ANALYTIC REPORT

The system of prevention of cardiovascular diseases and diabetes in Ukraine: current state and ways of improvement

PRophylactive Education & Actions for Cardiovascular diseases and diabeTes (PREACT)

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1. The Prevalence of diabetes and CVD as acute social issues in contemporary Ukraine and worldwide

Non-communicable diseases (NCD) affect people from all population groups and in all parts of the world and have devastating consequences for the health of individuals, families, and communities. Four major NCDs collectively killed about 33.3 million (UI: 24.5–43.3 million) people in 2019, a 28% increase compared to 2000. These major NCDs are cardiovascular disease (17.9 million, UI: 13.4–22.9 million), cancer (9.3 million, UI: 6.9–12.2 million), chronic respiratory disease (4.1 million, UI: 2.9–5.6 million) and diabetes (2.0 million, UI: 1.4–2.7 million). Preventing and controlling these diseases is a major development imperative in the 21st century.

Despite the NCD prevention efforts, there is an upward trend in the number of patients with CVD and type 2 diabetes (T2D), which is a consequence of adverse changes in modern lifestyles (urbanisation, excessive and unbalanced diet, sharp decline in physical activity, chronic stress, etc.) and the resulting increase in obesity prevalence [191].

Since the 1980s, the number of obese people has doubled, and the number of people with T2D has increased by almost 2.5 times [191]. According to WHO estimates, about 1.8 billion people worldwide are overweight, and 590 million are obese, which leads to a significant reduction in life expectancy by 9 years for women and 12 years for men.

In 2021, the International Diabetes Federation estimated the prevalence of diabetes in Ukraine to be 7.3%. According to the National Health Service of Ukraine as of December 2023 the number of patients with DM registered in the Digital healthcare system of Ukraine as of December 12, 2023 was 1,028,824, including 15,150 children under 18 years of age. The number of patients among adults and children receiving insulin in 2023 was 190,367. The number of adult and child patients with diabetes who were first diagnosed in 2023 was 223,769 [104]. Thus, data on diabetes prevalence are much higher than expected; in 2023, the number of newly diagnosed patients with diabetes was 10.8%. These data do not include statistics from the occupied territories and people who left the country due to Russia's military aggression.

Over the past few years, the incidence of CVD has been increasing in Ukraine. In 2021, the total number of patients with myocardial infarction was 42279 and the number of patients with hospital mortality was 6729 (15.92%). In 2022, the number of cases of myocardial infarction was 43843, indicating a significant increase despite a significant outflow of people who needed protection from the war. Nevertheless, a decrease in hospital mortality to 14% can be noted against the background of the introduction of state inpatient treatment programmes.

According to the National Health Service of Ukraine, the number of people with cerebral strokes treated under the programme of medical guarantees was 119821 in 2019, and there was a sharp increase in the number of strokes to 134477 in 2022 [140] despite a reduction in the population of Ukraine by almost 10 million people.

In general, the war in Ukraine has made adjustments to the morbidity of the Ukrainian population over the past two years. Experts in our country have recorded an increase in the number of patients with prediabetes and diabetes mellitus, as well as an increase in cardiovascular complications. It is well established that stress has a significant impact on metabolic functions in the human body. T2D can be triggered by both psychological and physical stress. Stress-induced release of catecholamines and increased serum glucocorticoid levels increase insulin demand and provoke insulin resistance. Persistent uncompensated hyperglycaemia in people with diabetes also can be caused by stress. Blood sugar levels rise due to the release of hormones in response to stress. Although this is an adaptive response for a healthy person, if stress becomes prolonged and chronic, such changes can cause insulin resistance and lead to diabetes and cardiovascular disorders. In addition, diabetes can cause dysregulation of stress hormones.

Currently, prevention of complications of CVD is based on the concept of total cardiovascular risk (CVR) [54]. Its essence lies in an integrated approach to CVR stratification, which allows to identify patients with an unfavourable prognosis and to modify risk factors more aggressively. Correction of cardiovascular risk factors is the main scientific-based strategy for the prevention of CVD. The global healthcare system has accumulated considerable experience in implementing practices for the prevention and correction of CVD in adults, which is reflected in numerous recommendations of the World Health Organization (WHO) and the European Centre for Disease Control and Prevention, as well as leading scientists' studies from around the world [228].

In practice, each of these risk factors is most often considered in isolation as an object of intervention, despite the fact that circulatory system diseases are multifactorial by definition. Meanwhile, there is a lack of research on the correction of these complications. A few studies were conducted, and the views of researchers are contradictory.

The above gives particular importance to the issue of scientific justification, development, and implementation of comprehensive programmes for the primary and secondary prevention of pathological conditions in people who are at clear risk of developing CVD.

