipose tissue, indicating the presence of leptin resistance [28].

Insulin, acting at the level of the central nervous system (CNS), likewise exerts an anorexigenic effect and serves as a signal of energy availability. In the course of obesity, central insulin resistance may also develop, weakening insulin's inhibitory effect on food intake and favouring a positive energy balance. The weight gain observed during insulin therapy in diabetes results predominantly from insulin's peripheral anabolic and glucose-low-

ering action rather than from a direct central effect. The pancreatic polypeptide and amylin secreted by the pancreas, in turn, increase the sensation of satiety [28].

In addition to homeostatic mechanisms, food intake is also subject to **hedonic regulation** linked to the reward system. This system encompasses, among other structures, the nucleus accumbens, the ventral tegmental area, and the prefrontal cortex; dopaminergic neurotransmission plays a central role within it. Hedonic regulation is responsible for the consumption of food irrespective of current energy needs, principally in response to its taste qualities or attractiveness. Excessive activation of this system may foster overeating and the development of obesity [29].

An important role in the control of eating behaviour is also played by the executive functions of the prefrontal cortex, which are responsible for planning, the inhibition of impulsive responses, and decision-making. Effective executive functioning enables refraining from impulsive eating and limits the influence of hedonic stimuli.

Gastrointestinal hormones are of considerable significance in the regulation of food intake. They may act directly on the hypothalamus, the brainstem, and reward centres, as well as indirectly via vagal afferent fibres which transmit signals from gastrointestinal mechano- and chemoreceptors activated after a meal [30].

Among the gastrointestinal hormones increasing food intake is **ghrelin**. It is secreted predominantly by the fundus of the stomach and the duodenum, with the highest blood concentrations occurring before the start of a meal [30]. Persons with obesity exhibit lower serum ghrelin concentrations than individuals of normal body weight, but a smaller postprandial decline [31].

The gastrointestinal tract also secretes hormones that increase the sensation of satiety. These include **peptide YY (PYY)**, **oxyntomodulin**, and **cholecystokinin (CCK)**. Of particular importance is **glucagon-like peptide-1 (GLP-1)** [30], secreted predominantly by the L-cells of the jejunum and ileum. GLP-1 is secreted in a biphasic manner in response to a meal: an early phase occurring a few minutes after the start of eating, and a late phase 30–60 minutes after the meal. This peptide reduces hunger, enhances satiety through delayed gastric emptying and activation of hypothalamic neurons, limits food intake, and acts on reward centres, reducing the hedonic drive to eat [28, 30]. In obesity, fasting GLP-1 concentrations are decreased and the postprandial response is attenuated compared with individuals of normal body weight [30]. It should be noted that the regulation of appetite may also be influenced by factors secreted by the liver.

Food intake is also regulated by macronutrients themselves, including:

- **glucose** – a rise in glycaemia and accompanying hormonal signals (e.g. insulin) are detected by hypothalamic centres, which suppress hunger and food intake;
- **free fatty acids** – in the intestine, these stimulate the secretion of PYY, GLP-1, and CCK, increasing postprandial satiety;
- **amino acids** – increase the secretion of satiety hormones;
- **dietary fibre** – slows gastric emptying, prolongs the action of satiety hormones, and prolongs the sensation of satiety [30];
- **sensory and gustatory components** – may stimulate the reward system and modulate appetite independently of energy needs; for example, the combination of sweet and fatty taste increases the motivation to eat [29].

In this way, food components affect both homeostatic regulation (hunger and satiety) and hedonic regulation (the pleasure of eating), acting in concert with gut hormones and hypothalamic neurons in the control of food intake.

3.1.2. Regulation of energy expenditure

The principal components of energy expenditure are: (1) resting energy expenditure (REE), which represents the largest component of total energy expenditure and accounts on average for approximately 60% (the value being variable and dependent on age, body composition, hormonal status, and physical activity level, among other factors); (2) the thermic effect of food (TEF); and (3) physical activity, encompassing both planned exercise and non-exercise activity thermogenesis (NEAT). A low REE may predispose to weight gain, especially when combined with excessive energy intake and low physical activity [26, 30].

Recent years have witnessed growing interest in the role of brown adipose tissue, which participates in thermogenesis and the maintenance of normal body temperature. The amount of brown adipose tissue in humans diminishes with age; the significance of changes in its quantity and activity in the pathogenesis of obesity, and its therapeutic potential, remain subjects of further investigation (Figure 3.1).

Increased energy intake is accompanied by increased energy expenditure, in part through enhancement of the TEF. Conversely, weight reduction leads to an adaptive decrease in energy expenditure, including a decrease in REE [26, 30]. These changes are partly independent of weight loss itself and result from neurohormonal adaptations such as decreased leptin and insulin concentrations and altered thyroid axis activity, which favour energy conservation. At the same time,

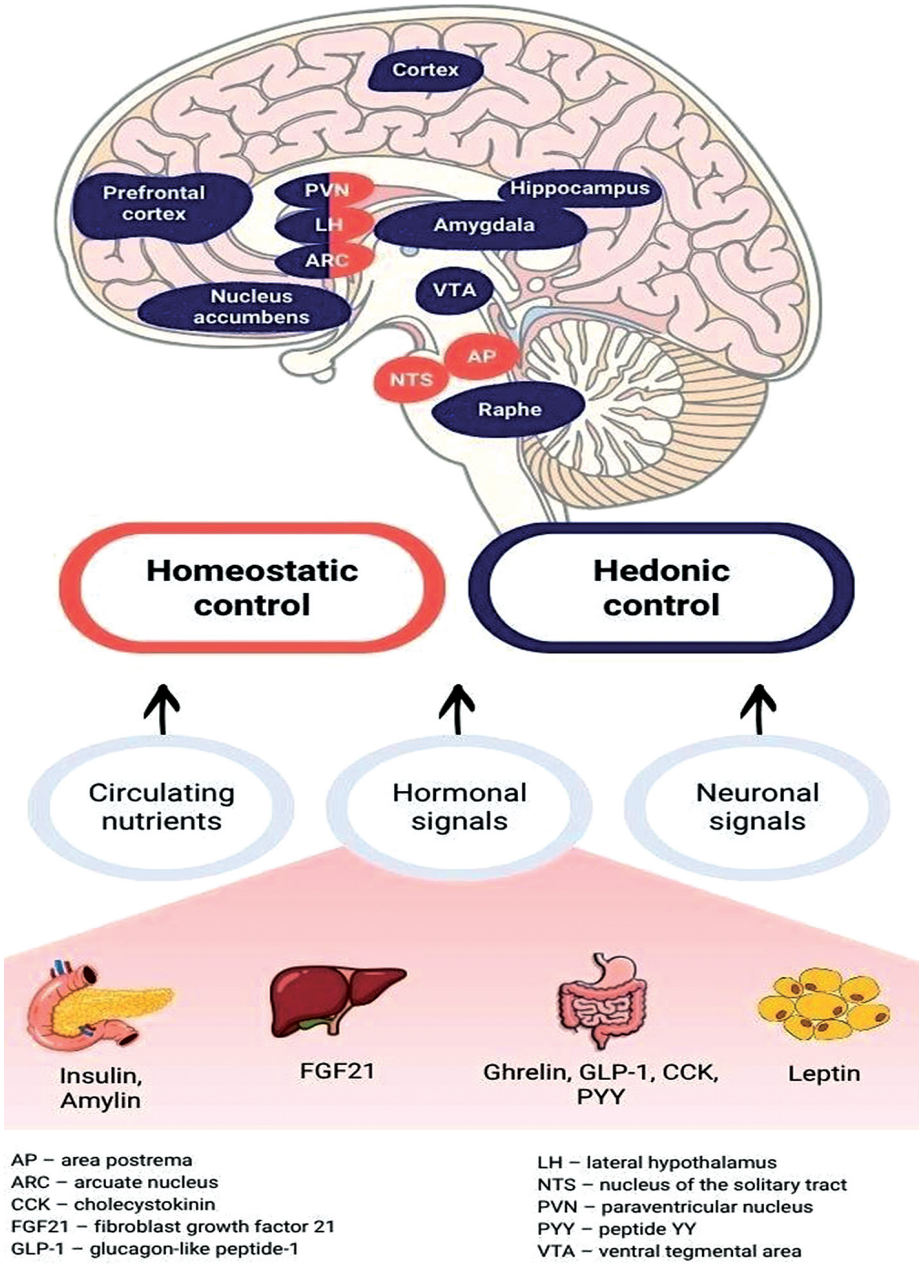


Figure 3.1. Regulation of appetite (after Stemmer *et al.* [28])

hunger intensifies and the motivation to eat increases, partly due to increased ghrelin secretion and activation of orexigenic neurons. Consequently, the lowered energy expenditure and intensified hunger that follow weight reduction make the long-term maintenance of normal body weight difficult and predispose to weight regain.

3.1.3. Adipose tissue during the development of obesity

As adipose tissue mass increases, insulin resistance develops within it. Despite compensatory hyperinsulinaemia, the antilipolytic action of insulin becomes attenuated, intensifying lipolysis and increasing the release of free fatty acids into the circulation. At the same time, hyperinsulinaemia favours the uptake of glucose and free fatty acids by adipocytes and *de novo* lipogenesis, leading to further triglyceride accumulation and adipocyte enlargement. High concentrations of free fatty acids further exacerbate insulin resistance [26, 28].

In this way, a self-perpetuating pathogenic cycle is established in which progressive insulin resistance promotes further expansion of adipose tissue, while increased adipose tissue mass and adipose-tissue dysfunction in turn exacerbate insulin resistance. This mechanism indicates that insulin resistance is not solely a consequence of

obesity but may also actively contribute to its development and perpetuation.

In population studies, insulin resistance is most often assessed by means of the indirect HOMA-IR index, based on fasting glucose and insulin concentrations, with higher values reflecting greater insulin resistance [32]. Difficulties in interpretation arise from the fact that proposed cut-off values differ depending on the criteria and the population studied. In the general population, a HOMA-IR value > 2.5 is most commonly considered to suggest insulin resistance. It must be emphasised, however, that this is not a diagnostic indicator [32].

Insulin resistance may also be assessed using indices derived from glucose and insulin measurements during an oral glucose tolerance test (OGTT), of which the Matsuda index is most commonly used; a low Matsuda index indicates reduced insulin sensitivity.

Additional limitations of these indices arise from the multifactorial regulation of glucose and insulin concentrations: glycaemia depends not only on insulin but also on glucagon, glucose absorption, the incretin effect, and the degree of glucagon suppression, while insulin concentrations depend on tissue insulin sensitivity and on insulin secretion, distribution, and degradation, as well as on the incretin effect.

For these reasons, the results of such indices require cautious interpretation in the clinical context, and the gold standard for the *in vivo* assessment of insulin sensitivity remains the hyperinsulinaemic – euglycaemic clamp.

It should also be noted that insulin-sensitivity measurements are influenced by individual factors such as stress, intense physical exertion before the measurement, restrictive dieting, and pharmacotherapy.

Dysfunctional adipose tissue additionally exhibits altered secretion of factors regulating appetite, such as leptin, adiponectin, and pro-inflammatory cytokines, leading to attenuation of satiety signals and intensification of orexigenic signals – further favouring the perpetuation of positive energy balance and the development of obesity.

3.2. The role of genetic factors in the development of obesity

Genetic and epigenetic factors play an important role in the pathogenesis of obesity. The greatest importance is attributed to polygenic factors in combination with environmental influences. This "polygenic obesity", driven by polymorphisms in many genes, is regarded as the most common form of obesity [33]. Although it is well established that environmental factors significantly influence the development of obesity, genetic predisposition is regarded as an important modulator influencing the individual's response to environmental conditions. Among the genes predisposing to obesity is the *FTO* gene (fat mass and obesity-associated gene), which was among the first genes associated with obesity [34]. Studies in the general population have shown that carriers of *FTO* genetic variants predisposing to obesity have increased food intake, while the effect on energy expenditure appears to be less pronounced. The findings indicate that, with the *FTO* rs9939609 polymorphism, individuals with the AA genotype have, on average, a body weight approximately 3 kg higher and a BMI approximately 0.8 kg/m² higher than individuals not carrying the risk-increasing alleles. Subsequent studies have identified numerous other genes – including *CPT1A*, *ABCG1*, *SLC7A11*, *RNF145*, and *SREBF1* – which exert genetic or epigenetic effects on the occurrence of obesity. Polymorphisms of these genes are not, however, routinely tested in the molecular diagnosis of obesity [33, 34].

3.3. The role of diet and physical activity in the development of obesity

Changes in food availability and dietary patterns over recent decades have played a key role in the development of the obesity epidemic [26]. Epidemiological data indicate that population-level weight gain is largely associated with increased energy intake, leading to a sustained positive energy balance. At the same time, sedentary behaviour has been increasing, including a substantial reduction in occupation-related energy expenditure, which may further intensify weight gain.

Diets rich in highly processed foods, simple sugars, and fats, and at the same time poor in fibre and other satiety-promoting components, are characterised by high energy density and a limited satiating capacity. Their wide availability, high sensory attractiveness, and intensive marketing favour excessive energy intake and, in consequence, the perpetuation of a positive energy balance and an increased risk of developing obesity. Furthermore, observational and interventional studies indicate that this type of diet is associated with a higher risk of developing T2DM independently of total caloric intake.

An important and often underappreciated component of energy expenditure is NEAT, which encompasses spontaneous everyday activities. NEAT levels are typically lower in individuals with obesity than in lean individuals and exhibit substantial inter-individual variability, suggesting that reduced NEAT may contribute independently to the development of obesity [26].

Increased physical activity alone is of limited effectiveness as a weight-reduction strategy, which is explained by compensatory mechanisms

of energy homeostasis – chiefly increased energy intake. Nevertheless, regular physical activity plays an important role in the maintenance of reduced body weight.

Physical activity plays a key role not only in the pathogenesis of obesity but also in glucose metabolism disorders [35]. Numerous studies show that higher physical activity levels are associated with a substantially lower risk of developing T2DM – including in individuals with overweight/obesity, partly independently of weight reduction. Low activity therefore represents an independent risk factor for the development of insulin resistance. Higher levels of moderate- and vigorous-intensity activity have been shown to be associated with a 20–30% lower risk of developing T2DM [35].

Prolonged sedentary behaviour is independently associated with intensified insulin resistance and an elevated risk of developing T2DM, even after adjustment for physical activity level and BMI [36]. Moreover, sitting time may be a stronger predictor of insulin resistance than total physical activity time, and breaking up sitting with brief bouts of movement improves postprandial glycaemia [36].

3.4. The role of psychological, social, and economic factors in the development of obesity

Obesity is a chronic disease of multifactorial aetiology in which a key role is played not only by biological and environmental factors but also by psychological and social determinants. These factors influence both the development of obesity and its course, the effectiveness of treatment, and the risk of metabolic complications [37–39].

Chronic psychological stress is among the best-documented factors contributing to weight gain. Activation of the hypothalamic – pituitary – adrenal axis leads to increased cortisol secretion, which may promote visceral adipose tissue deposition, intensify appetite, and increase the preference for energy-dense foods. In addition, stress is associated with reduced physical activity and a greater tendency towards emotional eating.

Sleep disturbances also play an important role. Shortened sleep duration, poor sleep quality, and circadian rhythm disturbances may affect the regulation of hormones controlling hunger and satiety, promoting increased energy intake and weight gain [37]. Sleep disturbances are also associated with impaired emotional functioning and increased levels of stress, further entrenching adverse health behaviours.

Psychological mechanisms regulating food intake constitute another important component of the pathogenesis of obesity. Emotional eating, stress-induced eating, and disturbed satiety perception may lead to excessive energy intake and impede weight reduction [37].

Mental disorders – particularly depression and anxiety disorders – co-occur with obesity more frequently than in the general population and may impede its treatment. They affect the level of physical activity, eating patterns, and adherence to therapeutic recommendations. The co-occurrence of mental disorders may also increase the risk of developing metabolic complications of obesity [37, 39].

Social and economic factors are likewise of substantial importance. Lower socioeconomic status, restricted access to healthy food, the absence of infrastructure conducive to physical activity, and a low level of health education foster the perpetuation of unfavourable health behaviours and increase the risk of obesity. Living environment, urbanisation, the availability of highly processed foods, and sedentary work all constitute additional factors promoting weight gain [39].

In recent years, increasing attention has been paid to the problem of stigmatisation of individuals with obesity [38, 39]. The experience of prejudice and discrimination may lead to increased psychological stress, lowered self-esteem, avoidance of contact with the healthcare system, and worsened adherence to therapeutic recommendations (Figure 3.2).

3.5. Distinct features of the pathogenesis of obesity in the developmental age

Obesity in the paediatric population constitutes a highly heterogeneous phenotype, dynamically shaped at successive stages of somatic and neuroendocrine development. The most common form, including in children and adolescents with glucose metabolism disorders, remains polygenic obesity of multifactorial aetiology. In contrast to the adult population, however, in cases of very early-onset obesity, marked hyperphagia, or coexisting developmental disorders, monogenic and syndromic forms must more often be considered, which has substantial diagnostic implications [40].

Unlike in adults, the pathogenesis of obesity in children is closely linked to the stage of bodily maturation. Of particular significance are the so-called critical periods of development, during which lasting "programming" of energy-balance regulation takes place.

3.5.1. Pre-conception and fetal period

The pre-conception stage and intrauterine life constitute a key window of metabolic susceptibility [40, 41]. Maternal factors modulate the child's future risk of obesity through epigenetic and neuroendocrine mechanisms. Among the best-documented modifiable determinants are: excess ma-

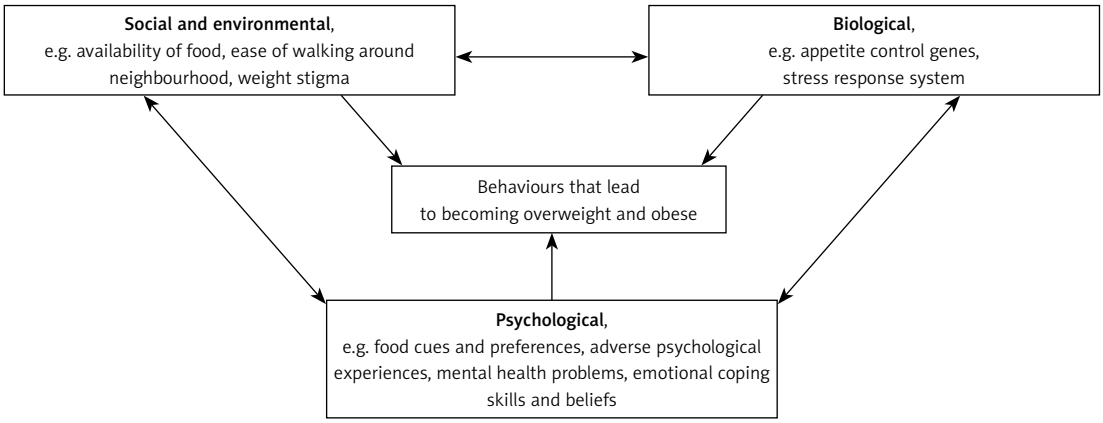


Figure 3.2. A biopsychosocial approach to obesity, after the British Psychological Society [39]

ternal body weight before pregnancy, abnormal gestational weight gain, hyperglycaemia, and tobacco-smoke exposure.

Birth weight and the rate of growth in the first months of life are strong predictors of subsequent obesity risk [40, 41]. High birth weight and the birth of a child large for gestational age (LGA) are associated with fetal exposure to an excess of energy substrates and predispose to a phenotype of increased adipose tissue accumulation. A different mechanism applies to children with intrauterine growth restriction or born small for gestational age (IUGR/SGA). Accelerated catch-up growth in infancy increases the risk of central obesity and insulin resistance, probably through a mismatch between thrifty metabolic programming and the high postnatal energy supply, together with unfavourable tissue allocation, including poorer development of muscle tissue and a greater tendency to visceral fat accumulation [40, 41].

3.5.2. Infancy and early childhood

The first 2 years of life constitute a stage of intensive adipocyte differentiation and maturation of the gut–brain axis. Rapid weight gain during this period is one of the strongest predictors of obesity in later life. Of importance are: the absence of breastfeeding, inappropriate introduction of complementary foods, sleep disturbances, and the early establishment of adverse taste preferences. Early occurrence of the so-called *adiposity rebound* (a reversal of the BMI trend before 5–6 years of age) is associated with an increased risk of obesity in school age and adulthood [40, 41].

3.5.3. School age

In the school years, environmental and behavioural patterns become entrenched – including low physical activity, prolonged sitting, and inappropriate dietary habits. At the same time, individual biological susceptibility related to genetic background and earlier metabolic programming becomes manifest [41].

3.5.4. Puberty

Adolescence represents a particular metabolic challenge. The physiological, transient deterioration of insulin sensitivity associated with hormonal changes (growth hormone, insulin-like growth factor 1 [IGF-1], sex steroids) may, in children with obesity, fail to normalise fully after the completion of puberty. This may favour the persistence of hyperinsulinaemia, progression to a prediabetic state, and the development of T2DM. Adolescence should be regarded as a critical window during which the risk of manifesting glucose tolerance disorders and accelerated β-cell dysfunction is particularly high [40].

In comparison with adults, the body of a child is characterised by greater metabolic plasticity. This means both a greater susceptibility to adverse programming during critical periods and a greater potential for reversibility of metabolic disturbances with early, comprehensive intervention.

4. SECONDARY CAUSES OF OBESITY

Key recommendations
• Patients with obesity should be evaluated for secondary causes when clinically indicated. [**A**]
• Levothyroxine is not recommended in individuals with obesity and normal thyroid function, nor in patients with subclinical hypothyroidism, solely for the purpose of weight reduction. [**B**]
• Routine screening for hypercortisolism is not recommended in patients with obesity. Diagnostic work-up should be initiated only on clinical suspicion of Cushing's syndrome. [**B**]
• Women of reproductive age with obesity, menstrual disturbances, and features of hyperandrogenism should be evaluated for polycystic ovary syndrome (PCOS). [**B**]
• In men with obesity and functional hypogonadism, lifestyle modification comprising dietary intervention and regular physical activity is recommended and, if ineffective, anti-obesity pharmacotherapy and/or bariatric treatment should be considered. [**B**]

- In women with obesity during the menopausal period, therapeutic management aimed at reducing body weight and the risk of metabolic complications associated with oestrogen deficiency should include lifestyle modification comprising dietary intervention and regular physical activity and, if ineffective, anti-obesity pharmacotherapy and/or bariatric treatment. [**B**]
- Syndromes combining monogenic obesity and monogenic diabetes provide examples of the co-occurrence of early-onset obesity with abnormalities of other systems and organs. [**A**]

Obesity is a disease of complex and heterogeneous aetiology, in which – alongside the dominant environmental and behavioural factors – endocrine disturbances may also play a substantial role. Excess body weight may be a consequence of secondary endocrine causes such as dysfunction of the hypothalamic – pituitary axis, hypothyroidism, hypogonadism, or growth hormone (GH) deficiency. Obesity occurs 2–3 times more frequently in women with PCOS. In rare cases, obesity may also have a monogenic genetic basis related to disturbances of central pathways regulating appetite and energy homeostasis. Recognition of these forms is of pivotal importance for appropriate diagnostic and therapeutic management [42].

4.1. The most common endocrine causes of obesity

4.1.1. Hypothyroidism

Overt hypothyroidism (↑ TSH, ↓ fT4) is found in approximately 14% of individuals with obesity, while subclinical hypothyroidism (↑ TSH, fT4 within reference range) occurs in a further 14.6% – a markedly higher proportion than in the general population, in which the prevalence of overt hypothyroidism is approximately 0.2–5.3% and that of subclinical hypothyroidism 4–10% [42].

Thyroid hormones play a substantial role in the regulation of metabolism, increasing thermogenesis and energy expenditure and intensifying lipolysis in adipose tissue. Their deficiency leads to a slowing of metabolic rate, decreased energy expenditure, and reduced thermogenesis, which manifests clinically with, among other features, cold intolerance. These changes are typically associated with modest weight gain, which in hypothyroidism results predominantly from water retention – caused by glycosaminoglycan deposition in tissues – rather than from a substantial increase in adipose tissue mass [42].

In children and adolescents, hypothyroidism is of particular clinical importance because thyroid hormones are critical for normal growth and maturation. The coexistence of hypothyroidism should be considered in cases of weight gain disproportionate to the rate of growth, or of growth deceleration [42].

Obesity may itself lead to elevated blood concentrations of thyroid-stimulating hormone (TSH). Increased leptin secretion by adipose tissue may stimulate the hypothalamic secretion of thyrotropin-releasing hormone (TRH), thereby raising TSH concentrations. In a proportion of individuals with obesity, slightly elevated TSH is observed – usually with normal fT4, and sometimes with higher fT3 – associated with increased type 2 deiodinase activity in adipose tissue. These changes are typically adaptive in nature and do not always indicate true hypothyroidism [42, 43].

Observational studies have also shown that obesity may be associated with a higher prevalence of thyroid autoimmunity markers, in particular elevated anti-TPO antibody titres, while the relationship with anti-TG antibodies is weaker. In addition, autoimmune hypothyroidism (Hashimoto's thyroiditis) is more frequently diagnosed in individuals with obesity, whereas no clear increase in the frequency of Graves-Basedow disease has been observed [44].

- Levothyroxine is not recommended for weight reduction in individuals with obesity and normal thyroid function (euthyroidism), in view of the lack of efficacy and the risk of iatrogenic hyperthyroidism manifesting, among other features, with arrhythmia, bone mass loss, and muscle catabolism [42].
- In patients with obesity, measurement of serum TSH is recommended as a screening test [42].
- Where TSH is elevated, fT4 should be measured; in clinically justified cases, antithyroid peroxidase (anti-TPO) antibodies should additionally be measured to assess autoimmune aetiology [42].
- Levothyroxine treatment should be instituted in cases of overt hypothyroidism.
- Subclinical hypothyroidism in individuals with obesity is not in itself an indication for treatment for the sole purpose of weight reduction; the therapeutic decision should be made individually, in accordance with endocrinology guidelines.
- Patients diagnosed with hypothyroidism should be referred for further endocrinological work-up to establish the aetiology of the disease and optimise treatment.

4.1.2. Hypercortisolism (Cushing's syndrome)

Hypercortisolism is a classic endocrinological cause of secondary obesity. The most common causes of hypercortisolism are endogenous overproduction of cortisol (Cushing's syndrome – adrenocorticotropic hormone [ACTH]-dependent or ACTH-independent) and exogenous exposure to glucocorticoids, the latter being the most common cause of cushingoid features [42].

Hypercortisolism intensifies the deposition of visceral adipose tissue, predisposes to insulin resistance and hyperglycaemia, increases appetite, and exerts catabolic effects on muscle – leading to a reduction in lean mass and lower energy expenditure. The result is central obesity accompanied by hypertension, dyslipidaemia, and T2DM [42].

At the same time, in individuals with obesity – particularly morbid obesity – *functional* hypercortisolism may be present, arising from chronic activation of the hypothalamic – pituitary – adrenal axis. It may also coexist with depression, chronic stress, alcohol abuse, obstructive sleep apnoea, and poorly controlled diabetes. Functional hypercortisolism is potentially reversible and may resolve following treatment of the underlying disease and weight reduction [42].

Particular clinical alertness should be prompted by highly discriminative clinical features, especially when they are multiple and progressive:

- facial plethora;
- easy bruising, thin skin, and delayed wound healing;
- proximal myopathy (weakness of the shoulder and pelvic girdle muscles, difficulty rising from a seated position);
- broad, purple striae (on the abdomen, thighs, and arms);
- in children: weight gain accompanied by growth deceleration [42].

Diagnostic work-up for hypercortisolism should always be carried out when adrenal incidentaloma is found on imaging [42].

In the diagnostic work-up of hypercortisolism, first-line screening tests are recommended for confirmation. The 1 mg overnight dexamethasone suppression test has the highest sensitivity. It must be borne in mind, however, that some medications (including oestrogen – progestogen contraception) may interfere with cortisol assays [42].

- Screening for hypercortisolism should be initiated only on clinical suspicion of Cushing's syndrome [42].
- Before starting diagnostic work-up, exposure to exogenous glucocorticoids (oral, inhaled, intranasal, topical) must be definitively excluded [42].
- In the event of abnormal screening test results or strong clinical suspicion of Cushing's syndrome, the patient should be referred to an endocrinologist for differential diagnosis and determination of the aetiology of the hypercortisolism [42].

4.1.3. Polycystic ovary syndrome

PCOS is a heterogeneous disorder characterised by androgen excess, which is associated with fertility problems and metabolic disturbances. Its pathogenesis includes genetic and environmental factors. PCOS is one of the more frequent endocrinopathies of women of reproductive age. Its prevalence is estimated at 6–20% depending on the diagnostic criteria adopted and ethnic background. In Europe, the Rotterdam criteria are used for the diagnosis of PCOS [45].

According to the literature, overweight/obesity affects approximately 60% of women with PCOS. Research data point to a relationship between obesity, insulin resistance, and PCOS [46]. Women with PCOS have a 2- to 3-fold increased risk of obesity and a higher risk of developing the metabolic syndrome, gestational diabetes mellitus (GDM), glucose tolerance disorders – both prediabetes and overt diabetes – and, consequently, of cardiovascular disease [45]. This is associated with obesity and insulin resistance [45]. Reduced insulin sensitivity may be detected in women with PCOS both with normal weight and obesity, but the presence of obesity substantially intensifies insulin resistance in this group [46]. Insulin resistance, with accompanying hyperinsulinaemia, is thought to drive increased androgen production by ovarian thecal cells, thereby influencing the clinical picture and consequences of PCOS [46]. It is worth emphasising that interventions which improve insulin sensitivity (behavioural management, weight-lowering pharmacotherapy, bariatric surgery) alleviate the manifestations of PCOS, reduce glucose metabolism disturbances, and improve fertility. In the case of glucose tolerance disturbances in women with PCOS, metformin is recommended. Drugs used in the treatment of obesity in the general population – particularly GLP-1-based therapies – are also used in the treatment of obesity in women with PCOS [47].

In view of the higher prevalence of glucose tolerance disturbances in women with overweight/obesity and PCOS, the recommended test for diagnosing glucose metabolism disorders is the OGTT [45].

Metformin is recommended for the treatment of glucose tolerance disturbances in women with PCOS.

4.1.4. Hypogonadism

Male hypogonadism

In adult men, testosterone plays a key role in maintaining muscle mass, bone mineral density, and sexual function. It exerts a beneficial effect on adipose-tissue metabolism, restricting fat accumulation – particularly visceral fat.

Low testosterone correlates positively with obesity, particularly with excess visceral adipose tissue. It exerts an anabolic effect on skeletal muscle, stimulating muscle protein synthesis and the

processes of regeneration and hypertrophy. Testosterone deficiency leads to loss of muscle mass, lowered basal metabolic rate, and increased risk of obesity and metabolic disturbances [48].

Testosterone improves tissue insulin sensitivity and reduces the risk of metabolic diseases such as T2DM, dyslipidaemia, and MASLD.

The relationship between low testosterone and obesity is bidirectional. On the one hand, lower testosterone favours weight gain. The cause may be hypergonadotropic hypogonadism (resulting from impaired testicular function) or hypogonadotropic hypogonadism (resulting from impaired hypothalamic – pituitary function). On the other hand, men may develop functional, obesity-related hypogonadism – male obesity-associated secondary hypogonadism (MOSH). This condition presents as hypogonadotropic hypogonadism but does not result from organic abnormalities of the hypothalamic – pituitary – testicular axis; rather, it is the consequence of obesity itself and of certain medications, among other factors [42]. This disorder affects approximately 40% of men with obesity.

The development of MOSH is driven by multiple mechanisms, including: enhanced peripheral conversion of androgens to oestrogens, with oestradiol-mediated inhibition of the pulsatile hypothalamic secretion of gonadotropin-releasing hormone (GnRH) and pituitary luteinising hormone (LH), thereby secondarily lowering testosterone production; suppression of hypothalamic kisspeptin gene expression as a consequence of leptin and insulin resistance, which likewise weakens pulsatile GnRH secretion; and reduced sex hormone-binding globulin (SHBG) concentrations in obesity and insulin resistance, which decreases the amount of biologically active free testosterone.

A further potential cause of obesity is age-related testosterone deficiency (late-onset hypogonadism, LOH), most commonly functional hypogonadotropic hypogonadism.

It has been shown that weight reduction leads to a substantial increase in blood testosterone concentration, in proportion to the extent of weight loss. Testosterone therapy has a limited effect on body weight, although it may favourably influence body composition.

Routine hormonal evaluation for hypogonadism is not recommended in men with obesity in the absence of clinical features suggestive of testosterone deficiency [42]. Hormonal screening is indicated in patients reporting symptoms suggestive of hypogonadism, such as reduced libido, erectile dysfunction (including absence of morning erections), chronic fatigue, low mood, decreased muscle mass, and difficulty in reducing body weight despite lifestyle modification and treatment of obesity.

- The basic test is the measurement of total serum testosterone in the morning between 7:00 and 10:00 a.m. in a fasting state. The measurement should be deferred in cases of acute inflammation or exacerbation of chronic disease. Total testosterone should be measured at least twice, using a reliable laboratory method.
- A persistent reduction in total testosterone (particularly < 8 nmol/l, i.e. < 230 ng/dl; values of 8–12 nmol/l, i.e. 230–350 ng/dl, are regarded as borderline) or a reduced free testosterone concentration measured directly by a reliable laboratory method or calculated from total testosterone and SHBG (e.g. < 220 pmol/l or < 65 pg/ml), in the presence of clinical symptoms, allows the diagnosis of hypogonadism.
- A patient diagnosed with hypogonadism should be referred to an endocrinologist, andrologist, or urologist to exclude organic causes and determine further diagnostic and therapeutic management.
- In men with obesity and functional hypogonadism, weight reduction frequently improves the functioning of the hypothalamic – pituitary – testicular axis.
- In men with obesity and functional hypogonadism, testosterone replacement therapy may be considered in cases of persistent testosterone deficiency and significant clinical symptoms after unsuccessful treatment of obesity and concomitant diseases. It always requires individual analysis of the potential benefits and risks and should be initiated and conducted by a specialist – an endocrinologist, andrologist, or urologist [42].

Female hypogonadism

Female hypogonadism is a state resulting from primary ovarian insufficiency or from secondary (central) disturbances of the hypothalamic – pituitary axis, occurring during the period from normal puberty to the menopause. It leads to deficiency of sex hormones, menstrual disturbances (including amenorrhoea), anovulation, and infertility, often accompanied by sexual or vasomotor symptoms. Biochemically, it is characterised by persistently low concentrations of 17β-oestradiol [49].

The menopause constitutes the physiological form of primary hypogonadism. Oestrogen deficiency, in addition to vasomotor and psychological symptoms, leads to reduced muscle mass, lowered basal metabolic rate, and weight gain – predominantly in the form of visceral adipose tissue. The menopause is also associated with an increased risk of T2DM and cardiovascular disease, in part through worsening of the lipid profile (↑ low-density lipoprotein cholesterol [LDL-C], ↓ high-density lipoprotein cholesterol [HDL-C]) [49]. Routine

hormonal evaluation of gonadal function is not recommended in women with obesity who do not have clinical symptoms.

- Hormonal testing is indicated when menstrual disturbances, infertility, or features of hyperandrogenism are present.
- Hormone replacement therapy (HRT) alleviates menopausal symptoms and improves quality of life but is not recommended as a treatment of obesity.
- In women with obesity during the menopausal period, lifestyle modification (appropriate diet and physical activity) is indicated in order to reduce the risk of obesity and metabolic complications associated with hypogonadism [42, 49].

4.1.5. GH deficiency

GH plays a substantial role in the regulation of body composition: it exerts anabolic effects mainly through IGF-1, and lipolytic effects on adipose tissue independent of IGF-1. The anabolic effect of GH is enhanced under conditions of positive energy balance and adequate insulin concentrations, while the lipolytic effect predominates between meals and during fasting. GH excess, as in active acromegaly, leads to a reduction in adipose-tissue mass and an increase in lean body mass, whereas GH deficiency favours adipose-tissue deposition, particularly visceral [50].

GH deficiency in adults is most commonly the consequence of damage to the hypothalamic – pituitary axis from neoplasms, strokes, inflammatory processes, or surgical treatment, among other causes. The symptoms of GH deficiency in adults are non-specific and include unfavourable changes in body composition, reduced muscle mass and bone mineral density, lipid abnormalities, insulin resistance and glucose tolerance disturbances, and decreased mood and life energy. In children, the dominant feature is short stature with disturbed body proportions [50].

In individuals with obesity, functional, potentially reversible suppression of GH secretion frequently occurs, associated with elevated free fatty acid concentrations and excess leptin secretion. These mechanisms inhibit the secretion of growth hormone-releasing hormone (GHRH) in the hypothalamus, leading to reduced GH secretion in the pituitary. Serum IGF-1 concentrations typically remain normal, with reductions seen mainly in severe obesity. Weight reduction results in improved functioning of the somatotropic axis [50].

In view of the favourable effects of GH on lipolysis and protein metabolism, this hormone has been investigated as a potential treatment for obesity; however, studies to date have not shown a substantial or lasting effect of GH therapy on weight reduction.

- Routine testing for growth hormone deficiency is not recommended in individuals with obesity.
- Evaluation of the somatotropic axis should be considered only in patients with suspected hypopituitarism, in which case the patient should be referred for further endocrine diagnostics.
- Activation of the somatotropic axis has no therapeutic application in the treatment of obesity.
- The use of GH as an adjunctive treatment in the therapy of obesity is not recommended [42, 50].

4.1.6. Hypothalamic damage

The hypothalamus is a key centre integrating the nervous and endocrine systems and is responsible for maintaining the homeostasis of the organism. It regulates, among other functions, hunger, thirst, thermogenesis, the sleep – wake rhythm, and emotional functions, and controls pituitary activity through the secretion of stimulating and inhibitory hormones (GnRH, corticotropin-releasing hormone [CRH], GHRH, TRH, somatostatin, dopamine). The hypothalamus also synthesises vasopressin and oxytocin, which are stored in the posterior pituitary lobe [51].

The most common cause of hypothalamic damage is tumours of this region (approximately 50% of cases), as well as trauma, surgical treatment and radiotherapy, inflammatory and vascular processes, and rare genetic syndromes (e.g. Kallmann syndrome, Prader-Willi syndrome).

Depending on the location and extent of damage, deficiency of hypothalamic hormones and secondary hypopituitarism – affecting one or several hormonal axes – may develop, which may favour the development of obesity [51, 52].

Damage to hypothalamic structures regulating appetite and energy expenditure may also lead to the development of *hypothalamic obesity*, characterised by hyperphagia and rapid weight gain. It affects approximately 25% of patients with substantial structural hypothalamic damage, most often in the course of craniopharyngioma or following surgical treatment and radiotherapy, and less commonly in genetic syndromes related to disturbance of the leptin – melanocortin pathway [51]. The pathogenesis comprises excessive activation of the orexigenic system, weakened satiety signals, hyperinsulinaemia resulting from parasympathetic activation, and reduced sympathetic activity leading to reduced energy expenditure. This form of obesity is often resistant to treatment, and the greatest weight gain is observed in the first year after hypothalamic damage [52].

- Of pivotal importance is the early identification of individuals at high risk of hypothalamic obesity, allowing the rapid implementation of preventive measures.

4.2. Monogenic obesity and obesity in the course of rare genetic syndromes

Monogenic obesity affects approximately 1–5% of patients with severe early-onset obesity, defined as obesity beginning before 5 years of age, the cause of which is a pathogenic variant in a single gene.

From a clinical standpoint, it can be divided into isolated monogenic obesity and syndromes combining monogenic obesity with monogenic diabetes.

In non-syndromic monogenic obesity, dynamic weight gain in the first years of the patient's life is accompanied by hyperphagia, endocrine disturbances and/or immunodeficiencies, and – less frequently – intellectual disability or neurodevelopmental disturbances. Underlying these are genes involved in the regulation of hunger/satiety, related to the leptin – melanocortin signalling pathway in the hypothalamus; in differential diagnosis, leptin levels should be considered. The most common form of this obesity is MC4R receptor deficiency due to mutations in the *MC4R* gene, accounting for 2–6% of cases of severe early-onset obesity. In addition to obesity, patients exhibit tall stature and hyperinsulinaemia. *MC4R* gene variants have also been described in patients with early-onset T2DM. Other forms of monogenic obesity include disturbances associated with pathogenic variants in the *LEP*, *LEPR*, *POMC*, and *PCSK1* genes [53].

A syndromic form of monogenic obesity is present when a genetic mutation gives rise to multiple clinical features. In addition to obesity, patients usually present with: marked insulin resistance, visual disturbances, neurodevelopmental abnormalities, neurological disturbances, and T2DM.

Among syndromic forms of monogenic obesity and diabetes, Alström syndrome (ALMS) and Bardet-Biedl syndrome (BBS) – both ciliopathies – should be mentioned. Their common clinical denominator is early-onset obesity with insulin resistance and pigmentary retinal degeneration, accompanied in subsequent decades of life by a broad spectrum of additional disturbances – chiefly T2DM, dyslipidaemia, hypertension, hearing impairment, cognitive impairment, and renal, hepatic, pulmonary, and cardiac abnormalities [54]. In ALMS associated with mutations in the *ALMS1* gene, intellectual disability does not occur, nor do additional digits or shortening or fusion of the fingers and/or toes, which are characteristic of patients with BBS.

It must be emphasised that the molecular diagnosis of monogenic diabetes and obesity syndromes is a demanding task – owing to the necessity of using next-generation sequencing (NGS) in each case and the potential difficulties in interpretation of the results obtained. The definitive diagnosis of the type of monogenic obesity is established on the basis of the genetic test result in conjunction with the patient's phenotype. The mode of inheritance of the defect may differ even within the same gene; in BBS, complex multigenic inheritance may also be encountered.

In the treatment of monogenic obesity and its syndromic forms, there are reports of beneficial effects of GLP-1-based therapies, as well as of targeted therapies using metreleptin (in patients with *LEP* mutations) and the MC4R receptor agonist setmelanotide (in patients with mutations in *LEPR*, *POMC*, *PCSK1*, and BBS) [53].

- Where obesity has its onset in early childhood, with marked hyperphagia or coexisting developmental disturbances, the possibility of monogenic and syndromic forms should be considered.

4.3. Medications associated with the development of obesity

In the choice of pharmacotherapy – particularly in individuals with overweight/obesity or at increased risk of its development – the influence of medications on body weight must be taken into account, and currently used preparations should be reviewed for their potential weight-promoting effect. Excess body weight increases the risk of insulin resistance, dyslipidaemia, the metabolic syndrome, T2DM, MASLD, cardiovascular diseases, neoplasms, and all-cause mortality.

Weight gain or unfavourable redistribution of adipose tissue are common adverse effects of many widely used drugs – particularly older-generation antidiabetic agents, neuropsychiatric drugs (including atypical antipsychotics), antidepressants, and antiepileptics [55]. The chronic use of glucocorticoids is likewise associated with redistribution of adipose tissue, the development of

Table 4.1. Medications associated with weight gain

Drug class	Drugs associated with weight gain	Mechanism leading to weight gain
Antipsychotic drugs	Clozapine – greatest weight gain; olanzapine – greatest weight gain; chlorpromazine; paliperidone; quetiapine; risperidone; thioridazine	Excessive food intake due to disturbance of neurotransmitter function in the hypothalamus

Table 4.1. Cont.

Drug class	Drugs associated with weight gain	Mechanism leading to weight gain
Mood stabiliser	Lithium	Increased thirst and increased intake of high-energy beverages; changes in food preferences through effects on hypothalamic centres controlling appetite; increased frequency of hypothyroidism (lithium inhibits the synthesis and release of thyroid hormones)
Antidepressants	Selective serotonin reuptake inhibitors (SSRIs): paroxetine (greatest weight gain); sertraline, citalopram, escitalopram, etc.	Appetite stimulation due to increased serotonin concentrations, particularly with long-term use; this results in desensitisation of 5-HT_{2C} receptors, leading to attenuation of the anorexigenic effect of serotonin; chronic modulation of the serotonergic system may lead to compensatory increases in appetite for high-carbohydrate foods
	Tricyclic antidepressants: amitriptyline, clomipramine, doxepin, imipramine, etc.	Chronic modulation of the serotonergic system may lead to compensatory increases in appetite for high-carbohydrate foods; effects on antihistaminergic and anticholinergic pathways
Antiepileptics	Valproic acid; gabapentin; perampanel; pregabalin; vigabatrin	Valproic acid: interactions with neuropeptides regulating appetite in the hypothalamus; effects on energy expenditure; intensification of leptin resistance; reduction of adiponectin concentration
Antihyperglycaemic drugs	Insulin	Anabolic action (increases protein synthesis, stimulates lipogenesis)
	Sulphonylureas	Increased endogenous insulin concentrations
	Pioglitazone	Fluid retention; intensified lipid storage; weight gain predominantly of subcutaneous adipose tissue
β-blockers	Metoprolol; atenolol; propranolol	Reduction of basal metabolic rate and postprandial thermogenesis; inhibition of lipolysis in response to adrenergic stimulation
	Carvedilol, nebivolol: smaller weight gain	More favourable effect on glycaemia and lipid profile; nebivolol: induction of lipolysis and reduction in lipid droplet size in adipocytes
α_1-blockers	Doxazosin; prazosin; terazosin	Increased extracellular fluid and plasma volume
Calcium-channel blockers	Flunarizine (calcium and histamine receptor antagonist)	Appetite stimulation
Glucocorticoids	Prednisone; prednisolone; dexamethasone; methylprednisolone; hydrocortisone	Increased food intake, particularly of high-energy foods; activation of the endocannabinoid system, which plays a role in the control of food intake and appetite; effects on adipose tissue distribution, predominantly increasing visceral adipose tissue
Hormonal agents	Synthetic progestogens: medroxyprogesterone, megestrol	Appetite stimulation, increased caloric intake
Antihistamines	First-generation H1 antihistamines: hydroxyzine, diphenhydramine, etc.; second-generation H1 antihistamines: cetirizine, desloratadine, fexofenadine	Sedation and increased appetite mediated by blockade of central hypothalamic H_1 histamine receptors
Antiretroviral drugs	Protease inhibitors: atazanavir, darunavir, etc.; integrase inhibitors: bictegravir, dolutegravir, raltegravir	Exacerbated central accumulation of adipose tissue; loss of subcutaneous adipose tissue in the limbs and face (lipodystrophy)

central obesity, and skeletal muscle catabolism and atrophy. Some antiretroviral drugs may be associated with weight gain and disturbances in adipose tissue distribution, including lipodystrophy [56].

A summary of medications predisposing to weight gain is presented in Table 4.1.

5. CLINICAL CONSEQUENCES OF OVERWEIGHT/OBESITY

Key recommendations
• Regular monitoring of individuals with overweight/obesity – particularly with abdominal obesity – for the presence of prediabetes and T2DM is necessary. [**A**]
• In every patient with overweight/obesity, cardiovascular risk should be routinely assessed, taking into account waist circumference, blood pressure, and features of organ damage, irrespective of BMI. [**B**]
• In patients with overweight/obesity and arterial hypertension, ambulatory or home blood-pressure monitoring is recommended in order to identify circadian-rhythm disturbances and enable precise risk stratification. [**A**]
• Obesity in individuals with glucose metabolism disorders is an independent risk factor for the development and progression of chronic kidney disease (CKD), irrespective of its underlying cause. [**A**]
• In patients with overweight/obesity and accompanying metabolic disturbances who report memory impairment, evaluation of cognitive function using screening tests is recommended. [**B**]
• Obesity should be regarded as an independent risk factor for the development of, and death from, many malignant tumours; in individuals with obesity, increased oncological vigilance in line with current screening programmes is recommended. [**A**]
• In patients with overweight/obesity, systematic monitoring of mental status should be considered at the various stages of treatment – particularly before starting anti-obesity pharmacotherapy, including GLP-1-based therapies, and during such treatment, especially in individuals with current or past mental disorders. [**B**]
• In patients with obesity, diagnostic work-up for MASLD is recommended, taking into account metabolic risk factors and non-invasive assessment of hepatic fibrosis. [**A**]
• In children and adolescents with glucose metabolism disorders and coexisting obesity, systematic assessment for cardiovascular–kidney–metabolic complications and disturbances of sexual maturation should be carried out. [**B**]
• In the developmental-age population, early identification and active treatment of obesity coexisting with glucose metabolism disorders are recommended in order to limit the accelerated progression to T2DM and early microvascular and cardiometabolic complications. [**A**]

Obesity constitutes a substantial and growing public-health problem, which directly causes – and significantly intensifies – the development of numerous metabolic and end-organ disturbances, including T2DM, cardiovascular disease, CKD, MASLD, neoplasms, and disturbances of CNS function. Its multifaceted character encompasses metabolic, pro-inflammatory, hormonal, immunological, and psychosocial components, which together determine the clinical course, complications, and prognosis of comorbid conditions.

5.1. Clinical consequences of obesity for glucose metabolism

Obesity – particularly abdominal obesity – is closely associated with the development of glucose metabolism disorders such as prediabetes and T2DM. Persons with prediabetes typically do not exhibit the classic symptoms of diabetes; however, they belong to a group at substantially elevated risk of developing T2DM, which accounts for approximately 90% of all cases of diabetes.

Data from prospective analyses indicate that the annual rate of progression from prediabetes to T2DM is approximately 4–6% in individuals with isolated IGT, 6–9% in individuals with isolated IFG, and may reach 15–19% per year in individuals with both abnormalities present concurrently. Patients with abdominal obesity and early glucose metabolism disturbances often already exhibit other features of the metabolic syndrome, such as dyslipidaemia or arterial hypertension. It has also been shown that, even at the prediabetic stage, the chronic microvascular complications characteristic of diabetes – including retinopathy, neuropathy, and renal complications – may already be present. Prediabetes is also associated with an elevated risk of cardiovascular disease [57, 58].

The early recognition of prediabetes is of pivotal importance for preventing the development of T2DM and its micro- and macrovascular complications. Therefore, even at this stage, restoration of normoglycaemia should be sought in order both to prevent T2DM and to improve the overall metabolic profile, which may contribute to the reduction of cardiovascular risk.

The likelihood of returning to normoglycaemia depends on the extent of the metabolic disturbances. Clinical studies indicate that, in individuals with obesity and more advanced prediabetes (HbA_{1c} in the range of 6.0 to < 6.5%), achieving normoglycaemia is substantially more difficult, which justifies the early implementation of intensive interventions – comprising lifestyle modification and, in selected patients, also consideration of pharmacological treatment of obesity for the prevention of T2DM (see Section 10.2).

5.2. Obesity, cardiovascular risk, and arterial hypertension

Obesity is recognised as an independent risk factor for cardiovascular disease. It constitutes a complex set of metabolic, haemodynamic, neurohormonal, and inflammatory disturbances that synergistically increase the risk of arterial hypertension, coronary artery disease, heart failure, cardiac arrhythmias, and stroke. Obesity should therefore be regarded not merely as a coexisting risk factor but as a key pathophysiological component directly involved in the development of cardiovascular disease [59, 60].

From an epidemiological standpoint, there is a strong relationship between rising BMI values and the incidence of cardiovascular disease and both all-cause and cardiovascular mortality. At the same time, the limitations of BMI as a sole risk indicator are becoming increasingly evident, with growing emphasis on the central importance of adipose-tissue distribution – and visceral obesity in particular. Visceral adipose tissue accumulation is associated with intensified inflammation, insulin resistance, endothelial dysfunction, and adverse haemodynamic changes, which determine cardiovascular risk to a greater extent than total body mass alone [60, 61].

Arterial hypertension is one of the most frequent and best-documented clinical consequences of obesity. The prevalence of hypertension increases in proportion to body weight and waist circumference, and obesity substantially increases the risk of developing essential hypertension, including resistant forms. The pathophysiological mechanisms underlying this relationship are multifactorial. They include increased sodium and water retention, leading to a rise in circulating blood volume and cardiac output; chronic activation of the sympathetic nervous system and the renin–angiotensin–aldosterone (RAA) system; and disturbances of renal function and increased vascular stiffness. Adipose tissue acts as an active endocrine organ secreting adipokines and pro-inflammatory cytokines that modulate vascular tone, insulin sensitivity, and the endothelial inflammatory response [61, 62].

A key element in the pathophysiology of obesity-related hypertension is endothelial dysfunction, leading to a reduction in nitric-oxide bioavailability and a predominance of vasoconstrictor factors. In parallel, remodelling of resistance vessels occurs, with increased stiffness and intensified oxidative stress. In many patients with obesity, disturbances of the circadian rhythm of blood pressure are observed, including the absence of a nocturnal blood-pressure dip (non-dipping), which further increases the risk of cardiovascular and end-organ complications. Coexisting obstructive sleep apnoea is often an additional factor intensifying sympathetic activation and haemodynamic instability.

The haemodynamic consequences of obesity also include substantial structural and functional cardiac changes. Chronic volume overload, increased cardiac output, and increased metabolic demand lead to left-ventricular hypertrophy, enlargement of the cardiac chambers, and disturbances of diastolic relaxation. In conjunction with arterial hypertension, this favours the development of heart failure – particularly heart failure with preserved ejection fraction (HFpEF), now recognised as the dominant phenotype of heart failure in individuals with obesity. An increased prevalence of atrial fibrillation is also observed in this population, related to left-atrial enlargement, fatty infiltration of the atria, and electrophysiological changes.

Obesity substantially accelerates atherogenesis. The mechanisms responsible for this effect include atherogenic dyslipidaemia, insulin resistance, chronic low-grade inflammation, haemostatic disturbances, and arterial hypertension. Elevated triglyceride concentrations, reduced HDL-C, and the presence of small, dense LDL particles favour lipid deposition in the vascular wall. At the same time, pro-inflammatory cytokines and adipokines intensify endothelial cell activation and the migration of inflammatory cells into the atherosclerotic plaque. Consequently, individuals with obesity are at higher risk of coronary artery disease, stroke, and peripheral arterial disease.

In the assessment of cardiovascular risk in patients with obesity, comprehensive clinical evaluation extending beyond BMI measurement is of pivotal importance. Routine assessment of waist circumference (as a simple indicator of visceral obesity), blood pressure (preferably using ambulatory or home monitoring), metabolic parameters, and early features of organ damage such as left-ventricular hypertrophy, microalbuminuria, or increased arterial stiffness is recommended. The recognition of coexisting disorders – including sleep apnoea – that modify cardiovascular risk and the clinical picture is also of importance.

In summary, obesity substantially increases cardiovascular risk through complex pathophysiological mechanisms leading to the development of arterial hypertension, atherosclerosis, heart failure, and cardiac arrhythmias. In clinical practice, this requires early identification of patients at the highest risk, appropriate risk stratification, and a holistic approach to diagnostic work-up and treatment.

5.3. Obesity and its renal consequences

Obesity is an independent risk factor for the development and progression of CKD, even after

correcting for the influence of arterial hypertension and T2DM. Obesity increases the risk of CKD development and progression by approximately 20–30% compared with individuals without this disease; the risk is markedly greater in patients with extreme obesity [63, 64].

Obesity-related glomerulopathy (ORG) is a diagnosis of exclusion and cannot be made solely on the basis of the clinical phenotype. In patients with obesity, the standard indications for renal biopsy should be applied; it should not be assumed *a priori* that proteinuria or a decline in estimated glomerular filtration rate (eGFR) is a consequence of ORG. The histopathological changes in ORG are non-specific and most often comprise focal and/or segmental glomerulosclerosis (FSGS). Obesity-related glomerulopathy typically manifests with proteinuria of varying severity (up to nephrotic range), although hypoalbuminaemia usually does not develop or is less pronounced. The disease is progressive, and it is estimated that in approximately one-third of patients (particularly those with extreme obesity) it may lead to advanced stages of renal injury, including end-stage renal disease [63].

Renal injury in obesity is multifactorial in nature and comprises:

- disturbances of renal microcirculatory haemodynamics with excessive afferent arteriolar dilatation and hyperfiltration;
- progressively worsening hypoxia developing and progressing in parallel with hyperfiltration-induced vascular damage;
- excessive activation of the systemic and tissue RAA axis, vasopressin secretion, and increased expression and activity of sodium–glucose cotransporters;
- the influence of pro-inflammatory and pro-fibrotic cytokines and adipokines derived from adipose tissue irrespective of its location (and from peri-renal adipose tissue [PRAT] in particular), together with increased sympathetic activation;
- the mechanical effects of PRAT, impairing renal haemodynamics at both the microcirculatory level and the level of the larger (especially venous) vessels – through compression of the kidneys by PRAT and increased intra-renal pressure (so-called renal tamponade) – and through compression by excessive adipose tissue at the renal hilum on the structures located there.

These mechanisms favour both the development of ORG and the progression of CKD of other aetiologies, justifying early multidirectional renoprotective management.

It is recommended to assess eGFR using the equation based on creatinine and cystatin C of the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI Cr-Cys), in view of its highest reliability against reference measurement methods. Owing to the limited availability of serum cystatin C measurement, the CKD-EPI Cr equation is recommended as an alternative for the assessment of renal function in individuals with obesity.

In clinical practice, when assessing and interpreting eGFR results, the following must be taken into account:

- the influence of sarcopenia or reduced muscle mass on serum creatinine;
- the possibility of underestimating the severity of CKD when relying solely on creatinine in patients with protein malnutrition;
- limitations in interpreting urinary albumin or protein excretion normalised to creatinine (urine albumin-creatinine ratio [UACR]; urine protein-creatinine ratio [UPCR]) in cases of variable creatinine excretion, e.g. in sarcopenia;
- the influence of overhydration on body weight in advanced stages of CKD.

Practical conclusions:

1. Muscle mass in patients with obesity may substantially affect the results of eGFR and UACR measurements and their interpretation.
2. Overhydration substantially affects anthropometric measurements in patients with obesity in advanced stages of CKD.
3. Obesity is an independent risk factor for the development and progression of obesity-related glomerulopathy, and for the development and progression of CKD irrespective of its cause. Specific criteria for the recognition, monitoring, and risk stratification of CKD in patients with obesity have not been defined; the guidelines applicable to other risk groups (e.g. arterial hypertension or diabetes) are therefore used.
4. Patients with obesity should undergo diagnostic renal biopsy in accordance with the general principles set out in nephrological guidelines. It should not be assumed *a priori* that proteinuria and/or reduced eGFR of unknown cause are caused by obesity-related glomerulopathy.

5.4. Consequences of obesity and metabolic disturbances in relation to neurodegeneration and cognitive impairment

Obesity is associated with impairment of cognitive function in the general population and with its deterioration in prospective observation. Furthermore, overweight or obesity in midlife is associated with a higher risk of dementia (Alzheimer's disease and vascular dementia) in later life, independently of comorbidities and other risk factors. This risk has been quantified as 35% higher in individuals with overweight and 74% higher in individuals with obesity, with the rela-

tionship being stronger in women. A similar association has been observed between anthropometric measures characterising obesity in midlife and the subsequent development of Parkinson's disease [65].

Overweight and obesity are associated with reduced cerebral blood flow – a risk factor for Alzheimer's disease – as well as reduced integrity of white and grey matter, and with brain atrophy and reduced neuronal viability. An important factor increasing the risk of neurodegenerative diseases and vascular dementia is insulin resistance and the metabolic disturbances associated with it, including prediabetes and T2DM [65, 66].

Insulin crosses the blood–brain barrier, and insulin receptors are expressed in various regions of the CNS, including the hypothalamus and cerebral cortex. The brain has also been shown to express the insulin-dependent glucose transporter GLUT4. Insulin influences neuronal electrical activity, the synthesis and release of neurotransmitters, synaptic plasticity, the metabolite content of the CNS, and cognitive function. Furthermore, owing to insulin's involvement in the degradation of amyloid β (Aβ) peptides, insulin resistance and hyperinsulinaemia may favour the accumulation of Aβ oligomers and deposits in the CNS, which play an important role in the pathogenesis of Alzheimer's disease.

In obesity and insulin resistance, lower blood concentrations of adiponectin and brain-derived neurotrophic factor (BDNF) are also found. These compounds exert neuroprotective effects. Leptin may have similar properties. In obesity, its blood concentrations are increased, but leptin resistance develops.

Chronic inflammation in adipose tissue may activate the inflammatory response in the CNS as well (neuroinflammation). The passage of pro-inflammatory cytokines across the blood–brain barrier may activate pro-inflammatory pathways, reduce synaptic plasticity, impair neurogenesis, and additionally activate microglial cells and astrocytes. These processes favour the development of neurodegenerative diseases.

In summary, elevated BMI constitutes a modifiable risk factor for neurodegenerative diseases. Prevention and treatment of obesity may be of substantial importance in the prevention of these conditions. For this reason, in patients with obesity – particularly with coexisting glucose metabolism disorders and other metabolic disturbances – who report memory impairment, assessment of cognitive function using screening tests such as the Mini-Mental State Examination (MMSE) or the Montreal Cognitive Assessment (MoCA) is recommended, with referral to appropriate diagnostic and therapeutic centres depending on the results obtained.

5.5. Obesity and the risk of cancer development and progression

Obesity is a risk factor for the incidence of most malignant tumours, and every increase in BMI of 5 kg/m² is associated with a substantial rise in the risk of practically all cancers. The greatest increase in risk in both sexes is observed for cancers of the liver, kidney, thyroid, colorectum, oesophageal adenocarcinoma, and pancreas. In women, the risk of uterine, ovarian, and post-menopausal breast cancer, as well as of gallbladder cancer, also rises highly significantly [67].

Hyperglycaemia plays a substantial role in the development and progression of malignant tumours. The greatest increase in cancer risk in individuals with diabetes has been demonstrated for cancers of the liver, endometrium, and pancreas. A very large cohort study conducted in China showed an elevated risk of malignant tumours in individuals with diabetes in the population aged < 70 years; in older age, the risk did not differ significantly. In men, obesity did not additionally increase this risk, but in women, the influence of obesity on increased risk was significant up to 70 years of age. The risk of cancer-related death in individuals with T2DM compared with the population without diabetes was likewise higher, and the greatest increase in this risk was found for cancers of the thyroid, liver, and pancreas [67, 68].

The increased cancer risk in diabetes – particularly type 2 – is associated principally with three phenomena: obesity, hyperglycaemia, and hyperinsulinaemia. Hyperinsulinaemia is of particular importance because the density of insulin receptors in tumour tissue is 2–3 times higher than in surrounding healthy tissue, and, in addition, type A receptors predominate in tumour tissue, principally activating the mitogen-activated protein kinase (MAPK) pathway.

Antihyperglycaemic drugs may modulate the risk of tumour development and progression. The lowering of glycaemia *per se* may reduce cancer risk by reducing the energy supply to tumour cells. Weight reduction and reduction of inflammation may also exert oncoprotective effects. The largest body of observational data concerns metformin and points to a protective effect of its use through activation of AMP-activated kinase, which inhibits angiogenesis and exerts antiproliferative effects, reducing cancer risk. It appears that newer drug classes – such as GLP-1-based therapies and sodium-glucose transport protein 2 (SGLT-2) inhibitors – also have anticancer potential, although longer-term observational cohort studies are required to confirm this.

In summary, obesity in conjunction with glucose metabolism disorders (including diabetes) increases the risk of developing malignant tumours.

Therefore, in this group of persons, heightened oncological vigilance is warranted, particularly with regard to gastrointestinal and renal tumours, and – in women – endometrial and breast cancer, especially in the post-menopausal period.

5.6. Psychosocial aspects of obesity and psychiatric complications

Obesity is a chronic disease with a documented, substantial impact on psychological and social functioning; psychosocial assessment should therefore form an integral part of diagnostic and therapeutic management. Obesity is associated not only with somatic burden but also with chronic psychological stress, decreased quality of life, and disturbances of interpersonal and occupational functioning. Routine assessment of health-related quality of life, body image, experiences of stigmatisation, and symptoms of psychological distress in clinical practice is recommended, irrespective of the severity of obesity as defined by BMI – which does not fully reflect the subjective and psychosocial dimensions of the disease [69].

In the course of obesity, mental disorders frequently coexist – particularly depressive disorders, anxiety disorders, sleep disturbances, and eating disorders, especially binge eating disorder. The available data point to a bidirectional relationship between obesity and mood disorders, conditioned by both biological and psychosocial factors. Biological mechanisms include chronic low-grade inflammation associated with the excessive activity of visceral adipose tissue and increased pro-inflammatory cytokine secretion; dysregulation of the hypothalamic–pituitary–adrenal axis, leading to disturbances of the stress response; and insulin resistance and disturbances of insulin signalling in the CNS. An important role is also played by changes in neurotransmitter systems and dysregulation of the central mechanisms controlling appetite and reward, which favour the entrenchment of impulsive and emotional eating patterns. In addition, an increasing body of data points to the role of the gut–microbiota–brain axis, in which gut dysbiosis, increased intestinal permeability, and activation of inflammatory mechanisms may influence mood regulation, stress reactivity, and eating behaviour.

The coexistence of these biological mechanisms with psychosocial factors – such as stigmatisation, self-stigmatisation, and limited access to social support – leads to a cumulative psychological burden and increases the risk of developing and entrenching mental disorders. The above relationships justify the necessity of systematic mental-status assessment of patients at the various stages of treatment, including before starting anti-obesity pharmacotherapy and during evaluation of eligibility for bariatric treatment. Unrecognised or untreated mental disorders may substantially reduce the effectiveness of therapeutic interventions, limit patient cooperation with the treatment team, and increase the risk of weight regain in long-term observation.

Inclusion of the psychosocial and psychiatric aspects of obesity – together with their biological underpinnings – represents an important condition for improving the long-term outcomes of treatment, the quality of life of patients, and the implementation of the principles of comprehensive, individualised medical care.

5.7. Distinct clinical features of the consequences of obesity in children and adolescents with glucose metabolism disorders

Obesity coexisting with glucose metabolism disorders in the developmental age is associated with earlier manifestation of metabolic and end-organ complications and with their more rapid progression than in obesity developing in adulthood. Of particular importance is the influence of obesity on the processes of growth, sexual maturation, and achieving peak bone mass [70].

The most important clinical particularities in the developmental-age population include:

- more rapid progression from IGT to T2DM than in adults;
- the development of early features of end-organ damage in the course of arterial hypertension (including left-ventricular hypertrophy and increased vascular stiffness) of substantial prognostic importance for later life;
- the influence of obesity during growth not only on mechanical loading of the joints but also on bone microarchitecture and the differentiation of precursor cells, which may result in worsened bone tissue quality despite increased body weight;
- a higher prevalence of postural defects, flat feet, knee valgus, slipped capital femoral epiphysis, and Blount's disease;
- an increased frequency of vitamin D deficiency resulting from its sequestration in adipose tissue, which may further disturb bone metabolism;
- disturbances of sexual maturation: in girls, earlier onset of puberty and an increased risk of menstrual disturbances and PCOS; in boys, the possibility of delayed puberty and relative hypogonadism with reduced testosterone concentrations;
- the influence of disturbances of the hypothalamic–pituitary–gonadal axis on final height, body composition, and future fertility;
- the association between early puberty and a higher cardiometabolic risk in adult life;

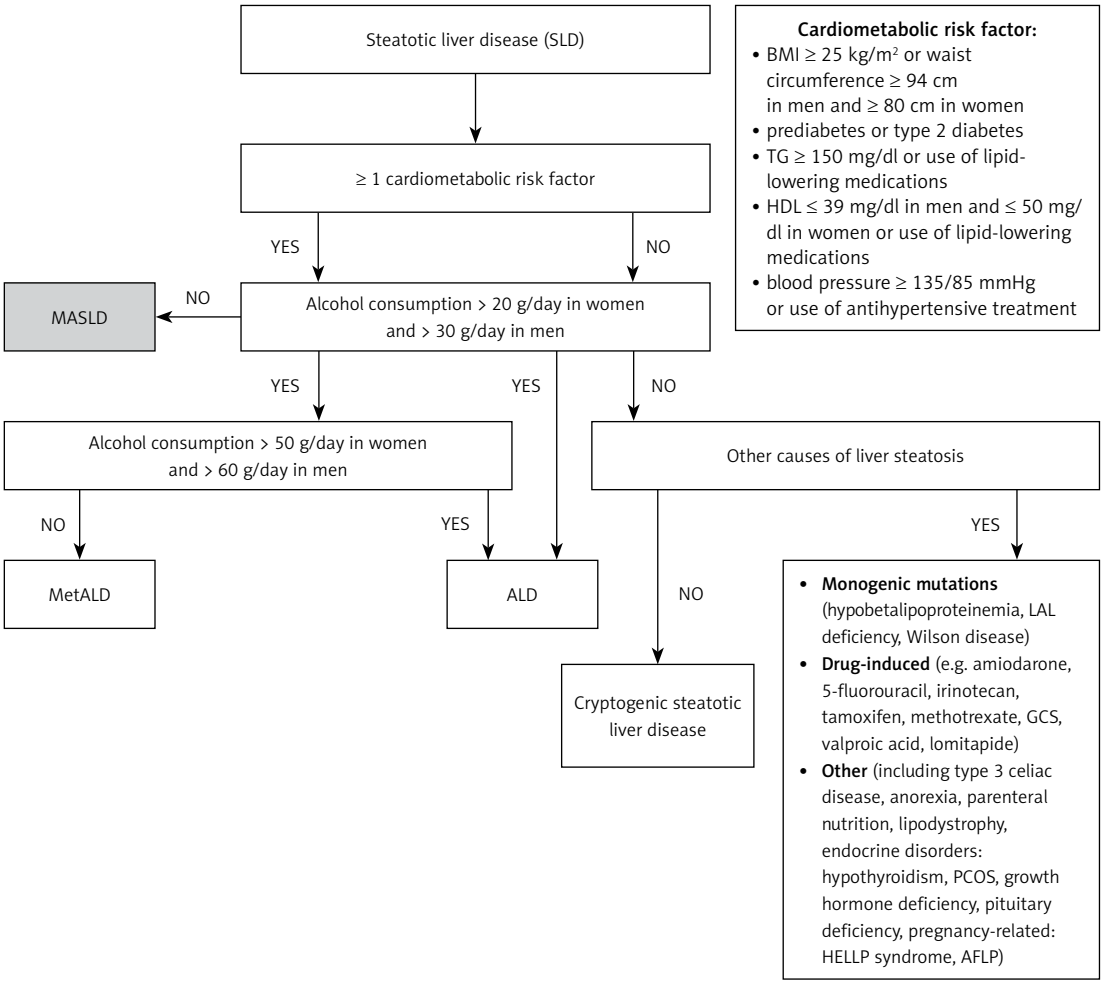
- substantial psychosocial consequences, including reduced self-esteem, stigmatisation, mood disturbances, and difficulties of functioning in the school environment; the coexistence of chronic disease additionally increases the risk of adjustment problems.

5.8. Other consequences of obesity: MASLD, hormonal disturbances

In recent years, growing attention has been paid to the role of obesity in the pathogenesis of MASLD (Figure 5.1). This disease affects more than 50% of individuals with T2DM and 90% of individuals with obesity. The presence of MASLD in individuals with prediabetes is a major risk factor for rapid progression to T2DM. The diagnosis of MASLD is associated with increased cardiovascular – kidney risk, and this state is consistent with the concept of cardiovascular–kidney–metabolic (CKM) syndrome. The disease may also lead to inflammatory changes in the liver, hepatic fibrosis with parenchymal remodelling, and consequently cirrhosis. Early clinical recognition and intervention are of substantial importance in order to prevent disease progression to the inflammatory and fibrotic stage (metabolic dysfunction-associated steatohepatitis – MASH) or to hepatocellular carcinoma (HCC) [71].

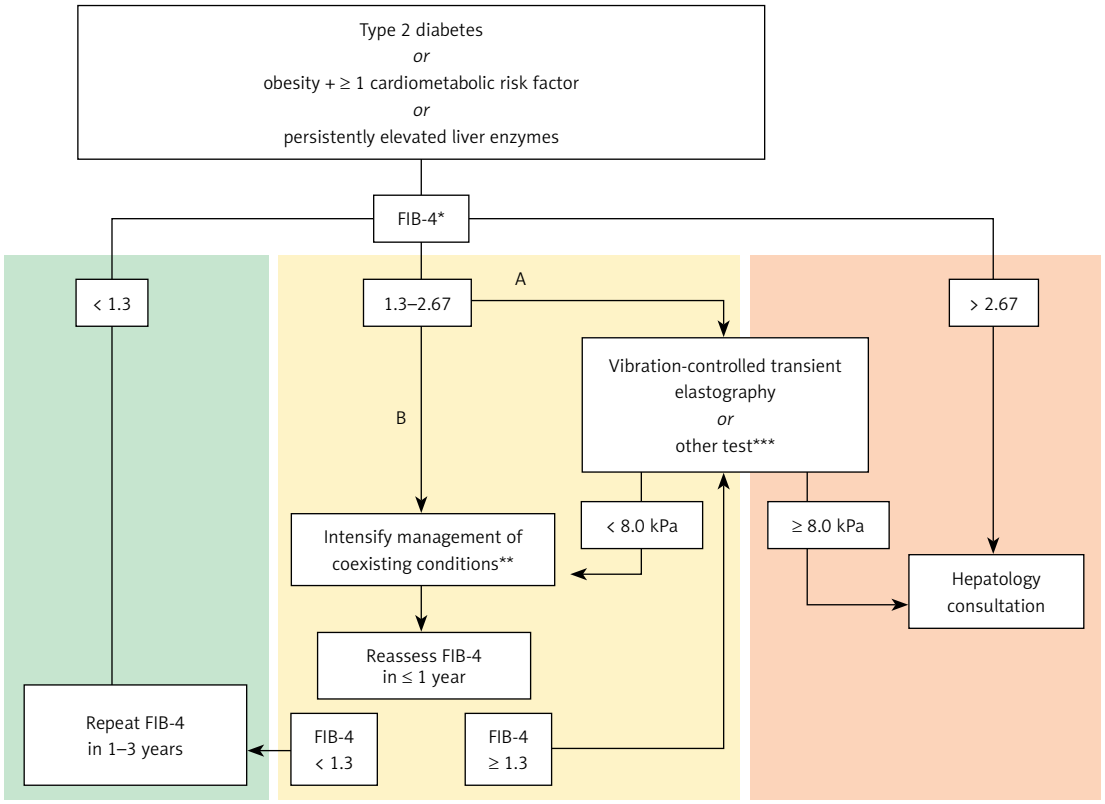
In patients with obesity, MASLD may have an asymptomatic course over a long period, and aminotransferase activity often remains within the normal range, hampering early diagnosis. The diagnosis of MASLD is based on the presence of hepatic steatosis on imaging, the coexistence of at least one metabolic risk factor (such as obesity, T2DM, dyslipidaemia, or arterial hypertension), and the exclusion of other causes of hepatic steatosis.

Current guidelines emphasise the central importance of assessing the stage of fibrosis, which



AFLP – acute fatty liver of pregnancy, ALD – alcohol-associated liver disease, GCS – glucocorticosteroid, HDL – high-density lipoprotein, LAL – lysosomal acid lipase, MASLD – metabolic dysfunction-associated steatotic liver disease, MetALD – metabolic dysfunction and alcohol-associated liver disease, PCOS – polycystic ovary syndrome, SLD – steatotic liver disease, TG – triglycerides.

Figure 5.1. Diagnostic algorithm for the differential diagnosis of steatotic liver disease (SLD) - modified from EASL – EASD – EASO [71]



**FIB-4 cut-off values for individuals aged ≤ 65. years (for individuals > 65. years, the lower cut-off value for FIB-4 is 2.0).*
***For example, lifestyle modification, treatment of coexisting conditions (e.g. GLP-1 receptor agonists), bariatric surgery.*
****For example, MRE (magnetic resonance elastography), SWE (shear wave elastography), ELF (enhanced liver fibrosis) with adjustment for applicable thresholds.*
A and B are options to be selected based on the patient's medical history, clinical context and available resoutces.

Figure 5.2. Proposed strategy for assessing the risk of advanced fibrosis and liver-related endpoints in individuals with MASLD, after EASL–EASD–EASO [71]

is the strongest prognostic factor for the development of cirrhosis, HCC, and death. To this end, non-invasive diagnostic tools are recommended – both indices based on laboratory parameters and patient age (e.g. FIB-4) and imaging methods assessing hepatic stiffness, in particular elastography. Magnetic resonance elastography remains the most precise non-invasive method, although its application in clinical practice is constrained by availability. A FIB-4 index < 1.3 (in individuals > 65 years of age, < 2.0) indicates a low risk of hepatic fibrosis, and a value > 2.67 indicates a high risk of this pathology. In cases of high or intermediate risk (1.3 [2.0]–2.67), confirmation of the diagnosis with elastography or other methods – for example, magnetic resonance imaging or liver biopsy – may be indicated. An elastography result > 8 kPa indicates clinically significant fibrosis requiring hepatological consultation and treatment (Figure 5.2).

Hormonal disturbances are a further important consequence of obesity. Excess adipose-tissue mass affects the functioning of the hypothalamic–pituitary–gonadal axis and the metabolism of steroid hormones. In women, obesity is associated with ovulatory disturbances, PCOS, infertility, and an increased risk of hormone-dependent cancers. In men, a reduction in testosterone concentration is observed, resulting from suppression of the gonadal axis and increased peripheral conversion of androgens to oestrogens in adipose tissue, predisposing to the development of hypogonadism, sarcopenia, and further progression of metabolic disturbances. Diabetes intensifies these disturbances; the cornerstone of treatment is weight reduction and optimal glycaemic control.

6. THE CARDIOVASCULAR–KIDNEY–METABOLIC SYNDROME IN INDIVIDUALS WITH OVERWEIGHT/OBESITY

Key recommendations
• In individuals with obesity and diabetes, active investigation for the other components of the CKM syndrome is appropriate. [**A**]
• In patients with obesity, T2DM, and MASLD, screening tests are recommended for the assessment of fibrosis risk and its stage. [**B**]

6.1. The role of dysfunctional adipose tissue in the pathogenesis of CKM syndrome

The substrate of the CKM syndrome is excess and/or dysfunctional adipose tissue. White adipose tissue is not only an energy reservoir but also the largest endocrine organ of the body. It produces and secretes numerous hormones, cytokines, extracellular matrix proteins, growth factors, and vasoactive factors that regulate energy expenditure, lipid and glucose homeostasis, food intake, immune function, and angiogenesis through autocrine, paracrine, and endocrine mechanisms [72–76].

The increase in adipose tissue mass occurs through two mechanisms: hypertrophy – an increase in adipocyte size – and/or hyperplasia, an increase in the number of adipocytes during adipogenesis, the process whereby new fat cells are formed from mesenchymal stem cells present in the stromal compartment of adipose tissue. As long as adipose tissue is able to store excess energy in adipocytes, metabolic disturbances do not develop [72, 73].

When the storage capacity of subcutaneous adipose tissue is exceeded, increased release of free fatty acids (FFA) into the bloodstream and ectopic lipid deposition occurs – including in skeletal muscle and the liver, in excessive amounts in visceral adipose tissue (which is characterised by intensified lipolytic activity), and in epicardial and peri-renal adipose tissue. Elevated free fatty acid concentrations and ectopic lipid accumulation, especially of their toxic forms, lead to the development of insulin resistance through inhibition of post-receptor insulin signalling [72, 73].

Dysfunctional adipose tissue is also characterised by increased accumulation of pro-inflammatory immune cells – particularly macrophages. Hypertrophic adipocytes and pro-inflammatory macrophages secrete increased amounts of pro-inflammatory adipokines, which induce insulin resistance. At the same time, dysfunctional adipose tissue produces decreased amounts of adipokines with anti-inflammatory and insulin-sensitising effects, such as adiponectin. Additionally, increased generation of reactive oxygen species (ROS) is observed. Inflammatory mediators stimulate pro-inflammatory signalling pathways. This leads to the development of chronic, low-grade inflammation [72, 73].

Insulin resistance constitutes the basis for the development of the metabolic syndrome – a cluster of features leading to T2DM, atherosclerosis, and cardiovascular and renal complications. The components of this syndrome are: abdominal obesity, glucose tolerance disturbances, hypertension, and atherogenic dyslipidaemia, comprising hypertriglyceridaemia, decreased HDL-C concentrations, and the presence of small, dense LDL particles. Insulin resistance – particularly hepatic insulin resistance – is also associated with the development of MASLD, which is an independent predictor of cardiovascular risk [72–77].

Insulin resistance contributes to the development of atherosclerosis through various mechanisms, including chronic low-grade inflammation, hyperinsulinaemia (the presence of insulin receptors in the endothelial-cell membrane indicates insulin's substantial role in maintaining vascular homeostasis), atherogenic dyslipidaemia, and reduced synthesis of nitric oxide (a vasodilator), increased activity of the RAA system, and increased prothrombotic readiness (increased secretion of plasminogen activator inhibitor 1 – PAI-1). Elevated glucose concentrations further promote inflammation through increased secretion of pro-inflammatory cytokines and ROS. Inflammatory mediators such as FFA, pro-inflammatory cytokines, and ROS contribute to the development of atherosclerosis and to the direct injury of the myocardium, glomerulosclerosis, tubulointerstitial inflammation, and renal fibrosis. Prevention and treatment of obesity may have substantial importance in preventing the development of dysfunctional adipose tissue and CKM syndrome [72–77].

6.2. The role of MASLD in the sequence of events of the CKM syndrome

MASLD is defined as the presence of hepatic changes in the form of steatosis on imaging or biopsy in individuals with at least one cardiometabolic risk factor: BMI ≥ 25 kg/m² or abdominal obesity; diabetes or prediabetes; hypertension; hypertriglyceridaemia; or reduced HDL-C concentration (or use of lipid-lowering drugs); and in whom weekly alcohol consumption does not exceed 140 g (20 g/day) in women or 210 g (30 g/day) in men [78, 79].

The fundamental pathophysiological mechanism leading to the development of hepatic steatosis and further progression to MASLD is increased energy delivery to the liver, resulting from excessive intake of foods rich in readily absorbable carbohydrates and saturated fats and from FFA derived from lipolysis. Saturated fats reaching the liver are metabolised and stored or exported as triglycerides (TG) in very-low-density lipoprotein (VLDL) lipoprotein particles. Simple sugars – both as monosaccharides and as products of digestion of di- and polysaccharides – and amino acids are substrates for hepatic *de novo* lipogenesis, in which they are transformed into saturated fatty acids. A particular role in this process is played by fructose, present in many food products. Unlike glucose metabolism, almost all fructose from portal blood is phosphorylated and subsequently undergoes *de novo* lipogenesis [72, 77, 79–81].

The delivery of energy substrates to the liver in amounts exceeding its capacity to export TG favours their accumulation in hepatocytes. In individuals with MASLD, hepatic TG export initially increases and reaches a plateau when intrahepatic TG content exceeds 10%. Under these conditions, increased formation of lipid metabolism products such as diacylglycerol and ceramides occurs, which initiates an inflammatory cascade, leads to activation of stellate cells, and promotes the development of fibrosis. All these phenomena contribute to dysfunction of the insulin receptor and appear to be the principal mediators of hepatic insulin resistance [72, 73, 77, 79–81].

The presence of insulin resistance at the hepatocyte level disturbs insulin's inhibitory effect on gluconeogenesis and reduces hepatic glycogen synthesis, which in turn leads to increased glucose concentration and consequent hyperinsulinaemia. Peripheral insulin resistance in muscle and adipose tissue causes reduced peripheral glucose utilisation and intensified lipolysis, which in turn leads to excessive, chronic delivery of FFA to the liver, thereby closing this vicious pathological cycle [72, 73, 77, 79–81].

The complete picture of the mechanisms leading to the development and progression of hepatic steatosis is further supplemented by genetic factors that may, in susceptible individuals, promote the development of MASLD, as well as by disturbances of intestinal microbiota composition that cause damage to the intestinal barrier, the development of smouldering inflammation in the submucosal layer, and disturbed secretion of gut hormones (including GLP-1) and functioning of the gut–liver axis [72, 73, 77, 79–82].

In addition, MASLD may progress, leading to inflammation (through the mechanisms outlined above) and, in a proportion of persons, to fibrosis, cirrhosis, and ultimately HCC. The systemic health consequences of MASLD include the development of T2DM, cardiovascular disease, increased risk of malignancies in extra-hepatic locations, and increased risk of CKD (Figure 6.1) [79, 83, 84].

6.3. Metabolic disturbances in the CKM syndrome

In the pathogenesis of CKM syndrome, glucose metabolism disturbances – in the form of prediabetes and T2DM – play a key role. In the development of hyperglycaemia, insulin resistance plays a pivotal role. At the hepatocyte level, it is responsible primarily for IFG, while at the level of peripheral tissues – particularly skeletal muscle – it is responsible for the development of IGT. Insulin resistance is initially compensated by increased insulin secretion by pancreatic β-cells. When β-cell insulin secretory function declines, diabetes develops [72, 73].

In CKM syndrome, end-organ complications result from the interaction of all its components. Hyperglycaemia, through multiple mechanisms, leads to small-vessel damage (microangiopathy) and large-vessel damage (macroangiopathy) and is responsible for chronic complications of diabetes, such as retinopathy, diabetic kidney disease, neuropathy, cardiovascular disease, peripheral vascular disease, cerebrovascular disease, and heart failure. The other components of the CKM syndrome amplify the risk of these complications [72–76].

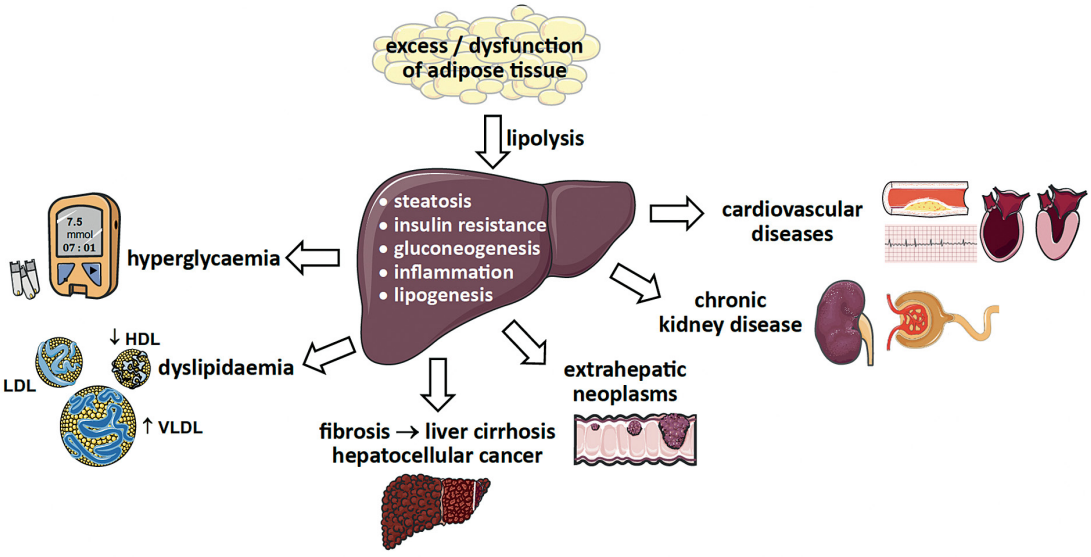


Figure 6.1. Schematic representation of the role of the liver in the pathogenesis of disturbances associated with the cardiovascular–kidney–metabolic (CKM) syndrome

Lipid metabolism disturbances very often coexist with carbohydrate metabolism disturbances. Atherogenic dyslipidaemia occurs in approximately 70–80% of patients with T2DM. It is one of the key metabolic disturbances increasing the risk of cardiovascular and cerebrovascular complications in CKM syndrome. The typical lipid disturbance in patients with CKM syndrome comprises hypertriglyceridaemia, decreased HDL-C concentration, and elevated concentrations of small, dense LDL particles. In the pathogenesis of dyslipidaemia in individuals with prediabetes/diabetes, insulin resistance, insulin secretion disturbances, and hyperglycaemia leading to lipoprotein glycation – altering their structure and function – play essential roles. Insulin is one of the principal hormones regulating lipid metabolism. Under physiological conditions, it inhibits lipolysis and increases lipogenesis. Under conditions of insulin resistance, lipoprotein lipase activity is inhibited, leading to intensified lipolysis and impaired catabolism of chylomicrons and VLDL. The result is an increase in FFA and TG concentrations. High VLDL concentrations favour the exchange of TG between lipoproteins, and hydrolysis of TG within LDL by hepatic lipase leads to the formation of small, dense LDL particles [72–76, 83, 84].

The coexistence of glucose tolerance disturbances and dyslipidaemia substantially increases the risk of cardiovascular disease; therefore, early diagnosis and effective treatment of lipid disorders in patients with obesity and prediabetes or diabetes are highly important. The effectiveness of lipid-lowering treatment depends to a large extent on the effectiveness of antihyperglycaemic treatment [72–76].

6.4. The cardiovascular system in the CKM syndrome

The key mechanism responsible for the cardiovascular component of CKM syndrome is the activation of neurohormonal axes, including the sympathetic nervous system and the RAA system. Activation of these systems favours sodium and water retention, increased circulating blood volume, increased peripheral resistance, and vascular remodelling, leading to the development of arterial hypertension and accelerated atherogenesis [74–76].

Chronic low-grade inflammation, initiated by dysfunctional adipose tissue, also plays a substantial role. Pro-inflammatory factors act directly on the vascular endothelium, leading to its dysfunction, reduced nitric-oxide bioavailability, and predominance of vasoconstrictor factors. Consequently, vascular stiffness increases, microcirculation is disturbed, and susceptibility to end-organ damage rises [74–76].

6.4.1. Hypertension and vascular remodelling

Hypertension is one of the earliest and most frequent components of CKM, constituting a key link between metabolic disturbances and end-organ damage. Its pathogenesis in CKM comprises both haemodynamic and metabolic factors, including insulin resistance, RAA activation, increased sympathetic activity, and endothelial dysfunction [74–76].

Chronically elevated blood pressure leads to vascular remodelling, increased vascular stiffness, and microcirculatory damage, contributing to the progression of heart failure, kidney disease, and cerebrovascular changes. In patients with CKM, disturbances of the circadian blood-pressure profile – including absence of nocturnal blood-pressure decline – are often observed, further increasing the risk of cardiovascular complications [74–76].

6.4.2. Atherosclerotic cardiovascular disease (ASCVD)

Patients with CKM syndrome are characterised by a particularly unfavourable atherosclerotic risk profile, comprising atherogenic dyslipidaemia, chronic inflammation, arterial hypertension, and glycaemic disturbances. The coexistence of CKD additionally intensifies the atherogenic process through disturbances of calcium – phosphate balance, oxidative stress, and accumulation of uraemic toxins [74–76].

The clinical picture features earlier development of coronary artery disease, more frequent multivessel disease, and a higher risk of cardiovascular events, including myocardial infarction and stroke. Importantly, in patients with CKM, the clinical manifestations of atherosclerosis may be less specific and the disease course more aggressive, hampering early diagnosis and risk stratification [74–76].

6.4.3. Heart failure as a central element of the CKM syndrome

Heart failure constitutes a key cardiovascular manifestation of CKM syndrome and results from the cumulative effects of haemodynamic, metabolic, and inflammatory disturbances. Obesity, diabetes, arterial hypertension, and CKD create conditions favourable for the development of both heart failure with reduced ejection fraction (HFrEF) and – increasingly often – HFpEF [74–76].

Heart failure with preserved left-ventricular ejection fraction is now regarded as a model cardiovascular disease (CVD) in CKM. Its pathogenesis comprises chronic inflammation, microcirculatory dysfunction, myocardial stiffness, and disturbances of diastolic function. In patients with

CKM, increased circulating blood volume, volume overload, and left-ventricular hypertrophy are also often observed, further worsening cardiac function [74–76].

Heart failure in CKM is a progressive, multi-organ disease, and its clinical course is substantially modified by coexisting renal and hepatic dysfunction, leading to frequent hospitalisations and worsening prognosis [74–76].

6.4.4. Cardiac arrhythmias, including atrial fibrillation

CKM syndrome substantially increases the risk of cardiac arrhythmias – particularly atrial fibrillation. The mechanisms responsible for this association include structural atrial remodelling, atrial enlargement, fatty infiltration, and electrophysiological changes resulting from chronic inflammation and oxidative stress. Arterial hypertension and heart failure, frequent comorbidities in CKM, additionally favour the development of arrhythmias [74–76].

Atrial fibrillation in patients with CKM is associated with a higher risk of thromboembolic complications, more difficult rhythm control, and more frequent arrhythmia recurrence. Coexisting CKD complicates assessment of bleeding risk and influences the safety of anticoagulant therapy, underscoring the clinical complexity of this patient population [74–76].

6.4.5. The importance of cardiovascular diagnosis and risk stratification

Owing to the complex, multi-organ nature of CKM, assessment of the cardiovascular component of the syndrome requires a holistic approach. Of pivotal importance is the early identification of patients with subclinical cardiovascular damage, encompassing assessment of blood pressure, cardiac function, features of atherosclerosis, and metabolic and renal parameters. In clinical practice, it is necessary to move away from isolated assessment of individual organs in favour of integrating clinical, laboratory, and imaging information [74–76].