2. Factors contributing to the development of DM and CVD in Ukraine

2.1. The impact of stress and of Covid-19 on initiating metabolic alterations and vascular dysfunction

Glucocorticoids (GCs) and catecholamines are the most important adrenal hormones involved in the adaptive response to stress. These hormones do not cause side effects in the acute phase, but in the long-term may disturb glucose homeostasis. This disturbed glucose homeostasis can result in chronic hyperglycaemia, which leads to insulin resistance and type 2 diabetes.

Glucocorticoids act by stimulating gluconeogenesis and causing glycogen depletion in the liver. The main regulator of glucose uptake is the glucose transporter type 4 (GLUT4), which is most abundant in muscles and is stimulated by insulin. In the presence of glucocorticoids, the translocation of GLUT4 to the cell surface in response to insulin is blocked, which leads to a decrease in the ability of skeletal muscle to absorb glucose, causing an increase in blood glucose levels [155].

Chronic stress can cause an increase in the activity of the sympathoadrenal system, which also contributes to a decrease in glucose tolerance and an increase in the likelihood of an acute cardiovascular event. Infusion of catecholamines stimulate an increase in glycolysis and glycogenolysis, increased gluconeogenesis, and may indirectly inhibit glycogenesis through insulin causing hyperglycaemia and hyperlactaemia. Activation of β-adrenergic receptors (AR) by epinephrine and norepinephrine leads to insulin resistance [10]. Since all of the above processes cause an increase in tissue resistance to insulin, they indirectly contribute to the development of type 2 diabetes.

The hypothalamic-pituitary-adrenal (HPA) axis and the sympathoadrenal system play a significant role in mediating stress response. Insulin resistance and stress hyperglycaemia are evolutionary responses to stress. The central and peripheral nervous systems, bone marrow, leukocytes and erythrocytes, and the reticuloendothelial system are among the tissues that use glucose most actively and are insulin-independent cells. In experimental models of haemorrhagic shock, injection of hypertonic glucose solution increased heart function, blood pressure, and survival [126]. By stimulating angiogenesis and antiapoptotic pathways, acute hyperglycaemia can prevent cell death after ischaemia. Both in vitro and in vivo studies have shown that cardiomyocytes exposed to an insulin-free environment with high glucose concentrations are resistant to pathological effects such as ischaemia, hypoxia and calcium overload, indicating that acute hyperglycaemia is an innate protective mechanism [121]. In addition to this, stress hyperglycaemia provides the immune system and brain with a source of energy during stress, trauma, or infection [145]. So, based on the mentioned above, we can say that acute hyperglycaemia during stress can be beneficial for the body and is part of the body's evolution, but under chronic stress conditions, it stimulates insulin production and causes the development of insulin resistance due to numerous factors, including chronic hyperglycaemia. This is the basis for the development of CVDin people with chronic stress.

Chronic stress also plays an immunomodulatory role. The innate and adaptive immune responses can be suppressed or disrupted by the ability of stress to alter the balance of type 1 and type 2 cytokines; GCs can disrupt leukocyte function, reduce the production of cytokines and inflammatory mediators, and suppress the effects of the latter on target tissues [48]. On the other hand, cytokines and other humoral inflammatory mediators are powerful activators of the central stress response, forming a feedback loop through which the immune/inflammatory system interacts with the hypothalamic-pituitary-adrenal axis, especially IL-6 and TNF-α [211].

Stress is not only a potential trigger for T1D but can also affect the compensation of the underlying disease in patients with T1D. In addition to general social stress, patients with T1D experience additional diabetes-specific stress due to daily self-monitoring, adherence to treatment regimens, etc [198].

Self-monitoring in children and adolescents with T1D is constant and complex, requiring the active participation of both patients and caregivers. Learning to cope with stressful events is an important factor in achieving better long-term outcomes in diabetes. Jasser et al. investigated coping strategies in adolescents with type 1 diabetes as predictors of adjustment and glycaemic control. The results showed that higher levels of stress were associated with poor use of adaptive coping strategies. Primary control coping strategies (e.g., problem solving) and secondary control coping strategies (e.g., positive thinking) lead to improved quality of life and reduced depressive symptoms. On the contrary, coping was found to be a significant predictor of glycaemic control [96].

According to the β-cell stress hypothesis, rapid growth, overweight, puberty, physical inactivity, injuries, infection, and glucose overload, all these factors causing increased insulin requirements are potentially significant in the development of T1D. Prolonged stress of the endoplasmic reticulum disrupts insulin synthesis and causes apoptosis of pancreatic β-cells [175].