6.5. The kidneys in the CKM syndrome

The influence of obesity *per se* on renal function has been described in detail in Section 5. The disturbances associated with CKM syndrome outlined above may substantially affect the development and progression of renal dysfunction. Each component of the syndrome plays a role here, but – as it appears – the most important are hypertension and hyperglycaemia. Increased reabsorption of glucose and sodium in the proximal convoluted

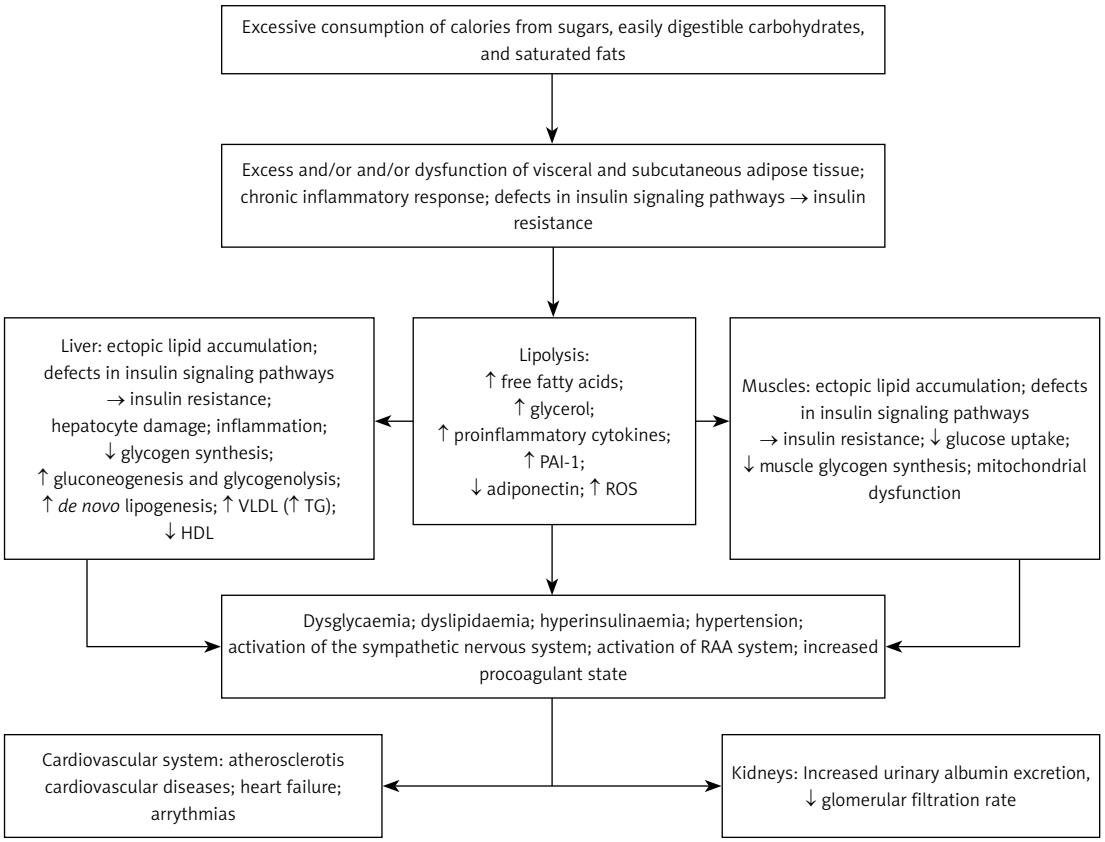


Figure 6.2. Diagram of the interrelationships between the components of CKM syndrome

tubule leads to activation of the RAA system. Together with a fall in adenosine concentration, this results in dilatation of the afferent arteriole and constriction of the efferent arteriole. The effect is hyperperfusion and hyperfiltration with elevated intraglomerular pressure. This in turn leads to damage to the intraglomerular structures, as well as thickening and increased permeability of the basement membrane, resulting in increased urinary albumin excretion. Hypertension contributes to renal injury by causing thickening of the walls of small renal arteries and arterioles, narrowing of the vascular lumen and impaired blood flow, which results in nephron ischaemia and further progression of renal damage. A further factor with a substantial influence on renal function in CKM syndrome is the formation of advanced glycation end-products (AGEs) related to hyperglycaemia. These compounds modify protein structures – such as collagen – in the glomerular basement membrane, eliciting oxidative stress and inflammation, and together with aldosterone they accelerate the process of fibrosis. A further phenomenon is endothelial dysfunction caused by circulating and locally acting pro-inflammatory cytokines and by oxidative stress; chronic inflammation activates mesangial cells and fibroblasts, leading to mesangial proliferation, gradual nephron loss, and ultimately a decline in glomerular filtration [74–76, 83, 84].

6.6. Clinical implications

Understanding the interactions between the heart, kidneys, metabolism, and liver is of pivotal importance for the appropriate identification of high-risk patients and for the design of effective models of care. In this context, the interdisciplinary approach to the patient with CKM is becoming increasingly significant, encompassing close collaboration between physicians of different specialties and integration of primary and specialist care, which may translate into earlier diagnosis, better risk stratification, and improved prognosis [72–77, 79–86] (Figure 6.2).

7. SEXUAL DYSFUNCTION ASSOCIATED WITH OVERWEIGHT/OBESITY

Key recommendations

General principle. Interventions directed at improving sexual function should be individualised, holistic in character (avoiding reductionism), encompass potential biomedical and psychosocial factors, increase the cumulative positive effect (i.e. the cumulative effect of various forms of intervention and lifestyle modification), and be tailored to the patient's goals, needs, and relational context [87–89]. [**E**]

Psychosocial interventions:
- Psychoeducation – individualised, encompassing sexual psychophysiology, the bio-psycho-social model of sexual response, and the influence of various groups of factors on sexuality, including a lifestyle conducive to sexual satisfaction and function [90]. [**E**]
- Individual psychotherapy – individualised, focused on work with body image, self-esteem, emotion regulation, and coexisting psychiatric and psychological problems [88, 89]. [**E**]
- Couples psychotherapy or counselling – in cases of coexisting relational problems, primary or secondary to obesity and/or sexual problems [87, 88]. [**E**]

Medical management:
- Treatment of coexisting mental disorders – in accordance with general principles, taking into account the influence of psychopharmacotherapy on sexual function and metabolic profile [88, 89]. [**E**]
- Treatment of coexisting metabolic disorders (particularly diabetes, glucose intolerance, and the metabolic syndrome). [**E**]
- Testosterone in men with obesity and hypogonadism [91]. [C]
- PDE-5 inhibitors in men with obesity and sexual distress [92]. [**C**]

7.1. Foundations of contemporary sexology

The foundations of contemporary sexology constitute the axiological and practical basis for incorporating sexuality and sexual health into the care of various patient groups, including individuals with obesity.

Sexuality is regarded as an integral aspect of human functioning, shaped by the interaction of biological, psychological, social, economic, cultural, and relational factors. In the context of obesity, the importance of these interactions is particularly evident, as the disease simultaneously affects biological functioning, body image, psychological well-being, and interpersonal relationships.

According to the WHO, sexual health denotes a state of physical, emotional, mental, and social well-being in relation to sexuality, and not merely the absence of disease or dysfunction. The achievement and maintenance of sexual health require a positive and respectful approach to sexuality and sexual relationships, together with the possibility of having pleasurable and safe sexual experiences, free from coercion, discrimination, and violence [87].

The bio-psycho-social model constitutes the foundational paradigm of contemporary sexology. It underpins, among others, the concept of the sexual tipping point and the dual control model, which emphasise the balance between excitatory and inhibitory factors in the regulation of sexual response [87].

The psychosexual response is also described by linear (DEOR) and circular (Basson) models, which take into account the differing mechanisms

of sexual motivation in women and men. This perspective assists in the interpretation of sexual difficulties in individuals with obesity, in whom biological, emotional, relational, and social factors often coexist [87].

7.2. Sexuality in individuals with obesity

Sexual problems in individuals with overweight or obesity remain relatively poorly characterised in the literature, and specific standards of care are limited. The available data, however, indicate that the prevalence of sexual dysfunction is elevated in this group, especially in the presence of coexisting metabolic disorders, body-image difficulties, depressive symptoms, or relational problems [88–95].

The risk of sexual dysfunction may additionally rise in the case of coexisting metabolic diseases, hormonal disturbances, mood disturbances, or chronic stress. Each of these factors may constitute an independent risk element, but in clinical practice they often overlap and reinforce one another [88, 89, 93].

The determinants of sexual dysfunction in individuals with overweight/obesity are complex and encompass both biomedical factors (e.g. hormonal disturbances, increased aromatisation of testosterone) and psychological and relational factors, including body dissatisfaction, avoidance of intimacy, depressive symptoms, anxiety, and interpersonal difficulties [88, 89].

In clinical practice, the division of factors into predisposing, precipitating, perpetuating, and contextual is helpful. Obesity itself may serve various functions – from a predisposing factor to a perpetuating factor of sexual disturbances [94].

Of substantial importance are also psychological factors that perpetuate sexual dysfunction, such as performance anxiety, excessive self-observation (spectatoring), and relational difficulties. These factors may sustain sexual disturbances even in the presence of relatively stable biological parameters [90, 96].

The largest body of evidence concerns the influence of weight reduction on the improvement of sexual function. Interventions encompassing diet and physical activity exhibit beneficial effects on sexual functioning in both women and men; improvement in sexual function has also been described after bariatric surgery, although the magnitude and durability of this effect may differ between studies and depend on sex, baseline dysfunction, relational context, and psychological factors [90, 96–101].

Direct evidence regarding the effectiveness of psychosocial interventions in the population with concurrent obesity and sexual dysfunction is limited, but their substantial clinical value is recognised. Treatment of coexisting mental disorders, work with body image and self-esteem, reduction of shame, and improvement of communication within the relationship may facilitate both sexual functioning and adherence to obesity treatment [87–89].

At present, recommendations cannot be formulated regarding the use of GLP-1-based therapies in individuals with obesity and sexual dysfunction, owing to the limited number of studies and their conflicting findings (e.g. both improvement and deterioration of erectile function in men have been reported, as has improvement in sexual satisfaction associated with improved body image, alongside cases of decreased libido and anorgasmia).

7.3. Psychological support for patients with obesity and sexual dysfunction – a clinical perspective

Sexual dysfunction coexisting with obesity is often multifactorial in character and requires an approach that takes into account not only biomedical aspects but also psychological and relational ones. Obesity is associated with an increased risk of body dissatisfaction, shame, avoidance of intimacy, lowered self-esteem, and sexual distress, which may contribute to the maintenance of sexual problems independently of metabolic factors [87–89].

Body image constitutes one of the key mediators of the relationship between obesity and sexual functioning. Negative perception of one's body may lead to avoidance of intimacy, decreased sexual satisfaction, and increased anxiety connected with sexual activity. In clinical practice, it is therefore important to assess not only the occurrence of sexual symptoms but also the patient's subjective experience of the body and sexuality [88, 89, 94, 95].

Another important element of psychological support is the identification of coexisting mental disorders – particularly depression, anxiety disorders, and eating disorders. These problems may affect sexual functioning both directly and indirectly, for example through fatigue, reduced libido, avoidance behaviours, low self-esteem, or the effects of psychopharmacotherapy [88, 89].

In the treatment of obesity and accompanying sexual dysfunction, a patient-centred approach taking into account the patient's psychological resources, relational context, and individual health goals is of particular importance. Psychological interventions may include psychoeducation, support for lifestyle change, work on emotion regulation, body image, and partner communication [90, 96].

The importance of counteracting stigmatisation of individuals with obesity within the healthcare system is also emphasised. The experience of prejudice or negative treatment may lead to avoidance

of contact with healthcare, concealment of sexual problems, and reduced readiness to engage in treatment [88, 89].

The inclusion of psychological support as a component of comprehensive management of individuals with obesity and sexual disturbances may foster improvements in quality of life, relational functioning, and the effectiveness of treatment of obesity [90, 94, 96].

8. GOALS AND MONITORING OF THE MANAGEMENT OF OVERWEIGHT/OBESITY

Key recommendations
• In individuals with overweight/obesity and glucose metabolism disorders, including T2DM, control of body weight should constitute one of the principal therapeutic objectives, on a par with improvement of glycaemic control. [**A**]
• Treatment goals should be set individually depending on the severity of obesity, its duration, the coexistence of obesity-related diseases and complications, and the expectations, needs, life circumstances, and preferences of the individual. [**C**]
• Treatment aimed at controlling body weight should be provided, with the aim of achieving weight reduction to any extent. A reduction in body weight by 5–7% of the initial weight leads to clinically significant improvement in glycaemic control and other cardiovascular risk factors and reduces the risk of progression from prediabetes to T2DM. [**A**]
• In individuals with obesity-related comorbidities and/or complications, sustained weight reduction of ≥ 10% should be sought. [**A**] Sustained loss of > 10% of body weight typically yields greater benefits, including disease-modifying effects and possible remission of T2DM, and may also improve long-term cardiovascular outcomes and reduce mortality. [**B**]
• In some cases, a reduction in body weight of ≥ 15% may be indicated, particularly in individuals with moderate or severe obesity-related conditions, in order to obtain greater therapeutic benefits. [**B**]
• In children and adolescents with obesity and glucose metabolism disorders, the aim of treatment is primarily improvement of metabolic status. [**A**]
• Treatment goals should be tailored to the patient's age, stage of maturation, and clinical situation. [**A**]
• In prepubertal children, the aim is stabilisation of body weight while body height continues to increase, and in adolescents, gradual reduction of body weight or BMI SDS (standard deviation score). [**A**]
• Treatment should improve glycaemic control, reduce insulin resistance, and limit the risk of obesity complications. [**A**]
• The goal of treatment is also to improve the quality of life and psychological well-being of the child and the family. [**A**]

Obesity is a chronic disease requiring long-term therapeutic management whose goals extend beyond weight reduction itself and also encompass reduction of the risk of coexisting diseases and complications, improvement of quality of life, and improvement of overall health. From this perspective, the principal aim of treatment should be not so much weight reduction *per se* as – perhaps above all – the reduction of the risk of developing the diseases and complications associated with excess adipose tissue and, where they have already occurred, reduction of the rate of progression to subsequent stages through optimisation of disease control or achievement of remission. In setting therapeutic goals, therefore, as in T2DM, account should be taken of the necessity for multidirectional management, of the causes that have led to the development of overweight or obesity, of the severity of obesity, of the duration of the disorder, and of the coexistence of associated diseases and complications. It must be remembered that the patient's expectations and preferences are key – both in defining the individual therapeutic goal and in optimising the management plan and timeline [102–104].

T2DM is, in the great majority of cases, a direct consequence of overweight or obesity, which are present in 80% of individuals with this type of diabetes. The prevalence of overweight (30–40%) and obesity (15–30%) in individuals with type 1 diabetes (T1DM) is comparable to that in the adult population without glucose metabolism disorders. In individuals with T1DM, obesity is associated with a greater risk of CVD and microvascular complications than in those without obesity. In this context, the development of evidence-based interventions in the treatment of obesity – particularly in T1DM – remains an unmet need.

Effective management of overweight or obesity should lead to improved metabolic control and improved outcomes of treatment of the many other diseases that are consequences of excess body weight – primarily arterial hypertension, dyslipidaemia, MASLD, MASH, CVD, musculoskeletal disorders, mental disorders, and eating disorders of various severity. It must be emphasised that, while weight reduction relative to initial weight is the fundamental objective of the treatment of overweight or obesity, treatment must absolutely encompass the totality of the patient's health [104–106].

Comprehensive treatment goals comprise:

- sustained, gradual reduction of body weight;
- sustained lifestyle change, including dietary habits and increased physical activity;
- improvement of metabolic status – that is, reduction of the risk of developing and/or improvement of control of T2DM, arterial hypertension, dyslipidaemia, obstructive sleep apnoea, MASLD, MASH, and osteoarthritis, and reduction of insulin resistance;

- reduction of the risk of microvascular and cardiovascular complications;
- improvement of quality of life and health (physical and psychological, including self-acceptance);
- maintenance of treatment effects (the long-term goal) – maintenance of reduced body weight and prevention of its renewed increase (the so-called yo-yo effect).

Treatment goals should be staged and individually defined on the basis of comprehensive patient assessment, taking into account the severity of overweight/obesity, the coexistence of obesity-related diseases and complications, the risk-to-benefit ratio, and the expectations, needs, motivation, life circumstances, and preferences of the individual. In individuals with T2DM and overweight/obesity who exhibit inadequate glycaemic control, blood pressure, and lipid parameters and/or other obesity-related metabolic complications, sustained weight reduction of 5–7% improves glycaemia, blood pressure values, and the lipid profile, and may reduce the need for disease-specific medications. In individuals with prediabetes, weight reduction of 5–7% reduces the risk of developing diabetes. Greater weight loss yields additional benefits, including reduction of all-cause and cardiovascular mortality [102, 103, 107].

In individuals with obesity-related comorbidities and/or complications, sustained weight reduction of ≥ 10% should be sought. An increasing body of data indicates that loss of ≥ 10% of body weight typically brings greater benefits in terms of normalisation of glycaemia and improvement of other coexisting metabolic disturbances, reduces cardiovascular risk and the risk of MASLD, MASH, and sleep apnoea, and improves comorbid diseases – thereby improving quality of life.

In some cases, a reduction in body weight of ≥ 15% may be indicated, particularly in individuals with moderate or severe obesity-related conditions, in order to obtain greater therapeutic benefits. The available evidence indicates that, although weight-reduction goals of ≥ 15% may be beneficial for some individuals with moderate-to-severe obesity-related diseases and/or complications, other patients may experience substantial improvement in health status with smaller weight loss. Personalised goals and treatment strategies therefore lead to long-term therapeutic effect (Figure 8.1) [102, 103, 105, 106, 108, 109].

In individuals with glucose metabolism disorders and overweight/obesity, the findings of trials concerning the prevention of and treatment for T2DM suggest that the magnitude of weight loss and the duration of the disorder are substantial determinants of the potential health benefits of intervention [102, 103, 105–107].

8.1. Treatment goals for overweight/obesity in children and adolescents with glucose metabolism disorders

In children and adolescents with overweight/obesity and glucose metabolism disorders, the principal aim of treatment is improvement of metabolic status, not solely weight reduction. Therapeutic goals should be tailored to the child's age, stage of maturation, and individual clinical situation [9, 110].

In younger children, the aim of treatment is most often stabilisation of body weight with simultaneous growth in height, leading to gradual

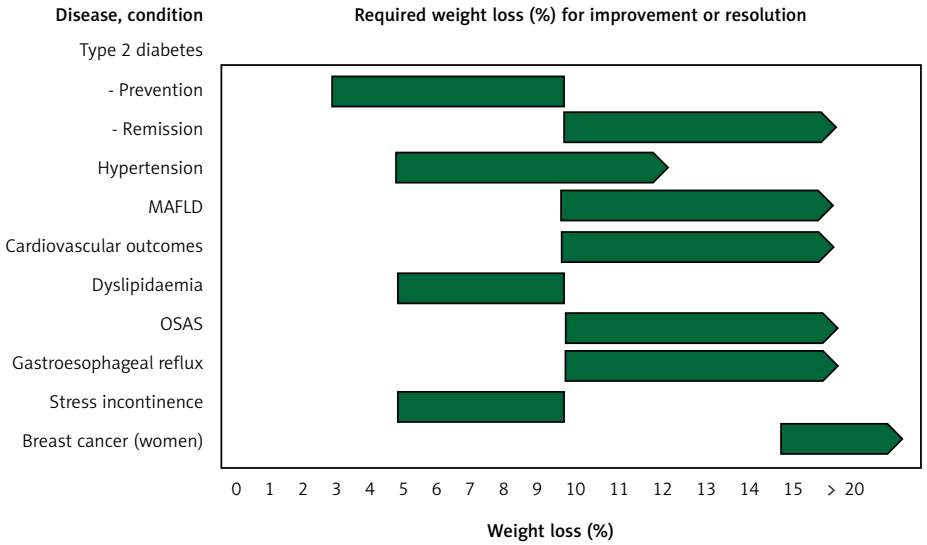


Figure 8.1. Influence of weight loss (%) on risk factors and on coexisting diseases and complications of obesity (after Blüher M [105])

reduction of BMI values (assessed against percentile charts), whereas in adolescents – after the completion of intensive growth – gradual, controlled reduction of body weight or BMI is feasible (assessed against percentile charts). Treatment should lead to improved glycaemic control, reduced insulin resistance, and limitation of the risk of development and progression of obesity complications.

A further important aim of therapy in children and adolescents is to improve quality of life, psychological well-being, and social functioning of the patient, as well as to establish lasting healthy dietary habits and physical activity within the family environment [9, 110].

9. THERAPEUTIC EDUCATION IN OVERWEIGHT/OBESITY

Key recommendations
• Therapeutic education constitutes an integral and indispensable element of the treatment of overweight/obesity in individuals with glucose metabolism disorders and should be implemented in parallel with behavioural, dietary, and pharmacological interventions. [**A**]
• Education should be conducted in a patient-centred model, taking into account the individual's health competences, family environment, and psychosocial factors. [**B**]
• The educational programme should encompass systematic monitoring of metabolic parameters and the development of self-care skills, including interpretation of glycaemia and other clinical indicators. [**A**]
• Education should incorporate elements of psychoeducation and counter the stigmatisation associated with obesity. [**B**]
• Owing to the chronic and progressive character of obesity, the educational process should be implemented in a structured, long-term manner by an interdisciplinary therapeutic team. [**A**]

Therapeutic education constitutes a key and integral element of the treatment of obesity – a progressive chronic disease – in individuals with glucose metabolism disorders, and cannot be regarded merely as a supplementary intervention. It should form the foundation for the implementation of comprehensive measures encompassing lifestyle modification, behavioural therapy, dietary intervention, and pharmacotherapy.

The educational process requires a patient-centred approach, using structured management models such as the 5A model (Ask, Assess, Advise, Agree, Assist). It includes early identification and systematic monitoring of glucose metabolism disorders, the parameters of the metabolic syndrome, and other complications of obesity [3].

Education increases the level of *health literacy* in respect of the making of informed health decisions, lifestyle modification, and glycaemic control. It should take into account the patient's environment, family context, and psychosocial factors. Important components are psychoeducational elements, encompassing emotion regulation, stress-coping strategies, and the strengthening of motivation for sustained behaviour change. Education of the patient and their environment also contributes to reducing stigmatisation and prejudice associated with obesity.

Therapeutic education should be conducted by an interdisciplinary team under the leadership of the physician coordinating treatment. The team comprises a physician, a nurse, a dietitian, a physiotherapist, and a psychologist. Owing to the chronic and progressive character of obesity, the educational process should be carried out systematically during medical visits and specialist consultations, and its scope adapted to the individual needs of the patient. The educational programme, closely coordinated with treatment, must be developed with the active participation of the patient and – where necessary – of the patient's caregivers and family. Of pivotal importance are the setting of realistic individual therapeutic goals and the conduct of education in a structured, staged, long-term manner [111, 112].

9.1. Outline of therapeutic education

Stage 1 – Initial assessment. Comprehensive assessment of the educational, clinical, and psychosocial needs of the patient (and the patient's family), encompassing analysis of metabolic status, previous therapeutic experiences, readiness for change, and environmental barriers.

Stage 2 – Setting therapeutic goals. Setting of realistic and measurable goals concerning:

- weight reduction and improvement of body composition;
- glycaemic control and other metabolic parameters;
- modification of health behaviours (diet, physical activity, sleep);
- improvement of quality of life.

Goals should be set jointly with the patient and subjected to periodic review.

Stage 3 – Educational intervention. The educational intervention encompasses the development of self-care skills and informed health decision-making. It includes in particular:

- the principles of rational nutrition and lifestyle modification;
- monitoring and interpretation of glycaemia (including the use of glucose meters and continuous glucose monitoring [CGM] systems);
- monitoring of weight and body composition, waist circumference, blood pressure, and the lipid profile;

- the principles of pharmacotherapy and correct technique of medication administration (including subcutaneous injections);
- recognition and management of acute states and early signs of complications;
- the use of modern digital tools supporting self-care.

The scope of education should be tailored to the individual needs and competences of the patient.

Stage 4 – Support and maintenance of effects. Therapeutic education is always long term in character and encompasses measures to prevent relapse and to support the maintenance of metabolic and behavioural achievements [113, 114].

9.2. Therapeutic education in the paediatric population

In children and adolescents with obesity and glucose metabolism disorders, therapeutic education should take into account the stage of somatic and emotional development and actively engage the family or legal guardians.

Paediatric education:

- is conducted in a family-based model, working in parallel with the child and the caregivers;
- takes into account the child's level of cognitive maturity and readiness for shared responsibility for the treatment process;
- encompasses the shaping of correct dietary patterns for the entire family, not only for the child;
- contains elements of building a sense of agency and strengthening intrinsic motivation, tailored to the child's age;
- encompasses education on physical activity, limitation of sedentary behaviours, and education on sleep and digital hygiene;
- requires particular linguistic sensitivity in order to counteract stigmatisation and negative effects on the child's self-esteem.

In the paediatric population, education has not only a therapeutic but also a developmental character – its aim is the lasting modification of environment and health behaviours during the period of growth, which may substantially affect the long-term course of obesity and the risk of progression of glucose metabolism disorders [115].

9.3. Education in the prevention of obesity in the offspring of individuals with obesity and glucose metabolism disorders

Persons with obesity and glucose metabolism disorders constitute a population at increased risk of transmitting an unfavourable metabolic phenotype to the next generation. Therapeutic education should encompass elements of intergenerational prevention, particularly with respect to women of reproductive age and prospective fathers.

In the pre-conception period and during pregnancy, education should encompass:

- the importance of normal body weight before planned pregnancy;
- optimisation of glycaemic control before conception and during pregnancy;
- control of gestational weight gain;
- smoking cessation;
- the importance of physical activity adapted to clinical status.

In the neonatal and infancy periods, parents should be educated in:

- the benefits of breastfeeding;
- avoidance of excessive energy and protein intake during infancy;
- correct introduction of complementary foods;
- monitoring of the child's rate of weight gain.

In the early childhood period, education should promote:

- the shaping of correct dietary patterns for the entire family;
- regular physical activity;
- limitation of screen time;
- sleep hygiene.

Education in the field of intergenerational prevention reduces the risk of perpetuating the "obesity cycle", may limit the prevalence of obesity and T2DM in the next generation, and constitutes an element of comprehensive treatment of obesity.

The inclusion of an offspring-prevention component in therapeutic education extends its scope from an individual intervention to a family- and population-level model [116].

10. RECOMMENDATIONS ON BEHAVIOURAL MANAGEMENT

10.1. Dietary recommendations for individuals with overweight/obesity and glucose metabolism disorders

Key recommendations for adults
• The use of interventions encompassing diet, physical activity, and behavioural therapy is recommended in individuals with overweight/obesity and glucose metabolism disorders, in order to improve weight control and health outcomes. [**B**]
• For weight reduction, intensive, structured behavioural interventions are recommended, directed at modification of diet, increased physical activity, attention to sleep quality, and achieving an energy deficit of approximately 500–750 kcal/day, irrespective of dietary macronutrient composition. [**A**]
• Dietary recommendations should be individualised and adapted to the patient's preferences, needs, and capabilities, with eating plans that produce an energy deficit consistent with the principles of healthy eating. [**A**]

- In planning dietary management, account should be taken of systemic, cultural, and socioeconomic determinants and other social determinants of health. [**C**]
- Long-term monitoring and support after weight reduction are recommended. [**E**]
- Effective weight-maintenance programmes ≥ 1 year typically include monthly contact, frequent self-monitoring, and an optimum of 300 min/week of physical activity. [**A**]
- Short-term, very-low-calorie nutritional interventions (800–1000 kcal/day) may be used only in carefully selected individuals, under the supervision of qualified specialists, in a medical-care setting, with simultaneous planning of long-term weight-maintenance strategies. [**B**]
- Dietary supplements are not recommended for weight reduction, owing to the absence of confirmed efficacy. [**A**]
- In individuals pursuing intentional weight reduction, regular monitoring of nutritional status is recommended, in order to prevent deficiencies of protein and micronutrients. [**E**]

Key recommendations for children and adolescents (general)

- Diet therapy should be a long-term process, integrated with the treatment of glucose metabolism disorders, physical activity, and psychological support. [**A**]
- The overarching aim is improvement of metabolic control, dietary quality, and lifestyle while maintaining normal growth and maturation; weight reduction is not always the primary objective. [**A**]
- Restrictive, very-low-calorie, ketogenic, and very-low-carbohydrate diets are not recommended in children and adolescents. [**A**]
- Nutrient-dense dietary patterns, particularly the Mediterranean diet and the DASH diet, are recommended, with limited intake of ultra-processed foods and free sugars. [**A**]
- Regular meals (typically 4–5 meals per day at intervals of 3–4 hours) are recommended, and skipping breakfast should be avoided. [**B**]
- Supplementation (e.g. with vitamin D) should be considered only in cases of deficiency. [**A**]

Key recommendations for children and adolescents (differential)

T1DM – pre-clinical stage
- Management in accordance with the principles of healthy eating is recommended, analogous to that in the general population of children with overweight and obesity. [**A**]
- The aim is normalisation of body weight relative to height, without restrictive diets. [**B**]

T1DM – clinical stage
- Weight reduction is not the primary objective; the priority is glycaemic safety. [**A**]
- Analysis of the total daily insulin dose, the proportion administered as boluses, and CGM/AID reports is recommended in order to limit iatrogenic hyperinsulinism. [**A**]
- Hypoglycaemia should be treated with glucose, avoiding excessive energy intake. [**A**]
- Adjustment of insulin dosing in relation to physical activity is recommended, rather than routine increase in carbohydrate intake. [**A**]
- In selected adolescents, cautious weight reduction (approximately 5% over 6–12 months) is permissible, provided that glycaemic control is stable. [**C**]

Prediabetes and T2DM
- Weight reduction is one of the principal primary aims of treatment. [**A**]
- In adolescents with obesity, weight reduction of ≥ 5–10% should be sought, where the stage of maturation and growth rate permit. [**A**]
- Gradual reduction of insulin doses with improving insulin sensitivity is recommended. [**A**]
- Pharmacotherapy supporting weight reduction may be used in accordance with current recommendations. [**A**]

Coexisting conditions

Coeliac disease
- A strict gluten-free diet (gluten ≤ 20 ppm) is recommended. [**A**]
- A nutrient-dense dietary pattern is recommended, with limited intake of ultra-processed gluten-free products. [**B**]
- Monitoring for micronutrient deficiencies is recommended. [**A**]

MASLD
- Normalisation of body weight and elimination of sweetened beverages are recommended. [**A**]
- In patients with T1DM, optimisation of insulin therapy is recommended in order to limit hepatic lipogenesis. [**B**]

10.1.1. Assessment of dietary intake – recommendations

It is recommended that the assessment of dietary intake be conducted in a structured, multidimensional manner and integrated with the patient's clinical and behavioural assessment, using standardised dietary tools. [**A**]

It is recommended that, during the consultation, a detailed dietary history be taken, encompassing both quantitative and qualitative assessment of intake, using methods such as the repeated 24-hour dietary recall or a food diary (3–7 days). [**A**]

Assessment of the dietary pattern is recommended, including the number and regularity of meals, their distribution throughout the day, and the context of consumption (e.g. emotional eating, snacking, evening intake). [**A**]

Analysis of dietary quality is recommended, with particular attention to the level of food processing, fibre intake, saturated fat intake and free sugars, and the overall nutrient density of the diet. [**A**]

Account should be taken of behavioural and environmental factors, including lifestyle, level of physical activity, sleep, stress, socioeconomic determinants, and food availability. [**B**]

Integration of dietary data with the assessment of nutritional status and clinical parameters (body weight and composition, glycaemia, lipid profile) is

recommended, and – in justified cases – the use of objectifying tools (e.g. CGM). [**A**]

10.1.2. Goals of dietary management

1. Goals of dietary management for adults

The fundamental goal of dietary management in individuals with overweight/obesity and glucose metabolism disorders is to achieve and maintain optimal metabolic control – particularly glycaemic control in individuals with diabetes – as well as sustained reduction of body weight and improvement of quality of life and overall metabolic health [117, 118].

A reduction in body weight of at least 5% per year (optimally ≥ 7% per year) relative to baseline weight is regarded as clinically meaningful, since it is associated with measurable improvements in metabolic parameters. Greater weight loss (≥ 10–15% per year) brings additional health benefits – including further improvement of glycaemic control and reduction of cardiovascular risk factors – and should be the therapeutic goal in selected individuals, provided that it can be achieved and maintained safely [117–119].

In individuals with diabetes – particularly T2DM – and coexisting overweight or obesity in whom inadequate glycaemic control, blood pressure, lipid profile, or other obesity-related metabolic complications are observed, moderate and sustained weight reduction (5–7% of baseline weight) leads to substantial improvement in metabolic control and may reduce the need for pharmacological treatment [117–119].

In individuals with prediabetes, weight reduction of 5–7% substantially reduces the risk of progression to overt T2DM and constitutes a key element of preventive management. In individuals in the pre-clinical stages of T1DM, normalisation and maintenance of body weight is also one of the fundamental elements of behavioural therapy, which slows the autoimmune process [117, 119, 120].

2. Goals of dietary management for children and adolescents

The fundamental goal of dietary management in children and adolescents with glucose metabolism disorders and overweight or obesity is to achieve and maintain optimal metabolic control – particularly glycaemic control, lipid profile, and hepatic parameters – while preserving normal growth, maturation, and psychophysical development. Diet therapy should also lead to lasting improvement in dietary quality, lifestyle, and the quality of life of the patient and the family [9, 120–122].

In children and adolescents, weight reduction does not always constitute the primary objective. In many cases, the clinically desirable outcome is stabilisation of body weight together with continued growth in height, leading to gradual normalisation of weight indices in relation to height (BMI SDS). This management is associated with improved insulin sensitivity and improved metabolic parameters, without the risk of compromising development [9, 121–123].

In children and adolescents with prediabetes and T2DM, in whom overweight and obesity constitute the key pathogenetic factor, weight reduction is the primary therapeutic objective. A weight reduction of 5–10% over 6–12 months is regarded as clinically meaningful, provided that it is adapted to the stage of pubertal maturation and growth rate and is achieved safely. Such reduction is associated with substantial improvement in glycaemia, reduction of insulin resistance, and limitation of the risk of disease progression and of its complications [9, 120–122].

In children and adolescents with T1DM, the priority of dietary management is glycaemic safety, prevention of hypoglycaemia and excessive glycaemic variability, and limitation of iatrogenic hyperinsulinism. Weight reduction may be considered only in selected adolescents with overweight or obesity, in a cautious and gradual manner (approximately 5% of body weight over 6–12 months), and only with stable metabolic control and close monitoring of insulin treatment [118, 120, 121].

In the pre-clinical stage of T1DM, the goal of diet therapy is normalisation and maintenance of body weight appropriate to height, improvement of dietary quality, and the establishment of lasting healthy eating habits, which may support overall metabolic health and limit additional risk factors [9, 120, 121].

Irrespective of the type of glucose metabolism disorder, an important goal of dietary management in children and adolescents is the prevention of energy, protein, and micronutrient deficiencies; support for normal bone mineralisation; and the development of a positive relationship with food. Equally important is dietary education of the entire family, the strengthening of caregivers' health competences, and the provision of long-term behavioural and psychological support – increasing the chances of lasting therapeutic effects and improvement of metabolic health into adulthood [9, 120–122].

10.1.3. Detailed recommendations – composition of the diet

1. Carbohydrates

Control of the quantity and quality of consumed carbohydrates is a key element of dietary management in children, adolescents, and adults with glucose metabolism disorders and overweight/obesity. No single optimal carbohydrate intake

appropriate for all age groups has been defined; the amount should be set individually, taking into account age, metabolic status, level of physical activity, treatment used, and the feasibility of long-term adherence [117, 118, 120, 121].

In clinical practice, approximately 45% of energy from carbohydrates may be taken as a starting point, with preference for complex carbohydrates of low glycaemic index and high fibre content. In individuals with T1DM, the amount of carbohydrate and the matching of insulin dose to the meal are of particular importance. In individuals with T2DM, the proportion of carbohydrates may be reduced or increased depending on metabolic goals, body weight, and glycaemic tolerance. In gestational diabetes, excessive carbohydrate restriction is not recommended; minimum carbohydrate intake should be 175 g/day, corresponding to approximately 35% of energy on a 2000-kcal diet. In individuals who are very physically active, carbohydrate intake often needs to be increased, particularly around training, in order to prevent hypoglycaemia and maintain performance [117, 118, 121, 124].

In adults, diets with moderate carbohydrate content (typically approximately 45% of total energy intake) are most often recommended in weight-reduction settings, whereas in children and adolescents, restrictive carbohydrate limitation is not recommended due to the risk of impaired growth and maturation. Low-carbohydrate and very-low-carbohydrate diets do not show a clear advantage in long-term improvement of metabolic parameters, and should not be used in children and adolescents – and in adults only exceptionally, short-term, and after individual clinical assessment [117, 118, 120, 121].

Irrespective of age, carbohydrate quality is of greater importance than the amount alone. Preference is recommended for products of low or moderate glycaemic index (GI < 55), which produce slower postprandial rises in glycaemia and favour better metabolic control. It is equally important to consider the meal's glycaemic load (GL), which reflects both the quality and the amount of carbohydrate consumed; aiming for low or moderate GL of meals and the daily diet allows postprandial glycaemic excursions to be limited [117, 118, 121].

In clinical practice, this entails choosing foods rich in dietary fibre and minimally processed, such as whole-grain foods, vegetables, legumes, and whole fruit, and combining carbohydrates with protein, fat, and fibre within meals to lower their glycaemic response. At the same time, intake of free sugars – particularly sweets, sugar, honey, juices, and sweetened beverages, which are characterised by high GI and GL – should be limited [117, 118, 121, 125, 126].

This approach promotes improved glycaemic control, improved metabolic health, and the development of lasting healthy eating habits across the life course, both in children and adolescents and in adults [117, 118, 121, 125].

2. Dietary fibre

Dietary fibre plays a substantial role in glycaemic control, body-weight regulation, and improvement of overall metabolic health by increasing the sensation of satiety, slowing glucose absorption, and exerting a beneficial effect on the intestinal microbiota. Recommendations for fibre intake differ according to age and energy requirements [117, 118, 125, 127].

In adults, the minimum recommended fibre intake is at least 25 g/day or approximately 15 g per 1000 kcal of consumed energy. Higher fibre intake may further favour weight control and metabolic improvement, provided that it is well tolerated. An increased proportion of resistant starch – which exhibits effects similar to dietary fibre – is also beneficial [117, 118, 127].

In children and adolescents, the recommended fibre intake should be adapted to age and development, and is typically 16–21 g/day; a practical approach is the rule of "age + 5–10 g" of fibre per day. Increase in fibre intake should be gradual, with appropriate hydration ensured [9, 121, 127].

Irrespective of age, the principal sources of fibre should be vegetables, fruit, whole-grain foods, legumes, and other nutrient-dense foods, which favour long-term improvement of metabolic control and dietary quality [118, 121, 125, 127, 128].

3. Protein

Protein intake in the diet of children, adolescents, and adults with glucose metabolism disorders and overweight/obesity should be set individually, taking account age, body weight and composition (including lean body mass), level of physical activity, treatment goal (weight reduction, weight stabilisation, or support of normal growth), the degree of energy deficit, comorbid conditions (including CKD), pharmacotherapy used (e.g. insulin), and the feasibility of long-term adherence [117, 118, 120, 121, 129, 130].

In adults with glucose metabolism disorders and/or obesity, protein intake similar to population norms is typically recommended – that is, approximately 15–20% of total energy, most often corresponding to 0.8–1.5 g of protein/kg body weight/day. There is no clear evidence that routine increase or reduction of protein intake beyond this range leads to substantial improvement of glycaemic control or reduction of cardiovascular risk. During weight reduction, moderately higher protein intake (20–30% of energy) may be considered,

in order to increase the sensation of satiety and protect lean body mass [117, 118, 127].

In patients receiving GLP-1-based therapies, adequate protein intake is of particular importance. These drugs substantially reduce appetite and total energy intake, promoting weight reduction, but may simultaneously lead to loss of lean body mass, including muscle mass. The available data indicate that a substantial proportion of weight reduction during GLP-1-based therapy may concern this very fraction, increasing the risk of impaired muscle function and the development of sarcopenia, particularly in older adults or those with low physical activity [117, 118].

In this group of patients, it is reasonable to consider higher protein intake – at least approximately 1.2 g/kg body weight/day, and often 1.2–1.5 g/kg body weight/day, particularly during weight reduction. Even distribution of protein throughout the day (approximately 25–30 g in main meals) is also recommended, as this favours the maintenance of muscle protein synthesis. Owing to reduced appetite in patients receiving GLP-1-based therapies, clinical practice often requires prioritising high-protein products in meals in order to prevent deficiencies and excessive loss of muscle mass [117, 118].

In addition, in order to protect lean body mass, the combination of adequate protein intake with regular physical activity – particularly resistance training – is recommended, since this exhibits synergistic effects in preventing muscle-mass loss during weight reduction.

In children and adolescents with glucose metabolism disorders and overweight/obesity, protein intake should cover requirements arising from age, sex, and developmental stage, in accordance with current paediatric nutritional standards [9, 120, 121, 127]. Routine increase or reduction of protein intake beyond age-appropriate norms is not recommended, since there is no evidence of additional metabolic benefits, and excessive protein intake may displace other essential nutrients from the diet [120, 121, 127].

The use of general protein-intake recommendations consistent with paediatric nutritional standards and diabetological recommendations is advised – typically at the level of approximately 15–25% of total dietary energy – while ensuring coverage of growth and developmental needs. The choice of protein intake should take account of age, body weight and composition, level of physical activity, and therapeutic goals (improvement of metabolic control, stabilisation, or weight reduction) [120, 121, 127].

The priority of dietary management remains ensuring normal growth, maturation, and development of the musculoskeletal system. In clinical practice, particular attention should be paid to the quality of protein sources (nutrient-dense foods), the protection of lean body mass, support for appetite control, and the feasibility of long-term adherence within a healthy, balanced dietary pattern [9, 120–122].

Irrespective of age, in order to support the maintenance of lean body mass and muscle function, even distribution of protein throughout the day – rather than concentrating most of it in a single meal – is recommended [117, 118].

The quality and sources of protein are of substantial importance. The choice of nutrient-dense foods is recommended – such as fish, low-fat dairy products, lean meat and poultry, eggs, and legumes. Partial replacement of animal protein with plant protein may bring metabolic and cardiovascular benefits, owing to lower saturated-fat content and higher fibre intake [117, 118, 128]. During higher-protein dietary interventions, attention should be paid to overall diet quality, particularly saturated fat intake, as well as nutritional status and renal function where clinically indicated [118, 129, 130].

In individuals with glucose metabolism disorders and coexisting CKD, routine reduction of protein intake below approximately 0.8 g/kg body weight/day is not recommended, since no metabolic benefits of such management have been demonstrated, and it may increase the risk of protein – energy malnutrition. More intensive high-protein strategies in this group require individual assessment and regular monitoring. In individuals treated with insulin or sulphonylureas, larger modifications of protein intake – particularly at the expense of carbohydrates – require assessment of the risk of hypoglycaemia and possible adjustment of treatment, with monitoring of glycaemia during the period of dietary change [129, 130].

4. Fats

No single universal share of energy from fats appropriate for all individuals with glucose metabolism disorders and obesity has been defined. In both adults and children and adolescents, the proportion of fat in the diet should be set individually, taking into account age, metabolic status, energy requirement, level of physical activity, coexisting lipid disorders, and the feasibility of long-term adherence. In assessing the influence of diet on glycaemic control and cardiovascular risk, the quality of fats – and not their amount alone – is of pivotal importance [117, 118, 120, 121, 127].

In adults, as in children and adolescents, total fat intake is generally consistent with recommendations for the general population and typically accounts for 30–40% of total energy intake; in

younger children, the upper end of the range may be justified by higher energy requirements [118, 121, 127].

Limitation of saturated-fat intake and maximum limitation of trans fatty acids – particularly those derived from ultra-processed foods (e.g. fast food, ready meals, biscuits) – is recommended [117, 118, 126]. Replacement of saturated fatty acids with mono- and polyunsaturated fatty acids promotes improvement of the lipid profile and reduction of cardiovascular risk, in both adults and children and adolescents. Replacement of saturated fats with refined carbohydrates is not recommended [117, 118].

In children and adolescents with glucose metabolism disorders and overweight/obesity, very-low-fat diets are not recommended, because they may compromise dietary quality and increase the risk of essential fatty acid deficiencies [9, 120, 121]. Particular attention should be paid to ensuring adequate intake of essential unsaturated fatty acids, including omega-3 fatty acids [118, 121, 127].

Dietary patterns should emphasise unsaturated plant fat sources, including vegetable oils, nuts, seeds, and avocado, together with regular fish intake [118, 125, 128, 131]. Coconut and palm oils are discouraged because of their high saturated fat content [118, 127].

5. Sweeteners

Sweeteners may be used by adults with glucose metabolism disorders and coexisting overweight/obesity, provided that consumption does not exceed the acceptable daily intake (ADI). The ADI value, expressed in mg per kg body weight per day, defines the amount of a given sweetener that can safely be consumed daily over a lifetime – including in the paediatric population [118, 132].

In adults, sweeteners may constitute an acceptable element of strategies for limiting energy and carbohydrate intake, provided that their use does not lead to compensatory increase in energy intake from other sources. They may facilitate the reduction of added sugars in the diet; however, their effectiveness depends on the context of the overall dietary pattern [117, 118, 132].

In children and adolescents with glucose metabolism disorders and overweight/obesity, the use of low-calorie sweeteners is not routinely recommended and should be limited to exceptional, clinically justified situations. The basis of dietary management in this age group should be to reduce preference for sweetness rather than reinforce it through habitual sweetener use [120, 121, 132].

Sweeteners should not be used as a permanent component of the diet of children and adolescents – particularly in beverages, desserts, and everyday products. Their use may be considered only in the short term, as a transitional tool in older adolescents, solely with the aim of limiting added-sugar intake, under strict specialist supervision and with adherence to ADI limits [120, 121, 132].

The use of sweeteners is not recommended in young children, and in school-age children and younger adolescents their use should be limited to the maximum extent possible. In this age group, the establishment of lasting, healthy taste preferences based on unsweetened or naturally low-sugar foods – such as water, unsweetened dairy products, and whole fruit instead of juices – is of particular importance [9, 121, 132].

Irrespective of age, sweeteners should not be regarded as a tool for weight reduction or as a means of improving dietary quality. Their use should not compensate for the consumption of ultra-processed foods, nor lead to a false sense of "safe" food choice [117, 118, 126, 132]. The priority in the treatment of children and adolescents remains dietary education of the child and the family, gradual reduction of sweet taste in the diet, and the establishment of dietary patterns conducive to long-term metabolic health [9, 120, 121, 132].

6. Sodium (table salt)

In adults, children, and adolescents with glucose metabolism disorders and overweight/obesity, restriction of sodium intake is recommended in line with general-population recommendations, taking into account age, clinical status, and coexisting cardiovascular and renal risk factors. The aim of such management is to improve blood-pressure control and reduce the risk of cardiovascular and renal complications, which are more frequent in individuals with diabetes and obesity [117, 118, 129–131].

In adults, sodium intake is recommended not to exceed 2300 mg/day, corresponding to approximately 5 g of table salt from all dietary sources. Further reduction of sodium intake may lead to additional lowering of blood pressure but should be considered individually, particularly in individuals with salt-sensitive hypertension. In such cases, more restrictive recommendations consistent with the principles of the DASH diet may be applied. The available data on the benefits of sodium reduction below 1500 mg/day in individuals with diabetes remain inconclusive [118, 131].

In children and adolescents, restriction of sodium intake is recommended in line with age-appropriate norms; in older children and adolescents, the upper limit of sodium intake should also not exceed 2300 mg/day. The adequate intake norm in children, depending on age, is 1000–1500 mg/day. Particular attention should be paid to the prevention of arterial hypertension from the earliest

Table 10.1.1. Macronutrient distribution and intake [117, 118, 120, 121, 126, 127, 129, 130]

Component	Adults	Children (from 4 years)	Adolescents (from 12 years)
Carbohydrates	40–50% of energy*	40–50% of energy*	40–50% of energy*
Free sugars	≤ 10% of energy, with preference for further reduction even to < 5% of energy	≤ 10% of energy, with preference for further reduction even to < 5% of energy	≤ 10% of energy, with preference for further reduction even to < 5% of energy
Total fat	30–40% of energy	30–40% of energy	30–40% of energy
Saturated fatty acids	< 10% of energy	< 10% of energy	< 10% of energy
Trans fatty acids	As little as can be achieved within a diet ensuring proper nutritional value	As little as can be achieved within a diet ensuring proper nutritional value	As little as can be achieved within a diet ensuring proper nutritional value
Protein	15–20% of energy, 0.8–1.5 g/kg body weight/day; 20–30%, ≥ 1.5 g/kg body weight/day in exceptional situations	Younger children: 0.9–1.1 g/kg body weight/day	1.0–1.2 g/kg body weight/day
Dietary fibre	25 g/day or 15 g/1000 kcal	"age + 5–10 g"	16–21 g/day (depending on age)
Fluids	2.0–2.5 l/day	1.6–2.5 l/day (rising with age)	1.6–2.5 l/day (rising with age)

Carbohydrate intake should be personalised; for example, a higher percentage of carbohydrates may be justified in physically active individuals and in those consuming plant-based diets. In patients with obesity, values of 40–45% are preferred.

years, especially in children with overweight, obesity, or T1DM and T2DM. Very-low-sodium diets are not recommended in the paediatric population without clear clinical indications and specialist supervision [9, 120, 121, 127, 131].

Restriction of sodium intake in the diets of adults, children, and adolescents should be implemented primarily through reduction of intake of processed and ultra-processed foods, which constitute the principal source of sodium in the diet, and through preference for fresh, minimally processed food products. Avoidance of additional salting of dishes – both in preparation and at the table – is recommended, as is the gradual development of tolerance to less salty taste, particularly in the paediatric population [118, 126, 131].

The planning of a low-sodium diet should take account of the patient's individual capabilities and needs, including taste acceptance, cultural and economic determinants, food availability, and the presence of comorbidities. This approach increases the long-term effectiveness and safety of dietary intervention, both in adults and in children and adolescents [117, 118, 131].

7. Vitamins, minerals, and dietary supplements

In adults, children, and adolescents with glucose metabolism disorders and overweight/obesity, routine use of dietary supplements – including vitamins, minerals, and herbal preparations – is not recommended, unless clinically meaningful deficiencies, signs of overt malnutrition, or specific medical indications have been identified. Both in adults and in the paediatric population, supplementation in the absence of confirmed deficiencies has not demonstrated clinical benefits in terms of improving glycaemic control, reducing body weight, or reducing cardiovascular complication risk [117, 118, 120, 121].

Antioxidant supplementation – including vitamin C, vitamin E, and β-carotene – is not recommended, owing to the absence of evidence of beneficial effects on metabolic parameters in individuals with glucose metabolism disorders and obesity, and the potential risk of adverse effects with long-term use. This applies to both adults and children and adolescents [117, 118, 120, 121].

Universal vitamin D supplementation in children, adolescents, and adults with T1DM or T2DM and obesity is not recommended in the absence of deficiency. Vitamin D_3 supplementation should be conducted in line with current recommendations for the general population, taking into account age, body weight, and sun exposure, and – where justified – based on individual measurement of 25(OH)D concentration [118, 127].

In adults treated long-term with metformin, and in adolescents receiving this drug, periodic assessment of vitamin B_{12} concentration is recommended, particularly in the presence of anaemia, peripheral neuropathy, or other symptoms suggesting deficiency. Vitamin B_{12} supplementation is indicated only where deficiency is confirmed [117, 118, 120].

In selected groups of patients – both adults and adolescents – such as women planning pregnancy, pregnant and breastfeeding women, older adults, children and adolescents on elimination diets (e.g. vegetarian and vegan), and individuals on very-low-calorie or restrictive dietary patterns,

supplementation with selected vitamins and minerals may be considered for the prevention of deficiencies, after prior individual clinical and dietary assessment [118, 121, 124, 127].

A particular exception remains folic acid supplementation in women planning pregnancy, which should be given at a dose of 400 µg/day for at least 12 weeks before planned conception and continued until the 12th week of pregnancy, in line with current recommendations [124, 133].

The basis of dietary management in adults, children, and adolescents with glucose metabolism disorders and obesity remains a balanced diet of high nutrient density; supplementation should serve only a complementary role and should not replace proper nutrition [117, 118, 121, 125].

8. Alcohol

There is no safe dose of alcohol. Alcohol consumption is not recommended as an element of the diet, and in children and adolescents alcohol is contraindicated. Alcohol may adversely affect glycaemic control, foster risky health behaviours, disturb psychophysical development, and increase the risk of acute metabolic complications, including severe hypoglycaemia [118, 134].

In adults with glucose metabolism disorders and/or obesity, alcohol consumption – if it occurs at all – should be limited and treated with great caution, with full awareness of potential risks. Alcohol may increase the risk of hypoglycaemia, particularly through inhibition of hepatic glucose production; this risk is increased when alcohol is consumed without simultaneous intake of a meal containing carbohydrate, and in individuals treated with insulin or sulphonylureas [118, 134].

Both in adults and in adolescents of legal drinking age, alcohol should not be used as an element of dietary strategy, and its consumption cannot compensate for energy deficiencies or substitute for healthy eating habits. For individuals who decide to consume alcohol, individual discussion of the risks, education on the prevention of hypoglycaemia, and monitoring of glycaemia during consumption and in the night-time hours are essential [118, 134].

The basis of dietary recommendations in individuals with glucose metabolism disorders and obesity remains the non-promotion of alcohol, and in the population of children and adolescents an unequivocal recommendation of avoidance [118, 134].

10.1.4. Timing of meals, regularity, and intermittent fasting

The timing of meals and their regularity are of substantial importance for metabolic control in adults, children, and adolescents with glucose metabolism disorders and overweight or obesity [117, 118, 120, 121]. Glucose metabolism is subject to circadian regulation, and consumption of meals at earlier times of day is associated with better glucose tolerance and a more favourable metabolic response than the consumption of meals in the late evening. Disturbances of the circadian rhythm – including shift work – are associated with an increased risk of prediabetes, T2DM, and obesity, and should be taken into account in individual planning of nutrition and therapeutic strategies [117, 118].

1. Adults

In adults with glucose metabolism disorders and obesity, intermittent fasting and time-restricted eating may be considered as optional strategies for weight reduction and improvement of glycaemic control [117, 118]. The available data indicate that these strategies lead to mild or moderate short-term weight reduction but do not show superiority over continuous caloric restriction in long-term weight control. Limitation of the eating window may be applied within various dietary patterns, provided that the principles of rational, balanced eating are observed during eating periods; dietary quality and total energy intake are of pivotal importance.

In adults with diabetes treated with insulin and/or sulphonylureas, the implementation of intermittent fasting requires particular caution, medical supervision, and possible modification of pharmacotherapy in order to limit the risk of hypoglycaemia. The choice of a time-restricted eating strategy should always be individualised, taking into account the patient's preferences, metabolic safety, and the feasibility of long-term application of the chosen intervention [117–119].

2. Children and adolescents

In children and adolescents with glucose metabolism disorders and overweight/obesity, the use of intermittent fasting or restrictive limitation of the eating window is not recommended. The priority in this age group is regularity of meals, ensuring adequate energy and nutrient intake, and the protection of normal growth and maturation [9, 120–122].

Planning of 4–5 meals per day (3 main meals and 1–2 supplementary meals) and maintenance of consistent meal times – typically at intervals of 3–4 hours (in some patients, 2–3 hours is permissible) – is recommended. Skipping meals is not recommended, particularly breakfast, the omission of which is associated with an increased risk of overweight and obesity [9, 121, 122]. Breakfast should be consumed as early as possible after the start of the day, ideally within an hour of waking [9, 118, 120, 121].

Table 10.1.2. Recommended distribution of energy across meals (4–5 meals/day) [9, 118, 121, 127]

Meal	Energy share (%)	Practical comments
1st breakfast	20–25	Key for control of glycaemia and appetite
2nd breakfast	5–10	Snack of low energy density
Lunch (main meal)	30–35	Largest meal of the day
Afternoon snack	5–10	Optional, particularly for younger children
Dinner (evening meal)	20–25	Light, consumed ≥ 2 hours before sleep

Each meal should be balanced and contain protein, carbohydrate, and fat with a favourable profile, in accordance with the principles of the *healthy plate* method (½ plate vegetables, ¼ source of protein, ¼ source of carbohydrates). The use of nutrient-dense foods is recommended – including whole-grain foods, vegetables and fruit, lean protein sources (e.g. fish, legumes, poultry, and low-fat dairy products), and plant-based fats (excluding coconut and palm oils). Consumption of at least one portion of fish per week is recommended, and 100% juice should be limited to ≤ 180 ml/day [9, 118, 121, 125, 127].

10.1.5. Dietary strategies for glucose metabolism disorders and obesity – adults and children and adolescents

Diet therapy is an integral element of the treatment of glucose metabolism disorders and obesity. It should be implemented from the moment of diagnosis and conducted long term, in conjunction with physical activity, education, behavioural therapy, and (where applicable) pharmacotherapy [117, 118, 120, 121].

There is no single universal dietary model effective in all individuals. The effectiveness of weight reduction and improvement of glycaemia depends primarily on (1) negative energy balance (where the goal is weight reduction), (2) dietary quality, and (3) the feasibility of long-term maintenance of the chosen dietary pattern [117–119].

In the paediatric population, treatment goals and the choice of strategy must additionally take into account the safety of growth and maturation; for this reason, dietary patterns of high nutrient density (e.g. Mediterranean, DASH) are preferred, and extremely restrictive strategies (e.g. ketogenic diet, intermittent fasting) are generally not recommended [9, 120–122, 125].

In practice, structured methods of meal planning are recommended (e.g. plate method, carbohydrate counting/estimation, qualitative approach), and CGM is increasingly used in personalising recommendations (assessment of postprandial response, identification of "problem" meals, adjustment of portion size and composition) [117, 118, 120, 121].

Common elements of best practice irrespective of age:

- Prefer high-quality patterns (Mediterranean, DASH, plant-based/flexitarian, well balanced) and limit ultra-processed foods [125, 126, 128, 131].
- Use structuring tools (plate method, portion planning, food-based work, CGM) rather than "prohibitions" and rigid menus [117, 118].
- Pursue long-term feasibility: preferences, culture, family/patient resources, lifestyle, and treatment safety [117, 118].

10.1.6. Strategies for weight reduction through energy deficit

1. General principles

Behavioural therapy constitutes the foundation of treatment of individuals with obesity and glucose metabolism disorders. It encompasses modification of dietary intake aimed at reducing energy supply and improving dietary quality, increased physical activity, and attention to sleep and circadian regularity. The intervention should be individualised, long-term, and conducted with regular monitoring of effects and safety [117, 118].

2. Adults

Goals and principles of energy deficit [117–119]:

- for clinically meaningful weight reduction, achievement of negative energy balance is recommended – most often through a reduction in energy intake of approximately 500–750 kcal/day;
- the recommended rate of weight reduction is typically 0.5–1.0 kg/week; the greatest fall is observed at the start of the intervention, after which the rate slows due to metabolic adaptations;
- after achieving ≥ 10% weight reduction, reassessment of energy requirements and adjustment of further management is recommended.

Energy value of weight-reducing diets (approximate) [117, 118, 127]:

- in most women, effective weight reduction is achieved with 1200–1500 kcal/day; in most men, with 1500–1800 kcal/day;

Table 10.1.3. Dietary strategies for glucose metabolism disorders and obesity – adults and children and adolescents [9, 118, 120–122, 125, 128, 131]

Strategy/model	Recommendation status – adults	Recommendation status – children/adolescents	Key characteristics	Limitations/risks	Practical comments (when to use/not use)
Mediterranean diet	Recommended (preferred)	Recommended (preferred)	Vegetables, fruit, whole grains, legumes, nuts; plant-based fats (olive oil); fish; low intake of highly processed foods	Typically no substantial limitations when properly balanced	First-choice model in long-term therapy; easy to combine with energy reduction
DASH diet	Recommended (particularly in HTN, dyslipidaemia)	Recommended (particularly in HTN, dyslipidaemia, MASLD)	High intake of vegetables and fruit, wholegrain products, low-fat dairy products; lower intake of sodium, SFA, and added sugars	In children, adjustment of energy portions may be required at high requirements	Beneficial in the "cardiometabolic" phenotype (HTN, dyslipidaemia)
Plant-based/flexitarian patterns	Recommended/permissible	Conditionally recommended	Predominantly plant-based pattern with moderate intake of meat/fish	Risk of deficiencies (Fe, B_{12}, Ca, Zn) with poor planning – greater in children	In children and adolescents, the flexitarian version is preferred, with dietitian oversight
Low-GI/GL diet + "qualitatively selected carbohydrates"	Recommended as a tool	Recommended as a tool	Nutrient-dense carbohydrate sources; GI/GL used as supportive tools	Substantial inter-individual variability of glycaemic response	Best combined with CGM and education; treatment should not be reduced to GI alone
Moderately low-carbohydrate diet (26–40% energy)	Conditionally permissible	Not recommended routinely	Restriction of carbohydrates below population standards	In adults: risk of poorer fat and fibre quality; in children: no long-term safety data	In adults only if the patient is able to maintain dietary quality and treatment safety; in adolescents only exceptionally and short-term, in specialist care
Very-low-carbohydrate/ketogenic diet	Not recommended routinely	Not recommended/contraindicated in obesity	Carbohydrates very limited: < 10% of energy; high fat intake	Risk of deficiencies; in T1DM, more difficult interpretation of ketonaemia and potential risk of DKA; in children, risk of growth disturbance	Not to be used in children and adolescents for the treatment of overweight/obesity; exceptions only for neurological indications (e.g. epilepsy)
Fasting/extremely restrictive diets	Not recommended	Not recommended	Severe restriction of energy intake or food groups	High risk of weight regain, deficiencies, eating disorders	Avoid in every age group; prefer lasting lifestyle change

CGM – continuous glucose monitoring; DKA – diabetic ketoacidosis; GI – glycaemic index; GL – glycaemic load; HTN – arterial hypertension; MASLD – metabolic dysfunction-associated steatotic liver disease; SFA – saturated fatty acids; T1DM – type 1 diabetes.

- these values require individual modification depending on age, body weight and composition, physical activity, and clinical status.

Safety [117, 118, 127]:

- the energy value of the diet should be determined based on the total energy expenditure (TEE);
- energy intake below basal metabolic rate is not recommended due to the risk of deficiencies and adverse effects;
- in individuals treated with insulin and/or sulphonylureas, energy deficit requires monitoring of glycaemia and possible adjustment of treatment.

3. Children and adolescents – goals and principles of energy deficit

Overarching principles [9, 120–123]:

- energy requirements must safeguard the needs of growth and maturation, even under reducing intervention;
- the reference point in diet therapy of obesity is the requirement for the body weight appropriate for height, not for the current body weight;
- diets < 1000 kcal/day are not recommended in children and adolescents.

Determination of requirements [127]:

- the basis is TEE (total energy expenditure), calculated according to the formula:
  TEE = REE (resting energy expenditure) × PAL (physical activity level), where:
  – REE is calculated from formulas appropriate for age and sex (example formulas in Table 10.1.4);
  – PAL is most often 1.4–1.6 in children with low/moderate activity.

Approximate ranges of energy requirement (TEE) by age and intervention goals [9, 123, 127]:

- pre-school children (3–6 years): approximate TEE 1200–1600 kcal/day; the intervention goal is most often stabilisation of body weight with continued growth in length/height;
- school-age children (7–10 years): approximate TEE 1600–2000 kcal/day; in overweight/obesity, moderate energy reduction – typically by 200–300 kcal/day – is feasible;
- adolescents (11 – 18 years): approximate TEE: girls 1800–2400 kcal/day; boys 2000–3000 kcal/day. In adolescents with obesity, controlled energy reduction is permissible, provided that growth and maturation are monitored.

Calculation of deficit – recommended approaches [9, 122, 123, 127]:

- reduction from TEE: by 200–300 kcal/day (younger children); by 300–500 kcal/day (adolescents);
- energy for the appropriate body weight: TEE for BMI 50th–75th centile; possible further reduction by 10–15% of energy;
- "no-deficit" strategy: in young children – maintenance of energy, improvement of dietary quality, and increased energy expenditure.

Safe rate of change [9, 123]:

- young children: ≤ 0.5 kg/month;
- older children and adolescents: up to 1–2 kg/month.

The overarching goal is improvement of metabolic status and quality of life, not solely weight reduction.

10.1.7. Particularities of diet therapy

1. Dietary recommendations for infants (0–12 months) – goals and principles

Overarching goal: Metabolic and neurodevelopmental safety (minimisation of hypoglycaemia and substantial glycaemic variability) while ensuring normal growth and development; weight reduction is not a treatment goal in infancy [118, 120, 121].

- Infant feeding in line with the principles of feeding for healthy children is recommended, with simultaneous adaptation of insulin therapy to the actual feeding pattern (variability is large and requires a flexible plan) [120, 121].
- Breastfeeding should be recommended on the same principles as in the general population; decisions on insulin therapy should be adapted to the actual feeding schedule [120, 121].
- Introduction of complementary foods: in line with the principles of infant feeding, typically from approximately 4 to approximately 6 months of age (depending on developmental readiness) [121, 127].
- A consistent feeding rhythm (routine) is recommended in an infant with glucose metabolism disorders, since this facilitates interpretation

Table 10.1.4. Example formulas for calculating resting energy expenditure (REE) in children and adolescents (after Rychlik *et al.* [127])

Age (years)	Boys (kcal/day)	Girls (kcal/day)
1–2	28.2 × W + 859 × H - 371	30.4 × W + 703 × H - 287
3–9	15.1 × W + 74.2 × H + 306	15.9 × W + 210 × H + 349
10–17	15.6 × W + 226 × H + 299	9.4 × W + 249 × H + 462
18	14.4 × W + 313 × H + 113	10.4 × W + 615 × H - 282

H – height (m); W – body weight appropriate for corrected height (kg).

Table 10.1.5. Estimated daily energy requirements for boys and girls aged 7–18 years (kcal/day) (after Rychlik *et al.* [127])

Age (years)	Boys (PAL 1.4)	Boys (PAL 1.6)	Boys (PAL 1.8)	Boys (PAL 2.0)	Girls (PAL 1.4)	Girls (PAL 1.6)	Girls (PAL 1.8)	Girls (PAL 2.0)
7	1504	1719	1934	–	1386	1584	1782	–
8	1599	1827	2055	–	1475	1686	1896	–
9	1693	1934	2176	–	1566	1790	2014	–
10	–	1965	2211	2456	–	1824	2051	2279
11	–	2074	2334	2593	–	1914	2153	2393
12	–	2217	2494	2771	–	2016	2268	2520
13	–	2384	2682	2980	–	2111	2375	2639
14	–	2558	2878	3198	–	2179	2451	2723
15	–	2712	3051	3390	–	2220	2497	2774
16	–	2834	3188	3543	–	2244	2524	2804
17	–	2933	3300	3666	–	2255	2537	2819
18	–	2707	3045	3383	–	2123	2388	2654

PAL – physical activity level. 1.4 – low physical activity; 1.6 – moderate physical activity; 1.8 – active lifestyle; 2.0 – very active lifestyle.

of glycaemia and choice of insulin doses. In practice, this may mean feeding approximately every 3–4 hours during the day, together with complementary feeding [120, 121].
- In infants and young children, excessive "feeding up" out of fear of hypoglycaemia should be avoided (risk of chronic energy excess and unfavourable glycaemic control); hypoglycaemia is treated with glucose at a dose adequate to body weight and age, avoiding "overfeeding" with carbohydrates [120, 121].
- Introduction of complementary foods is recommended in line with the principles of infant feeding, with emphasis on nutrient-dense foods (vegetables, whole-grain foods with higher fibre content appropriate for age, sources of protein and healthy fat) [121, 127].
- Avoidance of perpetuating preference for sweet taste is recommended: avoidance of additional sweetening and of sweetened beverages; juices (including 100% juices) – as a rule, not as an everyday drink [9, 121, 127].

2. Dietary recommendations for children and adolescents with glucose metabolism disorders, overweight/obesity, and coeliac disease
- A strict gluten-free diet (gluten ≤ 20 ppm) is recommended as the causal treatment of coeliac disease [118, 121].
- A nutrient-dense dietary pattern is recommended, preferably based on a gluten-free Mediterranean or DASH diet [118, 121, 125, 131].
- Low GI/GL carbohydrate sources are recommended, while ultra-processed gluten-free products should be avoided [118, 121, 126].
- Naturally gluten-free sources should be chosen: buckwheat, quinoa, amaranth, certified gluten-free oats, legumes, low-starch vegetables [118, 121].
- In individuals with overweight/obesity, a moderate energy deficit is permissible provided that normal growth and a nutrient-dense pattern are maintained [9, 121, 123].
- Owing to the gluten-free diet, monitoring of the risk of deficiencies (Fe, folate, B_{12}, vitamin D, Ca, Mg, Zn) is required [118, 121, 127].

3. Dietary recommendations for children and adolescents with glucose metabolism disorders, overweight/obesity, and MASLD
- Normalisation of body weight is recommended as the fundamental therapeutic objective in children and adolescents with MASLD, irrespective of the type of glucose metabolism disorder (T1DM, T2DM), with preservation of safe growth and maturation [9, 118, 121, 122].
- A nutrient-dense dietary pattern, preferably based on the Mediterranean or DASH diet, is recommended, with limited intake of ultra-processed foods, saturated fats, and free sugars [118, 121, 125, 126, 131].
- Strict limitation of sweetened beverages and of products rich in fructose is recommended, given their strong association with progression of hepatic steatosis and hepatic insulin resistance [118, 121, 126].
- Preference is recommended for low-GI and low-GL carbohydrates sources, with high intake of dietary fibre (vegetables, whole fruit, wholegrain foods, or naturally gluten-free products in individuals with coeliac disease) [118, 121, 127].
- Regularity of meals (4–5 per day) is recommended, with avoidance of energy excess from snacking, particularly in the evening hours [9, 118, 121].

Table 10.1.6. Energy requirements and goals of dietary intervention in children and adolescents [9, 123, 127]

Age group	Approximate TEE* (kcal/day)	Main goal of diet therapy	Recommended energy deficit	Clinical comments
1–3 years	900–1200	Stabilisation of body weight	Typically no deficit	Energy restriction unacceptable; concentrate on dietary quality
3–6 years	1200–1600	Decrease in BMI with continued growth	0–200 kcal/day	"Energy maintenance" strategy preferred
7–10 years	1600–2000	Reduction of excess body weight	200–300 kcal/day	Deficit calculated from TEE or from energy for the appropriate body weight
11–14 years	1800–2400	Controlled weight reduction	300–500 kcal/day	Monitoring of growth and maturation essential
15–18 years	2000–3000	Weight reduction/ metabolic improvement	300–500 kcal/day	Risk of restrictive diets and eating disorders

TEE – total energy expenditure (REE × PAL).

- In children and adolescents with T1DM and MASLD, optimisation of insulin therapy is recommended – including analysis of the daily insulin dose and CGM data – in order to limit iatrogenic hyperinsulinism, which favours hepatic lipogenesis [118, 120, 121].
- Weight reduction should not be conducted by restrictive methods; a moderate energy deficit, directed primarily at the elimination of energy excesses from ultra-processed foods, is permissible [9, 122, 123, 126].
- Long-term diet therapy in a multispecialist model is recommended, with the participation of a dietitian and – where necessary – a psychologist, since MASLD has a chronic and recurrent character [9, 118, 121, 122].

4. Dietary recommendations for individuals with glucose metabolism disorders and CKD

- Dietary therapy as an integral element of the treatment of individuals with glucose metabolism disorders and CKD is recommended, from the time of diagnosis and on a long-term basis [118, 129, 130].
- Dietary recommendations should be individualised, taking into account the stage of CKD (eGFR), albuminuria, nutritional status, age, comorbidities, and pharmacotherapy used [118, 129, 130].
- Dietary treatment by a dietitian with experience in nephrology is recommended, with regular monitoring of nutritional status (body weight, body composition, biochemical parameters) [129, 130].
- Adequate energy intake (typically 25–35 kcal/kg body weight/day) is recommended in order to prevent protein – energy malnutrition [129, 130].
- High-quality dietary patterns (e.g. Mediterranean, DASH, plant-based) with restriction of ultra-processed foods are recommended [126, 128–131].
- In patients with diabetes treated with insulin or drugs that increase the risk of hypoglycaemia, dietary changes require monitoring of glycaemia and possible modification of treatment [118, 129, 130].

Goals of dietary management [118, 129–131]

- Achievement and maintenance of optimal glycaemic control.
- Slowing CKD progression.
- Reduction of cardiovascular risk.
- Prevention of protein – energy malnutrition and sarcopenia.
- Improvement of patient quality of life.
- In individuals with overweight/obesity and early stages of CKD (G1–G3a), moderate weight reduction (5–7%) may be considered, conducted safely and under clinical supervision.
- In advanced CKD (G3b–G5), the priority is the maintenance of normal nutritional status; weight reduction is not the primary objective.

Protein [128–130]

- Adjustment of protein intake to CKD stage and treatment is recommended:
  - CKD G1–G3a: approximately 0.8–1.0 g/kg body weight/day;
  - CKD G3b–G5 (without dialysis): 0.6–0.8 g/kg body weight/day.
- Dialysis: ≥ 1.0–1.2 g/kg body weight/day.
- Protein intake < 0.6 g/kg body weight/day is not recommended without strict specialist supervision.
- High-quality protein sources are recommended, with a greater proportion of plant protein sources in the diet.
- In older adults with features of frailty syndrome, sarcopenia, or high risk of malnutrition, caution is advised in restricting protein intake.

Carbohydrates [118, 126, 129, 130]

- Individualisation of carbohydrate intake is recommended, taking into account glycaemic control and CKD stage.

- The following are recommended:
  – choice of products of low/moderate GI and GL;
  – restriction of free sugars and ultra-processed food;
  – preference for nutrient-dense foods.
- In advanced CKD, the potassium content of carbohydrate sources should be taken into account.

Fats [118, 128–130]
- The following are recommended:
  – restriction of saturated fats and trans fatty acids;
  – increased the intake of mono- and polyunsaturated fats;
  – preference for plant fats (with the exception of coconut and palm oils) and fish.
- Replacement of saturated fats with refined carbohydrates is not recommended.

Dietary fibre [118, 128–130]
- Fibre intake in line with population norms is recommended, taking into account tolerance and potassium control.
- Preference for natural sources of fibre (vegetables, fruit, legumes, whole-grain foods) is recommended.

Minerals and fluids [126, 129–131]
- Sodium: restriction of sodium intake to < 2 g/day (i.e. approximately 5 g NaCl) is recommended.
- Potassium: routine restriction of potassium in all patients is not recommended. Restriction should be considered in the case of hyperkalaemia or advanced CKD.
- Phosphorus: limitation of phosphate additives and ultra-processed foods is recommended. Preference for natural sources of phosphorus and monitoring of its serum concentration is recommended.
- Fluids: fluid intake should be individualised depending on CKD stage, urine output, and clinical status.

Additional dietary strategies [118, 126, 128–130]
- In patients with CKD G1–G4, an increased proportion of vegetables and fruit may be considered, in order to reduce the dietary acid load – while maintaining safety (potassium control).
- Restriction of ultra-processed foods – the principal source of sodium, phosphates, and food additives – is recommended.
- The following diets are not recommended:
  – high-protein diets;
  – very-low-carbohydrate/ketogenic diets;
  – extremely restrictive diets without specialist supervision.

Monitoring and safety [118, 129, 130]
- Regular monitoring is recommended: eGFR and albuminuria; potassium, phosphorus, and other electrolyte concentrations; nutritional status parameters (body weight, body composition); glycaemic control.
- Gradual introduction of dietary changes and adaptation to pharmacological treatment is recommended.

5. Dietary recommendations for women in pregnancy (and during pregnancy planning) with glucose metabolism disorders and obesity – goals and principles

Overarching goal: Achieving and maintaining optimal glycaemic control (with particular emphasis on postprandial glycaemia), while ensuring normal fetal development, limiting the risk of obstetric complications, and achieving appropriate gestational weight gain (not weight reduction) [118, 124, 133].

A. Pre-conception period (pregnancy planning)
- Assessment of body weight and counselling concerning the risk associated with obesity in pregnancy is recommended, together with implementation of lifestyle interventions (including dietetic consultation) before pregnancy – irrespective of the type of glucose metabolism disorder.
- In women with overweight/obesity and a history of GDM, weight reduction before the next pregnancy may reduce the risk of GDM recurrence – particularly with reduction of ≥ 5% of body weight (an element of pre-conception counselling) [118, 124, 133].

B. Pregnancy – principles of nutrition and weight gain
- Weight reduction during pregnancy is not recommended, including in women with obesity, owing to the risk of small-for-gestational-age (SGA) births; the goal is weight gain in line with the recommendations [124, 133].
- In women with obesity, the recommended total gestational weight gain is approximately 5–9 kg, and in women with overweight 7–11.5 kg [133].
- Avoidance of dietary patterns that severely restrict entire macronutrient groups – including the ketogenic diet – is recommended; in practice, pregnancy is a state predisposing to ketosis, and additionally, in women with diabetes, the importance of ketone safety increases [118, 124, 133].
- Stable/consistent carbohydrate intake and matching of insulin to the amount of carbohydrate are recommended, in order to limit hy-

poglycaemia and postprandial hyperglycaemia; cooperation with a dietitian is recommended to establish a feeding plan and weight-gain goals [118, 124].
- Protein intake in pregnancy (RDA): 0.8 g/kg body weight/day + 1 g/day (first trimester) + 9 g/day (second trimester) + 28 g/day (third trimester), calculated as additions to the protein intake recommendations for non-pregnant women of normal body weight [124, 127].
- Fat intake in the diet: the quality of fats is very important, 30–40% of energy, EPA + DHA 250 mg/day + a minimum of 200 mg DHA/day [118, 124, 127].
- Carbohydrate intake: 45–60% of energy. The minimum recommended carbohydrate intake in pregnancy is ≥ 175 g/day (in order to cover fetal needs, including brain development, and to limit the risk of ketonaemia from excessive carbohydrate restriction). Distribution of carbohydrates across several meals throughout the day (most often 3 main meals + 2–4 snacks) is recommended, in order to limit postprandial glycaemic peaks and reduce the risk of hypoglycaemia (particularly under insulin therapy) [118, 124].
- In clinical practice, limitation of large "carbohydrate loads" in single meals is recommended; moderate, repeatable portions are preferred (particularly under insulin therapy in T1DM/T2DM) [118, 124].
- A diet based on nutrient-dense foods is recommended (vegetables, fruit, legumes, whole grains, lean sources of protein, healthy fats), with restriction of ultra-processed foods and sweetened beverages; emphasis on carbohydrate quality may support glycaemic control [118, 124, 126].
- Excessive restriction of carbohydrate intake to improve glycaemia requires caution, as it may lead to increased dietary fat intake and adverse metabolic consequences. When excessive carbohydrate restriction is suspected, fasting ketone monitoring may be helpful [118, 124].
- Treatment of GDM begins with diet therapy, physical activity, and weight management (depending on pre-pregnancy BMI), and the feeding plan should ensure adequate energy intake for the health of mother and fetus and achieving glycaemic goals, while ensuring normal fetal development and weight gain in line with recommendations for pre-pregnancy BMI (without "slimming" in pregnancy) [118, 124, 133].
- In women with T1DM (and to a lesser extent T2DM) in pregnancy, the risk of DKA increases at lower glycaemia than outside pregnancy; education in prevention and early detection of ketonaemia/acidosis is recommended (an element of metabolic safety, also during dietary modifications) [118, 124].
- GDM + obesity: diet therapy is the first-line treatment; the priorities are distribution and quality of carbohydrates, avoidance of sweetened beverages, and achievement of the recommended weight gain. Pharmacotherapy is considered when glycaemic goals are not achieved despite proper implementation of dietary recommendations [124, 133].
- Intentional weight reduction in pregnancy is not recommended, including in women with obesity; the goal is controlled weight gain in line with the recommendations and improvement of dietary quality [124, 133].
- In the practice of treating GDM with obesity, some recommendations permit cautious energy restriction – for example, a limit of approximately 24 kcal/kg body weight/day or an energy reduction of approximately 30–33% in women with GDM and BMI ≥ 30 kg/m². The decision requires individualisation and monitoring of fetal growth and ketonaemia, and assessment of nutritional status [124, 133].

10.2. Recommendations on physical activity for individuals with overweight/obesity and glucose metabolism disorders

Key recommendations
• In individuals with obesity and T2DM, aerobic physical activity is recommended (at least 150 minutes of high-intensity exercise or 300 minutes of moderate-intensity exercise per week), combined with resistance training (at least 2–3 times per week), which beneficially affects glycaemic control, blood pressure, inflammation, cardiorespiratory fitness, and quality of life. [**A**]
• Regular aerobic physical activity of moderate and high intensity in individuals with obesity and prediabetes substantially reduces the risk of developing T2DM. [**B**]
• Resistance training at least twice per week prevents loss of muscle mass during weight reduction. [**B**]
• Persons with obesity and glucose metabolism disorders are advised to limit uninterrupted sitting time. [**B**]
• In individuals with obesity and diabetes treated with insulin, education on modification of insulin therapy in respect of physical activity and weight reduction is recommended, in order to reduce the risk of hypoglycaemia. [**C**]

Physical activity is a fundamental component of comprehensive obesity management. Recommendations on the type, intensity, and duration of physical activity should take into account the individual needs, capabilities, and preferences of the patient. It is recommended to choose forms of physical activity that bring pleasure and satisfaction. In conversations about physical activity, medical staff should take into account both motivating factors and barriers – an understanding of which favours the development of practical and

lasting solutions, particularly given that achieving full activity recommendations may be initially difficult for a substantial proportion of individuals with diabetes and obesity.

Increased physical activity in individuals with obesity promotes the reduction of adipose tissue – particularly visceral and ectopic fat (defatting of the liver, skeletal muscle, and heart) – even in the absence of weight reduction [1, 135].

10.2.1. Principles of undertaking physical activity

- The initial recommendations for physical activity should be moderate and adapted to the patient's exercise capacity, which is particularly important in patients with extreme obesity.
- For optimal effect, physical activity should be regular, undertaken at least every 2–3 days, ideally daily [1, 136].
- In children and adolescents, daily exercise of 10–20 minutes at moderate intensity is recommended, with gradual extension to 60 minutes per day. Regularity is more important than intensity; the total daily activity time may be achieved in several shorter sessions, which facilitates adherence – particularly in children with low fitness or clinically significant obesity [110].
- When starting intense physical activity, 5–10-minute warm-up exercises should be performed, with cool-down exercises at the end.
- In individuals treated with insulin, physical activity may increase the risk of hypoglycaemia during or immediately after exercise, and of delayed hypoglycaemia.
- Alcohol may increase the risk of hypoglycaemia after exercise.
- Attention should be paid to the prevention of dehydration, particularly under conditions of high ambient temperature and excessive sweating.
- The risk of foot injury during exercise should be borne in mind (especially with coexisting peripheral neuropathy and reduced pain threshold), as should the necessity of foot care and comfortable footwear [1].
- Persons with mobility limitations and with extreme obesity should be referred for physiotherapist consultation to identify exercises that can be performed in seated and/or supine positions. Analogous management is recommended in children and adolescents with clinically significant obesity, postural defects, or coexisting musculoskeletal conditions [135, 137, 138].
- In planning physical activity in individuals with obesity, it should be remembered that excess adipose tissue may prolong recovery time after exercise, irrespective of age. A regular exercise programme should last at least 6 months in order to achieve clinically meaningful reduction of adipose tissue mass and improvement of abnormal fat distribution and deposition [137].

10.2.2. Recommended type, intensity, and duration of physical activity

- The undertaking of physical activity by an individual with obesity and glucose metabolism disorders should be defined with reference to: assessment of health status (including the severity of obesity and the patient's level of activity – type, duration, intensity), any contraindications, and the patient's expectations, knowledge, and skills regarding hypoglycaemia prevention. Heart-rate monitoring and assessment of exercise intensity using the Borg scale are recommended. Heart-rate ranges and exercise intensity may be defined during electrocardiographic exercise testing. In this group of patients, moderate-intensity aerobic exercise (up to the point of breathlessness) is safe [135, 139].
- Persons with obesity are advised to undertake 200–300 minutes of physical activity per week, leading to an energy deficit of 500–750 kcal/day. In children and adolescents, at least 60 minutes of physical activity per day is recommended, mainly of moderate intensity, adapted to developmental age and psychophysical capabilities [1, 140].
- In everyday practice, information on the number of steps taken per day – obtained from an accelerometer, pedometer, or mobile application – should be used to assess the level of physical activity. Classification of physical activity based on pedometer data is presented in Table 10.2.1.
- In individuals with obesity – particularly with BMI > 35 kg/m² – exercises that excessively load the joints, such as jumping or running, are not recommended. Beneficial forms of physical activity in individuals with obesity are swimming, water aerobics, yoga, t'ai chi, cycling, and exercise on a stationary cycle ergometer or rowing ergometer. Other forms of recreational activity leading to measurable energy expenditure are also recommended – for example, sing-

Table 10.2.1. Classification of physical activity based on pedometer data

Number of steps per day	Level of physical activity
< 5000	Sedentary lifestyle/very low level of physical activity
5000–7499	Low level of physical activity
7500–9999	Moderate level of physical activity
10,000–12,500	High level of physical activity
> 12,500	Very high level of physical activity

ing with vocal exercises, which trained singers use to improve pitch and rhythm control, can be considered endurance physical activity of moderate intensity. In children and adolescents with obesity, this recommendation is of particular importance during the period of growth [1, 135, 140].

- Resistance training engaging all muscle groups should be undertaken no less than twice per week. Loading of large muscle groups and the performance of 8–12 repetitions, 2–3 times per week, is recommended. This recommendation is particularly important during weight reduction, in order to prevent loss of muscle mass and strength (sarcopenia). In children and adolescents, resistance training should be based predominantly on bodyweight exercises or low resistance, conducted under the supervision of a trained person, and directed at improvement of fitness and muscle strength rather than at maximisation of loads [1, 110, 137].
- In older adults with sarcopenic obesity, the use of diets with a small energy deficit (200–500 kcal/day) and increased protein intake (approximately 1.5 g/kg body weight/day) is recommended, provided that renal function is normal and proteinuria has been excluded. Regular physical activity – including exercises improving flexibility, balance, aerobic capacity, and resistance training – constitutes an important element of the management of obesity in older adults [137, 140].
- Health benefits also accrue from limitation of sitting time. The introduction of short breaks with physical activity yields additional health benefits. In individuals with T2DM, glycaemic benefits can be obtained by avoiding sitting for longer than 30 minutes at a time [140].
- Increases in physical activity should be gradual and directed at extending the duration, frequency, and intensity of exercise, and should be integrated with everyday life – for example, walking up stairs, working while standing, and travelling on foot or by bicycle.
- Cross-sectional findings indicate that afternoon and evening activity – but not nocturnal activity – provides greater metabolic benefit than morning activity, while morning activity is associated with the lowest risk of hypoglycaemia [141].
- In planning physical activity in children and adolescents, psychosocial aspects should be taken into account, including reduced self-esteem, fear of peer judgement, and previous negative experiences associated with physical activity. Forms of physical activity should be adapted to the child's preferences, based on play, and conducive to acceptance of physical activity, and should not lead to stigmatisation. Engagement of the family and promotion of joint forms of physical activity are recommended [110, 138].

10.2.3. Risks associated with physical activity in individuals with obesity and diabetes

Physical activity without adequate preventive measures may result in hypoglycaemia or hyperglycaemia (less commonly) and metabolic decompensation, as well as an increased risk of injury. These measures should encompass the pre- and post-exercise periods and long-term management (taking into account the improvement of physical fitness over time).

Intense physical activity and excessive load during resistance training may, in particular clinical situations, have an unfavourable effect on the patient's general status:

- proliferative diabetic retinopathy – risk of vitreous haemorrhage, retinal detachment;
- diabetic kidney disease – intensification of albumin excretion and proteinuria;
- autonomic neuropathy – presence of orthostatic hypotension;
- ischaemic heart disease – risk of acute myocardial ischaemia and life-threatening arrhythmia [1, 140].

10.2.4. Monitoring of health and glycaemia during physical activity

- In individuals treated with insulin, the use of CGM systems is recommended. The therapeutic team has a role in supporting the choice of CGM, education on the interpretation of results, individual programming of higher hypoglycaemia alarm thresholds, and securing of CGM during physical activity. The CGM system should be equipped with predictive alarms and alarms for the rate of glycaemic rise and fall [1, 140].
- Where self-monitoring of glycaemia is conducted by glucose meter, glycaemia should be measured up to 15 minutes before the start of physical activity, during it (frequency of measurement every 30–60 minutes or as needed), and after the end of activity. Informing companions during physical activity about diabetes substantially increases the safety of individuals with diabetes [1, 135, 140].
- In individuals with obesity and diabetes not treated with insulin, the use of CGM systems serves an educational role and increases motivation to adhere to therapeutic recommendations.
- The use of devices for monitoring health and activity increases adherence to recommendations and engagement in self-care; their use is therefore appropriate alongside exercise treatment [1].

10.2.5. Hypoglycaemia and hyperglycaemia in connection with physical activity

See: Section 7 of the *Clinical Guidelines on the Management of Patients with Diabetes* of Diabetes Poland 2026, and Figure 10.2.1.

10.2.6. Principles of physical activity in individuals with T2DM not requiring insulin treatment

- In individuals with diabetes who do not use insulin or sulphonylureas, the risk of hypoglycaemia is very low. Glycaemia values < 100 mg/dl do not require additional carbohydrate consumption.
- Regular physical activity improves insulin sensitivity and thereby increases the chances of delaying the initiation of insulin therapy [142].

10.2.7. Principles of physical activity in individuals treated with insulin

- Modification of insulin therapy should be directed at preventing hypoglycaemia, in order to limit the consumption of additional carbohydrate portions.
- Irrespective of the type of exercise, the target glycaemic range should be 126–180 mg/dl, or slightly higher for individuals with increased risk of hypoglycaemia and/or impaired hypoglycaemia awareness. Starting physical activity with glycaemia < 90 mg/dl is not recommended. For resistance exercise and where hyperglycaemia is anticipated, there are no contraindications to starting activity at a glycaemia of 90 mg/dl [1, 140].
- Physical activity undertaken within 2 hours of the administration of a rapid-acting insulin analogue requires reduction of insulin dose, if the activity lasts at least 30 minutes [1, 110].
- Physical activity 2–3 hours after the administration of a rapid-acting insulin analogue may require smaller carbohydrate portions. Bolus reduction may be 25–75%, depending on the duration and intensity of the activity [1, 110].
- In individuals with obesity, physical activity requires consumption of smaller amounts of carbohydrate – typically 0.2 g/kg body weight per hour of intense physical activity during the maximum action of an insulin bolus that has been reduced or that has been administered more than 2 hours from the start of the activity.

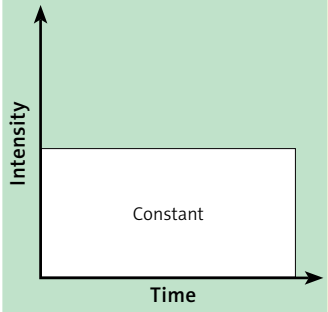
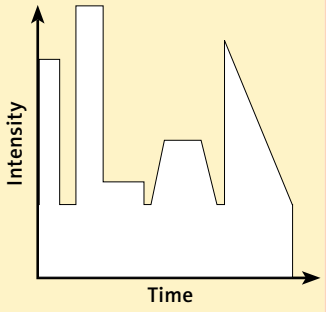
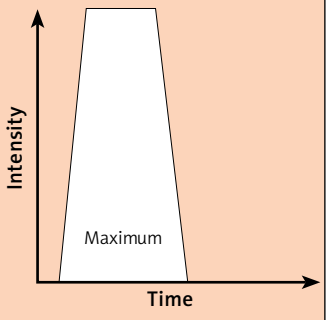
Type of exercise	**Aerobic** Examples: walking, Nordic walking, light cycling, jogging	**Mixed (aerobic-anaerobic)** Examples: team sports, running, swimming, interval cycling	**Anaerobic** Examples: sprints, resistance training with maximum load, explosive exercises
Intensity			
Heart rate range	< 55 (60)% HR_{max}	60–75 (80)% HR_{max}	> 75 (80)% HR_{max}
Borg scale	7–11	12–15	16–20
Expected glycaemic response	Decrease	Decrease and/or increase	Increase
Risk of hypoglycaemia	High	Increased	Low
Reduction of prandial insulin bolus for activity lasting > 30 minutes (not applicable to automated insulin delivery systems)	25% for low-intensity exercise 50% for higher-intensity exercise lasting > 45 minutes 75% for prolonged, intensive aerobic exercise lasting several hours	Reduction may be required 25% if a slight decrease in glycaemia is expected 50% for moderate-intensity exercise with an expected rapid decrease in glycaemia	Dependent on the athlete's experience No reduction of prandial bolus Administration of a small insulin bolus before or during physical activity

Figure 10.2.1. Types of physical exertion and their effect on glycaemia

- A 20% reduction of basal NPH insulin or a long-acting analogue should be considered for multi-hour or all-day endurance activity. A preceding 25% dose reduction of ultra-long-acting insulin analogues may be considered before multi-day activities.
- In treatment with personal insulin pumps, the maximum duration of pump disconnection during physical activity should not exceed 3 hours. The condition for pump disconnection is the presence of active insulin, the amount of which should be monitored using the bolus calculator function.
- During treatment with a personal insulin pump, reduction of the basal insulin flow rate by 20–80% – depending on the intensity and duration of exercise – is recommended, ideally 2 hours before its start.
- The use of a hybrid closed-loop system during physical activity requires multiple decisions and modifications of therapy by the patient. Separate education on this is recommended (see: *Clinical Guidelines on the Management of Patients with Diabetes; Position Statement of Diabetes Poland 2026*, Section 7.VII).

10.2.8. Physical activity in individuals with obesity and CKD

Physical activity should be recommended for individuals with overweight or obesity and CKD according to general principles. Account should be taken of limitations specific to this group of patients – particularly coexisting sarcopenia, mineral and bone disorders, fluid overload, and renal anaemia – and of the comorbidities common in this group, such as heart failure, peripheral arterial atherosclerosis, and difficult-to-control arterial hypertension, which may substantially impede the achievement of recommended physical-activity programmes.

Dietary interventions and physical activity allow weight reduction in patients with CKD of 5–10%. Studies assessing the effect of behavioural management on body weight and clinical parameters have lasted up to 24 months, and the durability of such management cannot therefore be assessed. Diet and physical activity, and the associated reduction of body weight, also have a beneficial effect on the rate of eGFR loss and on UACR/UPCR [1, 135].