Although it is not possible to completely eliminate stress, it is possible to prevent it from becoming too severe by using simple daily techniques. It is very important for the physician to encourage patients to engage in appropriate physical activity to reduce stress. Physical activity has been found to play a role in stress management and also has anxiolytic and antidepressant effects. Patients should be encouraged to make lifestyle and dietary changes, which can be a significant factor in reducing stress in patients. Patients can also use various relaxation techniques such as deep breathing, meditation, yoga, etc. Appropriate sleep is a very important part of our lifestyle. It has been found that lack of sleep can lead to increased stress in patients. Patients should be encouraged to make dietary and lifestyle changes that not only reduce obesity but also help to overcome insulin resistance in the body. To reduce calories and fat, patients should choose foods that are high in fibre. They should focus on whole grains, vegetables, fruits, and dairy products.

Another significant factor currently contributing to the development of carbohydrate metabolism disorders is COVID-19. SARS-CoV-2 infection and diabetes are linked in two ways. DMis one of the leading comorbidities that increases the severity of COVID-19. In addition, SARS-CoV-2 infection can trigger pancreatitis and the clinical manifestation of a new type of diabetes in healthy people without genetic immune vulnerability. Taken together, numerous studies show that SARS-CoV-2 infection damages the morphological structure and impairs the function of pancreatic cells.

SARS-CoV-2 infection leads not only to acute illness but also to long-term consequences. In a Canadian study, the authors showed [85] an increase in the incidence of diabetes after SARS-CoV-2 infection. A meta-analysis [189] of reports from the United States, Norway, the United Kingdom, Germany, and multi-site consortia found an overall 66% increase in the incidence of new-onset diabetes after SARS-CoV-2 infection. Another review found that 12 out of 14 population-based studies found a significant increase in the incidence of diabetes after COVID-19, with an excess of 11% to 26% compared to controls. Where sub-analyses were performed, rates were generally higher in men than in women, and new diagnoses tended to occur in the first few months after infection and were more likely in patients with more severe COVID-19 infection [102].

Some studies show that post-COVID-19 diabetes is more severe and more often accompanied by ketoacidosis than diabetes diagnosed before the pandemic [141].

State Institution «V.P. Komisarenko Institute of Endocrinology and Metabolism» has conducted research on the course of the acute period of COVID-19 and the post-COVID period in patients with diabetes mellitus. It has been established that the presence of complications in the acute period of COVID-19 in patients with T2D is mainly observed in overweight and obese patients with increased HbA1c levels and comorbidities. Furthermore, overweight and obesity in patients increases the risk of developing comorbidities and complications in hospital. It was shown that men are 6.3 times more likely to have severe COVID-19 than women. With a BMI of 25.0 to 29.9 kg/m^2, the risk of inpatient complications is 3.4 times higher, and with a BMI of 30.0 or more kg/m^2, the risk is 11.5 times higher than with a BMI of 24.9 or less. Compared with the group of patients with HbA1c of 6.4% or less, the risk of complications is 2.5 times higher in patients with HbA1c levels ranged from 6.5 to 7.0%, 6.3 times higher in patients with HbA1c of 7.1 to 8.0%, and 14.6 times higher in patients with HbA1c of 8.1 or more. During the acute period of COVID-19, overweight and obesity along with carbohydrate metabolism disorders with HbA1c levels higher than 6.4% are significant risk factors for the development of complications in hospital, even without taking into account comorbidities. The presence of comorbidities significantly increases the chances of severe COVID-19 in patients with and without carbohydrate metabolism disorders. The presence of T2D can be considered a risk factor for post-COVID syndrome [151]. In contrast, it was found that the onset of anxiety/depression after COVID-19 is probably not related to the presence of carbohydrate metabolism disorders. Vitamin D levels in patients with T2D did not depend on COVID-19 [201].

Prevention of metabolic disorders is especially important during pandemic. A number of negative trends that have characterised the health of the Ukrainian population in recent years indicate the need to raise awareness of both the population and physicians about risk factors and ways to prevent their harmful effects. There is also a need to continue the research to find new ways of early diagnosis and correction of metabolic disorders.

2.2. The carbohydrate metabolism disorders as a risk factor for cardiovascular complications

Insulin resistance and hyperinsulinaemia are triggers for the development of all subsequent metabolic, haemodynamic and haemostatic disorders. All these negative changes lead to the development of endothelial dysfunction, hypertension, and thrombosis, which cause coronary heart disease (CHD).

Given the peculiarities of the combination of links in this mechanism and the health status of patients, since 2019, the European Society of Cardiology (ESC) guidelines for the management of patients with diabetes, prediabetes, and CVD have proposed ranking patients by cardiovascular risk: moderate, high and very high, with the vast majority (almost 90%) of all patients with T2D being at high and very high risk.