10.3. Recommendations on psychological support for individuals with overweight/obesity and glucose metabolism disorders

Key recommendations
• Routine psychosocial assessment should constitute an integral element of the behavioural treatment of obesity and should encompass at least the assessment of stress, sleep, depressive and anxiety symptoms, emotional eating, and episodes of loss of control over eating [117]. [**A**]
• Behavioural interventions (behavioural weight-loss [BWL]/lifestyle modification) based on self-monitoring, goal-setting, stimulus control, skills training, and relapse prevention should constitute the standard of management in the treatment of obesity and form the fundamental component of behavioural treatment [143, 144]. [**A**]
• In the case of dominant stress, emotional eating, and entrenched strategies of regulating tension through eating, targeted techniques of stress and emotion regulation (CBT/ACT components, mindfulness training, relaxation techniques) should be implemented as part of the weight-reduction programme [37, 145, 146]. [**B**]
• Where binge eating disorder (BED) or substantial episodes of loss of control over eating are suspected, the priority is treatment directed at the eating disorder (psychotherapy with documented effectiveness, most often CBT/CBT-E or interpersonal psychotherapy [IPT]); weight reduction should be integrated with this management [147, 148]. [**A**]
• Sleep and circadian rhythm should be regarded as a modifiable determinant of the effectiveness of obesity treatment. Sleep deficiency, insomnia, sleep apnoea, and disturbance of the circadian rhythm (e.g. social jetlag) require diagnosis and treatment, since they affect appetite regulation, dietary choices, and the capacity for self-control [149–152]. [**A**]
• In chronic insomnia, the first-line treatment is cognitive behavioural therapy for insomnia (CBT-I). Sleep hygiene constitutes an element of psychoeducation but is typically not a sufficient monotherapy in chronic insomnia [153]. [**A**]

10.3.1. Description of the problem: why behavioural treatment without "psychology" often fails

Obesity is a chronic disorder in which behavioural treatment requires long-term change of habits and maintenance of a new lifestyle despite fatigue, stress, social pressure, and fluctuations in motivation. In clinical practice, the maintenance phase is particularly demanding and often proves more difficult than the initial implementation of recommendations. For this reason, psychological support should not be regarded as a supplementary element but as an essential condition for increasing the effectiveness of behavioural treatment in real-world clinical conditions [143, 144].

From a mechanistic perspective, in many patients several mutually related factors co-occur: chronic stress and overload, sleep disturbances, difficulties in emotion regulation, and patterns of reward-based or impulsive eating. These factors may mutually reinforce one another. Worsening sleep quality increases stress reactivity and impulsivity, stress fosters emotional eating, and eating in the function of tension reduction may become entrenched through reward-system mechanisms [37, 145, 146, 149].

In the psychological context, the capacity for self-regulation and the functioning of cognitive control processes also play an important role. Chronic stress, fatigue, and sleep deficiency may lead to weakening of the capacity to inhibit impulsive responses and to make decisions that favour immediately rewarding behaviours at the expense of long-term goals [146, 149, 154].

10.3.2. Stress and the HPA axis: how stress biologically and behaviourally supports weight gain

Chronic stress activates the hypothalamic–pituitary–adrenal (HPA) axis and favours sustained elevation of cortisol concentrations. Cortisol affects glucose and lipid metabolism and, in clinical terms, is associated with an increased tendency towards visceral adipose-tissue deposition and increased appetite – particularly for high-energy foods. Chronic activation of the HPA axis may also influence adipose-tissue distribution and the regulation of glucose and lipid metabolism. These changes favour the entrenchment of an unfavourable metabolic phenotype, in which high-energy eating serves as a quick strategy for the reduction of emotional tension [145].

In parallel, stress acts on the reward system. The reward-based stress eating model indicates that stress and highly palatable food may activate reward mechanisms and reinforce the habit of reaching for food as a quick method of tension reduction. In the short term, the patient may experience subjective relief; however, in the long term, the behavioural loop becomes entrenched: stress → eating → momentary relief → entrenchment of pattern [145, 146].

10.3.3. Emotional eating and loss of control over eating

Emotional eating is a behavioural pattern in which the trigger for eating is emotion (most often tension, overload, sadness, or frustration), not physiological hunger. In the population of individuals with obesity, this phenomenon is frequent and clinically significant, since it is associated with greater susceptibility to evening eating, high-energy choices, and difficulties in adhering to therapeutic recommendations. In population studies, emotional eating is also associated with greater variability of energy intake and with difficulties in maintaining long-term weight reduction. In behavioural-treatment practice, it is essential to distinguish between the patient experiencing occasional emotional eating and the occurrence of episodes of loss of control over eating. In the latter case, the probability of coexisting eating disorders increases, and the intervention requires more targeted therapeutic management [37].

10.3.4. BED: why it must be diagnosed and treated with targeted therapy, not diet alone

BED is the most common eating disorder in the adult population and frequently coexists with obesity. The NCS-R study has demonstrated a substantial prevalence of BED in the population and its association with other mental disorders. The disorder is characterised by episodes of binge eating combined with a sense of loss of control and substantial psychological distress. In the context of weight reduction, this is of pivotal importance: if a patient struggles with binge episodes, intensifying dietary restriction alone may lead to escalation of the cycle of restriction → tension → binge → shame → renewed restriction. For this reason, psychiatric guidelines recommend psychotherapeutic treatment directed at the disorder (CBT/CBT-E, IPT) as management with documented effectiveness [147, 148].

10.3.5. Depression and anxiety: barriers to behavioural treatment

Depressive and anxiety symptoms occur more frequently in individuals with obesity, and this relationship is bidirectional. A meta-analysis of longitudinal studies confirms a mutual increase in the risk of depression and obesity. Clinically, this means that, with more severe depression, drive and capacity for implementing physical activity are reduced, the risk of emotionally driven eating as a means of reduction increases, and sleep quality deteriorates. In anxiety disorders, tension increases and impulsive coping strategies are observed more frequently. Recognition and treatment of these conditions may be a precondition for the effectiveness of a behavioural-treatment programme in some patients [155].

10.3.6. Sleep and circadian rhythm: a "core" element of lifestyle treatment

Influence of sleep on body weight

Data indicate that sleep deficiency and circadian-rhythm dysregulation increase the risk

of obesity and impede treatment. A review in *Nature Reviews Endocrinology* indicates that insufficient sleep and circadian misalignment affect appetite, food choice, energy expenditure, and the risk of obesity. Mechanistically, changes in appetite regulation are of importance. In the classic experimental study, sleep curtailment was shown to be associated with decreased leptin concentrations, increased ghrelin concentrations, and intensification of hunger and appetite. In addition, sleep deprivation affects the cerebral mechanisms of reward valuation and impulse control. A neuroimaging study showed an increase in susceptibility to food craving after sleep deprivation. Sleep deficiency also affects executive functions – including inhibitory control, planning, and decision-making – which play a key role in maintaining lifestyle changes and adhering to therapeutic recommendations [149, 152, 154].

Circadian rhythm and social jetlag

Even with similar sleep duration, a discrepancy between the biological and social clocks (social jetlag) is associated with higher BMI. This phenomenon consists of the difference between the sleep rhythm on working days and the sleep rhythm on days free from work, leading to chronic dysregulation of the circadian rhythm. Clinically, this means that, in many patients, the problem is not solely shortened sleep duration but the irregularity of sleep and the compensatory "catching up" of sleep at weekends. From a clinical-practice standpoint, this means the necessity of assessing not only sleep duration but also its regularity. Stability of sleep and wake times favours synchronisation of the biological clock and improvement of sleep quality, which may indirectly affect appetite regulation and eating behaviour [151].

Sleep disorders common in obesity: insomnia and sleep-disordered breathing (SDB)/obstructive sleep apnoea (OSA)

In the population of individuals with obesity, SDB – including OSA – occurs more frequently, and obesity is one of the strongest risk factors for its occurrence. Updated epidemiological data confirm a high prevalence of SDB in the population and its association with obesity. Obstructive sleep apnoea causes sleep fragmentation, excessive daytime sleepiness, and poorer exercise tolerance, as well as reducing the ability to engage in physical activity. This disorder also frequently coexists with low mood, worsened cognitive function, and a reduced capacity for actions requiring sustained self-control. For this reason, in patients with obesity, clinical vigilance for symptoms suggestive of OSA – such as loud snoring, observed apnoeas, excessive daytime sleepiness, and morning headaches – is recommended. Where these are present, referral for further investigation of sleep-disordered breathing should be considered [150].

Sleep hygiene: what specifically to recommend

Sleep hygiene constitutes an important element of psychoeducation and should be discussed practically and in a way that is feasible in everyday functioning. Discussion with the patient of the following areas is recommended:

- regular sleep rhythm – as consistent a wake time as possible every day, including at weekends, since this stabilises the functioning of the biological clock;
- light and screen exposure – limitation of exposure to bright light and screen devices in the 1–2 hours before sleep; in the morning, exposure to daylight is advisable, as it favours synchronisation of the circadian rhythm;
- caffeine, alcohol, and nicotine – caffeine is best avoided in the afternoon and evening; alcohol worsens sleep architecture; nicotine increases arousal and may impede falling asleep;
- physical activity – regular physical activity favours improvement of sleep quality, but very intense exercise undertaken late in the evening may impede falling asleep;
- evening eating – large meals consumed late in the evening may worsen sleep quality and favour evening snacking; this should be considered in conjunction with work on emotional eating;
- environmental conditions – quiet, darkness, and a moderately cool room favour falling asleep; strengthening of the association of the bed with sleep – rather than with work or telephone use – is also advisable.

Chronic insomnia: the standard is CBT-I

In chronic insomnia, the use of CBT-I is recommended as first-line treatment. European guidelines clearly indicate that sleep hygiene alone is typically not a sufficient therapeutic intervention. This therapy includes stimulus control, restriction of time spent in bed, cognitive restructuring, and arousal-reduction techniques [153].

The aim of CBT-I is to modify the factors that perpetuate insomnia – such as irregular sleep rhythm, excessive focus on the problem of falling asleep, and safety behaviours that perpetuate sleep difficulties. The inclusion of CBT-I in therapeutic management may contribute not only to improvement of sleep but also to an increase in the patient's capacity to maintain lifestyle changes [153].

10.3.7. Psychological and behavioural interventions: "what we do" in the behavioural treatment of obesity

Structure of behavioural treatment (behavioural weight-loss – BWL)

Effective BWL programmes are based on a structured process encompassing goal-setting, self-monitoring, behavioural planning, work on environmental cues, skills training, problem-solving, and relapse prevention. These principles are described in the review literature and constitute the basis of contemporary lifestyle interventions [143, 144].

The key components in clinical practice include:

- self-monitoring of food, physical activity, and body weight, which constitutes one of the most important elements of behavioural treatment;
- environmental stimulus control, encompassing modification of food availability and the planning of shopping and meals;
- planning of health behaviours, including the planning of meals, breaks from eating, and strategies for coping in social situations;
- training in skills such as assertiveness, communication, and coping with difficult emotions;
- relapse prevention strategies, encompassing the preparation of plans for periods of increased stress, travel, holidays, or fall in motivation.

CBT in obesity: what is "psychological" in BWL

Cognitive behavioural therapy in the treatment of obesity encompasses work on beliefs and cognitive schemas that may impede the maintenance of lifestyle change. Among the most commonly observed are:

- dichotomous thinking ("all-or-nothing");
- catastrophising in response to a single deviation from the eating plan;
- shame and avoidance related to experiences of stigmatisation;
- automatic eating patterns occurring without a conscious decision.

In clinical practice, CBT encompasses identification of triggers of eating behaviour, functional analysis of behaviour (A-B-C), modification of responses, training in alternative coping strategies, and the development of tolerance of emotional discomfort [143, 144].

Functional analysis of behaviour allows for the identification of the sequence of events preceding episodes of unplanned eating – including situational, cognitive, and emotional factors – enabling the development of more precise behaviour-change strategies.

Stress – emotion interventions: how to incorporate them into the programme

If stress constitutes the dominant trigger for eating, the inclusion of brief, repeatable techniques of emotion and tension regulation is recommended, such as:

- breathing and relaxation training;
- mindfulness directed at the recognition of hunger, satiety, and emotional-state signals;
- work on response delay (a pause before deciding to eat);
- problem-solving strategies;
- preparation of an action plan for high-risk situations – for example, evening emotional eating.

The rationale for these interventions arises from the stress–reward–eating model and from data indicating the role of dopaminergic mechanisms in reward-based behaviours [145, 146].

10.3.8. BED: integrated management

In BED, the behavioural intervention should be integrated with treatment of the eating disorder (CBT/CBT-E, IPT). Increasing dietary restrictions without parallel treatment of binge episodes may lead to perpetuation of the cycle of symptoms. The recommendations of the American Psychiatric Association emphasise the role of psychotherapy as a fundamental element of BED treatment [147].

Depression/anxiety: when to intensify parallel treatment

In the case of substantial depressive or anxiety symptoms, behavioural treatment should encompass parallel psychotherapeutic or psychiatric management. Without improvement of mood, reduction of anxiety, and improvement of sleep quality, the patient may have difficulty maintaining lifestyle changes [155].

10.3.9. Minimum standard of office assessment

In the behavioural treatment of obesity, inclusion of a brief screening assessment that can be conducted in routine clinical practice is recommended (Table 10.3.1) [117].

10.3.10. Summary

Effective behavioural treatment of obesity requires simultaneous action on health behaviours and on the psychological factors that destabilise the maintenance of those behaviours. Chronic stress – through activation of the HPA axis and reward-system mechanisms – favours the consumption of high-energy foods and the entrenchment of emotional eating. Eating disorders – including BED – require treatment directed at the disorder, not solely the intensification of dietary restriction. Mood and anxiety disorders constitute substantial barriers to treatment and, in some patients, require parallel therapeutic management [37, 143–148].

Table 10.3.1. Minimum standard of behavioural assessment in the medical office

Domain	Content
Sleep	Sleep duration, sleep quality, and daytime sleepiness; if OSA is suspected, further investigation is indicated
Insomnia	Duration, severity, and perpetuating factors of symptoms; with chronic character, CBT-I should be considered
Stress	Identification of principal stressors and coping strategies; assessment of whether eating serves a tension-reducing function
Emotional eating/ loss of control	Characterisation of episodes, situational and emotional context; if BED is suspected, referral for psychotherapy is indicated
Mood and anxiety	Assessment of whether symptoms impede the achievement of therapeutic recommendations and worsen sleep; with substantial severity, parallel treatment is indicated

Sleep and the circadian rhythm have the character of a biological – behavioural determinant: short sleep, insomnia, obstructive sleep apnoea, and social jetlag affect appetite regulation, dietary choices, and the capacity for self-control. For this reason, they should be routinely identified and treated. In chronic insomnia, the first-line treatment remains CBT-I [149–153].

11. GENERAL PRINCIPLES OF PHARMACOLOGICAL TREATMENT OF OVERWEIGHT/OBESITY IN INDIVIDUALS WITH GLUCOSE METABOLISM DISORDERS

Key recommendations

- The indication for pharmacological treatment of overweight/obesity is the lack of effect of behavioural management in individuals with obesity (BMI ≥ 30 kg/m²) or overweight (BMI ≥ 27 kg/m²) in the presence of at least one obesity-related complication. [**A**]
- In the pharmacological treatment of overweight/obesity, GLP-1-based pharmacotherapy should be considered, taking into account the effectiveness of these drugs in the prevention of T2DM (liraglutide, semaglutide, tirzepatide) and the reduction of cardiovascular risk (semaglutide) in individuals with overweight/obesity. [**A**]

11.1. General principles of pharmacological treatment

The aim of pharmacological treatment of overweight/obesity is improvement of overall health and prevention of the development of the numerous diseases and complications associated with obesity. Furthermore, overweight/obesity are among the substantial factors increasing the risk of CVD [156]. To achieve the goal of treatment of overweight/obesity, reduction of adipose-tissue mass is necessary. This goal should be set individually, taking into account the severity of overweight/obesity, the patient's health complications, preferences, and economic capabilities, and contraindications to a given type of treatment – or, in the longer term, its tolerance. An important element of treatment is the realisation that this is chronic pharmacotherapy, requiring at the same time changes in patient engagement, lifestyle, and often in close family members. Pharmacotherapy of overweight/obesity requires cooperation not only with the physician but also with a dietitian, a physiotherapist, and a psychologist. All therapeutic decisions concerning the treatment of overweight/obesity should be taken jointly with the patient, after obtaining their acceptance. The indication for pharmacological treatment of overweight/obesity is the lack of effect of behavioural management in individuals with obesity (BMI ≥ 30 kg/m²) or overweight (BMI ≥ 27 kg/m²) in the presence of at least one obesity-related complication. The BMI threshold of 27 kg/m² as an indication for pharmacotherapy was adopted on the basis of the registration trials of anti-obesity drugs; this does not mean, however, that no therapeutic action should be taken in the BMI range 25.0–26.9 kg/m².

11.2. Drugs used for the treatment of obesity in Poland

The drugs currently available in Poland for the treatment of obesity are: incretin-based drugs – liraglutide, semaglutide, tirzepatide; the fixed combination of naltrexone hydrochloride and bupropion hydrochloride; orlistat; and phentermine with topiramate (Table 11.1).

The mainstay drugs in the therapy of overweight/obesity are at present GLP-1 receptor agonists (GLP-1 RAs) – liraglutide and semaglutide – and the dual agonist of the GLP-1 and GIP receptors, tirzepatide [157–159]. Use of this group of drugs results in reduced hunger, increased satiety through direct action on the CNS, slowing of gastric emptying, and increased glucose-dependent insulin secretion [160]. In most individuals, the effect of these drugs is substantial weight loss and improvement of glucose metabolism [160]. Moreover, clinical trials have shown their cardioprotective effects (semaglutide at a dose of 2.4 mg, liraglutide at a dose of 1.8 mg, and tirzepatide at doses

up to 15 mg in T2DM) and renoprotective effects (liraglutide and semaglutide in T2DM).

In light of the published trial findings, these drugs are also recommended for the treatment of overweight/obesity, both in the prevention of T2DM and in established diabetes and other special populations (see Section 12). In individuals with BMI ≥ 27 kg/m² and prediabetes, pharmacotherapy with GLP-1-based therapies of proven efficacy in reducing the risk of developing T2DM (liraglutide, semaglutide, tirzepatide) [157, 158, 161], in addition to behavioural treatment, should be considered.

The remaining drugs have much more limited application. Orlistat is an inhibitor of intestinal lipase, the effect of which is reduced fat absorption. This drug does not suppress appetite. As a weakly acting and poorly tolerated drug (gastrointestinal symptoms – flatulence, fatty diarrhoea), it is now rarely used [162].

The fixed combination of naltrexone hydrochloride and bupropion hydrochloride suppresses appetite and consequently food intake, principally through a central mechanism. Both active substances act mainly in two regions of the brain – the arcuate nucleus and the mesolimbic dopaminergic reward system [163].

In situations where the effectiveness of a given pharmacotherapy is less than desired, combination of anti-obesity drugs with different mechanisms of action is possible (e.g. a GLP-1 analogue with a preparation containing naltrexone and bupropion). Similarly, in patients after surgical treatment of obesity, in the case of insufficient weight loss or secondary weight regain (these problems affect as many as 20–30% of patients within several years of surgery), anti-obesity drugs are used as a supplement to surgical treatment and may be implemented both for the optimisation of weight reduction after the operation and for the treatment of obesity recurrence (most often, GLP-1-based therapies are used).

12. PHARMACOLOGICAL TREATMENT OF OVERWEIGHT/OBESITY IN SPECIAL POPULATIONS

12.1. Pharmacological treatment of overweight/obesity in individuals with glucose metabolism disorders and other cardiovascular risk factors

Key recommendations
• In individuals with overweight/obesity, weight loss of 5–7% of baseline body weight improves glycaemia and other cardiovascular risk factors. [**A**]
• Sustained weight loss > 10% typically yields still greater benefits in terms of reducing cardiovascular risk factors – including disease-modifying effects and potential remission of T2DM – and may also improve long-term cardiovascular outcomes and reduce mortality. [**B**]

Table 11.1. Drugs available for the treatment of overweight/obesity (2026)

Substance	Trade name	Route	Dose range	Weight reduction	Mean weight loss (kg)	Continuation criterion	Direct effect on glycaemia	Cardiovascular risk	Most common adverse effects	Contraindications
Orlistat	Xenical	*p.o.*	120 mg three times daily	≈ 3% above placebo	≈ -3 kg	≥ 5% at 3–6 months	=	=	Fatty diarrhoea, flatulence	Malabsorption syndrome, cholestasis
Naltrexone + bupropion	Mysimba	*p.o.*	32 mg/360 mg per day	≈ 5–6%	≈ -5 kg	≥ 5% at 16 weeks	=	=	Nausea, insomnia, ↑ BP	Epilepsy, bipolar affective disorder, MAOI use, opioid use
Liraglutide 3.0 mg	Saxenda, Plyzari, Polidia	s.c. once daily	0.6 → 3.0 mg/day	≈ 8%	≈ -8 kg	≥ 5% at 16 weeks	↓	↓ (1.8 mg in type 2 diabetes)	Nausea, vomiting, diarrhoea	Hypersensitivity
Semaglutide 2.4 mg	Wegovy	s.c. once weekly	0.25 → 7.2 mg/week	≈ 15% (2.4 mg); ≈ 19% (7.2 mg)	≈ -17 kg (2.4 mg); ≈ -21.5 kg (7.2 mg)	≥ 5% at 16–20 weeks	↓↓	↓ (2.4 mg)	Nausea, vomiting, diarrhoea	Hypersensitivity
Tirzepatide	Mounjaro	s.c. once weekly	2.5 → 15 mg/week	≈ 15–22%	≈ -16 to -23 kg	≥ 5% at 16–20 weeks	↓↓	↓ (in individuals with type 2 diabetes)	Nausea, vomiting, diarrhoea	Hypersensitivity
Phentermine + topiramate	Qsiva	*p.o.*	3.75 + 23 → 15 + 92 mg/day	≈ 7–11%	≈ -7 to -10 kg	≥ 5% at 12 weeks	=	No data on long-term safety; no EMA registration	Paraesthesias, headache and dizziness, insomnia, dry mouth	Hypersensitivity, MAOI use, hyperthyroidism, glaucoma

"=" – no effect, "↓" – reduction; "↓↓" – significant reduction. BP – blood pressure; MAOI – monoamine oxidase inhibitors.

- In individuals with overweight/obesity and hypertension, the obesity treatment plan should include drugs of proven efficacy in reducing blood pressure values. [**A**]

On the basis of the findings of analyses of 112 cohort studies conducted in 34 countries with a combined population of 1,518,028 individuals, it has been shown that 5 principal modifiable cardiovascular risk factors (BMI, systolic blood pressure, non-HDL-C, smoking, and diabetes) are responsible for 57.2% of cardiovascular disease cases in women and 52.6% in men, and for 22.2% and 19.1% of all-cause deaths in women and men respectively over a 10-year follow-up period [106]. The study did not analyse the subgroup of individuals with overweight/obesity and accompanying glucose metabolism disorders; however, it can be assumed that, in this special population, the recorded indices would be analogous or higher. In view of the foregoing, it appears extremely important to undertake actions aimed at controlling risk factors in this group of individuals.

Overweight and obesity constitute key pathophysiological factors underlying diabetes and other cardiovascular risk factors and, ultimately, cardiovascular–kidney–metabolic disease itself [103].

In the assessment of cardiovascular risk in patients with overweight/obesity, comprehensive clinical evaluation extending beyond BMI measurement is of pivotal importance [103]. Routine inclusion of waist circumference (as a simple indicator of visceral obesity), assessment of blood pressure (preferably with ambulatory or home monitoring), assessment of metabolic parameters, and identification of early features of end-organ damage – such as left-ventricular hypertrophy, albuminuria, or increased arterial stiffness – is recommended. Recognition of coexisting disorders, including sleep apnoea, that modify cardiovascular risk and the clinical picture is also important [103].

Management arising from the nature of obesity – particularly in the population of individuals with established cardiovascular risk factors – is multidirectional therapy aimed not only at weight reduction but also at normalisation of carbohydrate and lipid parameters and blood-pressure values, in accordance with current treatment standards [103]. Management should comprise behavioural modifications (see Section 10) and appropriate pharmacotherapy. It is highly important that, in individuals with established cardiovascular risk factors, drugs of proven benefit be used for both weight reduction and for their impact on the aforementioned risk factors. Each time, the medications taken for other indications should also be analysed for their potential influence on weight gain [103].

In line with data from clinical studies, achieving even a 5% weight reduction is associated with health benefits – including improvement of cardiometabolic risk factors. In individuals with additional comorbidities accompanying overweight/obesity, achieving a 10–15% reduction of baseline body weight has allowed substantial improvement of glycaemia, blood-pressure values, and the lipid profile compared with reductions at the 5% level. In most cases, the reduction of cardiovascular risk factors is directly proportional to the degree of weight reduction. This is confirmed by the data from studies in which it has been shown that at least a 15% weight reduction resulted in greater improvement of systolic blood pressure values and the lipid profile compared with groups in which weight reduction was lesser [103, 164–167].

One of the mechanisms by which drugs intended for the treatment of obesity beneficially affect cardiovascular risk factors is weight loss *per se*. All drugs approved for use exhibit a weight-reducing effect, but only for GLP-1-based therapies do we have findings from randomised trials conducted in the population of individuals with glucose metabolism disorders [103].

Hypertension is associated with excess body weight, the reduction of which translates directly into improvement of blood-pressure values. Most drugs registered for the treatment of obesity exhibit a blood-pressure-lowering effect through weight reduction. This does not apply to the naltrexone – bupropion combination, which is contraindicated in individuals with uncontrolled hypertension [103, 164–168].

Weight reduction of at least 5% translates into improvement of the lipid profile in patients with overweight/obesity. This is brought about not only by weight reduction (which is observed for every registered preparation) but also additionally by the action of the molecule itself – as has been demonstrated for GLP-1-based therapies [103, 109, 169].

As already mentioned, in individuals with cardiovascular risk factors, drugs of proven potential in both weight reduction and control of the aforementioned risk factors should be chosen. The findings of cardiovascular safety studies of GLP-1-based therapies are described in Subsection 12.5. Discussing the cardiovascular safety of phentermine plus topiramate, it is worth noting that an analysis of short-term studies did not demonstrate a substantial increase in the risk of cardiovascular disease or death; however, the absence of long-term cardiovascular safety studies of this drug should be borne in mind. In view of this limitation, the drug has not received marketing authorisation from the European Medicines Agency [170]. In the case of the bupropion – naltrexone combination, an attempt was made to assess car-

diovascular safety; however, the early termination of the LIGHT trial (for non-medical reasons) did not allow the assumed hypothesis to be proven, and the cardiovascular safety of the drug remains uncertain [103, 168].

12.2. Pharmacological treatment of overweight/obesity in individuals with prediabetes

Key recommendations
• In individuals with obesity and prediabetes, weight reduction of at least 5–7% of baseline body weight, together with its maintenance, is recommended in order to reduce the risk of developing T2DM. [**A**]
• In individuals with overweight/obesity and prediabetes, GLP-1-based anti-obesity pharmacotherapy – with proven efficacy in reducing the risk of developing T2DM and beneficial cardiovascular effects – should be considered the preferred first-line option. [**A**]
• In patients with BMI ≥ 27 kg/m² and advanced prediabetes, anti-obesity pharmacotherapy should not be delayed; this is supported by clinical trials indicating greater intervention efficacy at earlier stages of glucose metabolism disorders. [**B**]

Treatment of overweight/obesity prevents the development of numerous obesity-related diseases – including T2DM. A particularly high risk of developing T2DM pertains to individuals with visceral obesity, marked insulin resistance, and prediabetes. In individuals with IGT, the greatest intensity of insulin resistance is observed. Maintenance of normal glucose tolerance requires its compensation through increased insulin secretion by pancreatic β-cells. Decline in β-cell function constitutes the principal mechanism of progression from prediabetes to T2DM. For this reason, the treatment of obesity at the prediabetes stage is of pivotal importance in the prevention of T2DM development [1].

12.2.1. The role of non-pharmacological treatment in the prevention of T2DM

The basis of obesity therapy is behavioural management, encompassing dietary treatment and physical activity appropriately adapted to the severity of obesity (see Section 10.2).

In individuals with overweight/obesity and prediabetes, weight reduction of 5–7% reduces the risk of progression of this state to T2DM [1, 171].

In the *Diabetes Prevention Program*, in the group of individuals with obesity and prediabetes, non-pharmacological management – comprising a diet with a 450 kcal/day caloric deficit aimed at a 7% body-weight reduction, and physical activity of at least 150 minutes per week – produced a reduction in the incidence of diabetes of 58% [171].

The greater (> 7%) and more durably maintained the weight reduction, the greater the benefits in terms of glycaemic normalisation and reduction of the risk of T2DM development [1, 171].

12.2.2. The role of pharmacological treatment in the prevention of T2DM

Since effective prevention of T2DM is closely associated with weight reduction, every pharmacological treatment (see Section 11) leading to substantial and sustained weight loss may reduce the risk of its development.

The indication for pharmacological treatment of obesity is the absence of efficacy of behavioural management in individuals with obesity (BMI ≥ 30 kg/m²) or overweight (BMI ≥ 27 kg/m²) in the presence of at least one obesity-related complication – including prediabetes. Pharmacological treatment should always be conducted in combination with behavioural treatment (see Section 10).

1. GLP-1-based therapies

For liraglutide, semaglutide, and tirzepatide, clinical trial data demonstrate that their use in combination with behavioural management reduces the risk of T2DM development in individuals with prediabetes.

In the placebo-controlled randomised trial SCALE, it was found that liraglutide at a dose of 3.0 mg used in obesity therapy substantially reduced the risk of developing T2DM. After 1 year of treatment, normoglycaemia was achieved in 69.7% of patients with prediabetes, and after 3 years of treatment the risk of developing T2DM was reduced by approximately 80% [172].

In the STEP trials, the use of semaglutide in the therapy of overweight/obesity at a dose of 2.4 mg resulted in restoration of normoglycaemia in approximately 89% of individuals with prediabetes [173–175]. In the STEP 10 trial, in which only individuals with overweight/obesity and confirmed prediabetes participated, normoglycaemia was achieved by approximately 81% of patients after 52 weeks of treatment with semaglutide 2.4 mg [175]. Additional data supporting the potential for remission of prediabetes are provided by the STEP UP trial, in which, among individuals with prediabetes treated with semaglutide 7.2 mg once weekly, approximately 73.8% achieved restoration of normoglycaemia after 72 weeks of treatment, which was associated with greater weight loss and improvement of insulin sensitivity [176].

In the SELECT trial, it was found that semaglutide 2.4 mg used together with behavioural intervention in individuals with BMI ≥ 27 kg/m² and established cardiovascular disease – both with and without prediabetes – substantially reduced

the risk of developing T2DM (approximately 73%) and the risk of major cardiovascular events [161] (see Subsection 12.5).

Among individuals with prediabetes and baseline HbA_{1c} levels of 5.7 to < 6.0%, normoglycaemia was achieved by 71.4% of patients treated with semaglutide, and in the group with HbA_{1c} from 6.0% to < 6.5% by 47.3%, supporting the early initiation of anti-obesity pharmacotherapy in individuals with prediabetes, which should not be delayed [161].

Another agent with proven efficacy in the prevention of T2DM is tirzepatide. In the SURMOUNT-1 trial, normoglycaemia was achieved by 95.3% of patients with prediabetes treated for overweight or obesity. After approximately 3 years of follow-up, treatment with tirzepatide was associated with an approximately 94% reduction in the risk of progression to T2DM compared with placebo [157]. In addition, beneficial effects of tirzepatide have been demonstrated in patients with obesity and HFpEF [177] (see Subsection 12.5).

2. Non-incretin drugs

Other medications used for the treatment of overweight and obesity (see Section 11), owing to weight reduction, may reduce the risk of developing T2DM. However, no evidence currently demonstrates cardiovascular benefit with these agents.

Metformin, which is not registered for the treatment of obesity, may be used in patients with prediabetes for the prevention of T2DM. Its effect on weight reduction is modest.

In individuals with BMI ≥ 27 kg/m² and prediabetes, in addition to behavioural treatment, anti-obesity pharmacotherapy with proven efficacy in reducing the risk of developing T2DM and beneficial cardiovascular effects should be considered.

12.3. Pharmacological treatment of overweight/obesity in individuals with glucose metabolism disorders and MASLD

Key recommendations
• Treatment of obesity in individuals with MASLD encompasses behavioural management and pharmacological treatment. [**A**]
• Weight loss of ≥ 5% substantially reduces hepatic steatosis; weight loss of 7–10% limits the degree of inflammation; and weight loss of ≥ 10% leads to gradual reduction of fibrosis. [**A**]
• In the pharmacological treatment of individuals with obesity and MASLD, GLP-1-based therapies are recommended. [**C**]

MASLD is closely associated with abdominal obesity and the metabolic syndrome and currently affects up to 38% of the population [178]. It is defined as the presence of hepatic steatosis with the exclusion of other potential causes of steatosis and of excessive alcohol consumption, in the presence of at least one criterion of cardiovascular or metabolic disturbances. The disease is divided into simple steatosis (metabolic dysfunction-associated steatotic liver – MASL), MASH, and cirrhosis on the basis of steatotic disease (see Section 5). Steatohepatitis can only be diagnosed on the basis of a histopathological examination, which encompasses assessment of hepatocyte steatosis, inflammation, and ballooning degeneration [71].

The aim of treatment in individuals with obesity and MASLD is not only weight reduction by at least 5% (with a target of 10%), but also regression of steatotic and fibrotic changes, or prevention of the progression of hepatic steatosis and fibrosis. It has been shown that weight loss > 5% substantially reduces hepatic steatosis; weight loss of 7–10% limits the degree of inflammation; and weight loss of ≥ 10% leads to gradual reduction of fibrosis. The basis of treatment is lifestyle change through the introduction of a diet and physical activity individually tailored to the patient's preferences and capabilities. The diet of choice in the treatment of MASLD is the Mediterranean diet (based on vegetables, fruit, whole-grain products, nuts, olive oil, unprocessed dairy products, and fish), with elimination of ultra-processed fast-food-type products, simple sugars, and saturated fats [71]. Physical activity is also indicated (see Section 10). At present, the drugs approved for the treatment of MASH with F2–F3 fibrosis are resmetirom (a thyroid hormone receptor B1 agonist) and semaglutide. For the treatment of obesity in individuals with MASLD, the use of incretin drugs is recommended (GLP-1 receptor agonists – liraglutide, semaglutide; or the dual GIP/GLP-1 agonist tirzepatide) [179–181]. It must be emphasised that, to date, randomised clinical trials with the aforementioned drugs have been conducted in groups of patients with MASH confirmed on histopathological examination. The effects of liraglutide, semaglutide, and tirzepatide use are presented in Table 12.3.1. It appears that the beneficial outcomes observed with GLP-1-based therapies in individuals with obesity and pre-existing hepatic fibrosis in the course of MASLD result not only from weight reduction but also from indirect drug effects – for example, through the anti-inflammatory action of GLP-1 receptor agonists.

A particular group of individuals with MASLD comprises patients with established cirrhosis. Before the introduction of dietary recommendations, their nutritional status and hepatic functional capacity should be assessed. In the case of sarcopenia and decompensated cirrhosis, a high-calorie,

Table 12.3.1. Summary of trials concerning the use of GLP-1-based therapies in the treatment of obesity in individuals with metabolic dysfunction-associated steatohepatitis (MASH)

Drug	Trial duration	Drug dose	Study group	Effect
Liraglutide vs. placebo (LEAN trial) [179]	48 weeks	1.8 mg	Patients with MASH confirmed on histopathology, *N* = 52	No worsening of fibrosis in 39% vs. 9% in the placebo group; weight reduction of 5.5%
Semaglutide vs. placebo (ESSENCE trial) [180]	72 weeks	2.4 mg	Patients with moderate fibrosis at stage F2/F3 confirmed on histopathology, *N* = 800	Reduction of hepatic steatosis without progression of fibrosis in 62.9% vs. 34.3% in the placebo group reduction of fibrosis without progression of hepatic steatosis in 36.8% vs. 22.4% in the placebo group concurrent reduction of MASH and hepatic fibrosis significantly more frequent in the semaglutide group (32.7% vs. 16.1%); weight reduction of 10.5%
Tirzepatide vs. placebo (SYNERGY-NASH trial) [181]	52 weeks	5 mg, 10 mg, 15 mg	Patients with moderate fibrosis at stage F2/F3 confirmed on histopathology, *N* = 190	Complete resolution of MASH without progression of hepatic fibrosis observed in 44%, 56%, and 62% for tirzepatide doses of 5 mg, 10 mg, and 15 mg, respectively, compared with 22% in the placebo group reduction of fibrosis stage by at least one stage without worsening of MASH in 55%, 51%, and 51% for tirzepatide 5 mg, 10 mg, and 15 mg, and in 30% in the placebo group; weight reduction at the maximum dose of tirzepatide of 15.6%

high-protein diet is recommended, with avoidance of long fasting periods and inclusion of an additional meal just before sleep. In individuals with cirrhosis and obesity, slow, gradual weight reduction is recommended with a high-protein diet and physical activity, to prevent the development of sarcopenia.

Where treatment with GLP-1 receptor agonists or the dual GIP/GLP-1 agonist is not feasible, or in the absence of effects of their use, the next step is consideration of bariatric surgery (in patients with grade II and III obesity) (Figure 12.3.1) [71].

12.4. Pharmacological treatment of overweight/obesity in individuals with glucose metabolism disorders and CKD

Key recommendations

- The principles of pharmacotherapy of overweight/obesity in CKD do not differ from those adopted for the general patient population, but they require adjustment of the drug and its dosing to the eGFR value. [**A**]

Obesity affects no less than 30–50% of all patients with CKD; its prevalence rises up to stage

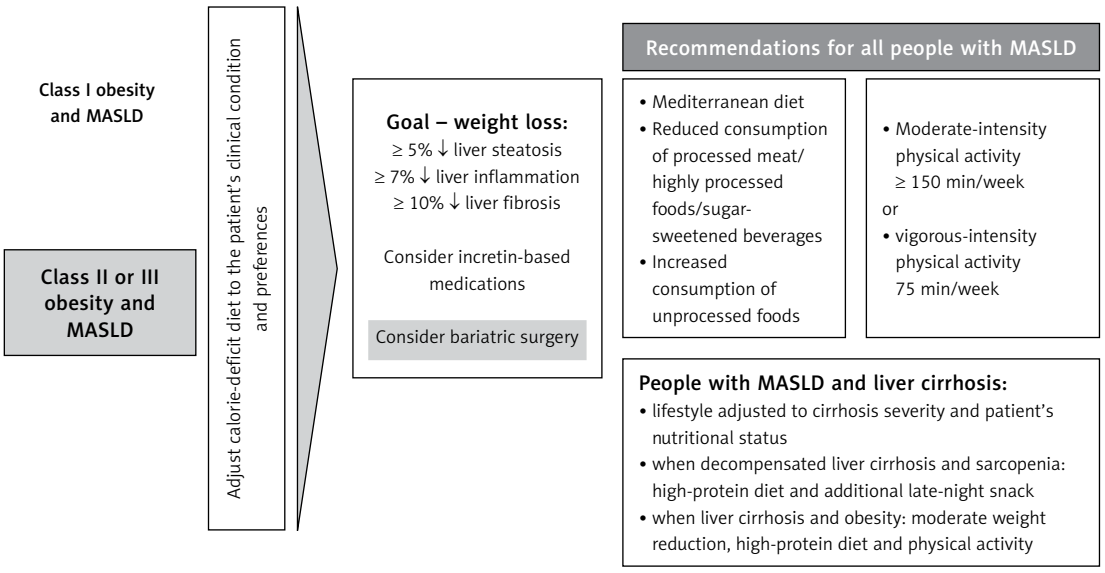


Figure 12.3.1. Management algorithm for individuals with overweight/obesity and MASLD (modified from EASL–EASD–EASO [71])

3B, falling slightly at stages 4 and 5, in association with the progressive catabolic character of uraemic intoxication [182–184].

Pharmacotherapy

1. The use of GLP-1-based therapies with proven cardiovascular and renal benefit is recommended in individuals with T2DM and CKD with eGFR ≥ 25 ml/min/1.73 m² and albumin-to-creatinine ratio (ACR) ≥ 100 mg/g. Semaglutide is the first GLP-1 receptor agonist for which an effect on slowing the rate of GFR loss and on reducing the risk of all-cause and renal-cause death across a wide spectrum of eGFR values (25–75 ml/min/1.73 m²; the FLOW trial) has additionally been demonstrated [185–190].
2. GLP-1-based therapies used in the treatment of obesity reduce the risk of CKD progression and of cardiovascular complications in individuals with T2DM and CKD [185–190].

For GLP-1 RAs (liraglutide, semaglutide), it has been shown that, in patients with T2DM, weight reduction was independent of eGFR value. However, no analyses have been identified that assess the efficacy of these drugs as a function of renal function exclusively in individuals with overweight/obesity and coexisting T2DM [185–190]. In the landmark FLOW trial in nephrodiabetology, in patients with T2DM receiving semaglutide at a target dose of 1 mg/week s.c., weight reduction averaged -5.5 kg compared with -1.45 kg in the placebo group (the baseline mean BMI of 32.0 [6.3] kg/m² indicated that most participants had obesity). Baseline eGFR was 47 ± 15.2 ml/min/1.73 m², and patients in each of the following eGFR ranges were represented: ≥ 60, 45–60, 30–45, and < 30 ml/min/1.73 m². However, no analyses have yet appeared assessing the effect of weight reduction as a function of renal function in subgroups with overweight or obesity [190]. The effect of tirzepatide on weight reduction in patients with obesity and diabetes is also independent of the eGFR value; however, as in the case of semaglutide, separate analyses assessing the efficacy of this drug as a function of renal function in patients with overweight/obesity are lacking. Likewise, in the trials assessing the effect of tirzepatide on the treatment of obesity in patients without diabetes, drug efficacy was not analysed as a function of eGFR [191].

The doses of liraglutide, semaglutide, and tirzepatide do not require modification irrespective of eGFR value, and these drugs may be used at advanced stages of CKD (including end-stage) [192].

3. The scientific literature lacks data permitting the assessment of the efficacy of obesity drugs such as phentermine/topiramate, naltrexone/bupropion, and orlistat in terms of weight reduction as a function of GFR range. On the basis of the published data, it can be concluded that pharmacokinetic studies of these drugs were conducted at various stages of renal injury [193]. The findings indicate that:
   - phentermine/topiramate and bupropion/naltrexone have not been studied in patients on dialysis;
   - no dose adjustment of orlistat is required based on GFR values (< 2% of this drug is excreted in the urine);
   - phentermine/topiramate should be used at a maximum dose of 7.5 mg/46 mg/day at eGFR < 50 ml/min/1.73 m²; 80% of phentermine and 70% of topiramate is excreted in the urine in unchanged form;
   - naltrexone/bupropion should be used at a maximum dose of 2 × 8 mg/90 mg in patients with moderate and severe renal function disturbances (the terms "moderate" and "severe" renal failure have not, however, been defined); up to 80% of naltrexone and up to 87% of bupropion is excreted in the urine;
   - numerous publications point to a risk of hyperoxaluria (excessive excretion of oxalates) in patients treated with orlistat, which may cause or worsen the course of oxalate nephrolithiasis and may also cause acute kidney injury related to hyperoxaluria.

12.5. Pharmacological treatment of overweight/obesity in individuals with glucose metabolism disorders and established cardiovascular disease

Key recommendations
• Pharmacotherapy of obesity in patients with established CVD should be aimed at achieving ≥ 10–15% sustained weight reduction and at reducing the risk of cardiovascular events. [**A**]
• The first-choice drugs in this population are GLP-1-based therapies. [**A**]
• The only preparation for which a reduction in the 3-point MACE (cardiovascular death, myocardial infarction, stroke) has been demonstrated in patients with overweight/obesity and established CVD without diabetes is semaglutide 2.4 mg administered *s.c.* once weekly (the SELECT trial). [**A**]
• Treatment selection should take into account the haemodynamic profile of the drug, coexisting heart failure, and blood pressure control. [**B**]
• During intensive weight reduction, modification of antihypertensive drug doses should be considered. [**C**]

The principles of pharmacotherapy for obesity in patients with established cardiovascular disease (CVD) generally do not differ from the general principles of obesity treatment; however, in this population, the choice of preparations with document-

ed safety and beneficial effect on cardiovascular prognosis is of particular importance [194].

The efficacy of pharmacotherapy is enhanced by the simultaneous implementation of dietary interventions and regular physical activity, the individual adaptation of which is particularly important in patients with CVD or heart failure.

In patients with chronic coronary syndrome, post-myocardial-infarction, post-stroke/transient ischaemic attack (TIA), peripheral arterial disease, and/or heart failure, the treatment of obesity constitutes an element of secondary prevention.

Overweight and obesity intensify haemodynamic loading, sympathetic nervous system activation, and RAA system activation, fostering chronic inflammation and insulin resistance, which lead to worsening of symptoms, reduced exercise tolerance, and an unfavourable effect on prognosis.

The aim of pharmacotherapy is typically to achieve ≥ 10–15% sustained weight reduction, since this range of reduction is associated with clinically meaningful improvement in blood pressure, glycaemic, and lipid control, and reduction in symptomatic burden. In this group, drugs with a documented beneficial effect on cardiovascular risk and a neutral or favourable haemodynamic profile, acting without adrenergic stimulation, are preferred.

Semaglutide at a dose of 2.4 mg administered *s.c.* once weekly is the only preparation for which, in patients with overweight/obesity and established CVD without diabetes, a reduction in cardiovascular risk measured by the 3-point MACE (cardiovascular death, myocardial infarction, stroke) has been demonstrated, in addition to substantial weight reduction [157, 195]. Furthermore, in patients without diabetes with HFpEF, semaglutide 2.4 mg led to a reduction in symptom severity and a reduction in body weight [196]. Liraglutide at a dose of 3.0 mg administered *s.c.* once daily exhibits efficacy in weight reduction and improvement of cardiovascular risk factors in individuals without diabetes; in T2DM, the

Table 12.5.1. Cardiovascular disease and the choice of obesity pharmacotherapy

Disease entity (established)	Preferred anti-obesity drugs	Rationale	Potential risks
Stable coronary disease/post-MI	Semaglutide 2.4 mg; alternatively, tirzepatide or liraglutide 3.0 mg	Semaglutide: reduction of MACE in CVD without diabetes	Avoid drugs ↑ HR/↑ BP (naltrexone/bupropion in unstable/poorly controlled patients)
Post-stroke/TIA (atherosclerotic)	Semaglutide 2.4 mg; tirzepatide or liraglutide as alternatives	Semaglutide: reduction of MACE including stroke in CVD without diabetes	Caution with drugs raising BP/HR; blood-pressure control is the priority
PAD	Semaglutide 2.4 mg; alternatively, tirzepatide or liraglutide 3.0 mg	Semaglutide: reduction of MACE in CVD without diabetes	As above; attention to exercise tolerance and wound healing (indirectly: weight reduction helps)
HFpEF	Semaglutide 2.4 mg; tirzepatide	Semaglutide improves symptoms, limitations, and exercise capacity in HFpEF with obesity; tirzepatide reduces the composite endpoint of CV death or worsening heart failure	Avoid drugs ↑ HR/↑ BP; monitor volume status/BP during intensive weight reduction (medication-dose changes)
HFrEF	Individualisation (limited data)	Priority: optimisation of HFrEF treatment; weight reduction may aid symptomatically but requires haemodynamic monitoring	Carefully observe HR, BP, and tolerance
Arterial hypertension	Semaglutide/tirzepatide or liraglutide	Typically lower BP together with weight reduction (indirect and haemodynamic effect)	Naltrexone/bupropion contraindicated in uncontrolled hypertension; caution even with controlled hypertension
Atrial fibrillation/ arrhythmias	Typically prefer GLP-1 or GIP/GLP-1	Weight reduction reduces atrial loading and the frequency of episodes (indirect effect)	Avoid drugs potentially ↑ HR; monitor heart rate with every therapy

SGLT-2 inhibitors are often used in patients with obesity and CVD due to cardiological indications. The use of these drugs is associated with moderate weight reduction. BP – blood pressure, CVD – cardiovascular disease, HR – heart rate, HFpEF – heart failure with preserved ejection fraction, HFrEF – heart failure with reduced ejection fraction, MACE – major adverse cardiovascular events, MI – myocardial infarction, PAD – peripheral arterial disease, TIA – transient ischaemic attack.