Observations have shown that the risk of developing cardiovascular complications is the same in people with diabetes and in patients with CVD, so recently, diabetes has been increasingly referred to as a cardiovascular disease. Also, diabetes is considered as a pathogenetic link in general disorders of the body, so it is believed that glycaemic control alone does not sufficiently reduce the risk of CHD in diabetes [45]. According to current guidelines, comprehensive correction of glycaemia, hyperlipidaemia, and arterial hypertension (AH) is the main target of therapy aimed at reducing the risk of developing CHD in patients with diabetes.

The increasing prevalence of excessive visceral obesity and obesity-related cardiovascular risk factors is, in turn, closely linked to the rising incidence of cardiovascular disease and type 2 diabetes. The close relationship between increased visceral fat, metabolic disorders, including low-grade inflammation, and cardiovascular disease, and the unique anatomical connection to the portal venous system of the liver has led to intensive attempts to elucidate the specific endocrine functions of visceral fat [45].

Most importantly, an increase in total and visceral fat mass is closely associated with chronic systemic inflammation, in particular, increased production of proinflammatory cytokines such as tumour necrosis factor-α (TNF-α) and interleukin-6 (IL-6) [28]. The increase in adipose tissue mass during weight gain can occur at the cellular level, both by increasing the size of adipocytes (hypertrophy) and by increasing their number (hyperplasia). In addition to simple weight gain, the tissue additionally undergoes a process of remodelling characterised by excess production of extracellular matrix, increased infiltration of immune cells, and a greater pro-inflammatory response.

Another depot that is positively correlated with BMI and waist circumference is epicardial adipose tissue (EAT), and it can be significantly increased even in lean individuals. EAT thickness is positively associated with increased fasting insulin levels, diastolic blood pressure, coronary heart disease, and atrial fibrillation [91; 235].

Obesity and T2Dare independent common risk factors for cerebrovascular disease that require early diagnosis and appropriate treatment [158].

The main effect of elevated BMI is on the vascular endothelium, which is the main regulator of vascular homeostasis, due to its interaction with both circulating cells and those in the vascular wall. Endothelial cells (ECs) are extremely sensitive to any changes in haemodynamic parameters and respond instantly to the release of various biologically active substances.

According to the analysis of ultrasound examination data of the head and neck vessels performed in our centre, the majority of patients with T2Dand obesity showed compaction and thickening of the walls of brachiocephalic vessels and an increase in the frequency of stenotic atherosclerotic lesions in the main head arteries. In 52.27 % of patients, haemodynamically significant stenoses were detected due to the development of atherosclerotic plaques in the extracranial carotid arteries. Of these, the atherosclerotic process in one of the carotid arteries was found in 43.48 % of cases, and in both was found in 13.04 % of cases. Most often (56.52 % of cases), atherosclerotic plaques were localised in the bifurcation of the common carotid artery (the area of the vascular bed with the most developed subendothelial layer).

In these patients with carbohydrate and lipid metabolism disorders, endothelial dysfunction was detected by flow-dependent vasodilation, which may indicate a decrease in the compensatory capacity of regional blood flow. This can be regarded as a response of the vessel wall to haemodynamic load caused by an increase in body weight. Thus, the presence of overweight and obesity is one of the main risk factors for atherosclerotic lesions in patients with type 2 diabetes. One of the leading factors of such changes is the lipid metabolism disorder characteristic of such patients, namely, the accumulation of low-density lipoproteins in the serum may be due to the irreversible non-enzymatic glycosylation of apoproteins (proteins of lipoproteins) in patients with diabetes, which disrupts the receptor interaction between the cells and lipid transport forms. These processes are especially pronounced in overweight patients, as obesity contributes to the deterioration of lipid disorders. Furthermore, glycosylated lipoprotein complexes have an altered antigenic structure. In the arterial intima, modified lipoprotein complexes are absorbed by fixed macrophages, which is accompanied by thickening of the intima-media complex and trigger atherosclerotic plaque development and so-called macroangiopathies, leading to a deterioration in blood supply to organs and tissues, thus causing their chronic and/or ischaemic damage. Glycolysation of protein components in the tissues also causes the damage to the vascular endothelium with impairment of its biological function, i.e. the ability to control regional blood flow at the level of muscle-type arteries depending on the functional needs of the body. The inability of regional mechanisms to provide an appropriate level of blood supply leads to the need to involve systemic levels of haemodynamic regulation, in particular, an increase in systemic blood pressure. Thus, endothelial dysfunction is a marker of the vascular system ability to control the level of optimal blood flow at the regional level. This is of considerable practical importance, as it allows detecting a number of diseases at the preclinical stage of functional changes and monitoring the effectiveness of treatment [150].