1.8 mg dose was associated with a reduction in the risk of cardiovascular events [161, 197].

The dual GIP/GLP-1 receptor agonist tirzepatide, administered at doses of 5–15 mg *s.c.* once weekly, is characterised by very high efficacy in weight reduction and improvement of cardiovascular risk factors; in patients with HFpEF, a reduction in the composite endpoint comprising cardiovascular death or worsening of heart failure has been demonstrated, and in patients with T2DM, a beneficial effect on cardiovascular prognosis has been confirmed [158, 177, 198].

The naltrexone/bupropion preparation is not a first-line drug in patients with obesity and coexisting CVD or heart failure, owing to the risk of substantial increases in blood pressure and heart rate; it is contraindicated in uncontrolled hypertension and requires particular caution in patients with CVD [159, 199].

12.6. Pharmacological treatment of overweight/obesity in individuals with T2DM

Key recommendations
• Restoring the appropriate body weight in individuals with T2DM and overweight/obesity is one of the therapeutic goals in diabetes. [**A**]
• Treatment of overweight/obesity in individuals with T2DM encompasses behavioural management and pharmacological treatment. [**A**]
• Loss of 5–10% of body weight improves the metabolic control of diabetes, while loss of 10–15% of body weight or more modifies the course of diabetes and may lead to its remission. [**A**]
• In the pharmacological treatment of individuals with overweight/obesity and T2DM, the use of GLP-1-based therapies is recommended – also due to the antihyperglycaemic action of these medications. [**A**]
• The benefits of weight loss arise not only from improvement of metabolic control but also from reduction of cardiometabolic risk factors and improvement of quality of life. [**A**]

T2DM is regarded as the principal clinical consequence of obesity (see Section 5). Obesity/overweight and/or abnormal adipose tissue distribution occur in approximately 80–90% of individuals with T2DM. The rising incidence of T2DM is also associated with the growing epidemic of obesity. Accordingly, in the therapy of T2DM with accompanying overweight/obesity, both non-pharmacological management (diet, physical activity) and pharmacological management aimed at weight loss are recommended. The principles of dietary treatment and the recommended physical activity are described in Section 10.

In the pharmacological treatment of obesity in individuals with T2DM, the following medications are recommended: GLP-1 receptor agonists (liraglutide, semaglutide) and the dual GIP/GLP-1 receptor agonist (tirzepatide) – also due to the antihyperglycaemic action of these medications [158, 200, 201]. The use of semaglutide and tirzepatide is recommended, since these medications produce the greatest weight-reduction effects. Additionally, they have cardioprotective properties in individuals with T2DM (liraglutide at a dose of 1.8 mg, semaglutide, tirzepatide) and renoprotective properties (semaglutide) [190]. In the STEP-2 trial, in which semaglutide at a dose of 2.4 mg was used in individuals with T2DM and obesity, a 9.6% reduction in body weight and a 1.5% reduction in HbA_{1c} were observed [200]. In the STEP UP T2D trial, with semaglutide at a dose of 7.2 mg in individuals with T2DM and obesity, a 13.2% reduction in body weight and a 1.7% reduction in HbA_{1c} were obtained [202]. On the basis of the findings of the SURMOUNT-2 trial with tirzepatide, the medication at a dose of 15 mg produced a 14.7% reduction in body weight and a 2.1% reduction in HbA_{1c} [201]. Other groups of antihyperglycaemic medications (metformin, SGLT-2 inhibitors) may also produce weight loss; however, their effect is substantially smaller (< 5% weight reduction). It must be emphasised that women of reproductive age receiving incretin-based therapies should simultaneously use effective contraception (the detailed principles are described in Subsection 12.8). Where these groups of medications cannot be used in the therapy of overweight/obesity in individuals with T2DM, consideration of other medications used in the pharmacological treatment of obesity and metabolic surgery is indicated.

Before initiating treatment of overweight/obesity in individuals with T2DM, it is important to check whether the patient is chronically taking medications that cause weight gain. These include glucocorticoids, antipsychotic medications, antiallergic medications, and certain antidepressive therapies. Where chronic use of these medications is necessary, this should be taken into account in the choice of therapy for overweight/obesity. In addition, attention should be paid to symptoms suggesting an endocrinopathy associated with the development of obesity and worsening of metabolic control of diabetes (see Section 4).

During the treatment of overweight/obesity in individuals with T2DM, the use of other antihyperglycaemic medications – including insulin – should be monitored. Chronic therapy is most often associated with the necessity of reducing insulin doses (in some cases, discontinuation of insulin is possible) and of other medications that may cause hypoglycaemia.

It must be remembered that the effects of treatment of overweight/obesity in individuals with T2DM concern not only metabolic control and

weight loss. Additionally, beneficial effects on cardiovascular disease risk factors (lowering of blood pressure, reduction of lipid concentrations), inhibition of hepatic steatosis and fibrosis in MASLD, and improvement of quality of life are observed.

12.7. Pharmacological treatment of overweight/obesity in individuals with T1DM

Key recommendations
• Overweight/obesity constitute a growing clinical problem in individuals with T1DM and substantially increase their cardiovascular risk and mortality. [**B**]
• In individuals with T1DM and coexisting obesity, owing to the limited effectiveness of non-pharmacological management, pharmacotherapy of obesity should be considered as a substantial or fundamental element of treatment. [**E**]
• The use of GLP-1 receptor agonists or GLP-1/GIP receptor agonists in the treatment of obesity in individuals with T1DM may be effective and safe, but requires caution in view of potentially increased risk of hypoglycaemia or ketoacidosis. [**A**]
• During the initiation and dose selection of pharmacotherapy of obesity in individuals with T1DM, the use of CGM systems is recommended. [**E**]
• Pharmacotherapy of obesity is safest in individuals with T1DM using automated insulin delivery (AID) systems. [**B**]
• In individuals with T1DM, the use of lower or moderate doses of GLP-1-based therapies is preferred, in view of the favourable benefit–risk ratio. [**B**]

Overweight and obesity are becoming an increasingly important clinical problem also among individuals with T1DM [203]. Recent epidemiological data indicate that the percentage of patients with T1DM and overweight/obesity is systematically rising. For individuals with T1DM, the coexistence of overweight/obesity is all the more dangerous given that, irrespective of body weight, individuals with T1DM are characterised at baseline by substantially elevated cardiovascular risk [204, 205]. Obesity is an independent risk factor for premature death in individuals with T1DM [206]. Treatment of obesity in individuals with T1DM should be conducted with at least equal effectiveness and consistency as in other patient groups, taking into account – and in many cases requiring – pharmacotherapy. Unfortunately, studies on the treatment of obesity in individuals with T1DM are lacking.

At present, none of the drugs with a well-documented role in the pharmacological treatment of obesity is registered for use in individuals with T1DM. At the same time, in most cases, T1DM is not on the list of contraindications to the use of these drugs.

Taking into account the serious health consequences of untreated obesity in individuals with T1DM and the limited effectiveness of non-pharmacological management (with the exception of metabolic surgery), it must be acknowledged that, in most individuals with T1DM, there is no alternative to pharmacological treatment. Such a position has been expressed in the *Diabetes Poland Guidelines 2026*. Most of the available studies in this area concern GLP-1 receptor agonists or GLP-1/GIP agonists. Data on other drug classes used in the treatment of obesity in individuals with T1DM are very limited or practically non-existent.

12.7.1. Effectiveness of pharmacotherapy in reducing excess body weight

In the ADJUNCT ONE and ADJUNCT TWO trials, the addition of liraglutide to insulin therapy in adults with T1DM produced weight reduction from 2.2 to 5.1 kg, depending on the dose of liraglutide and the duration of the intervention [207, 208]. Meta-analyses including the use of various GLP-1 receptor agonists in individuals with T1DM indicate weight reduction of approximately 2–4 kg [209–211]. Studies concerning semaglutide and tirzepatide indicate the possibility of achieving weight reduction of 7–10%, even with the use of doses lower than the maximum [212, 213]. The scale of weight reduction observed is comparable to the effects achieved in individuals without diabetes or with T2DM for corresponding drug doses and baseline BMI [214]. It must be emphasised that the discontinuation of therapy in individuals with T1DM, as in other populations, may be associated with the risk of recurrence of obesity and renewed weight gain.

12.7.2. Safety – hypoglycaemia

In the ADJUNCT ONE and ADJUNCT TWO trials, the frequency of symptomatic hypoglycaemia was substantially higher in the groups receiving liraglutide compared with placebo [207, 208]. In other studies and meta-analyses, a substantial increase in the risk of hypoglycaemia has not been confirmed, or has been only marginally higher than in the placebo group. The risk of hypoglycaemia appears to depend on the drug dose and the manner of insulin-therapy modification [209–214]. A recent study with semaglutide in patients using an AID system demonstrated the possibility of safe weight reduction without increased risk of hypoglycaemia or ketoacidosis [215].

12.7.3. Safety – hyperglycaemia and ketoacidosis

In the ADJUNCT ONE and ADJUNCT TWO trials, the proportion of patients with hyperglycaemia and ketosis was higher for liraglutide than for placebo, with the risk being greatest in the first

weeks of therapy in ADJUNCT TWO, particularly for the highest dose of liraglutide [207, 208]. The data from meta-analyses are inconclusive – ranging from a small increase in the frequency of ketosis to no differences in this respect [209–211]. In the trial with tirzepatide, no cases of diabetic ketoacidosis were observed [213]. In the meta-analysis concerning semaglutide, no episodes of clinically overt ketoacidosis were observed [212].

12.7.4. Safety – other adverse effects

The frequency of other adverse effects in patients with T1DM – primarily gastrointestinal – was comparable to that observed in other patient populations treated with GLP-1 receptor agonists [207–213]. These symptoms were most often mild or moderate in nature and rarely led to discontinuation of therapy.

It must be emphasised that, among individuals with T1DM taking drugs in the therapy of obesity, there may be women of reproductive age, who throughout the duration of treatment should use effective contraception.

In summary, the use of GLP-1-based therapies in the treatment of obesity in individuals with T1DM may be effective, and in many situations is necessary; it requires, however, caution in view of the increased risk of hypoglycaemia or diabetic ketoacidosis. This risk is substantially smaller with the use of lower or moderate drug doses, and with appropriate, individually tailored modification of insulin therapy. The use of the maximum doses of these drugs in this population should be avoided.

12.7.5. Practical guidance on the use of GLP-1 or GLP-1/GIP receptor agonists in the treatment of obesity in individuals with T1DM

The data cited indicate that the use of GLP-1 or GLP-1/GIP receptor agonists in the treatment of obesity in individuals with T1DM is highly effective for weight reduction; however, appropriate precautionary measures are necessary in order to minimise adverse effects associated with therapy. In the opinion of the authors of these guidelines, the use of GLP-1 or GLP-1/GIP receptor agonists in the treatment of obesity in individuals with T1DM should be based on the following principles:

1. Treatment should be initiated only in individuals cooperating well with the therapeutic team. Owing to the time needed to form an opinion on the quality of cooperation with the patient, initiation of therapy at the first or second medical visit is not advised.
2. Each instance of initiation of pharmacological treatment should be preceded by intensive education on the glycaemic effects of the implemented treatment and the appropriate modification of insulin therapy.
3. Initiation of treatment requires intensified glycaemic monitoring by the patient – and ideally constant use of CGM systems.
4. On the basis of the available data, pharmacotherapy is safest in patients using AID, where adjustment of insulin doses to the falling insulin requirement that accompanies weight reduction occurs almost entirely automatically (over time, correction of the insulin-to-carbohydrate ratio and other device settings may be indicated).
5. Regular monitoring of ketonaemia is recommended, particularly during the period of treatment initiation, dose escalation, reduction of carbohydrate intake, and during infections and other clinical conditions that increase insulin requirements, and in the event of technical problems with insulin-delivery devices (e.g. occlusion of an insulin pump infusion set).
6. Patients using methods of insulin therapy other than AID should remember the need for adequate, dynamic reduction of insulin doses, particularly at the start of treatment. Data from studies in individuals with T1DM treated with AID – a method that allows objective assessment of changes in insulin requirements and may indirectly serve as a guide for individuals with T1DM using other forms of treatment – indicate that an approximately 10% reduction in insulin dose may be expected by the end of the first week of drug use, and an approximately 20% reduction in dose by approximately the 10th week of therapy [216].
7. Use of the maximum doses of these drugs should be avoided.
8. These drugs should not be used in patients on a ketogenic diet.
9. Initiation of pharmacotherapy in women of reproductive age must take into account the absence of data on the safety of pharmacotherapy during pregnancy and pregnancy planning. The use of effective contraception is unconditionally necessary.

The principles of GLP-1 receptor agonist use in T1DM in individuals using AID systems (for various indications) have been broadly discussed in the consensus by Shah *et al*., published in 2025 [217].

12.8. Pharmacological treatment of overweight/obesity in individuals with glucose metabolism disorders during pregnancy planning and pregnancy

Key recommendations
• Diabetes and obesity in the mother are among the strongest risk factors for pregnancy and neonatal complications, and may negatively affect fetal developmental programming. [**A**]

- Multidisciplinary, integrated care for women with obesity and glucose metabolism disorders in the pre-conception period and during pregnancy is essential for the improvement of obstetric outcomes. The recommended period of preparation for pregnancy is at least 3 months. [**B**]
- The recommended pre-pregnancy weight loss is 5–10%; even a 5% weight reduction increases the chances of conception, normal course of pregnancy, and improved obstetric outcomes. [**B**]
- The basis of treatment of obesity is behavioural modification – encompassing the healthy eating model, regular physical activity, and psychological support. In many cases, however, simultaneous implementation of effective pharmacotherapy or bariatric surgery is necessary. [**A**]
- In pharmacotherapy, the key role is played by incretin-based drugs: GLP-1 receptor agonists (liraglutide, semaglutide) and the dual GLP-1/GIP receptor agonist tirzepatide. These drugs improve metabolic disturbances (glycaemia, lipid profile, blood pressure, coagulation parameters) and at the same time exert beneficial effects on the functions of the reproductive system. [**B**]
- The safety of these drugs in pregnancy has not been confirmed; therefore, during therapy, the use of effective contraception is necessary. The drugs should be discontinued 4–8 weeks before planned conception; this period will differ for individual preparations: liraglutide – at least 2 weeks; tirzepatide – at least 4 weeks; semaglutide – at least 8 weeks. [**B, C**]
- Folic acid supplementation 3 months before pregnancy and until the 12th week of pregnancy and vitamin D_3 supplementation until the end of pregnancy are recommended for women with overweight/obesity. [**A**]

Obesity is a chronic, progressive metabolic disease with a substantial influence on the reproductive health of women, the course of pregnancy, and the short- and long-term health of offspring [218]. In women of reproductive age, excess body weight and obesity often coexist with glucose metabolism disorders, which substantially increases the risk of infertility, obstetric complications such as gestational diabetes, arterial hypertension, and pre-eclampsia, and unfavourable metabolic programming of the fetus. Obesity disrupts the hypothalamic–pituitary–ovarian axis, causing irregular menstruation, anovulation, and consequently infertility. Adipose tissue, through the secretion of adipokines and inflammatory mediators, negatively affects oocyte maturation and gamete quality. Even with normal ovulatory function and regular cycles, women with obesity more frequently experience fertility problems and a higher risk of miscarriage. In women with BMI ≥ 30 kg/m², an approximately 4% decrease in the rate of pregnancy achievement is observed for every increase in BMI of 1 kg/m² [219].

Multidisciplinary, integrated care of women with obesity and glucose metabolism disorders in the pre-conception period and during pregnancy is essential for the improvement of obstetric outcomes [220–224].

When initiating obesity therapy in a patient of reproductive age, the physician should include education in family planning. This arises from the fact that weight reduction substantially increases fertility, which – without appropriate protection – may lead to unplanned pregnancy [220].

12.8.1. Pre-conception care

Preparation for pregnancy in a woman with excess body weight should last a minimum of 3 months – and longer in the absence of expected weight reduction and improvement of metabolic parameters. The aims of pre-conception care (pregnancy planning) are as follows [220–224]:

- weight reduction – the recommended pre-pregnancy weight loss is 5–10% of baseline weight, with even a 5% loss being associated with improvement of pregnancy course and obstetric outcomes;
- early diagnosis and treatment of comorbid conditions, including diabetes, arterial hypertension, hepatic, renal, thyroid, and cardiac function disturbances, as well as consideration of investigation of OSA – treatment should be selected in such a way that it can be continued during pregnancy;
- implementation of effective pharmacotherapy of obesity, aimed at improvement of metabolic disturbances – disturbances of glucose metabolism, lipids, blood pressure, and coagulation – with simultaneous beneficial effects on reproductive system functioning;
- consideration of bariatric treatment in women with BMI > 30 kg/m² and coexisting diabetes; after bariatric surgery, postponement of pregnancy planning by 12–18 months is recommended, until weight stabilisation and correction of nutritional deficiencies;
- implementation of vitamin supplementation:
  – folic acid at a dose of 0.8–5 mg/day for at least 3 months before conception (a daily dose of 0.8 mg, double the general-population dose, is recommended, including 0.4 mg in the form of active folates); the dose should be individualised through measurement of serum folic acid concentration after 4–6 weeks of supplementation; if the concentration is below 28 nmol/l, an increase in dose to 5 mg/day, until a maximum of the 12th week of pregnancy, is recommended;
  – vitamin D_3 at a dose of 2000 IU/day, and after bariatric surgery 4000–8000 IU/day;
- absolute cessation of cigarette smoking and tobacco-like products, and total prohibition of alcohol consumption;
- in case of preparation for assisted reproduction procedures, analogous methods of pregnancy preparation apply.

12.8.2. Pharmacotherapy

The basis of management in obesity is lifestyle modification based on a healthy eating model and regular physical activity, together with psychological support. In many women, however, pharmacotherapy is also a necessary element of treatment.

Pharmacotherapy should be considered in every woman with BMI ≥ 30 kg/m², and in the presence of even one excess-weight-related complication, at BMI ≥ 27 kg/m². For women with obesity and T2DM, T1DM, prediabetes, or other components of the metabolic syndrome, drugs from the group of GLP-1-based therapies are recommended: liraglutide and semaglutide – GLP-1 receptor agonists; and tirzepatide – the dual GLP-1 and GIP receptor agonist. These drugs, acting centrally, suppress appetite, and peripherally slow gastrointestinal motility, thereby prolonging the sensation of satiety. In women, an improvement in reproductive functions can be expected, since GLP-1 receptors are present in the ovaries, and their stimulation may reverse the inhibition of gonadotropin secretion, affecting both indirectly the hypothalamic–pituitary–ovarian axis and directly the activity of gonadotropin-releasing hormone (GnRH) neurons in the hypothalamus [225, 226].

The benefits arising from pharmacotherapy with incretin receptor agonists encompass weight reduction with the use of liraglutide, semaglutide, and tirzepatide, which is associated with prevention or remission of T2DM, improvement of insulin sensitivity, reduction of HbA_{1c}, reduction of the daily insulin dose in women with T1DM, reduction of androgen concentrations and menstrual disturbances and the achievement of ovulatory cycles, and additionally lowering of blood pressure, improvement of the lipid profile, and reduction of the severity of hepatic steatosis.

Notwithstanding the unquestionable advantages and established position of GLP-1-based therapies in the treatment of obesity, they do not constitute universal therapy for all women, owing to the multifactorial and heterogeneous pathogenesis of obesity. Studies have shown that approximately 30–40% of women with obesity exhibit features of emotional eating or dominant, entrenched feelings of hunger. A drug of proven efficacy in the treatment of overweight and obesity associated with emotional eating is naltrexone with bupropion. Even when receiving this drug, the use of effective contraception is necessary.

Animal studies have shown harmful effects of liraglutide on embryonic development (including malformations), and safety in humans has not been fully confirmed. Similarly, direct evidence of safety for the remaining drugs is lacking – animal studies have shown that exposure to semaglutide and to tirzepatide during organogenesis may lead to fetal malformations and low birth weight, or miscarriage [227–229].

12.8.3. Contraception during pharmacological treatment of obesity

Obesity may reduce the effectiveness of oral contraceptives because of altered pharmacokinetics associated with obesity, of which the patient should be informed. For this reason, when using oral contraception, additional non-hormonal contraception should also be employed. The safest and preferred method of contraception in women with obesity and diabetes is the use of preparations containing progestogens (single-component oral preparations or intrauterine devices) [220–224].

In the case of combined hormonal contraception – which is permissible but not preferred – given the 2- to 3-fold elevated risk of venous thromboembolic disease, a preparation containing the lowest possible dose of ethinylestradiol (20–30 µg ethinylestradiol) should always be used.

Pharmacotherapy of obesity must be discontinued immediately in the event of unplanned pregnancy. The time for elimination of the drugs from the body and the wash-out period before planned pregnancy should be adapted to the pharmacokinetics of individual preparations, with the recommendation that the drug be discontinued for at least 5 of its half-lives. Generally, the time for drug discontinuation is 4–8 weeks before planned conception, with this period differing slightly for individual preparations: the duration of action of tirzepatide is approximately 5 days (120 hours); however, for complete elimination from the body, discontinuation of the drug at least 25–30 days before pregnancy is recommended, and to ensure complete safety, 60 days before pregnancy. Semaglutide has a longer half-life of approximately 7 days, meaning that complete drug elimination occurs after 5 weeks. Semaglutide should be discontinued at least 2 months (8 weeks) before planned conception. Short-acting liraglutide has a half-life of approximately 13 hours. In theory, therefore, discontinuation of the drug 3 days before planned conception suffices; however, to maintain a safe clinical margin, discontinuation of therapy 10–14 days before planned pregnancy is recommended [227, 228, 230].

Contraception should be used during pharmacotherapy of obesity until elimination of the drug from the body.

In the period between discontinuation of pharmacotherapy of obesity and conception, behavioural management – encompassing healthy eating, regular physical activity, and psychological support – should be continued. In women with diabetes or prediabetes, metformin therapy may be

continued until the 12th week of pregnancy. During this period, the risk of renewed weight gain and worsening of glycaemic control should be reckoned with; therefore, maintenance of established habits and motivational support of the patient are of pivotal importance.

In the time from drug discontinuation to conception, the following should be monitored [220–224]:

1. Body weight – the goal is the maintenance of the achieved weight reduction, with the only acceptable method of therapy being the continuation of behavioural management.
2. Glycaemic targets – even in women in whom normoglycaemia was achieved through pharmacotherapy, worsening should be expected after drug discontinuation; in prediabetes this particularly concerns fasting glycaemia, and in diabetes – both fasting and postprandial glycaemia. Possible pharmacotherapy options include metformin (until the 12th week of pregnancy) and insulin therapy adapted to the glycaemic disturbance profile.

- The use of CGM is recommended; in the event of worsening glycaemic control, insulin therapy should be implemented immediately according to general principles.
- Glycaemic targets at the pregnancy planning stage encompass all of the following:
  – fasting glycaemia: 70–90 mg/dl;
  – 2-hour postprandial glycaemia: < 140 mg/dl;
  – $HbA_{1c} \leq 6.5\%$;
  – on CGM systems: time in range 70–140 mg/dl > 90% in women with T2DM and GDM, and > 70% in women with T1DM.

3. Other metabolic parameters: blood-pressure control and optimisation of antihypertensive treatment, taking into account the safety of therapy in pregnancy.

12.8.4. Care during pregnancy

The aim of care during pregnancy is the control of weight gain, glycaemia, and accompanying diseases. Overweight and obesity are among the strongest risk factors for gestational diabetes; investigation in this direction should therefore be performed immediately upon confirmation of pregnancy, in accordance with the schema presented in Figure 12.8.1.

1. Goals of weight-gain control (Table 12.8.1)

The recommended values of weight gain for pregnant women with BMI ≥ 30 kg/m² are 5–9 kg; for pregnant women with BMI ≥ 40 kg/m², minimal weight gain or no weight gain in pregnancy should be considered, and in justified cases even a weight reduction of 5–7 kg, under strict supervision of the therapeutic team [220, 223, 224].

The approximate daily caloric requirement for a pregnant woman with overweight is 25–30 kcal/kg of appropriate body weight, and in women with obesity approximately 20 kcal/kg.

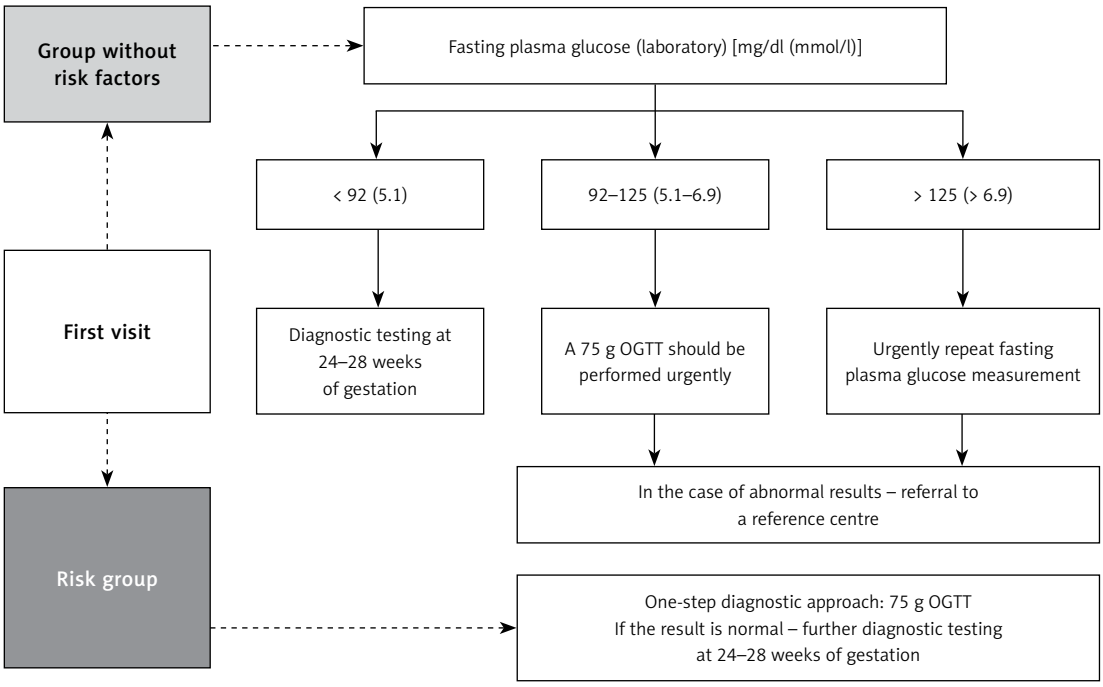


Figure 12.8.1. Schema for diagnosis of glucose metabolism disorders in pregnant women

OGTT – oral glucose tolerance test. Note: A single fasting glycaemia in a pregnant woman in the first trimester of pregnancy of > 92 mg/dl but < 125 mg/dl cannot serve as the basis for the diagnosis of hyperglycaemia in pregnancy.

Table 12.8.1. Recommendations for weight gain in pregnancy

Pre-pregnancy BMI [kg/m²]	Recommended weight gain [kg]	Recommended weight gain in 2nd and 3rd trimester [kg/week]
< 18.5	12.5–18.0	0.51 (0.44–0.58)
18.5–24.9	11.5–16.0	0.42 (0.35–0.50)
25.0–29.9	7.0–11.5	0.28 (0.23–0.33)
30.0–39.9	5.0–9.0	0.22 (0.17–0.27)
≥ 40	< 5	0.11 (0.0–0.15)

Assuming weight gain in the first trimester of pregnancy of 0.5–2.0 kg.

The recommended form of physical activity is walking for 10–15 minutes, ideally after each substantial meal.

In all women with overweight and obesity, consultation with a qualified dietitian is indicated, particularly in the case of a 1500–1800 kcal/day diet. Rational use of vitamin supplementation is necessary.

2. Diagnostic work-up for glucose metabolism disorders

Note: In pregnant women after bariatric surgery, the OGTT 75 g test is not performed. Carbohydrate tolerance can be investigated on the basis of laboratory measurement of fasting glucose concentration and HbA_{1c} value, or by use of a CGM system [223, 224].

In every pregnant woman with excess pre-pregnancy body weight, irrespective of the recognition of the type of glucose metabolism disorder, dietary management and moderate, safe physical activity should be continued, and dietary education repeated.

In pregnant women with obesity and glucose metabolism disorders [223, 224]:

1. Glycaemic targets in pregnancy for all pregnant women, irrespective of coexisting conditions, remain the same and are:
- fasting glycaemia: 70–90 mg/dl;
- 1-hour postprandial glycaemia: < 140 mg/dl;
- HbA_{1c}: ≤ 6.5% in the 1st trimester and ≤ 6.0% in the second and third trimesters;
- on CGM – time in the target range for pregnancy (63–140 mg/dl) > 90% in women with T2DM and gestational diabetes, and > 70% in women with T1DM;
- the preferred method is CGM systems;

2. The recommended pharmacotherapy in women with obesity, glucose metabolism disorders, and diabetes does not differ from the standard therapy of diabetes during pregnancy; insulin therapy using insulin analogues should be adapted to the profile of glycaemic disturbances:
- in gestational diabetes, basal insulin is most often sufficient;
- in T2DM, multiple insulin injections are often necessary;
- in T1DM, therapy with a personal insulin pump integrated with CGM is preferred;

3. During pregnancy, the following are recommended:
- regular blood-pressure monitoring and maintenance of values in line with current obstetric recommendations;
- folic acid supplementation during the first 3 months of pregnancy (see pregnancy planning);
- in women after bariatric surgery – monitoring of vitamin concentrations (D_3, B-group vitamins, folic acid) and iron;
- prophylactic management should be implemented in patients with at least one high-risk factor or at least two moderate-risk factors. **High-risk factors** are: arterial hypertension in a previous pregnancy and chronic hypertension, CKD, systemic lupus, antiphospholipid syndrome, T1DM and T2DM. **Moderate-risk factors** include: age > 40 years, first pregnancy, interval between pregnancies > 10 years, BMI > 35 kg/m², multiple pregnancy, pre-eclampsia in the mother;
- in women with overweight and obesity, consideration of indication for thromboprophylaxis with low-molecular-weight heparin; pregnant women with at least grade II obesity and with grade I obesity and additional risk factors should receive thromboprophylaxis from the start of pregnancy and throughout the puerperium with low-molecular-weight heparins at a dose dependent on body weight before pregnancy;
- early prenatal investigation for chromosomal aberrations and the planning of follow-up ultrasound examinations for the early detection of fetal malformations, in accordance with the standards of perinatal care and the recommendations of the Polish Society of Gynaecologists and Obstetricians.

12.8.5. Postpartum care

After delivery, breastfeeding is recommended in both women with obesity and women with diabetes. A beneficial effect of feeding on postpartum weight reduction and glycaemic control has been demonstrated. During breastfeeding, behavioural management should be continued. Energy expenditure during breastfeeding is approximately 400–

500 kcal/day, which should be taken into account in dietary advice for the breastfeeding woman with obesity [223, 224].

In women with obesity in whom glucose metabolism disorders occurred during pregnancy, postpartum diagnostic work-up should be performed again in line with the recommendations of Diabetes Poland. If disturbances or diabetes persist, metformin therapy may be implemented [224].

Data on the safety of GLP-1 and GLP-1/GIP receptor agonist use during breastfeeding are lacking; for this reason, they should not be implemented. The use of metformin is permissible (it does not pass into milk) [231, 232]. The use of metformin in the prevention of diabetes in women with previous GDM may also be considered.

12.9. Pharmacological treatment of overweight/obesity in individuals with glucose metabolism disorders treated psychiatrically

Key recommendations
• In patients receiving psychiatric treatment, the differential metabolic profile of psychotropic drugs should be taken into account, and where clinically possible, drugs with lower risk of weight gain and disturbances of carbohydrate metabolism should be preferred [233–236]. [**A**]
• In patients with overweight/obesity – particularly those with sudden weight gain, prediabetes, T2DM, or other metabolic disturbances associated with psychiatric treatment – modification of psychiatric pharmacotherapy should be considered, provided that this is not associated with a substantial risk of worsening of mental status [234, 236, 237]. [**B**]
• Metformin may be used in patients receiving psychiatric treatment to limit weight gain and improve metabolic parameters – particularly in disturbances induced by antipsychotic drugs – although it is not registered for the treatment of overweight/obesity [238]. [**A**]
• GLP-1 receptor agonists, in particular liraglutide and semaglutide, are an effective option for the treatment of overweight/obesity in patients receiving psychotropic drugs and may also be used in this population, while observing standard safety principles [239–243]. [**A**]
• Tirzepatide may be considered in patients receiving psychiatric treatment with obesity, although data concerning this population are still limited [243, 244]. [**C**]
• The combination of naltrexone with bupropion should be used in psychiatric patients with particular caution, taking into account the current psychopharmacotherapy, the risk of antidepressant polypharmacy, and the risk of seizures. [**B**]
• In psychiatric patients with obesity, recognition and treatment of coexisting conditions that increase the risk of metabolic disturbances or impede weight reduction should be sought – such as binge eating disorder, bulimia nervosa, night eating syndrome (NES), sleep-related eating disorder (SRED), alcohol use disorders, and endocrinological diseases [234]. [**B**]
• Effective treatment of overweight/obesity in individuals receiving psychiatric treatment requires interdisciplinary care encompassing cooperation between a psychiatrist, primary-care physician, internist, diabetologist or endocrinologist, dietitian, psychologist or psychotherapist, and – where necessary – physiotherapist [233–235]. [**A**]

Patients receiving psychiatric treatment belong to the high-risk group for overweight/obesity and glucose metabolism disorders. This risk arises from the overlap of unfavourable lifestyle, psychopathological symptoms, biological factors, and the action of psychotropic drugs [245–247].

The greatest clinical importance attaches to antipsychotic drugs – particularly olanzapine, clozapine, phenothiazines, and chlorprothixene – which most strongly increase the risk of weight gain, insulin resistance, and diabetes. Among mood stabilisers, the greatest metabolic risk is associated with valproates, and among antidepressants, with tricyclic antidepressants, mirtazapine, mianserin, and paroxetine [233, 234, 236].

Some drugs – such as aripiprazole, lurasidone, ziprasidone, lamotrigine, bupropion, and fluoxetine – are characterised by a more favourable or relatively neutral metabolic profile [234, 236, 237].

Overweight/obesity and metabolic disturbances in individuals with severe mental disorders worsen not only the somatic but also the psychiatric prognosis, increasing the risk of poorer treatment response, cognitive disturbances, and premature mortality [245–247].

For this reason, in all patients receiving psychiatric treatment, systematic monitoring of metabolic parameters is necessary from the very start of psychopharmacotherapy [233–235].

In patients with mental illness, the treatment of obesity is of particular importance in view of the elevated metabolic and cardiovascular risk. Effective management encompasses both non-pharmacological interventions and pharmacological options adapted to the specific features of this group.

12.9.1. Treatment

Modification of psychiatric pharmacotherapy

Where possible, the choice of psychotropic drugs with a safer metabolic profile, or switching to a drug with a more favourable profile, is recommended, together with monitoring of body weight and glycaemia from the first weeks of treatment. Such a strategy may limit weight gain, although it is not always feasible, owing to the need for effective control of the symptoms of mental disorders. In patients treated with olanzapine, clozapine, or quetiapine, where switching to an antipsychotic drug with low risk is not possible, consideration should be given to adding aripiprazole or lurasi-

done – a strategy that, in single studies in patients with schizophrenia, has been associated with weight reduction and improvements in metabolic parameters within several weeks [234, 236, 237].

In the psychopharmacotherapy of a patient struggling with weight gain or metabolic syndrome, additional avoidance – to the extent possible – of drugs causing daytime sedation and somnolence, dry mouth (because of the risk of excessive consumption of caloric beverages), insomnia, and constipation is recommended [234, 235].

Pharmacotherapy of overweight/obesity

- Metformin – although not registered for the treatment of overweight/obesity, is most often used in the context of weight gain and glycaemic disturbances induced by antipsychotic drugs. A meta-analysis published in 2025 has shown that metformin may reduce body weight by an average of 3–4 kg over 12–24 weeks, improve insulin sensitivity, and is relatively well tolerated [238].
- GLP-1 receptor agonists (liraglutide, semaglutide) demonstrate, in clinical analyses, effective weight reduction in patients with obesity receiving psychotropic drugs. In studies in patients with schizophrenia or other psychiatric disorders treated with liraglutide, weight loss was greater than in the placebo group, and semaglutide in longer follow-up led to substantial weight reduction (e.g. up to ~15% of body weight after several dozen weeks), together with improvement of glycaemia and the lipid profile [239–243].
- Systematic reviews and meta-analyses have shown that GLP-1 receptor agonists in this population are effective and well tolerated, do not worsen the patients' mental status, and do not intensify psychiatric symptoms – in some studies, improvement of mood and quality of life has even been observed. It must be remembered that some psychotropic drugs, similarly to GLP-1 receptor agonists, increase the risk of pancreatitis; these are mainly clozapine, valproate, olanzapine, and mianserin – a fact that requires caution but does not constitute a contraindication to combining these drugs [239, 243].
- Tirzepatide – data on the use of this dual GLP-1 and GIP receptor agonist in psychiatric patients are still limited; however, in view of the many similarities in mechanism of action to GLP-1 receptor agonists and similar tolerability, it can also be used in patients receiving psychiatric treatment [243, 244].
- The naltrexone + bupropion combination may be considered individually but with caution, in view of the following aspects:
  - it should be analysed whether the patient at the current stage of treatment requires an antidepressant such as bupropion, and whether it will not adversely affect psychopathology;
  - it should be checked whether the patient is not concurrently receiving other antidepressants and whether the addition of bupropion will not become an element of irrational antidepressant polypharmacy;
  - the risk of cumulative pro-convulsive effects of bupropion with other drugs or with patient conditions that increase the risk of seizure should be taken into account.

Other pharmacotherapies investigated in patients with mental disorders and weight gain

- In overweight/obesity accompanying – and particularly induced by – antipsychotic drugs, weight reduction and/or improvement of metabolic parameters has been demonstrated after the addition of [234]:
  - topiramate (efficacy of the intervention confirmed in a meta-analysis, and possibly additionally associated with improvement of general psychopathology);
  - reboxetine.
- Promising preliminary results have been observed with the use of probiotics combined with a high-fibre diet in patients treated with olanzapine and experiencing therapy-related weight gain [234].

12.9.2. Treatment of coexisting conditions

Identification and treatment of coexisting conditions in serious psychiatric disorders that are associated with increased risk of obesity or metabolic syndrome should be sought, such as [234]:

- BED (also known as binge eating syndrome, pathological binge eating);
- bulimia nervosa;
- NES;
- SRED;
- pathological alcohol use;
- endocrinological disorders.

13. METABOLIC SURGERY

Key recommendations
• Surgical treatment of obesity should be considered in persons – including children and adolescents – with T2DM and BMI ≥ 35 kg/m², particularly where conservative treatment of obesity is ineffective and especially in the case of coexisting other diseases and unsatisfactory glycaemic control with the use of behavioural therapy and antihyperglycaemic drugs. [**A**]
• The procedure should be performed in a centre specialised in metabolic surgery and equipped with a multispecialist team. [**A**]

Metabolic surgery is an effective method of treating obesity and associated diseases – particularly T2DM [248, 249]. A multidisciplinary approach permits the appropriate selection of patients for metabolic surgery and the selection of the appropriate surgical technique.

In 2023, approximately 9100 metabolic surgery operations were performed in Poland (a 5-fold increase compared with 2014 – to a large extent thanks to the KOS-BAR programme); in 2025, this number exceeded 10,000. In Europe in 2021, the number of procedures was 178,000, and in 2025 approximately 220,000. It is estimated that, worldwide in 2023, approximately 600,000 bariatric operations were performed. Despite the rising number of operations of this type, still < 1% of individuals with obesity are treated by this method.

13.1. Principles of eligibility assessment for procedures within the field of metabolic surgery

1. A procedure within the field of metabolic surgery should be considered in every person with T2DM and BMI ≥ 35 kg/m², particularly with coexisting additional accompanying diseases – for example, arterial hypertension and lipid disturbances. In particular, eligibility assessment for procedures of metabolic surgery should be considered when T2DM and obesity respond inadequately to pharmacological and behavioural therapy. This applies also to children and adolescents [250–252].
2. Assessment for a procedure of metabolic surgery is recommended in every person with BMI ≥ 40 kg/m² and T2DM or prediabetes [250, 251].
3. Taking into account the preferences of the person with T2DM, surgical treatment of obesity may also be considered in individuals with grade I obesity (BMI 30.0–34.9 kg/m²) in whom non-surgical methods (primarily GLP-1-based therapies) do not produce stable weight reduction and improvement of control of accompanying diseases [252].
4. For procedures of metabolic surgery in individuals with T2DM, patients between 18 and 65 years of age are considered eligible [252]. The upper age limit may, in justified cases, be extended to 70 years, provided that the individually considered surgical risk is lower than the achievable benefits from the operation.

- Procedures may be considered in children ≥ 12 years of age, if there are severe complications of obesity. Achieving a specific stage of pubertal development or final body height is no longer required if the benefits outweigh the risks [253].

5. Qualification for bariatric surgery should be carried out by a team of physicians comprising at least a diabetologist and a general surgeon with substantial experience in metabolic surgery. It is recommended that, in the multidisciplinary team of specialists participating in eligibility assessment, there should additionally be a cardiologist, pulmonologist, psychologist/psychiatrist, anaesthesiologist, and dietitian, as well as a nurse and a social worker [250, 251].
6. In the case of children, the team should include a paediatric diabetologist or a specialist in paediatric endocrinology and diabetology. The decision on eligibility should be preceded by at least 12 months of treatment encompassing modification of diet and physical activity, and – in selected cases – pharmacotherapy [253].
7. Bariatric procedures in children should be performed exclusively in highly specialised centres by an experienced interdisciplinary team providing long-term care [250, 251].

13.2. Types of metabolic surgery procedures performed

1. It is recommended that patients be considered for surgical procedures performed by minimally invasive techniques (laparoscopy).
2. In light of the available trial findings, in individuals with T2DM and prediabetes, eligibility assessment for the following procedures is recommended in the first instance: laparoscopic Roux-en-Y gastric bypass; laparoscopic mini gastric bypass (one-anastomosis gastric bypass); laparoscopic sleeve gastrectomy; laparoscopic biliopancreatic diversion; and laparoscopic single-anastomosis duodeno-ileal bypass (SADI) [250–252, 254].

- In children and adolescents, sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB) are recommended [253].

3. The decision regarding the type of procedure performed should be made after surgical consultation and individual consideration of the advantages and disadvantages of each of the aforementioned methods of metabolic surgery.
4. It is recommended that, before the decision on a procedure of metabolic surgery, patients familiarise themselves with the informed consent forms for the procedure prepared by the Society of Polish Surgeons. The pre-condition is obtaining informed consent from the patient – and, in the case of children, also from the parents – with full understanding of the nature of the procedure and the associated risks and benefits.

13.3. Complications associated with metabolic surgery in T2DM

In the 30-day period after the operation, mortality associated with the performance of a metabolic-surgery procedure has been calculated at

0.1–0.3%, identical to mortality associated with laparoscopic cholecystectomy – the risk is described as low. Among the most frequently occurring complications after metabolic surgery procedures are: anastomotic leak (3.1%), surgical site infection (2.3%), respiratory complications (2.3%), and gastrointestinal bleeding (1.7%) [255–258].

13.4. Assessment of the outcomes of metabolic surgery in T2DM

T2DM resolves in 40–95% of patients, depending on its duration, the degree of baseline obesity, and the type of surgical procedure performed. Resolution of prediabetes occurs even more rapidly [252, 257, 259]. The following method of assessing the outcomes of surgical treatment of T2DM is recommended:

Resolution of disease and accompanying conditions

Resolution of disease may be considered after the discontinuation of pharmacotherapy, when:

- HbA_{1c} value is < 6.5%;
- the patient does not experience episodes of hypoglycaemia;
- total cholesterol concentration is < 4 mmol/l, LDL cholesterol < 2 mmol/l;
- triglyceride concentration is < 2.2 mmol/l;
- blood pressure values are < 140/90 mmHg;
- weight loss is > 15% relative to the state at the time of assessment for surgery.

Improvement in disease course

Improvement in the course of disease after a metabolic surgery procedure may be considered when, with reduced doses of drugs taken before the operation:

- HbA_{1c} value falls by > 20%;
- LDL-C concentration is < 2.6 mmol/l;
- blood pressure values are < 140/90 mmHg.

13.5. Recommendations after surgical treatment of obesity in individuals with T2DM or prediabetes

1. Every person after surgical treatment of diabetes should permanently remain under the care of a diabetologist and general surgeon.
2. Permanent supplementation with vitamins and microelements is necessary in order to prevent deficiencies.
3. Every child after surgical treatment should continue to remain under the care of a paediatric diabetologist or paediatric endocrinologist and diabetologist.
4. Long-term metabolic, nutritional, and psychological monitoring is necessary, particularly in children and adolescents, in view of the risk of vitamin and mineral deficiencies and of recurrence of diabetes and obesity. DXA monitoring until achieving peak bone mass is recommended.

13.6. Pregnancy and metabolic surgery procedures

1. There are no contraindications to becoming pregnant in women after procedures of metabolic surgery, provided that 24 months have elapsed from the date of the bariatric procedure.
2. Before becoming pregnant, and during pregnancy, regular contact with the diabetologist providing care for the patient is recommended.

13.7. Contraindications to metabolic surgery procedures in individuals with T2DM or prediabetes

Absolute contraindications:

- lack of acceptance by the person with diabetes or prediabetes of surgical treatment of obesity;
- alcohol or drug dependence (eligibility for surgical treatment of obesity may be considered in the case of a documented period of abstinence of at least 1 year);
- mental illnesses not amenable to control despite treatment and pharmacotherapy;
- high cardiovascular risk associated with performance of the procedure;
- endocrinological diseases constituting the substrate of obesity (e.g. Cushing's syndrome);
- the impossibility of participation in regular, long-term follow-up after the operation;
- the 24-month period preceding planned pregnancy; breastfeeding.

Relative contraindications:

- increase in body weight in the period directly preceding the operation, indicating lack of cooperation with the patient;
- active peptic ulcer disease – requires treatment before the surgical procedure; in the case of patients with asymptomatic *Helicobacter pylori* infection, eradication before the operation is recommended but not absolutely necessary;
- in the case of individuals treated for cancer in the past, oncological consultation is necessary, documenting effective cure of the tumour.

13.8. Metabolic surgery in individuals with obesity and T1DM

Bariatric surgery in individuals with obesity and T1DM remains outside standard guidelines, owing to the paucity of high-quality data and long-term randomised trials. The available trial findings indicate that bariatric surgery has led to substantial improvement in body weight and cardiometabolic parameters, with moderate improvement in glycaemic control. The most frequently reported met-

abolic complications were episodes of hypoglycaemia and ketoacidosis [260].

13.9. Surgical treatment combined with pharmacotherapy of obesity

Pharmacotherapy of obesity plays an increasingly important role in patients after bariatric operations – particularly in the context of insufficient weight reduction or secondary weight gain (weight regain), which affect as many as 20–30% of patients within several years of the procedure. Anti-obesity drugs are used in this group as a supplement to surgical treatment, not as an alternative, and may be implemented both for the optimisation of weight reduction after the operation and for the treatment of obesity recurrence. The greatest body of data concerns GLP-1 receptor agonists (liraglutide, semaglutide), which exhibit good efficacy and safety in this population, leading to additional weight reduction in the order of 5–10% with simultaneous improvement of glycaemic control and metabolic parameters. Pharmacotherapy may be particularly beneficial in patients after sleeve gastrectomy (SG), where the risk of secondary weight gain is higher than after gastric bypass. The individualisation of treatment is of pivotal importance, taking into account the type of procedure, the mechanisms of failure (behavioural vs. hormonal), the metabolic profile, and treatment tolerance. In clinical practice, pharmacotherapy after bariatric surgery now constitutes an integral element of long-term, multidisciplinary treatment of obesity [252].

14. TREATMENT OF OVERWEIGHT/OBESITY IN CHILDREN AND ADOLESCENTS WITH GLUCOSE METABOLISM DISORDERS

Key recommendations
• In all children and adolescents with obesity and glucose metabolism disorders – including T1DM and T2DM, monogenic diabetes, and genetic syndromes – treatment of excess body weight should be conducted long term, in parallel with diagnostic work-up, monitoring, and treatment of obesity-disease complications (arterial hypertension, dyslipidaemia, MASLD, obstructive sleep apnoea, PCOS, psychosocial problems). [**A**]
• In all children and adolescents, behavioural therapy (preferentially family-based) should be implemented, encompassing lifestyle modification – including dietary management and appropriate physical activity. Health education is a very important element of therapy. [**A**]
• Pharmacotherapy of obesity in children and adolescents (typically aged ≥ 6 years) should be considered as treatment additional to behavioural therapy in the case of insufficient response – particularly in severe obesity and/or in the case of coexisting complications. [**A**]
• In adolescents with obesity, the drugs with the best-documented efficacy in reducing body weight and obesity-related complications are GLP-1 receptor agonists: semaglutide and liraglutide. [**A**]
• In children with T1DM, pharmacotherapy of obesity requires particular diabetological supervision (modification of insulin doses, continuous glucose monitoring, principles of ketone monitoring, and implementation of strategies reducing the risk of diabetic ketoacidosis and hypoglycaemia). [**E**]
• In children and adolescents with T2DM, glucose-lowering drugs that simultaneously favour weight reduction – particularly GLP-1-based therapy – should be preferred as part of the strategy of treating T2DM with obesity. SGLT-2 inhibitors may alternatively be considered. [**A**]
• SGLT-2 inhibitors are not recommended as adjunctive therapy in the treatment of obesity in children with T1DM, owing to the increased risk of diabetic ketoacidosis – including euglycaemic – and the weak effect on weight reduction. [**B**]
• In children and adolescents with overweight/obesity and prediabetes, glucose-lowering drugs that simultaneously favour weight reduction – particularly GLP-1 analogues – should be preferred. [**A**]
• In adolescents with severe obesity and/or its intensified complications – including T2DM – bariatric treatment in a referral centre should be considered in the absence of efficacy of pharmacotherapy or where it cannot be used. [**B**]
• In monogenic and syndromic obesity, targeted treatment in a specialist centre should be considered. [**A**]

In recent years, a substantial increase in the prevalence of obesity in children and adolescents – including severe obesity – has been observed. This phenomenon is associated with the growing prevalence of glucose metabolism disorders, including T2DM, in the developmental-age population. At the same time, the proportion of overweight and obesity is rising among children and adolescents with T1DM and other types of disease (see Section 2) [203].

In a substantial proportion of patients with obesity, metabolic and end-organ complications develop (see Section 5), justifying the necessity of implementing effective treatment methods directed at weight reduction and reduction of adipose-tissue content, and at the prevention of the development of obesity-disease complications or their regression [9, 110].

14.1. Diagnostic work-up for obesity in children and adolescents

In children and adolescents, excess body weight is defined on the basis of the BMI value referred to age- and sex-specific centiles. Individual scientific societies adopt different threshold values for the diagnosis of overweight and obesity [9].

Diabetes Poland adopts the position that the Polish OLA/OLAF centile charts should currently be used; according to these, overweight is defined as BMI > 85th centile, and obesity as BMI > 97th centile. In further investigation, the body's adipose

tissue content should be assessed. Direct measurement of adipose tissue can be performed by densitometry (DXA, the gold standard) or by bioimpedance. In everyday clinical practice, anthropometric measurements are of particular importance – including waist circumference and hip circumference.

Abdominal obesity is recognised at a waist circumference ≥ 90th centile for sex and age. Additionally, the WHtR may be calculated; abdominal obesity is recognised at WHtR > 0.5 (see Section 1).

14.2. Diagnostic work-up and monitoring of obesity-disease complications

After the diagnosis of obesity, an assessment of its complications and comorbidities should be conducted in parallel. This encompasses, among other things, blood-pressure measurement, assessment of the severity of glucose metabolism disorders, the lipid profile, hepatic function and morphology, investigation of obstructive sleep apnoea, assessment for PCOS, and assessment of mental health (see Section 5). Treatment of obesity and its complications should be conducted in parallel with the establishment of therapeutic goals (see Section 8).

14.3. Non-pharmacological interventions in obesity

The standard of management in all paediatric patients with obesity is the implementation of behavioural therapy encompassing lifestyle modification – including dietary management (see Subsection 10.1) and appropriately tailored physical activity (see Subsection 10.2). An important element of therapy is psychological support (see Subsection 10.3). The family approach and consideration of the child's environment are of pivotal importance. In this age group, social and family barriers affecting adherence to therapeutic recommendations play a particularly large role. A highly important element of therapy is health education (see Section 9).

In the paediatric population, the goals of obesity-disease therapy must take into account normal somatic and pubertal development. Energy restrictions and elimination diets should be conducted under the supervision of a paediatric team, in particular a dietitian.

In children with diabetes, the type of diabetes, the risk of hypoglycaemia and diabetic ketoacidosis, the insulin-therapy regimen, and the use of diabetes technologies (CGM systems, insulin pumps, AID systems) should additionally be taken into account.

14.4. Pharmacotherapy of obesity

In children and adolescents with obesity and glucose metabolism disorders, pharmacotherapy should be considered after the failure of intensive behavioural treatment – particularly in patients with severe obesity and in the case of coexisting obesity-disease complications [138]. Pharmacological treatment should be introduced after 3–6 months of lack of effect of behavioural therapy or in a situation of patient non-adherence. Drugs with documented efficacy in paediatric trials and approved for use in this age group should be preferred. At present, the drugs registered in Poland for the treatment of obesity in children and adolescents are GLP-1 receptor agonists: semaglutide (from age 12 years) and liraglutide (from age 6 years). Behavioural treatment should be continued in parallel with pharmacotherapy.

14.4.1. Children and adolescents with T1DM

The aim of treating obesity in patients with T1DM is reduction of BMI while maintaining metabolic safety and without an increased risk of hypoglycaemia, ketonaemia, and diabetic ketoacidosis.

At present, only sparse data are available concerning the use of pharmacotherapy directed at the treatment of obesity in children with T1DM. For this reason, in clinical practice, data from paediatric trials in the general population with obesity and from trials in adults with T1DM and obesity are used [217].

Taking into account the favourable findings of trials of obesity treatment in children with the use of GLP-1 receptor agonists, their administration may also be considered in adolescents with T1DM and obesity [261]. Particular attention must, however, be paid to the risk of acute complications of diabetes. Insulin therapy should always be optimised with regard to weight loss and reduced appetite (see Section 12.7).

Therapy with GLP-1 receptor agonists (semaglutide or liraglutide at anti-obesity doses) may be conducted in adolescents with T1DM and obesity only in an experienced centre of paediatric diabetology, with the application of an insulin-dose-reduction protocol, continuous glucose monitoring, and clear principles of ketone monitoring (see Section 9). Optimally, treatment should be conducted using AID.

It must be emphasised that, in the developmental-age population, greater glycaemic variability and the influence of pubertal development on insulin sensitivity, together with frequent non-adherence to the principles of diabetes therapy, may substantially increase the risk of acute complications of diabetes compared with the adult population.

In 2025, a meta-analysis was published concerning the use of metformin in adolescents aged 10–19 years with T1DM. It was found that metformin therapy at a dose of ≤ 2000 mg/day is as-

sociated with a small weight reduction, reduced insulin requirements, and limitation of weight gain. For this reason, metformin may be considered in adolescents with T1DM and obesity – particularly in the case of high insulin requirements and the presence of features of insulin resistance, especially when more effective pharmacotherapy is not available. Substantial or sustained improvement in HbA_{1c} values, however, or significant weight reduction, should not be expected. Metformin should not be used in individuals with HbA_{1c} > 9%.

SGLT-2 inhibitors are not recommended as therapy aimed at weight reduction in children with T1DM, owing to the increased risk of developing diabetic – including euglycaemic – ketoacidosis, and the absence of documented substantial weight reduction with the use of these drugs.

Treatment of obesity in children and adolescents with pre-clinical stages of T1DM is also indicated. According to the accelerator hypothesis, higher BMI accelerates manifestation of the disease.

14.4.2. Children and adolescents with T2DM or prediabetes

T2DM treatment in children and adolescents should be conducted in line with current Diabetes Poland guidelines, preferring drugs that support weight reduction and improvement of cardiometabolic risk [224].

In adolescents, metformin remains the basic therapy, provided it is well tolerated. In the case of insufficient metabolic control and coexisting obesity, the use of GLP-1-based therapy and/or SGLT-2 inhibitors (e.g. empagliflozin – data from the DINAMO trial) should be considered [262–264].

In situations where weight reduction is a primary therapeutic goal (e.g., in cases of severe obesity and/or obesity-related complications), treatment strategies with proven efficacy in reducing BMI in adolescents – particularly GLP-1 receptor agonists and dual GLP-1/GIP receptor agonists – should be preferred as part of a comprehensive treatment approach, in accordance with their regulatory approval and availability [265].

It must be remembered that intensive lifestyle intervention together with metformin use in adolescents with T2DM has limited efficacy, and pharmacotherapy frequently requires escalation.

14.4.3. Other types of diabetes – including genetically determined diabetes – with coexisting obesity

In a child with obesity and diabetes of atypical phenotype, a differential diagnostic work-up should be considered – e.g. maturity-onset diabetes of the young (MODY), mitochondrial diabetes, and other syndromic diabetes – since the choice of antidiabetic treatment and the risk of complications depend on the aetiology of the disturbances.

Treatment of obesity in monogenic diabetes should be conducted analogously to that in the general population (lifestyle modification and anti-obesity pharmacotherapy in line with age and registration), unless targeted therapy exists for the given cause of obesity.

In children with severe early-childhood obesity and hyperphagia, investigation for monogenic obesity should be considered. In monogenic and syndromic obesity, treatment should be conducted in a multidisciplinary manner (endocrinologist/diabetologist, hepatologist, nephrologist, cardiologist, ophthalmologist, dietitian, psychologist).

In children with Bardet-Biedl syndrome and severe early-childhood obesity with hyperphagia, targeted treatment with setmelanotide (an MC4R agonist) should be considered in a referral centre, in line with eligibility criteria and availability [266]. A phase 3 trial demonstrated clinically meaningful reduction of body weight and hunger in patients with Bardet-Biedl syndrome.

In Alström syndrome, setmelanotide is not currently recommended therapy. Therapeutic decisions require individualisation, and in clinical practice, strategies as in multifactorial obesity are more frequently used (including GLP-1 receptor agonists, if eligibility criteria are met and there are no contraindications).

14.4.4. Consequences of GLP-1-based therapy use in children and adolescents with dysglycaemia and obesity

Owing to the relatively short period of use of GLP-1-based therapies in children and adolescents, it is difficult to assess the long-term consequences of their chronic use. It must be remembered that the balance between energy intake and expenditure affects key growth hormones – including GH and IGF-1 [267].

The mechanism of action of GLP-1-based therapies – encompassing appetite suppression and reduction of the pleasure derived from eating (anti-hedonic action) – may potentially disturb this balance during critical periods of growth and development. Additional attention is paid to the possible influence of these drugs on muscle-mass development (risk of sarcopenia) and on achieving peak bone mass [268, 269].

Before the implementation of pharmacotherapy, contraindications, the risk of adverse effects (including gastrointestinal symptoms and cholelithiasis), potential interactions with concurrently used drugs, the patient's mental health status, and the family's readiness for lifestyle change and thera-

py monitoring should be assessed. In individuals treated with insulin, the family's ability to modify insulin dosing should additionally be assessed – particularly when methods other than AID systems are used.

14.5. Metabolic/bariatric treatment

In adolescents with severe obesity and its complications (including T2DM), in the absence of efficacy of pharmacotherapy or where it cannot be used, bariatric treatment performed in a referral centre should be considered.

Determining eligibility for bariatric treatment requires assessment of the patient's psychosocial maturity, psychiatric consultation, stable family support, analysis of the risk of nutritional deficiencies, and the planning of long-term monitoring.

The management algorithm in children and adolescents with obesity is presented in Section 16.

15. TREATMENT OF OVERWEIGHT/OBESITY IN INDIVIDUALS OVER 65 YEARS OF AGE WITH GLUCOSE METABOLISM DISORDERS

Key recommendations
• When initiating therapy in individuals with overweight/obesity and glucose metabolism disorders over 65 years of age, therapeutic goals should be individually assessed depending on the patient's health status, comorbidities, complications of diabetes, cognitive abilities, and social and living conditions. [**B**]
• Regular, comprehensive assessment of the nutritional status of older individuals is recommended, encompassing changes in body weight, risk of malnutrition, and assessment of muscle function and strength – and not BMI alone – and assessment of energy and protein intake. [**C**]
• The diet of older individuals should take into account the increased risk of dehydration; regular assessment of hydration and adaptation of meal consistency and structure to chewing and swallowing capabilities is recommended. [**B**]
• The initiation of pharmacotherapy of overweight/obesity in this age group should be accompanied by dietetic consultation, and pharmacologically induced weight reduction should be combined with appropriate protein intake, resistance training, and monitoring of muscle function and functional parameters. [**A**]

Diabetes and obesity in older individuals are characterised by substantial clinical heterogeneity arising from differences in functional status, the presence of comorbidities, frailty, sarcopenia, and cognitive and social limitations. The aging process is associated with unfavourable changes in body composition, including an increase in the proportion of visceral adipose tissue and progressive loss of skeletal muscle mass and quality, which increases the risk of sarcopenia and sarcopenic obesity, and impedes the use of physical activity [270, 271].

In this population, interventions directed solely at weight reduction may intensify undesirable loss of fat-free mass, worsen physical performance, and increase the risk of falls and loss of independence. In consequence, the goals of treatment of obesity in individuals aged ≥ 65 years should encompass improvement of functioning, quality of life, and metabolic control, with simultaneous protection of muscle mass and function – not be directed exclusively at weight reduction. Such an approach to weight reduction is important in every age group; however, it is of particular importance in individuals aged ≥ 65 years [118, 272].

15.1. The importance of comprehensive nutritional assessment

Dietary treatment of individuals aged ≥ 65 years with diabetes and obesity should always be preceded by multidimensional nutritional assessment, encompassing not only body weight and BMI but also analysis of body composition, functional fitness, and the presence of features of malnutrition, sarcopenia, and frailty, and assessment of dietary intake with respect to energy and nutrient consumption. In the older population, BMI has limited diagnostic value, since it does not reflect the redistribution of adipose tissue and the loss of muscle mass [271].

Nutritional status assessment should encompass screening for the risk of malnutrition (e.g. Mini Nutritional Assessment – Short Form; MNA-SF), analysis of the dynamics of body weight changes, and identification of unintended weight loss, which in older individuals is associated with an increased risk of complications, hospitalisation, and mortality, irrespective of baseline body weight. During intentional weight reduction, regular monitoring of nutritional status is necessary in order to distinguish desired loss of adipose tissue from unfavourable loss of fat-free mass [118, 273].

15.2. Goals of nutritional treatment in older persons

The fundamental aim of nutritional therapy in older individuals with diabetes and coexisting obesity is achieving optimal metabolic control – particularly glycaemic control – while maintaining or improving physical fitness and quality of life. Clinically meaningful weight reduction (typically a few percent of baseline weight) may bring metabolic benefits; however, in older persons, it should be achieved in a cautious, gradual, and monitored manner, with individual assessment of the benefit-to-risk balance.

In clinical practice, therapeutic success in individuals aged ≥ 65 years encompasses improvement of exercise tolerance, reduction of pain and

obesity-related symptoms, improvement of glycaemic control and cardiovascular risk factors, and the maintenance or improvement of muscle strength and motor function. In some patients – particularly those with frailty, sarcopenia, advanced comorbidities, or cognitive disturbances – the maintenance of stable body weight may constitute a more appropriate goal than its further reduction [270–272].

15.3. Planning energy intake and energy deficit

In older persons, careful planning of energy intake is recommended, taking into account reduced total energy expenditure and reduced metabolic reserve. In the case of weight reduction, the energy deficit should be moderate, with emphasis on high nutrient density of the diet. Excessive restriction of energy intake increases the risk of protein – energy malnutrition and accelerated loss of muscle and bone mass [272].

Quantitative dietary assessment should encompass analysis of actual energy and macronutrient intake (on the basis of dietary history or a food diary), with particular attention to protein intake. Ensuring adequate protein intake constitutes a precondition for the safety of reducing therapy, and its deficiency is one of the principal risk factors for sarcopenia and worsening fitness. The distribution of remaining macronutrients should be set individually, taking into account glycaemic control, lipid profile, comorbidities, and patient preferences [118, 272].

15.4. Protein as a key element of dietary therapy after age 65

One of the most important particularities of dietary treatment in this age group is the increased protein requirement, arising from the anabolic resistance of skeletal muscle. In individuals aged ≥ 65 years, protein intake of at least 0.8 g/kg body weight/day is recommended, with consideration of higher intake (e.g. 1.0–1.5 g/kg body weight/day) in individuals with diabetes, chronic diseases, those at risk of sarcopenia, or undergoing weight reduction, after individual assessment of clinical status and renal function.

Of substantial importance is not only total protein intake but also its distribution throughout the day. The intake of protein in 3–4 meals daily, with the provision of approximately 20–30 g of protein per single meal, is preferred – this promotes the stimulation of muscle protein synthesis. Attention should be paid to protein quality, with preference for sources of high biological value rich in leucine; in plant-based diets, appropriate combination of protein sources is necessary [274].

15.5. Dietary quality and dietary patterns

In older persons, qualitative assessment of the diet is of equal importance to its energy value. It should encompass analysis of meal nutrient density, dietary diversity, and the frequency of consumption of products that are sources of protein, dietary fibre, vitamins, and minerals. A diet of low nutrient density may coexist with micronutrient deficiencies, even with excessive energy intake.

Dietary patterns of documented metabolic and functional benefits are preferred, such as the Mediterranean diet, DASH diet, or flexitarian models – characterised by high intake of vegetables, fruit, wholegrain products, legumes, fish, nuts, and fermented dairy products, with simultaneous restriction of highly and ultra-processed foods. Qualitative assessment of the diet should also take into account the regularity of meal consumption, portion size, and adaptation of the consistency and structure of dishes to chewing and swallowing capabilities.

In older persons, dietary recommendations should take into account aspects characteristic of this age group. In some older patients, decreased appetite occurs; for this reason, the diet used should take into account limitations arising from this disturbance so as not to increase the risk of malnutrition. In addition, a common problem in this age group is constipation; the use of dietary components rich in soluble fibre, which will facilitate – or at least not impede – the bowel-emptying process, is therefore advised [118, 272].

15.6. Dietary treatment and incretin-based pharmacotherapy in older persons

In individuals aged ≥ 65 years treated with GLP-1-based therapies, particular caution is necessary. These therapies, although effective in reducing body weight and improving glycaemic control, may increase the risk of excessive weight loss, dehydration, malnutrition, excessive reduction of appetite, and loss of fat-free mass. In this group, slower dose escalation and frequent assessment of treatment tolerance and nutritional status are recommended.

Pharmacologically induced weight reduction should always be combined with appropriate protein intake, resistance training, and monitoring of muscle function and functional parameters – the so-called muscle-protection package [275–277].

15.7. The importance of physical activity and functional monitoring

After initial determination of the patient's individual risk and exercise capacity, physical activity characterised by a slow start and slow finish, with avoidance of straining and breath-holding

exercises and with attention to the risk of injury – particularly the risk of developing diabetic foot disease – should be recommended.

In line with WHO guidelines, older individuals are recommended to perform aerobic physical activity of moderate intensity for at least 150–300 minutes, or of high intensity for at least 75–150 minutes, or an equivalent combination of moderate- and high-intensity activity [278].

Older individuals should also perform resistance exercises of moderate or high intensity strengthening the muscles, encompassing all major muscle groups, on at least 2 days per week, in order to counteract sarcopenia (loss of muscle mass and strength).

In order to increase functional capacity and prevent falls, as part of weekly physical activity, older individuals should engage on at least 3 days per week in multicomponent physical activity that emphasises functional balance and strength training of moderate or high intensity [118, 278].

Older individuals should limit the time spent in a sitting position. Replacing sitting time with physical activity of any intensity (including low intensity) provides health benefits [118, 271, 273].

16. ORGANISATION OF CARE FOR INDIVIDUALS WITH OVERWEIGHT/OBESITY, RISK FACTORS FOR THE DEVELOPMENT OF DIABETES, AND GLUCOSE METABOLISM DISORDERS

Key recommendations
• Prevention of obesity should take place in the setting of primary health care.
• The primary-care physician, in assessing accompanying disorders and possible secondary causes of obesity, takes the decision on referral of the patient to a diabetology specialist.
• Treatment of obesity in a patient with glucose metabolism disorders requires comprehensive engagement of the diabetology therapeutic team – physicians, nurses providing education or educators, and dietitians, psychologists, and physiotherapists.
• Treatment of individuals with obesity requires medical visits constituting a separate provision within ambulatory specialist care in diabetology.
• Education of patients with obesity requires educational, dietetic, psychological, and physiotherapeutic consultations, which should constitute separate provisions within ambulatory specialist care in diabetology.
• The development of an interdisciplinary therapeutic pathway for patients requiring bariatric surgery should be sought.
• In children and adolescents, management should be individualised and encompass active engagement of the patient's family. Regular follow-up visits and care coordination by a single attending physician should be ensured, with consideration of preparation for transition from paediatric to adult diabetological care.

The care of patients with obesity requires structural and systemic solutions [1, 279]. The limited number of procedures within the package of guaranteed health benefits and the limitations on the provision of services within healthcare make it necessary to refer to ambulatory specialist care only those patients whose treatment in primary health care is ineffective. The therapeutic pathway on the basis of which patients should be referred to a diabetology clinic is presented in Figure 16.1.

As part of the reform of the Polish healthcare benefit system and the *Inverted Pyramid of Services* project, supported by the European Union (European Funds for Social Development), a package of visits has been developed enabling comprehensive and coordinated care for the patient with obesity. The introduction of these provisions should be accompanied by the assurance of appropriate funding and the standardisation of action in clinical practice.

The decision on referral of patients to the diabetes outpatient clinic should be preceded by physical examination and the performance of basic laboratory investigations – particularly a full diagnostic work-up defining the type of glucose metabolism disorder. A further factor determining the mode of patient referral is assessment of cardiovascular risk.

16.1. Organisational requirements

The requirements for diabetes outpatient clinics are set out in the *Diabetes Poland Clinical Guidelines* [224].

Of pivotal importance for the effective treatment of obesity is the educational infrastructure – that is, separate rooms for group or individual education, equipped with educational tools, including multimedia.

In the education and self-education of patients, digital methods should be used, including tele-education, webinars, mobile applications, and reliable websites.

Teleconsultations may complement care and be used for motivational purposes and for the support of behavioural therapy. Additionally, during remote visits, the use of pharmacotherapy, its adverse effects, and any change in dosing should be monitored.

A further piece of equipment necessary for the treatment of patients with obesity is a body composition analyser. Body composition assessment using bioelectrical impedance should be performed before the start of treatment and during it.

In the clinic, the patient should be given the opportunity to use a dietetic consultation and/or be referred for a psychological consultation if required [117]. In addition, initial eligibility assessment for surgical treatment of obesity – taking into account

the indications and any contraindications for surgical treatment – should take place in the clinic.

16.1.1. Dietetic consultation

In Poland, the implementation of dietary education in diabetes outpatient clinics is justified for the realisation of the provision of care for patients with obesity [224]. Dietetic consultation should be provided as a separate service, on the order of the physician in the diabetes outpatient clinic, and requires the maintenance of separate documentation.

Dietetic consultation should encompass: assessment of the patient's habitual eating pattern, nutritional diagnosis, establishment of the goal and assumptions of dietary intervention, dietary intervention (individual and/or group counselling), creation of dietary plans taking into account the energy deficit aimed at weight reduction, monitoring of the eating pattern and assessment of therapeutic effects, and correction of dietary assumptions in the case of failure to achieve the established therapeutic goal. The recommendations conveyed should be adapted to the patient's cognitive abilities, and – in the case of disabled persons – also to the needs and competences of their caregivers. The educational process during the dietetic consultation should take into account accompanying diseases, the patient's clinical status, and the current model of treatment – particularly insulin therapy.

In the case of patients with T2DM, in whom weight reduction may be the dominant element of treatment [171], the discontinuation of insulin therapy may be achievable, which constitutes a clinically substantial change for patients but will also save money for the healthcare system.

The dietetic consultation should conclude with the issuing of the most important recommendations in written form.

Duration of the consultation: 45 minutes.

16.1.2. Psychological consultation

The psychological consultation should be conducted by a clinical psychologist or psychotherapy specialist experienced in working with patients with metabolic diseases, on the order of a physician or at the request of the patient. The aim of the consultation is to support the patient in adapting to the diagnosis of obesity as a disease, in coping with the emotional aspects of obesity, and in motivating lifestyle change [37].

Indications for referral:

- depressive or anxiety symptoms coexisting with obesity;
- low motivation for lifestyle change;
- difficulties in emotion regulation (e.g. eating under the influence of stress, loneliness);
- recognised eating disorders (emotional eating, night eating);
- negative body image and low self-esteem;
- difficulties in social relationships, stigmatisation, withdrawal;
- lack of effects in weight reduction despite repeated attempts.

The psychological consultation should conclude with the issuing of the most important recommendations in written form.

Duration of the consultation: 45 minutes.

16.1.3. Physiotherapeutic consultation

In selected cases, the patient should be referred for a physiotherapeutic consultation, thanks to which an increase in physical activity will be conducted in a manner safe for the musculoskeletal system.

16.1.4. Benefits of treating obesity for patients and the payer

- Reduction of costs associated with the treatment of complications of obesity and diabetes.
- Reduction of expenditure on medications.
- Increase in treatment effectiveness.
- Prevention of T2DM [171, 280].
- Improvement of quality of life.

16.2. Particularities of the organisation of care for children and adolescents

The organisation of care for children and adolescents with obesity and glucose metabolism disorders shows substantial particularities compared with care for adults, arising from the specifics of the physical and psychosocial development of the paediatric patient and the need to involve legal guardians.

Care should be conducted by a therapeutic team comprising a specialist physician in paediatric endocrinology and diabetology (or a physician undergoing specialist training after at least the first year of training), a dietitian, a physiotherapist, a psychologist, and – in justified cases – also a child and adolescent psychiatrist [9, 110] (Figure 16.2).

The basic organisational model is the family-centred approach, in which therapeutic interventions encompass both the patient and the family environment.

Management should take into account individual clinical determinants, including the aetiology of glucose metabolism disorders, age, developmental stage, severity of obesity, and psychosocial and environmental factors. Active inclusion of the family in the therapeutic process increases treatment efficacy and the durability of the achieved effects.

Of substantial importance is the adaptation of communication and health education to the age

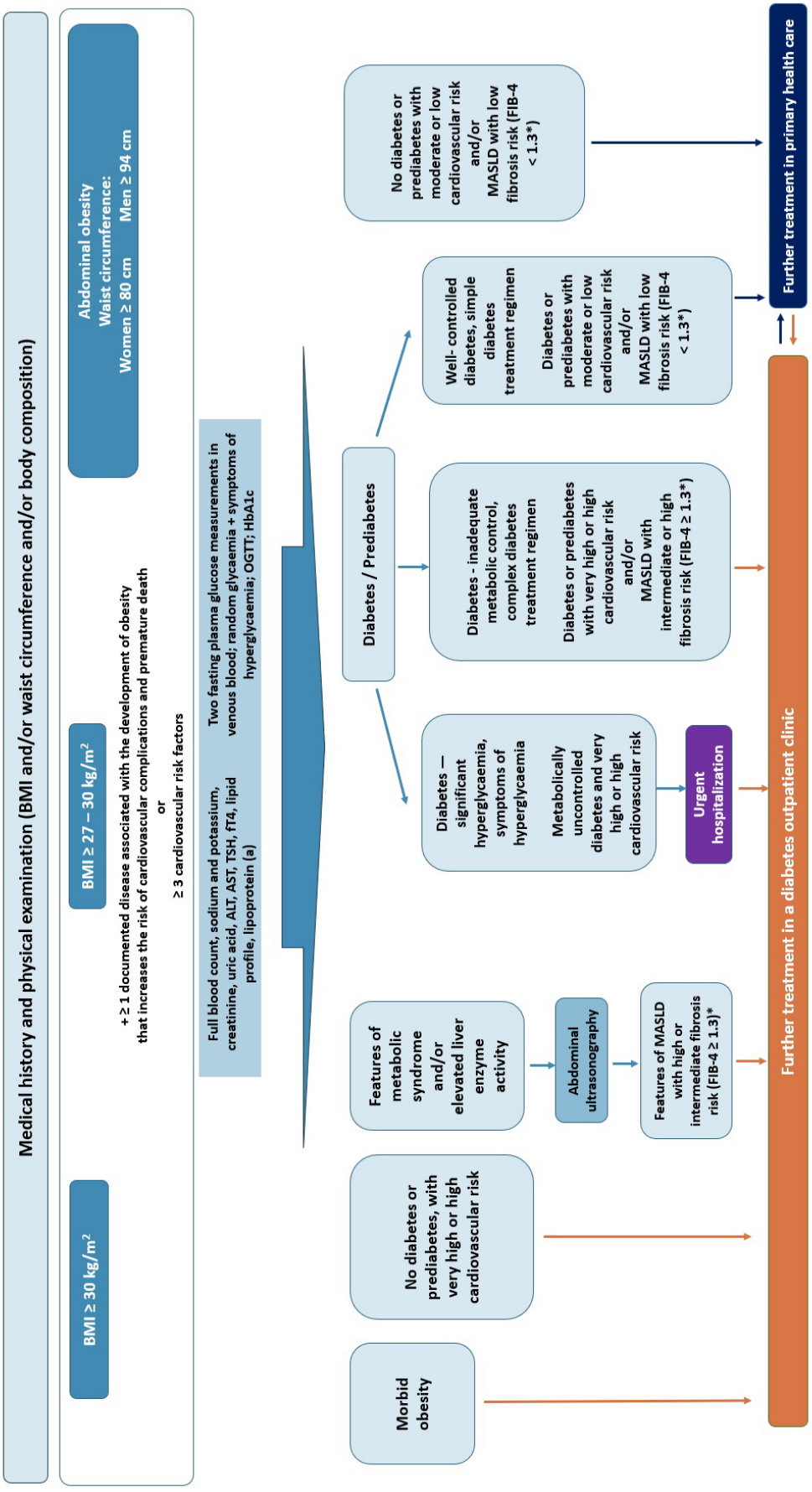


Figure 16.1. Management algorithm in individuals with obesity

and level of cognitive development of the child, with simultaneous consideration of emotional and social aspects, such as stigmatisation and functioning in the peer group.

Dietetic consultation in children should have a family character and encompass education of caregivers and modification of the lifestyle of the entire family. Of pivotal importance is consideration of the developmental needs of the child and the prevention of nutritional deficiencies.

Psychological consultation in the paediatric population should be systematic and long-term

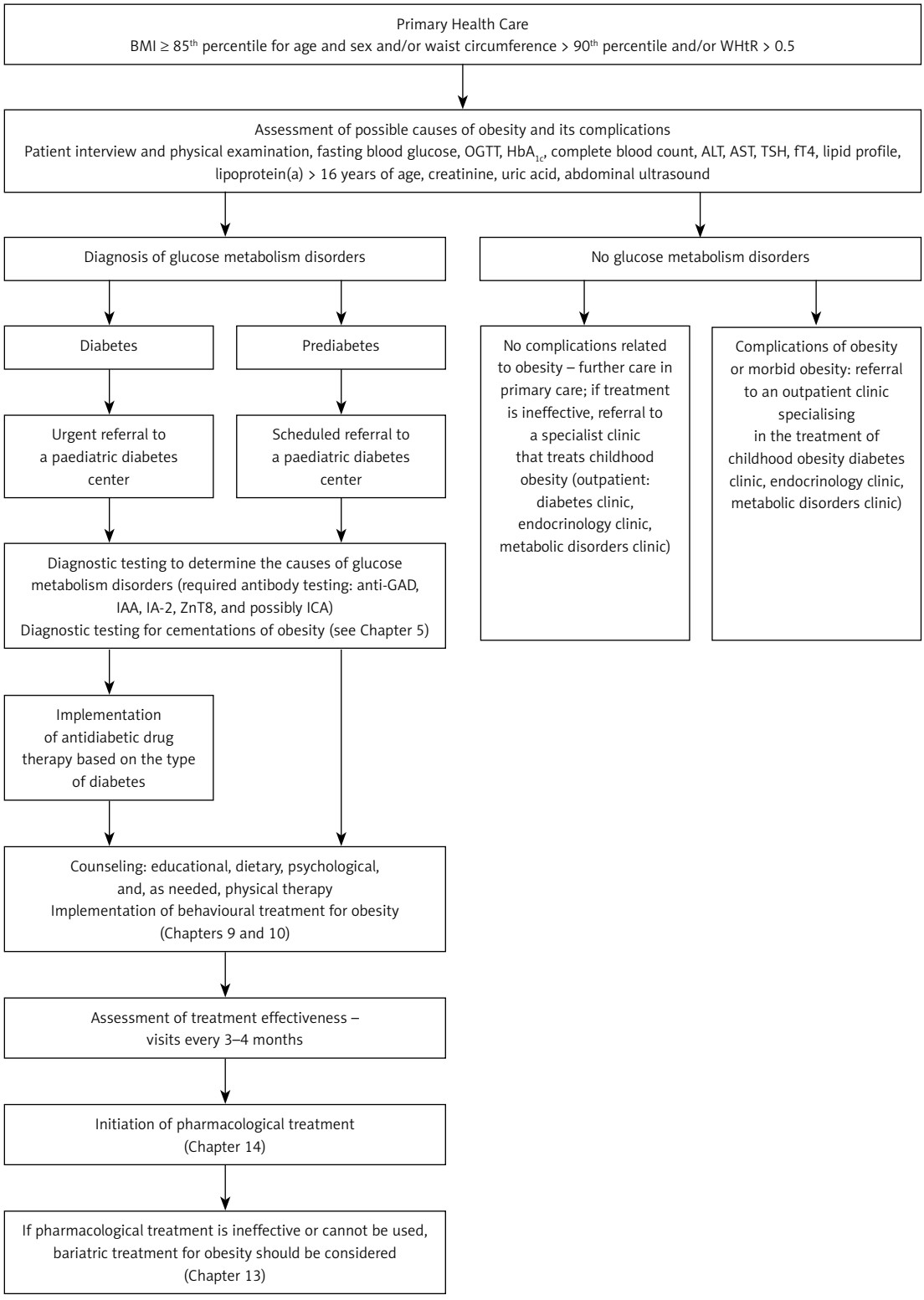


Figure 16.2. Management algorithm in children and adolescents with obesity

in nature and encompass both the child and the family, with particular consideration of support with respect to motivation, body image, and social functioning.

Physiotherapeutic consultation should encompass comprehensive assessment of the child's physical fitness and the development of an individual physical-activity programme adapted to age, severity of obesity, and comorbidities. The programme should take into account the patient's functional capabilities and be subject to modification during treatment.

A further particularity is the necessity of ensuring continuity of care over a long time horizon, encompassing the period of pubertal development and the preparation of the patient for transition to the adult care system.

Of particular importance is the early identification of metabolic disturbances and the rapid implementation of therapeutic interventions, which enables effective prevention of complications.

Follow-up visits at intervals of every 3–4 months are recommended, in order to monitor the effects of therapy, assess its efficacy, and modify management. It is recommended that the patient remain under the care of a single attending physician, responsible for the coordination of treatment, which favours improvement of therapeutic cooperation.

Within the healthcare benefit system, the so-called "obesity package" has been developed, intended to function within the *Inverted Pyramid of Services* project, which enables comprehensive and coordinated care for the patient. Consultations conducted within this package should be classified and accounted for as obesity-related consultations, which will provide appropriate financing for the services and the standardisation of action in clinical practice.

The organisation of care should take into account close cooperation between levels of the healthcare system (primary health care and specialist care) and the use of modern technologies, including continuous glucose monitoring systems, in the diagnosis and monitoring of glucose metabolism disorders.

Such an approach enables early intervention, effective secondary prevention, and improvement of long-term health outcomes, minimising the risk of metabolic, cardiovascular, and psychosocial complications associated with obesity and glucose metabolism disorders.

References

1. American Diabetes Association Professional Practice Committee for Diabetes. 8. Obesity and weight management for the prevention and treatment of diabetes: Standards of care in diabetes – 2026. Diabetes Care 2026; 49 (Supplement_1): S166-82.
2. Bray GA, Ryan DH. Beyond obesity. Med Sci (Basel) 2025; 13: 176.
3. Rubino F, Cummings DE, Eckel RH, et al. Definition and diagnostic criteria of clinical obesity. Lancet Diabetes Endocrinol 2025; 13: 221-262.
4. World Health Organization. Obesity and overweight [Internet]. Geneva: World Health Organization; 2025.
5. Lau DCW, Wharton S. Canadian Adult Obesity Clinical Practice Guidelines: The Science of Obesity. Available at: https://obesitycanada.ca/guidelines/science (accessed: 27 April 2026).
6. Dunkel KA. New Obesity Definitions – Watch or Warning? JAMA Netw Open 2025; 8: e2549012.
7. Fourman LT, Awwad A, Gutiérrez-Sacristán A, et al. Implications of a new obesity definition among the All of Us cohort. JAMA Netw Open 2025; 8: e2537619.
8. Ciudin A, Baker JL, Belančić A, et al. Framework for the pharmacological treatment of obesity and its complications from the European Association for the Study of Obesity (EASO): 2026 update. Nat Med 2026; 32: 1962-1966.
9. Mazur A, Zachurzok A, Baran J, et al. Childhood obesity: position statement of Polish Society of Pediatrics, Polish Society for Pediatric Obesity, Polish Society of Pediatric Endocrinology and Diabetes, the college of family physicians in poland and Polish association for study on obesity. Nutrients 2022; 14: 3806.
10. World Health Organization. WHO child growth standards: length/height-for-age, weight-for-length, weight-for-height and body mass index-for-age. Geneva: WHO; 2006.
11. European Association for the Study of Obesity (EASO). The heavy burden of obesity in Europe. Obes Facts 2023; 16: 113-120.
12. World Health Organization. Obesity and overweight. Fact sheet. Geneva: World Health Organization; 2024.
13. World Obesity Federation. World Obesity Atlas 2025: Overweight, obesity and non-communicable diseases. London: World Obesity Federation; 2025.
14. OECD. Health at a Glance: Europe 2022 – State of Health in the EU Cycle. Paris: OECD Publishing; 2022.
15. Stahl-Pehe A, Bächle C, Castillo K, et al. Prevalence of type 1 and type 2 diabetes in children and adolescents in Europe. Pediatr Diabetes 2022; 23: 1009-1019.
16. Drygas W, Niklas AA, Piotrowski W, et al. Multi-centre national population health examination survey (WOBASZ III) – assumptions, methods and selected results. Kardiol Pol 2022; 80: 697-708.
17. Narodowy Fundusz Zdrowia [National Health Fund]. Cukrzyca. Raport NFZ 2023 [Diabetes. NFZ Report 2023]. Warsaw: NFZ; 2023.
18. Zdrojewski T, Więcek A, Rutkowski M, et al. PolSenior2 study – design and selected results concerning cardiometabolic risk in older adults. Kardiol Pol 2021; 79: 1183-1191.
19. Han C, Zhang H, Luo X, et al. Global prevalence of prediabetes in children and adolescents: a meta-analysis. J Diabetes 2022; 14: 673-690.
20. WHO Regional Office for Europe. WHO European Childhood Obesity Surveillance Initiative (COSI): report on the sixth round of data collection, 2022-2024. Copenhagen: WHO Regional Office for Europe; 2025.
21. Zhang X, Liu J, Ni Y, et al. Global prevalence of overweight and obesity in children and adolescents: a systematic review and meta-analysis. JAMA Pediatr 2024; 178: 800-813.
22. Brzeziński M, Jankowski M, Jankowska A, et al. Is there a rapid increase in prevalence of obesity in Pol-

ish children and adolescents? Arch Med Sci 2017; 14: 22-29.
23. Chylińska-Frątczak A, Michalak A, Baranowska-Jaźwiecka A, et al. Incidence of hyperglycaemic disorders in children and adolescents with obesity. Pediatr Endocrinol Diabetes Metab 2022; 28: 274-280.
24. Fijałkowska A, Oblacińska A, Korzycka M, et al. Childhood obesity surveillance initiative (COSI) in Poland – implementation of two rounds of the study. J Mother Child 2020; 24: 29-38.
25. Wu H, Lau ESH, Ma RCW, et al. Worldwide estimates of incidence of type 2 diabetes in children and adolescents in 2021. Diabetes Res Clin Pract 2022; 185: 109785.
26. Matthews DR, Seeley RJ, Zeltser LM, et al. Obesity pathogenesis: an Endocrine Society scientific statement. Endocr Rev 2017; 38: 267-296.
27. Betley JN, Xu S, Cao ZF, et al. Neurons for hunger and thirst transmit a negative-valence teaching signal. Nature 2015; 521: 180-185.
28. Stemmer K, Muller ID, DiMarchi RD, et al. CNS-targeting pharmacological interventions for the metabolic syndrome. J Clin Invest 2019; 129: 4058-4071.
29. Egecioglu E, Skibicka KP, Hansson C, et al. Hedonic and incentive signals for body weight control. Physiol Behav 2011; 104: 748-753.
30. Koliaki C, Liatis S, Dalamaga M, et al. The implication of gut hormones in the regulation of energy homeostasis and their role in the pathophysiology of obesity. Curr Obes Rep 2020; 9: 255-271.
31. Karczewska-Kupczewska M, Stefanowicz M, Nikołajuk A, et al. Weight-reducing dietary intervention increases the ability of hyperinsulinemia to suppress serum ghrelin concentration in individuals with obesity. J Nutr 2024; 154: 1631-1639.
32. Ascaso JF, Pardo S, Real JT, et al. Diagnosing insulin resistance by simple quantitative methods in subjects with normal glucose metabolism. Diabetes Care 2003; 26: 3320-3325.
33. Loos RJF, Yeo GSH. The genetics of obesity: from discovery to biology. Nat Rev Genet 2022; 23: 120-133.
34. Frayling TM, Timpson NJ, Weedon MN, et al. A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity. Science 2007; 316: 889-894.
35. Ekelund U, Steene-Johannessen J, Brown WJ, et al. Does physical activity attenuate the detrimental association of sitting time with mortality? Lancet 2016; 388: 1302-1310.
36. Helmerhorst HJF, Wijndaele K, Brage S, et al. Objectively measured sedentary time may predict insulin resistance independently of moderate- and vigorous-intensity physical activity. Diabetologia 2009; 52: 1776-1779.
37. Konttinen H. Emotional eating and obesity in adults: the role of depression, sleep and genes. Proc Nutr Soc 2020; 79: 283-289.
38. Cyranka K, Snoek F, Hermanns N, et al. Obesity-related distress and obesity burnout: towards a conceptual framework for disease-specific emotional burden in obesity. Diabetes Obes Metab 2026; 28: 3457-3461.
39. British Psychological Society. The causes of obesity – a complex interaction. In: Psychological perspectives on obesity: Addressing policy, practice and research priorities. British Psychological Society; 2019.
40. Umano GR, Bellone S, Buganza R, et al. Early roots of childhood obesity: risk factors, mechanisms, and prevention strategies. Int J Mol Sci 2025; 26: 7388.
41. Blaauwendraad SM, Kamphuis ASJ, Ruiz-Ojeda FJ, et al. Risk factors in the first 1000 days of life associated with childhood obesity: a systematic review and risk factor quality assessment. Obes Rev 2026; 27: e70025.
42. 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: 1-32.
43. Ambrosi B, Masserini B, Iorio L, et al. Relationship of thyroid function with body mass index and insulin resistance in euthyroid obese subjects. J Endocrinol Invest 2010; 33: 640-643.
44. Song RH, Wang B, Yao QM, et al. The impact of obesity on thyroid autoimmunity and dysfunction: a systematic review and meta-analysis. Front Immunol 2019; 10: 2349.
45. Krentowska A, Kowalska I. Metabolic syndrome and its components in different phenotypes of polycystic ovary syndrome. Diabetes Metab Res Rev 2022; 38: e3464.
46. Kowalska I, Strączkowski M, Nikołajuk A, et al. Serum visfatin in relation to insulin resistance and markers of hyperandrogenism in lean and obese women with polycystic ovary syndrome. Hum Reprod 2007; 22: 1824-1829.
47. Forslund M, Wändell P, Forsberg L, et al. GLP-1 receptor agonist treatment in women with polycystic ovary syndrome: a systematic review and meta-analysis. Eur J Endocrinol 2026; 194: 25.
48. Salonia A, Capogrosso P, Boeri L, et al. EAU guidelines on male sexual and reproductive health: 2025 update. Eur Urol 2025; 88: 76-102.
49. Jayasena CN, Devine K, Barber K, et al. Female hypogonadism guideline. Clin Endocrinol (Oxf) 2024; 101: 409-442.
50. Hjelholt A, Høgild M, Bak AM, et al. Growth hormone and obesity. Endocrinol Metab Clin North Am 2020; 49: 239-250.
51. Jameson JL, De Groot LJ. Endocrinology: Adult and Pediatric. 7th ed. Philadelphia (PA): Elsevier; 2016.
52. Roth CL, McCormack SE. Acquired hypothalamic obesity. Diabetes Obes Metab 2024; 26: 34-45.
53. Collet TH, Schwitzgebel V. Precision medicine in rare obesity. Front Nutr 2024; 11: 1509994.
54. Dollfus H, Lilien MR, Maffei P, et al. Bardet-Biedl syndrome. Eur J Hum Genet 2024; 32: 1347-1360.
55. Gill H, Gill B, El-Halabi S, et al. Antidepressants and weight change. Obesity (Silver Spring) 2020; 28: 2064-2072.
56. VA/DoD Clinical Practice Guideline for the Management of Adult Overweight and Obesity. Version 4.0. Washington (DC): U.S. Department of Veterans Affairs, Department of Defense; 2025.
57. Rooney MR, Wallace AS, Echouffo Tcheugui JB, et al. Prediabetes is associated with elevated risk of clinical outcomes even without progression to diabetes. Diabetologia 2025; 68: 357-366.
58. Schlesinger S, Neuenschwander M, Barbaresko J, et al. Prediabetes and risk of mortality, diabetes-related complications and comorbidities: umbrella review of meta-analyses of prospective studies. Diabetologia 2022; 65: 275-285.
59. Bianchettin RG, Lavie CJ, Lopez-Jimenez F. Challenges in cardiovascular evaluation and management of