Thus, the development and improvement of the methods for the early diagnosis of vascular and metabolic complications can significantly improve the quality of life and prognosis in obese and overweight patients. It was found that overweight patients are at high risk of developing cardiovascular disease in terms of structural and functional damage to the vascular wall and cardiac muscle, and Doppler examination is an effective non-invasive method of early detection of pathological changes to develop methods of prevention and appropriate treatment of cardiovascular disease at the early stages of its development. Timely identification of overweight and treatment can significantly affect the life prognosis and quality of life in this category of patients.

2.3 Obesity and overweight as independent predictors of carbohydrate metabolism disorders and cardiovascular disease

According to the data of the Global Obesity Observatory for 2021, the prevalence of overweight and obesity in Ukraine is: men: obesity – 20.1%, overweight – 37.8%; women: obesity – 29.8%, overweight – 30.4%; adults in general: obesity – 24.8%, overweight – 34.3%; boys under 18: obesity – 2.3%, overweight – 11.5%; girls under 18: obesity - 1.8%, overweight - 8.5% [229].

There are several possible explanations for the rise in obesity: first, increased food availability has led to a significant increase in average daily calorie intake (in the United States, this figure increased by 24.5 %, or ~ 530 calories, between 1970 and 2000) [163]; secondly, a change in diet with an increase in the consumption of refined carbohydrates, sugar, animal and vegetable fats and a decrease in the consumption of fruits, vegetables and legumes; thirdly, the mechanisation of labour and development of transport has significantly decreased energy consumption; fourthly, the improvement of clothing and heating systems has reduced the importance of adaptive thermogenesis [40]. At the same time, the contribution of genetic factors to the development of obesity should not be overestimated: it is only about 20 %. The development of the pandemic of metabolic disorders is mainly due to environmental factors [119].

About 80 % of patients with T2D are overweight or obese. It has been proven that obesity and T2D are pathogenetically closely related. Data from large epidemiological studies confirm the role of overweight in the development of carbohydrate metabolism disorders [107]. Timely weight loss not only slows down the progression from prediabetes to diabetes, but also helps to improve glycaemic control and reduce the need for hypoglycaemic drugs in T2D. Body weight loss is most effective at the early stages of T2D, when β-cell dysfunction is still reversible [152]. According to current concepts, adipose tissue is one of the key links in the development of carbohydrate metabolism disorders. Excessive calorie intake leads to energy storage in the form of fat. Adipose tissue receives up to 90% of all fatty acids consumed with food, which leads to adipocyte remodelling: hypertrophy and hyperplasia to accommodate the increasing amount of triglycerides.

Hypertrophied adipocytes are less sensitive to insulin. They increase the expression of genes for inflammatory proteins and peptides, which leads to an increase in the production of cytokines, chemokines, and other inflammatory mediators, such as 12-lipoxygenase.

Chronic inflammation of adipose tissue is considered to be one of the main factors in the pathogenesis of obesity-related insulin resistance. Several mechanisms are involved in this process. Firstly, the hyperproduction of proinflammatory cytokines characteristic of adipose tissue can lead to the expression of cytokine signal suppressor 3 (SOCS3), which, in turn, blocks the interaction between the insulin receptor and the insulin receptor substrate, thus contributing to insulin resistance [54]. Secondly, proinflammatory cytokines activate numerous intracellular kinases, such as C-Jun-N-terminal kinase (JNK) and κB kinase inhibitor. These serine kinases inhibit insulin action at different levels. An increase in circulating free fatty acids inhibits insulin activity due to serine phosphorylation of the insulin receptor substrate and can lead to insulin resistance in skeletal muscle and liver. The systemic inflammatory response in obesity contributes to a decrease in the mass of functioning β-cells and systemic insulin resistance, which causes T2D [160].

Excess of circulating free fatty acids, which are formed as a result of lipolysis of subcutaneous and visceral adipose tissue, also contribute to the development of insulin resistance in the liver and skeletal muscle [30].

In addition, free fatty acids have a toxic effect on pancreatic β-cells (the so-called lipotoxicity phenomenon), which leads to a loss of the first phase of insulin secretion, suppression of insulin gene expression, acceleration of apoptosis in β-cells, and activation of oxidative stress. Free fatty acids also inhibit the ability of insulin to inhibit gluconeogenesis, which is accompanied by an increase in endogenous glucose production. Lipotoxicity is one of the main reasons for the decrease in the mass of functioning β-cells in patients with T2D [160].