obese patients: JACC state-of-the-art review. J Am Coll Cardiol 2023; 81: 490-504.
60. Kim MS, Kim WJ, Khera AV, et al. Association between adiposity and cardiovascular outcomes: an umbrella review and meta-analysis of observational and Mendelian randomization studies. Eur Heart J 2021; 42: 3388-3403.
61. Liao J, Qiu M, Li J, Li Y, Han Y. Association of visceral adipose tissue with hypertension: Results from the NHANES 2011-2018 and Mendelian randomization analyses. J Clin Hypertens (Greenwich) 2025; 27: e14953.
62. NCD Risk Factor Collaboration (NCD-RisC). General and abdominal adiposity and hypertension in eight world regions: a pooled analysis of 837 population-based studies with 7.5 million participants. Lancet 2024; 404: 851-863.
63. D'Agati VD, Chagnac A, de Vries AP, et al. Obesity-related glomerulopathy: clinical and pathologic characteristics and pathogenesis. Nat Rev Nephrol 2016; 12: 453-471.
64. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int 2024; 105 (Suppl 4): S117-S314.
65. Dhurandhar Y, Tomar S, Das A, et al. Chronic inflammation in obesity and neurodegenerative diseases: exploring the link in disease onset and progression. Mol Biol Rep 2025; 52: 424.
66. Karczewska-Kupczewska M, Tarasów E, Nikołajuk A, et al. The effect of insulin infusion on the metabolites in cerebral tissues assessed with proton magnetic resonance spectroscopy in young healthy subjects with high and low insulin sensitivity. Diabetes Care 2013; 36: 2787-2793.
67. Wang J, Yang DL, Chen ZZ, Gou BF. Associations of body mass index with cancer incidence among populations, genders, and menopausal status: a systematic review and meta-analysis. Cancer Epidemiol 2016; 42: 1-8.
68. Deshmukh B, Ajay AK, Bhat MK. Obesity and cancer: relevance of DNA damage response. Transl Oncol 2026; 65: 102657.
69. Brown A, Flint SW, Batterham RL. Pervasiveness, impact and implications of weight stigma. EClinicalMedicine 2022; 47: 101408.
70. Jebeile H, Kelly AS, O'Malley G, Baur LA. Obesity in children and adolescents: epidemiology, causes, assessment, and management. Lancet Diabetes Endocrinol 2022; 10: 351-365.
71. European Association for the Study of the Liver (EASL), European Association for the Study of Diabetes (EASD), European Association for the Study of Obesity (EASO). EASL–EASD–EASO clinical practice guidelines on the management of metabolic dysfunction-associated steatotic liver disease (MASLD). J Hepatol 2024; 81: 492-542.
72. Roden M, Shulman GI. The integrative biology of type 2 diabetes. Nature 2019; 576: 51-60.
73. James DE, Stöckli J, Birnbaum MJ. The aetiology and molecular landscape of insulin resistance. Nat Rev Mol Cell Biol 2021; 22: 751-771.
74. Ndumele CE, Neeland IJ, Tuttle KR, et al. A synopsis of the evidence for the science and clinical management of cardiovascular-kidney-metabolic (CKM) syndrome: a scientific statement from the American Heart Association. Circulation 2023; 148: 1636-1664.
75. Ndumele CE, Rangaswami J, Chow SL, et al. Cardiovascular-kidney-metabolic health: a presidential advisory from the American Heart Association. Circulation 2023; 148: 1606-1635.
76. Vora J, Cherney D, Kosiborod MN, et al. Inter-relationships between cardiovascular, renal and metabolic diseases: Underlying evidence and implications for integrated interdisciplinary care and management. Diabetes Obes Metab 2024; 26: 1567-1581.
77. Byrne CD, Armandi A, Pellegrinelli V, et al. Metabolic dysfunction-associated steatotic liver disease: a condition of heterogeneous metabolic risk factors, mechanisms and comorbidities requiring holistic treatment. Nat Rev Gastroenterol Hepatol 2025; 22: 314-328.
78. Younossi ZM, Kalligeros M, Henry L. Epidemiology of metabolic dysfunction-associated steatotic liver disease. Clin Mol Hepatol 2025; 31 (Suppl): S32-S50.
79. Huang DQ, Wong VWS, Rinella ME, et al. Metabolic dysfunction-associated steatotic liver disease in adults. Nat Rev Dis Primers 2025; 11: 14.
80. Stefan N, Yki-Järvinen H, Neuschwander-Tetri BA. Metabolic dysfunction-associated steatotic liver disease: heterogeneous pathomechanisms and effectiveness of metabolism-based treatment. Lancet Diabetes Endocrinol 2025; 13: 134-148.
81. Cusi K, Abdelmalek MF, Apovian CM, et al. Metabolic dysfunction-associated steatotic liver disease (MASLD) in people with diabetes: the need for screening and early intervention. A consensus report of the American Diabetes Association. Diabetes Care 2025; 48: 1057-1082.
82. Yang W, Jin Q, Xiao D, et al. Interaction mechanism and intervention strategy between metabolic dysfunction-associated steatotic liver disease and intestinal microbiota. Front Microbiol 2025; 16: 1597995.
83. Chan KE, Ong EYH, Chung CH, et al. Longitudinal outcomes associated with metabolic dysfunction-associated steatotic liver disease: a meta-analysis of 129 studies. Clin Gastroenterol Hepatol 2024; 22: 488-498.e14.
84. Bilson J, Mantovani A, Byrne CD, et al. Steatotic liver disease, MASLD and risk of chronic kidney disease. Diabetes Metab 2024; 50: 101506.
85. Bian H, Ma J, Qu S, et al. The evolving concept from Cardiovascular-kidney-metabolic syndrome to metabolic associated liver-cardiovascular-kidney syndrome: insights from endocrinology. Rev Endocr Metab Disord Published online February 2, 2026.
86. Theodorakis N, Nikolaou M. From cardiovascular-kidney-metabolic syndrome to cardiovascular-renal-hepatic-metabolic syndrome: proposing an expanded framework. Biomolecules 2025; 15: 213.
87. Porst H, Reisman Y, editors. The ESSM Syllabus of Sexual Medicine. Amsterdam: Medix Publishers; 2012.
88. Kolotkin RL, Zunker C, Østbye T. Sexual functioning and obesity: a review. Obesity (Silver Spring) 2012; 20: 2325-2333.
89. Saadedine M, Faubion SS, Grach SL, et al. Association between obesity and female sexual dysfunction: a review. Sex Med Rev 2024; 12: 154-163.
90. Li H, Xu W, Wang T, et al. Effect of weight loss on erectile function in men with overweight or obesity: a meta-analysis of randomised controlled trials. Andrologia 2022; 54: e14250.
91. Ng Tang Fui M, Hoermann R, Prendergast LA, et al. Testosterone treatment in dieting obese men with low testosterone levels: randomized placebo-controlled trial. Int J Obes 2017; 41: 420-426.

92. Aversa A, Francomano D, Bruzziches R, et al. Effects of vardenafil on sexual distress in men with obesity. Int J Impot Res 2012; 24: 122-125.
93. Biernikiewicz M, Szuster E, Pawlikowska-Gorzelańczyk A, et al. Prevalence and incidence of erectile dysfunction in men with overweight and obesity: a systematic literature review. Obes Rev 2026; 27: e70053.
94. Salari N, Hasheminezhad R, Sedighi T, et al. The global prevalence of sexual dysfunction in obese and overweight women: a systematic review and meta-analysis. BMC Womens Health 2023; 23: 375.
95. Ferrández Infante A, Novella Arribas B, Khan KS, et al. Obesity and female sexual dysfunctions: a systematic review with meta-analysis. Semergen 2023; 49: 102022.
96. Gao Z, Liang Y, Deng W, et al. Impact of bariatric surgery on female sexual function in obese patients: a meta-analysis. Obes Surg 2020; 30: 352-364.
97. Aversa A, Bruzziches R, Francomano D, et al. Weight loss by multidisciplinary intervention improves endothelial and sexual function in obese fertile women. J Sex Med 2013; 10: 1024-1033.
98. Esposito K, Giugliano F, Di Palo C, et al. Effect of lifestyle changes on erectile dysfunction in obese men: a randomized controlled trial. JAMA 2004; 291: 2978-2984.
99. Loh HH, Shahar MA, Loh HS, et al. Female sexual dysfunction after bariatric surgery in women with obesity: a systematic review and meta-analysis. Scand J Surg 2022; 111: 14574969211072395.
100. Xu J, Wu Q, Zhang Y, et al. Effect of bariatric surgery on male sexual function: a systematic review and meta-analysis. Sex Med 2019; 7: 270-281.
101. Syed AH, Chandnani A, Khan A, et al. Association of weight loss with improved sexual function in females. Cureus 2021; 13: e16849.
102. American Diabetes Association Professional Practice Committee. 8. Obesity and weight management for the prevention and treatment of type 2 diabetes: standards of care in diabetes – 2025. Diabetes Care 2025; 48: 167-180.
103. American Diabetes Association Professional Practice Committee for Obesity. Pharmacologic treatment of obesity in adults: Standards of care in overweight and obesity. BMJ Open Diabetes Res Care 2026; 13 (Suppl 1): e005729.
104. Baum A, Scarpa J, Bruzelius E, Tamler R, Basu S, Faghmous J. Targeting weight loss interventions to reduce cardiovascular complications of type 2 diabetes: a machine learning-based post-hoc analysis of heterogeneous treatment effects in the look AHEAD trial. Lancet Diabetes Endocrinol 2017; 5: 808-815.
105. Blüher M. An overview of obesity-related complications: the epidemiological evidence linking body weight and other markers of obesity to adverse health outcomes. Diabetes Obes Metab 2025; 27: 3-19.
106. Global Cardiovascular Risk Consortium, Magnussen C, Ojeda FM, et al. Global effect of modifiable risk factors on cardiovascular disease and mortality. N Engl J Med 2023; 389: 1273-1285.
107. Taylor R. Type 2 diabetes and remission: practical management guided by pathophysiology. J Intern Med 2021; 289: 754-770.
108. Malhotra A, Grunstein RR, Fietze I, et al. Tirzepatide for the treatment of obstructive sleep apnea and obesity. N Engl J Med 2024; 391: 1193-1205.
109. Miranda S, Choudhari J, Chauhan N, Parmar MS. Impact of semaglutide on lipid profiles in overweight and obese non-diabetic adults: a systematic review and meta-analysis of randomized controlled trials. Eur J Pharmacol 2025; 1003: 177953.
110. Hampl SE, Hassink SG, Skinner AC, et al. Clinical practice guideline for the evaluation and treatment of children and adolescents with obesity. Pediatrics 2023; 151: e2022060640.
111. Nishi SK, Kavanagh ME, Ramboanga K, et al. Effect of digital health applications with or without gamification on physical activity and cardiometabolic risk factors: a systematic review and meta-analysis of randomized controlled trials. EClinicalMedicine 2024; 76: 102798.
112. Norman K, Burrows L, Chepulis L, et al. Understanding weight management experiences from patient perspectives: qualitative exploration in general practice. BMC Prim Care 2023; 24: 45.
113. Ramos-Lopez O, Martinez-Urbistondo D, Navas-Carretero S, et al. Health and liver diagnostic markers influencing glycemia in subjects with prediabetes: preview study. Diagnostics (Basel) 2024; 14: 2895.
114. Aroda VR, Krause-Steinrauf H, Kazemi EJ, et al. Clinical and metabolic characterization of adults with type 2 diabetes by age in the GRADE cohort. Diabetes Care 2022; 45: 1512-1521.
115. Brauchmann J, Laudenbach L, Kapp P, et al. Discrepancies between recommendations in evidence-based guidelines for the management of obesity in adolescents and adults: an evidence map. Obes Rev 2025; 26: e13945.
116. Tuccinardi D, Masi D, Watanabe M, et al. Precision obesity medicine: a phenotype-guided framework for pharmacologic therapy across the lifespan. J Endocrinol Invest 2025; 48: 2761-2798.
117. American Diabetes Association Professional Practice Committee for Diabetes. 5. Facilitating positive health behaviors and well-being to improve health outcomes: standards of care in diabetes – 2026. Diabetes Care 2026; 49 (Suppl 1): S89-S131.
118. Polskie Towarzystwo Diabetologiczne [Diabetes Poland]. Zalecenia kliniczne dotyczące postępowania u osób z cukrzycą – 2026. Stanowisko Polskiego Towarzystwa Diabetologicznego [Clinical Recommendations on the Management of Individuals with Diabetes – 2026. Position Statement of Diabetes Poland]. Curr Top Diabetes 2026; 6: 1-172.
119. Lean ME, Leslie WS, Barnes AC, et al. 5-year follow-up of the randomised Diabetes Remission Clinical Trial (DiRECT): extension study. Lancet Diabetes Endocrinol 2024; 12: 233-246.
120. American Diabetes Association Professional Practice Committee. 14. Children and adolescents: standards of care in diabetes – 2025. Diabetes Care 2025; 48 (Suppl 1): S283-S305.
121. International Society for Pediatric and Adolescent Diabetes (ISPAD). ISPAD clinical practice consensus guidelines 2022-2024: Nutrition, obesity, and type 2 diabetes in children and adolescents. Pediatr Diabetes 2022-2024; 23 (Suppl 27): 1-350.
122. Kelly AS, Auerbach P, Barrientos-Perez M, et al. A framework for pediatric obesity management. N Engl J Med 2024; 390: 451-463.
123. Skrzypek M, Krzyszycha RM, Goral K, et al. Nutritional intervention for management of obesity in children and adolescents. Med Og Nauk Zdr 2021; 27: 13-22.
124. Cheong L, Law LSC, Tan LYL, et al. Medical nutrition therapy for women with gestational diabetes: current

practice and future perspectives. Nutrients 2025; 17: 1210.
125. Calcaterra V, Verduci E, Milanta C, et al. Benefits of the Mediterranean diet on inflammaging in childhood obesity. Nutrients 2024; 16: 1286.
126. Yao Q, de Araujo CD, Juul F, et al. Isocaloric replacement of ultraprocessed foods and weight loss in the POUNDS lost trial. Obesity (Silver Spring) 2024; 32: 1281-1289.
127. Rychlik E, Stoś K, Woźniak A, et al. Normy żywienia dla populacji Polski [Nutritional norms for the Polish population]. Narodowy Instytut Zdrowia Publicznego PZH-PIB; 2024.
128. Sullivan VK, Kim H, Caulfield LE, et al. Plant-based dietary patterns and incident diabetes in the ARIC study. Diabetes Care 2024; 47: 803-809.
129. KDIGO 2022 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney International; 2022.
130. KDOQI Clinical Practice Guideline for Nutrition in CKD: 2020 Update. Am J Kidney Dis 2020; 76 (Suppl 1): S1-S107.
131. Pilla SJ, Yeh HC, Mitchell CM, et al.; DASH4D Collaborative Research Group. Dietary patterns, sodium reduction, and blood pressure in type 2 diabetes: the DASH4D randomized clinical trial. JAMA Intern Med 2025; 185: 937-946.
132. Lohner S, Kuellenberg de Gaudry D, Toews I, et al. Non-nutritive sweeteners for diabetes mellitus. Cochrane Database Syst Rev 2020; 5: CD012885.
133. Weight gain during pregnancy. Committee opinion no. 548. American College of Obstetricians and Gynecologists. Obstet Gynecol 2013; 121: 210-212.
134. Llamosas-Falcón L, Rehm J, Bright S, et al. Alcohol consumption, BMI, and type 2 diabetes: systematic review and dose-response meta-analysis. Diabetes Care 2023; 46: 2076-2083.
135. AL-Mhanna SB, Batrakoulis A, Wan Ghazali WS, et al. Effects of combined aerobic and resistance training on glycemic control, blood pressure, inflammation, cardiorespiratory fitness and quality of life in patients with type 2 diabetes and overweight/obesity: a systematic review and meta-analysis. PeerJ 2024; 12: e17525.
136. Chen Y, Chen Z, Pan L, et al. Effect of moderate and vigorous aerobic exercise on incident diabetes in adults with obesity: a 10-year follow-up of a randomized clinical trial. JAMA Intern Med 2023; 183: 272-275.
137. Mian Li, Jie Li, Yu Xu, et al. Effect of 5:2 regimens: Energy-Restricted diet or low-volume high-intensity interval training combined with resistance exercise on glycemic control and cardiometabolic health in adults with overweight/obesity and type 2 diabetes: a three-arm randomized controlled trial. Diabetes Care 2024; 47: 1074-1083.
138. Warnick JL, Darling KE, Swartz Topor L, Jelalian E. Barriers to healthy behaviors: perspectives from teens with comorbid type 1 diabetes and overweight/obesity, caregivers, and pediatric endocrinologists. J Pediatr Psychol 2024; 49: 874-881.
139. Stanford KI, Goodyear LJ. Exercise and type 2 diabetes: molecular mechanisms regulating glucose uptake in skeletal muscle. Adv Physiol Educ 2014; 38: 308-314.
140. WHO guidelines on physical activity and sedentary behaviour. Available at: https://apps.who.int/iris/bitstream/handle/10665/336656/9789240015128-eng.pdf.
141. Stein MJ, Weber A, Bamberg F, et al. Diurnal timing of physical activity in relation to obesity and diabetes in the German National Cohort (NAKO). Int J Obes (Lond) 2025; 49: 921-930.
142. Zihao H, Xiaodong Z, Rihua H, et al. Physical activity and weight loss among adults with type 2 diabetes and overweight or obesity. A post hoc analysis of the look AHEAD trial. JAMA Network Open 2024; 7: e240219.
143. Butryn ML, Webb V, Wadden TA. Behavioral treatment of obesity. Psychiatr Clin North Am 2011; 34: 841-859.
144. Wadden TA, Tronieri JS, Butryn ML. Lifestyle modification approaches for the treatment of obesity in adults. Am Psychol 2020; 75: 235-251.
145. Adam TC, Epel ES. Stress, eating and the reward system. Physiol Behav 2007; 91: 449-458.
146. Volkow ND, Wang GJ, Baler RD. Reward, dopamine and the control of food intake: implications for obesity. Trends Cogn Sci 2011; 15: 37-46.
147. Crone C, Fochtmann LJ, Attia E, et al. The American Psychiatric Association practice guideline for the treatment of patients with eating disorders. Am J Psychiatry 2023; 180: 167-171.
148. Hudson JI, Hiripi E, Pope HG Jr, et al. The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. Biol Psychiatry 2007; 61: 348-358.
149. Chaput JP, McHill AW, Cox RC, et al. The role of insufficient sleep and circadian misalignment in obesity. Nat Rev Endocrinol 2023; 19: 82-97.
150. Peppard PE, Young T, Barnet JH, et al. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol 2013; 177: 1006-1014.
151. Roenneberg T, Allebrandt KV, Merrow M, et al. Social jetlag and obesity. Curr Biol 2012; 22: 939-943.
152. Spiegel K, Tasali E, Penev P, et al. Brief communication: Sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite. Ann Intern Med 2004; 141: 846-850.
153. Riemann D, Espie CA, Altena E, et al. The European insomnia guideline: an update on the diagnosis and treatment of insomnia 2023. J Sleep Res 2023; 32: e14035.
154. Greer SM, Goldstein AN, Walker MP. The impact of sleep deprivation on food desire in the human brain. Nat Commun 2013; 4: 2259.
155. Luppino FS, de Wit LM, Bouvy PF, et al. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. Arch Gen Psychiatry 2010; 67: 220-229.
156. The Global Cardiovascular Risk Consortium. Global effect on cardiovascular risk factors on lifetime estimates. N Engl J Med 2025; 393: 125-138.
157. Jastreboff AM, Aronne LJ, Ahmad NN, et al. SURMOUNT-1 investigators. Tirzepatide once weekly for the treatment of obesity. N Engl J Med 2022; 387: 205-216.
158. Pi-Sunyer X, Astrup A, Fujioka K, et al. SCALE Obesity and Prediabetes NN8022-1839 Study Group. A randomized, controlled trial of 3.0 mg of liraglutide in weight management. N Engl J Med 2015; 373: 11-22.
159. Wilding JPH, Batterham RL, Calanna S, et al.; STEP 1 Study Group. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med 2021; 384: 989-1002.
160. Muller TD, Finnan B, Bloom SR, et al. Glucagon like peptide-1 (GLP-1). Mol Metabolism 2019; 30: 72-130.
161. Lincoff AM, Brown-Frandsen K, Colhoun HM, et al.; SELECT Trial Investigators. Semaglutide and cardio-

vascular outcomes in obesity without diabetes. N Engl J Med 2023; 389: 2221-2232.
162. Torgerson JS, Hauptman J, Boldrin MN, et al. XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an ADJUNCT to lifestyle changes for the prevention of type 2 diabetes in obese patients. Diabetes Care 2004; 27: 155-161.
163. Greenway FL, Fujioka K, Plodkowski RA, et al.; COR-I Study Group. Effect of naltrexone plus bupropion on weight loss in overweight and obese adults (COR-I): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2010; 376: 595-605.
164. Ala M, Moheb Aleaba M. The blood pressure-lowering property of subcutaneous semaglutide: a systematic review, meta-analysis, and meta-regression. J Endocrinol Invest 2025; 48: 283-294.
165. Krumholz HM, de Lemos JA, Sattar N, et al. Tirzepatide and blood pressure reduction: stratified analyses of the SURMOUNT-1 randomised controlled trial. Heart 2024; 110: 1165-1171.
166. Siebenhofer A, Winterholer S, Jeitler K, et al. Long-term effects of weight-reducing drugs in people with hypertension. Cochrane Database Syst Rev 2021; 1: CD007654.
167. 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.
168. Nissen SE, Wolski KE, Prcela L, et al. Effect of naltrexone – bupropion on major adverse cardiovascular events in overweight and obese patients with cardiovascular risk factors. JAMA 2016; 315: 990-1004.
169. Mahar MU, Mahmud O, Ahmed S, et al. The effects of tirzepatide on lipid profile: a systematic review and meta-analysis of randomized controlled trials. J Obes Metab Syndr 2024; 33: 348-359.
170. European Medicines Agency. Available at: https://www.ema.europa.eu/en/documents/other/qsiva-epar-scientific-conclusions-and-grounds-refusal-marketing-authorisation-qsiva_en.pdf (accessed: 27 April 2026).
171. Knowler WC, Barrett-Connor E, Fowler SE, et al.; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med 2002; 346: 393-403.
172. le Roux CW, Astrup A, Fujioka K, et al. Three years of liraglutide versus placebo for diabetes risk reduction and weight management in individuals with prediabetes. Lancet 2017; 389: 1399-1409.
173. Wadden TA, Bailey TS, Billings LK, et al. Effect of subcutaneous semaglutide on weight loss and glycaemic control in adults with overweight or obesity and prediabetes (STEP 3). Diabetes Care 2021; 44: 1042-1051.
174. Rubino DM, Greenway FL, Khalid U, et al. Effect of continued weekly subcutaneous semaglutide vs withdrawal on weight loss maintenance (STEP 4). JAMA 2021; 325: 1414-1425.
175. McGowan BM, Brune JM, Capehorn M, et al. Efficacy and safety of once-weekly semaglutide 2.4 mg versus placebo in people with obesity and prediabetes (STEP 10): a randomised, double-blind, placebo-controlled, multicentre phase 3 trial. Lancet Diabetes Endocrinol 2024; 12: 631-642.
176. Wharton S, Freitas P, Hjelmesæth J, et al. Once-weekly semaglutide 7.2 mg in adults with obesity (STEP UP): a randomised, controlled, phase 3b trial. Lancet Diabetes Endocrinol 2025; 13: 949-963.
177. Packer M, Zile MR, Kramer CM, et al. Tirzepatide for heart failure with preserved ejection fraction and obesity. N Engl J Med 2025; 392: 427-437.
178. Wong VWS, Ekstedt M, Wong GLH, Hagström H. Changing epidemiology, global trends and implications for outcomes of NAFLD. J Hepatol 2023; 79: 842-852.
179. Armstrong MJ, Gaunt P, Aithal GP, et al. Liraglutide safety and efficacy in patients with non-alcoholic steatohepatitis (LEAN): a multicentre, double blind, randomised, placebo-controlled phase 2 study. Lancet 2016; 387: 679-690.
180. Sanyal AJ, Newsome PN, Kliers I, et al. Phase 3 trial of semaglutide in metabolic dysfunction-associated steatohepatitis. N Engl J Med 2025; 392: 2089-2099.
181. Loomba R, Hartman ML, Lawitz EJ, et al. Tirzepatide for metabolic dysfunction-associated steatohepatitis with liver fibrosis. N Engl J Med 2024; 391: 299-310.
182. Furth SL, Colhoun HM, Kanbay M, et al. The relationship between obesity and chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) controversies conference. Kidney Int 2026; 109: 442-464.
183. Grant CH, Bell S. Obesity and chronic kidney disease: the dual epidemic in cardiovascular health. Eur Cardiol 2025; 20: e28.
184. Camilleri B, Bridson JM, Sharma A, Halawa A. From chronic kidney disease to kidney transplantation: the impact of obesity and its treatment modalities. Transplant Rev (Orlando) 2016; 30: 203-211.
185. Abasheva D, Ortiz A, Fernandez-Fernandez B. GLP-1 receptor agonists in patients with chronic kidney disease and either overweight or obesity. Clin Kidney J 2024; 17: 19-35.
186. Alicic RZ, Neumiller JJ, Tuttle KR. GLP-1 receptor agonists and next-generation metabolic hormone therapies in chronic kidney disease. Nat Rev Nephrol 2026; 22: 265-282.
187. Bergmann NC, Davies MJ, Lingvay I, Knop FK. Semaglutide for the treatment of overweight and obesity: a review. Diabetes Obes Metab 2023; 25: 18-35.
188. Thong KY, Walton C, Ryder REJ. Safety and efficacy of liraglutide 1.2 mg in patients with mild and moderate renal impairment: the ABCD nationwide liraglutide audit. Pract Diab 2013; 30: 71-76.
189. Cherney DZI, Hadjadj S, Lawson J, et al. Hemoglobin A1c reduction with the GLP-1 receptor agonist semaglutide is independent of baseline eGFR: post hoc analysis of the SUSTAIN and PIONEER programs. Kidney Int Rep 2022; 7: 2345-2355.
190. Perkovic V, Tuttle KR, Rossing P, et al. Effects of semaglutide on chronic kidney disease in patients with type 2 diabetes. N Engl J Med 2024; 391: 109-121.
191. Apperloo EM, Tuttle KR, Pavo I, et al. Tirzepatide associated with reduced albuminuria in participants with type 2 diabetes: pooled post hoc analysis from the randomized active- and placebo-controlled SURPASS-1-5 clinical trials. Diabetes Care 2025; 48: 430-436.
192. American Diabetes Association Professional Practice Committee for Diabetes. Chapter 11. Chronic Kidney Disease and Risk Management: Standards of Care in Diabetes-2026 Diabetes Care 2026; 49 (Suppl.): S246-S260.
193. Chintam K, Chang AR. Strategies to treat obesity in patients with CKD. Am J Kidney Dis 2021; 77: 427-439.
194. Drug and Therapeutics Bulletin. Naltrexone/bupropion for obesity. DTB 2017; 55: 126-129.

195. European Medicines Agency. Mysimba (naltrexone hydrochloride/bupropion hydrochloride): product information (Article 20 procedure – product information). EMA; 2025 (updated document).
196. Kosiborod MN, Abildstrøm SZ, Borlaug BA, et al.; STEP-HFpEF Trial Committees and Investigators. Semaglutide in patients with heart failure with preserved ejection fraction and obesity. N Engl J Med 2023; 389: 1069-1084.
197. Marso SP, Daniels GH, Brown-Frandsen K, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. N Engl J Med 2016; 375: 311-322.
198. Nicholls SJ, Pavo I, Bhatt DL, et al. Cardiovascular outcomes with tirzepatide versus dulaglutide in type 2 diabetes. N Engl J Med 2025; 393: 2409-2420.
199. Visseren FLJ, Mach F, Smulders YM, et al. 2021 ESC guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J 2021; 42: 3227-3337.
200. 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.
201. Garvey WT, Frias JP, Jastreboff AM, et al. Tirzepatide once weekly for the treatment of obesity in people with type 2 diabetes (SURMOUNT-2): a double-blind, randomised, multicentre, placebo-controlled, phase 3 trial. Lancet 2023; 402: 613-626.
202. Lingvay I, Bergenheim SJ, Buse JB, et al. Once-weekly semaglutide 7·2 mg in adults with obesity and type 2 diabetes (STEP UP T2D): a randomised, controlled, phase 3b trial. Lancet Diabetes Endocrinol 2025; 13: 935-948.
203. Kueh MTW, Chew NWS, Al-Ozairi E, le Roux CW. The emergence of obesity in type 1 diabetes. Int J Obes (Lond) 2024; 48: 289-301.
204. Dahlstrom EH, Sandholm N, Forsblom CM, et al. Body mass index and mortality in individuals with type 1 diabetes. J Clin Endocrinol Metab 2019; 104: 5195-5204.
205. Karamanakos G, Kokkinos A, Dalamaga M, et al. Highlighting the role of obesity and insulin resistance in type 1 diabetes and its associated cardiometabolic complications. Curr Obes Rep 2022; 11: 180-202.
206. Livingstone SJ, Looker HC, Hothersall EJ, et al. Risk of cardiovascular disease and total mortality in adults with type 1 diabetes: Scottish registry linkage study. PLoS Med 2012; 9: e1001321.
207. Mathieu C, Zinman B, Hemmingsson JU, et al. Efficacy and safety of liraglutide added to insulin treatment in type 1 diabetes: the ADJUNCT ONE Treat-To-Target randomized trial. Diabetes Care 2016; 39: 1702-1710.
208. Ahrén B, Hirsch IB, Pieber TR, et al. Efficacy and safety of liraglutide added to capped insulin treatment in subjects with type 1 diabetes: the ADJUNCT TWO randomized trial. Diabetes Care 2016; 39: 1693-1701.
209. Park J, Ntelis S, Yunasan E, et al. Glucagon-like pepti-de 1 analogues as adjunctive therapy for patients with type 1 diabetes: an updated systematic review and meta-analysis. J Clin Endocrinol Metab 2023; 109: 279-292.
210. Purcell AR, Zhen Xi M, Wong J, et al. Glucagon-like peptide-1 receptor agonist treatment reduces body weight and improves glycaemic outcomes in patients with concurrent overweight/obesity and type 1 diabetes: a systematic review and meta-analysis. Diabetes Obes Metab 2026; 28: 296-305.
211. Tan X, Pan X, Wu X, et al. Glucagon-like peptide-1 receptor agonists as add-on therapy to insulin for type 1 diabetes mellitus. Front Pharmacol 2023; 14: 975880.
212. Dutta D, Karmul-Hasan ABM, Jindal R, et al. Impact of semaglutide use on glycemic and metabolic profile in adults with type 1 diabetes having overweight or obesity: a systematic review and meta-analysis. Medicine (Baltimore) 2025; 104: e46446.
213. Snaith JR, Frampton R, Samocha-Bonet D, et al. Tirzepatide in adults with type 1 diabetes: a phase 2 randomized placebo-controlled clinical trial. Diabetes Care 2026; 49: 161-170.
214. Galli M, Benenati S, Laudani C, et al. Cardiovascular effects and tolerability of GLP-1 receptor agonists: a systematic review and meta-analysis of 99,599 patients. J Am Coll Cardiol 2025; 86: 1805-1819.
215. Pasqua MR, Tsoukas MA, Kobayati A, et al. Subcutaneous weekly semaglutide with automated insulin delivery in type 1 diabetes: a double-blind, randomized, crossover trial. Nat Med 2025; 31: 1239-1245.
216. Pasqua MR, Tsoukas MA, Haidar A. Changes to insulin requirements over time with semaglutide in adults with type 1 diabetes on insulin pump therapy: a post-hoc analysis of a double-blinded, randomised, crossover trial. Diabetes Obes Metab 2026; 28: 427-433.
217. Shah VN, Peters AL, Umpierrez GE, et al. Consensus report on glucagon-like peptide-1 receptor agonists as adjunctive treatment for individuals with type 1 diabetes using an automated insulin delivery system. J Diabetes Sci Technol 2025; 19: 191-216.
218. Malhotra R, Garcia de Paredes J, Smith A, et al. Obesity epidemic and its impact on female fertility: current understanding and future directions. Cureus 2025; 17: e87283.
219. Pirkola J, Pouta A, Bloigu A, et al. Risks of overweight and abdominal obesity at age 16 years associated with prenatal exposures to maternal prepregnancy overweight and gestational diabetes mellitus. Diabetes Care 2010; 33: 1115-1121.
220. Filippi-Arriaga F, Agrawal N, Rodriguez-Martins D, et al. EASO Position Statement: Women with Obesity across the Reproductive Life – Fertility, Preconception, Pregnancy, Postpartum, and Breastfeeding. Obes Facts 2025; 18: 625-639.
221. Maxwell CV, Shirley R, O'Higgins MC, et al.; on behalf of the FIGO Committee on Impact of Pregnancy on Long-term Health and the FIGO Division of Maternal and Newborn Health. Management of obesity across women's life course: FIGO Best Practice Advice. Int J Gynecol Obstet 2023; 160 (Suppl 1): 35-49.
222. Bomba-Opon D, Gutaj P, Kedzia M, et al. Guidelines of the Polish Society of Gynecologists and Obstetricians on the obstetric care of women with obesity. Ginekol Pol 2023; 94: 1011-1029.
223. Wyckoff JA, Lapolla A, Asias-Dinh BD, et al. Preexisting diabetes and pregnancy: an Endocrine Society and European Society of Endocrinology joint clinical practice guideline. Eur J Endocrinol 2025; 193.
224. Araszkiewicz A, Borys S, Broncel M, et al. Clinical Recommendations on the Management of Individuals with Diabetes – 2026. Position Statement of Diabetes Poland. Current Topics in Diabetes 2026; 6: 1-172.
225. Jatin CH, Beniwal SS, Pithalla LB, et al. Managing obstetric and gynecologic complications in obese women: evidence-based strategies for optimizing outcomes and reducing risks. Ann Med Surg 2025; 87: 3586-3595.

226. Papaetis GS, Kyriacou A. GLP-1 receptor agonists, polycystic ovary syndrome, and reproductive dysfunction: current research and future horizons. Adv Clin Exp Med 2022; 31: 1265-1274.
227. Claire H, Parker BS, Slattery C, et al. Glucagon-like peptide 1 (GLP-1) receptor agonists' use during pregnancy: safety data from regulatory clinical trials. J Pharmacol 2025; 27: 4102-8.
228. Drummond RF, Seif K, Reece A. Glucagon-like peptide-1 receptor agonist use in pregnancy – a review. AJOG 2025; 232: 17-25.
229. Mandal L, Udby Andersen L, Møller Luef B, et al. Impact of semaglutide exposure on fetal and neonatal outcomes in pregnant women: a systematic review. Eur J Obstet Gynecol Reprod Biol 2026; 317: 114836.
230. National Institute for Health and Care Excellence (NICE). Tirzepatide: local formulary information. 2024. Available at: https://www.nice.org.uk/guidance/ta1026/resources/tirzepatide-local-formulary-information-pdf-17647359110341.
231. Dao K, Shechtman S, Weber-Schoendorfer C, et al. Use of GLP1 receptor agonists in early pregnancy and reproductive safety: a multicentre, observational, prospective cohort study based on the databases of six teratology information services. BMJ Open 2024; 14: e083550.
232. Muller DRP, Stenvers DJ, Malekzadeh A, et al. Effects of GLP-1 agonists and SGLT2 inhibitors during pregnancy and lactation on offspring outcomes: a systematic review of the evidence. Front Endocrinol 2023; 14: 1215356.
233. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. Diabetes Care 2004; 27: 596-601.
234. Cooper SJ, Reynolds GP, Barnes T, et al. BAP guidelines on the management of weight gain and metabolic disturbances associated with psychosis and antipsychotic drug treatment. J Psychopharmacol 2016; 30: 717-748.
235. DeJongh BM. Clinical pearls for the monitoring and treatment of antipsychotic-induced metabolic syndrome. Ment Health Clin 2021; 11: 311-319.
236. Pillinger T, McCutcheon RA, Vano L, et al. Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia: a systematic review and network meta-analysis. Lancet Psychiatry 2020; 7: 64-77.
237. American Psychiatric Association. The American Psychiatric Association practice guideline for the treatment of patients with schizophrenia. Am J Psychiatry 2021; 178: 868-872.
238. Carolan A, Hynes-Ryan C, Agarwal SM, et al. Metformin for the prevention of antipsychotic-induced weight gain: guideline development and consensus validation. Schizophr Bull 2025; 51: 1193-1205.
239. Bak M, Fransen A, Janssen J, et al. Glucagon-like peptide-1 receptor agonists for antipsychotic-induced weight gain: a systematic review and meta-analysis. Acta Psychiatr Scand 2024; 149: 85-96.
240. Larsen JR, Vedtofte L, Jakobsen MSL, et al. Effect of liraglutide treatment on prediabetes and overweight or obesity in clozapine- or olanzapine-treated patients with schizophrenia spectrum disorder. JAMA Psychiatry 2017; 74: 719-728.
241. Patino LR, Strawn JR, Adler CM, et al. Exenatide for olanzapine-associated weight gain in severe mental illness: randomized placebo-controlled trial. Diabetes Obes Metab 2025; 27: 1123-1132.
242. Siskind DJ, Russell AW, Gamble C, et al. Treatment of clozapine-associated obesity and diabetes with exenatide once weekly: a randomized controlled trial. Diabetes Obes Metab 2018; 20: 1050-1055.
243. Vasiliu O. Therapeutic management of atypical antipsychotic-related metabolic dysfunctions using GLP-1 receptor agonists: a systematic review. Exp Ther Med 2023; 26: 355.
244. Varghese JS, Goldsmith DR, Cotes RO, et al. Weight change from incretin-based weight loss medications across categories of second-generation antipsychotics. Int J Obes (Lond) 2025; 49: 2544-2548.
245. Dong K, Wang S, Qu C, et al. Schizophrenia and risk of type 2 diabetes: a systematic review and meta-analysis. Psychoneuroendocrinology 2024; 158: 106115.
246. Jackson CA, Fleetwood K, Kerssens J, et al. Incidence of type 2 diabetes in people with a history of hospitalization for major mental illness in scotland, 2001-2015: a retrospective cohort study. Diabetes Care 2019; 42: 1879-1885.
247. Lindekilde N, Rutters F, Eriksson L, et al. Psychiatric disorders as risk factors for type 2 diabetes: an umbrella review. Diabetes Res Clin Pract 2021; 176: 108855.
248. Janez A, Muzurovic E, Bogdanski P, et al. Modern management of cardiometabolic continuum: from overweight/obesity to prediabetes/type 2 diabetes mellitus. Recommendations from the Eastern and Southern Europe Diabetes and obesity expert group. Diabetes Ther 2024; 15: 1865-1892.
249. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric/metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow up of an open-label, single-centre, randomised controlled trial. Lancet 2015; 386: 964-973.
250. De Luca M, Shikora S, Eisenberg D, et al. Scientific evidence for the updated guidelines on indications for metabolic and bariatric surgery (IFSO/ASMBS). Surg Obes Relat Dis 2024; 20: 991-1025.
251. Eisenberg D, Shikora SA, Aarts E, et al. 2022 American Society for Metabolic and Bariatric Surgery (ASMBS) and International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO): indications for metabolic and bariatric surgery. Surg Obes Relat Dis 2022; 18: 1345-1356.
252. Rubino F, Nathan DM, Eckel RH, et al. Metabolic surgery in the treatment algorithm for type 2 diabetes: a joint statement by international diabetes organizations. Diabetes Care 2016; 39: 861-877.
253. Pratt JSA, Browne A, Browne NT, et al. ASMBS pediatric metabolic and bariatric surgery guidelines, 2018. Surg Obes Relat Dis 2018; 14: 882-901.
254. Zaveri H, Surve A, Cottam D, et al. Mid-term 4-year outcomes with single anastomosis duodenal-ileal bypass with sleeve gastrectomy surgery at a single US center. Obes Surg 2018; 28: 3062-3072.
255. Adams TD, Gress RE, Smith SC, et al. Long term mortality after gastric bypass surgery. N Engl J Med 2007; 357: 753-761.
256. Arterburn DE, Olsen MK, Smith VA, et al. Association between bariatric surgery and long-term survival. JAMA 2015; 313: 62-70.
257. Sjostrom L, Lindroos AK, Peltonen M, et al.; Swedish Obese Subjects Study Scientific Group. Lifestyle, dia-

betes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med 2004; 351: 2683-2693.
258. Sjostrom L, Narbro K, Sjostrom CD, et al.; Swedish Obese Subjects Study. Effects of bariatric surgery on mortality in swedish obese subjects. N Engl J Med 2007; 357: 741-752.
259. Schauer PR, Bhatt DL, Kirwan JP, et al.; STAMPEDE Investigators. Bariatric surgery versus intensive medical therapy for diabetes – 5-year outcomes. N Engl J Med 2017; 376: 641-651.
260. Parmar C, Appel S, Lee L, et al. Choice of bariatric surgery in patients with obesity and type 1 diabetes mellitus? An up-to-date systematic review. Obes Surg 2022; 32: 3992-4006.
261. Cengiz E, Danne T, Ahmad T, et al. ISPAD clinical practice consensus guidelines 2024: insulin and adjunctive treatments in children and adolescents with diabetes. Horm Res Paediatr 2024; 97: 584-614.
262. Shah AS, Barrientos-Pérez M, Chang N, et al. ISPAD clinical practice consensus guidelines 2024: type 2 diabetes in children and adolescents. Horm Res Paediatr 2024; 97: 555-583.
263. Laffel LM, Danne T, Klingensmith GJ, et al. Efficacy and safety of the SGLT2 inhibitor empagliflozin versus placebo and the DPP-4 inhibitor linagliptin versus placebo in young people with type 2 diabetes (DINAMO): a multicentre, randomised, double-blind, parallel group, phase 3 trial. Lancet Diabetes Endocrinol 2023; 11: 169-181.
264. Tamborlane WV, Barrientos-Pérez M, Fainberg U, et al. Liraglutide in children and adolescents with type 2 diabetes. N Engl J Med 2019; 381: 637-646.
265. Hannon TS, Chao LC, Barrientos-Pérez M, et al. Efficacy and safety of tirzepatide in children and adolescents with type 2 diabetes (SURPASS-PEDS): a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet 2025; 406: 1484-1496.
266. Haqq AM, Muehlbauer MJ, Clément K, et al. Setmelanotide in Bardet – Biedl syndrome and Alström syndrome: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Diabetes Endocrinol 2022; 10: 859-868.
267. Cooper DM, Rothstein MA, Amin A, et al. Unintended consequences of glucagon-like peptide-1 receptor agonist medications in children and adolescents: a call to action. J Clin Transl Sci 2023; 7: e184.
268. Kelly AS, Auerbach P, Barrientos-Pérez M, et al. A randomized, controlled trial of liraglutide for adolescents with obesity. N Engl J Med 2020; 382: 2117-2128.
269. Weghuber D, Barrett T, Barrientos-Pérez M, et al. Once-weekly semaglutide in adolescents with obesity. N Engl J Med 2022; 387: 2245-2257.
270. American Diabetes Association Professional Practice Committee. 13. Older adults: Standards of care in diabetes – 2026. Diabetes Care 2026; 49 (Suppl 1): S277-S296.
271. Di Vincenzo O, Minnetti M, Baker JL, et al. European Association for the Study of Obesity (EASO) position statement on the diagnosis and management of obesity in older adults. Obes Facts 2025; 1-20.
272. Narodowy Instytut Zdrowia Publicznego PZH-PIB [National Institute of Public Health PZH-NRI]. Normy żywienia dla populacji Polski [Nutritional norms for the Polish population]. Warsaw: NIZP PZH-PIB; 2024.
273. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults. N Engl J Med 2011; 364: 1218-1229.
274. Koopmans L, van Oppenraaij S, Heijmans MWF, et al. Dietary protein intake and distribution patterns in community-dwelling older adults. Clin Nutr 2025; 47: 177-184.
275. Mozaffarian D, Agarwal M, Aggarwal M, et al. Nutritional priorities to support GLP-1 therapy for obesity. Am J Clin Nutr 2025; 122: 344-367.
276. Prado CM, Batsis JA, Donini LM, et al. Sarcopenic obesity in older adults: a clinical overview. Nat Rev Endocrinol 2024; 20: 261-277.
277. Sievenpiper JL, Ard J, Blüher M, et al. Nutritional and lifestyle supportive care recommendations for management of obesity with GLP-1-based therapies. Obesity Pillars 2026; 17: 100228.
278. Villareal DT, Aguirre L, Gurney AB, et al. Aerobic or resistance exercise, or both, in dieting obese older adults. N Engl J Med 2017; 376: 1943-1955.
279. Narodowy Program Zdrowia na lata 2021-2025 [National Health Programme for the years 2021-2025]. Available at: https://www.gov.pl/web/mswia/narodowy-program-zdrowia-na-lata-2021--2025.
280. Knowler WC, Doherty L, Edelstein SL, et al.; DPP/DPPOS Research Group. Long-term effects and effect heterogeneity of lifestyle and metformin interventions on type 2 diabetes incidence over 21 years in the US Diabetes Prevention Program randomised clinical trial. Lancet Diabetes Endocrinol 2025; 13: 469-481.