In the last decade of the 20th century, the traditional view of adipose tissue as a passive energy storage has changed significantly. Previously, it was believed that the main role of adipose tissue was to store energy in the form of triglycerides and release it in the form of free fatty acids, depending on the needs of the body. In the late 1980s, it was discovered that adipose tissue is the site of metabolism of sex steroids. The subsequent isolation of a number of active molecules secreted by adipocytes, and especially the discovery of leptin in 1994, convinced us that adipose tissue is a complex, hormonally active organ that plays a crucial role in regulating energy balance and homeostasis of the body (Fig. 1) [164].

The pathogenesis of obesity is based on an imbalance between energy intake and energy expenditure. In humans, individual energy expenditure depends on three factors: the first is the basal metabolic rate, which corresponds to the energy expenditure to maintain basic physiological functions under normal conditions; the second is the specific dynamic effect (thermic effect) of food, which accounts for about 5-10% of total energy expenditure and is associated with additional energy expenditure for digestion; and the third is physical activity associated with the greatest energy expenditure.

Excess energy intake is caused by excessive energy value of diet with a predominance of fats and a disturbed daily dietary regimen. Nowadays, a lot of new research data on the pathogenetic mechanisms of obesity development is emerging. Both the central mechanisms of regulating energy intake and expenditure and the impact of adipose tissue itself on the development and progression of obesity and associated diseases are being studied. Progress in the study of adipocyte biology allows us to consider adipose tissue not a passive energy depot, but an important endocrine organ that plays a key role in energy homeostasis. It synthesises a large number of biologically active substances (adipocytokines), which are considered to be possible mediators of metabolic disorders and endothelial dysfunction.

Obesity can be an independent disease or a syndrome that develops in the setting of other diseases. Obesity and associated metabolic disorders are an urgent problem in modern medicine, as they lead to the development of a number of serious diseases. The most significant of these are type 2 diabetes, CVD, cancer, etc. Thus, body weight loss is one of the main aspects of the treatment of carbohydrate metabolism disorders combined with obesity and obesity-related diseases. Even a small reduction in body weight leads to improved glycaemic control, cardiovascular and metabolic outcomes. Today, the management of T2D is based on lifestyle changes, weight loss medications, and, if indicated, bariatric surgery [202].

2.4. Nutrition as a risk factor for disease development DMand CVD

The industrial revolution and subsequent advancements in animal husbandry and agriculture have changed our diets and the nutritional content of our foods. Improvements food processing technologies have also allowed humans to combine food types and nutrients in novel ways. Today, in the world, including in Ukraine, the Western diet is widespread, which mainly consists of processed food products, soft drinks and fast food products, which are poor in nutrients and rich in energy. This diet also comprises large amounts of red and processed meat, which have been linked to an increased risk of CVD and colorectal cancer [41].

Treatment of obesity is aimed at reducing the risk of CVD and T2D. The first and most important step is to introduce a new lifestyle with changes in diet and physical activity, as well as the adoption of healthy habits. Behavioural interventions make it easier for people to incorporate and maintain these changes into their daily routines. Weight loss has been the primary goal of most intervention studies. Even moderate weight loss (about 7%) was shown to lead to significant reductions in blood pressure, as well as glucose, triglyceride, and total cholesterol levels [37; 157]. In addition, weight loss improves adipokines and inflammatory markers such as adiponectin and tumour necrosis factor alpha levels [232]. A reasonable first goal for obese patients is to lose approximately 10% of initial body weight in six months. If they achieve this goal, insulin resistance will improve along with a reduced risk of metabolic syndrome and CVD. Even smaller weight loss (from 5% to 10% of initial body weight) improves insulin sensitivity by 30 to 60%, thus having an effect greater than that observed with insulin-sensitising drugs [142].

Considering all therapeutic options, calorie restriction is a very effective intervention, as most people with metabolic syndrome are obese and sedentary. Changes in physical activity are always part of lifestyle interventions for people with metabolic syndrome, and current scientific evidence supports the role of exercise as an effective treatment strategy for the syndrome. Along with dietary changes, a regular physical exercise programme also may lead to a reduction in insulin resistance and cardiovascular disease risk [101].

Tab.1 Stepped Approach to Treating Obesity [214; 75].

	BMI 25-26.9 kg/m^2	BMI 27-29.9 kg/m^2	BMI 30-34.9 kg/m^2	BMI 35-39.9 kg/m^2	BMI ≥40 kg/m^2
Diet, activity, and behaviours	+	+	+	+	+
Pharmacotherapy		with comorbidity	+	+	+
Surgery				with comorbidity	+

The data presented below pertains to the dietary strategies and financing, as well as the national food policy in Ukraine as of the year 2022, according to the "Global Food Report for 2022".

Tab. 2 National food policy implemented [75].

Food-based guidelines	Legislation for mandatory salt iodisation	Sugar-sweerened beverage tax
No	No	No
Policy to reduce salt/sodium consumption	Policy to limit saturated fatty acid intake	Policy to eliminate industrially produced trans fatty acids
Yes	Yes	Yes
Policy to reduce the impact of marketing of foods ans beverages high in saturated fats, trans fatty acids, free sugars, or salt on children	Operational policy, strategy, or action plan ti reduce unhealthy diet related to non-communicable diseases	Operational, multisectoral policy, strategy or action plan for non-communicable diseases
No	Yes	Yes

Tab. 3 National policy targets. Inclusion of targets related to the global nutrition targets in national policies [75]

Reduce anaemia among women	Reduce number of infants born with low birth weight	Increase prevalence of exclusive breastfeeding in infants 0-5 months
No	No	Yes
Reduce adolescent and adult overweight	Reduce salt/sodium intake	Reduce raised blood pressure prevalence
Yes	Yes	No
Reduce blood sugar levels/diabetes prevalence	Multisectoral comprehensive nutrition plan	-
No	Yes	-

2.5. Physical inactivity

Physical inactivity is one of the most aggressive, independent risk factors for the development of cardiovascular disease and mortality. According to the World Health Organization (WHO), it accounts for 6% of deaths worldwide (up to 3.18 million per year) [51]. Thus, it was found that regular physical activity compared to a sedentary lifestyle is associated with a 22-36% reduction in overall mortality and a 25-35% reduction in cardiovascular mortality, with the greatest reduction in CVD recorded at high levels of physical activity [118]. According to the WHO, one in four adults in the world is not active enough: 27.5% of adults and 81% of adolescents do not meet the aerobic exercise recommendations provided in the Global Physical Activity Guidelines. It is important to note that the prevalence of physical inactivity is often higher than that of other risk factors. Studies have shown that the population risk of cardiovascular disease associated with a sedentary lifestyle is higher than other risk factors (including high body mass index, smoking, and high blood pressure). According to the results of the international INTERHEART study, regular physical activity contribute to significant reduction of the risk of developing myocardial infarction (MI) [238]. Furthermore, the data of the INTERSTROKE study demonstrate that physical inactivity makes a significant contribution to the risk of stroke along with hypertension [146]. The functional state of the cardiovascular system is extremely sensitive to changes in physical activity levels and habitual exercises.

In Ukraine, there was no significant progress in engaging the population in recreational physical activity until the 21st century. According to official statistics, the number of people engaged in so-called “physical culture” has traditionally been overstated to demonstrate the benefits of the prevailing ideology. The apparent increase in the number of people involved in sports has never corresponded to the level of health of the population. The results of an all-Ukrainian survey show that at the beginning of the 21st century, only 3% of the population aged 16 to 74 had a sufficient level of recreational physical activity (at least 4 to 5 sessions per week, with each session lasting at least 30 minutes), 6% had a moderate level (2 to 3 sessions per week), and 33% had a low level (1 to 2 sessions per week). The majority of the adult population is characterised by hypokinesia. The popularity of sedentary leisure activities is growing among children. According to the report “The Global Status Report on Physical Activity 2022: Country Profiles”, the profile of the Ukraine shows that the prevalence of sedentary behaviour among adolescents aged 11-17 years was 71% for boys and 83% for girls. Sedentary behaviour was typical for 19% of men and 20% of women aged 18-60. For people over 70, the percentage of inactive people was 30% among men and 33% among women. Chronic non-communicable diseases cause 92% of deaths in Ukraine.

2.6. Smoking as a risk factor for metabolic and CVD

Smoking remains a significant public health concern in Ukraine. According to the Global Adult Tobacco Surveys (GATS), smoking prevalence stood at 28.8% in 2010 [206]. This high smoking prevalence is reflected in substantial social costs, with an estimated 85,000 Ukrainians dying from smoking-related diseases in 2010

[156]. Furthermore, smoking causes significant damage to the country's economy, resulting in an annual loss of approximately 3.2% of Ukraine's GDP due to early disability and healthcare expenditures related to smoking-related diseases [76].

In 2017 there was progress in the fight against smoking, as evidenced by a decrease in smoking prevalence to 22.8% [92]. Simultaneously, the use of electronic cigarettes (e-cigarettes), or vaping, has been on the rise among Ukrainian adults. The prevalence of vaping increased from 1.7% in 2010 to 3% in 2017 [92; 206].

In 2017, to tackle the health and economic burden of smoking Ukraine adopted a plan to annually increase the specific excise tax on cigarettes until 2025 [208]. In addition, Ukraine started taxing e-cigarette liquids with and without nicotine in 2021 [210]. From July 2023, the country prohibited vaping in public places as well as advertising, sponsorship, and promotion of e-cigarettes [209]. The law also banned the sale of flavored e-liquids other than tobacco flavor, while nicotine concentration was limited to 2%.

At the same time, an increasing number of countries are recognizing the effectiveness of harm reduction policies that enable access to non-cigarette alternatives, such as e-cigarettes [127; 138; 184]. Recent scientific literature has demonstrated that vaping is a less harmful alternative to smoking [127; 21] and can aid in smoking cessation [33;39; 83; 100;115; 127]. Furthermore, studies have indicated that the associations between vaping and smoking initiation are driven by shared risk factors of tobacco use in general, and e-cigarettes may serve as a substitute for combustible cigarettes, thereby reducing smoking initiation among adolescents and young adults [185]. Moreover, simulation studies found that reductions in smoking prevalence were most pronounced among younger smokers who are also more likely to use e-cigarettes [112; 113; 114; 129].

2.7. Genetic and epigenetic factors in the development of DM and CVD

The 1986 Chernobyl nuclear power plant (ChNPP) accident, the largest in nuclear history, exposed 3.4 million Ukrainians, including 1.2 million children, to ionizing radiation, leading to widespread DNA damage and mutations [77; 233].

This exposure, in particular, has led to increased damage to the genome in children, both evacuees and those continuously exposed to radiation over the past 30 years [70]. Research suggests links between this damage and the development of diabetes and cardiovascular disease (CVD). Studies of clean-up workers show a dose-related increased risk of CVD and cerebrovascular disease [86; 105; 106]. High sensitivity of pancreatic beta cells to radiation may explain the high prevalence of DM(up to 23%) among ChNPP survivors, compared to 3-7% in the general Ukrainian population [98; 26]. Exposure to ionizing radiation, as in cancer treatment, has been associated with insulin resistance and type 2 diabetes [120]. A mouse study suggests that epigenetic mechanisms may play a role in this process [144]. However, there is some, inconsistent, evidence for genetic effects among offspring of exposed persons [20].

Various types of DMand CVD are etiologically heterogeneous diseases with different proportions of hereditary factors and external factors influencing the development of the disease. According to theory, the rise in metabolic diseases is linked to reduced selective pressure from the industrial revolution, leading to an increase in disease-prone alleles in the human genome [38,188].

The genetic architecture of such diseases, including the number, frequency and magnitude of the effect of inherited genetic variants contributing to individual risks, is actively debated in the scientific literature [69; 84; 169; 236], and the degree of inheritance varies widely.

Recent advances in genomic technologies and molecular methods have extended our knowledge on the pathogenesis of these diseases and greatly facilitated the identification of the biomarkers. Modern approaches to the interpretation of genomic data are able to identify gene variants with phenotypic manifestations that contribute to the development of complex diseases such as diabetes and CVD [236]. Modern prediction methods are of great importance for research and clinical applications. A critical assessment of genome interpretation has shown that methods for interpreting missense variants in monogenic diseases are able to assess biochemical effects with maximum accuracy [196]. Molecular genetic analysis allows us to accurately determine the cause of the disease and adjust treatment approaches.

Genetics and epigenetics of diabetes. Type I diabetes (T1D) is an antigen-associated disease with a strong genetic predisposition, the genetic risk factors for which have been thoroughly identified over the past few decades [169]. Twin studies, linkage studies, and genome-wide association studies (GWAS) have highlighted that a significant proportion of T1D risk is genetically determined. The risk of T1D in the general population is 0.4%, while siblings of patients with T1D have a risk of 6-7%; and the risk of T1D is 1.3-4% in children of a female patient and 6-9% in the children of a male patient [136].

About 50 % of T1D heritability is explained by human leukocyte antigen (HLA) alleles, and the rest by several (about 50) non-HLA loci. More than 50 additional loci associated with T1D have been mapped using different approaches (candidate gene studies and GWAS). All identified genetic factors can explain approximately 80% of T1D heritability. In another study, more than 60 loci outside the HLA region were also associated with T1D including common variants identified by GWAS in genes involved in immune regulation [66; 79]. Modern methods for assessing the genetic risk of T1D are based on combining information from HLA and non-HLA alleles to improve diagnostic accuracy, and have been developed and validated in various settings and populations There are several genetic scales that combine risk information from multiple genetic factors to optimise the use of genetic information and ultimately improve the prediction and diagnosis of T1D [169].

The rapidly growing epidemic of T2D and its devastating complications have prompted greater efforts to study the genetics of T2D. There is convincing evidence that individual risk of developing T2D is largely dependent on genetic factors [222]. Inherited genetic characteristics can significantly increase the lifetime risk of developing T2D. The presence of T2Din only one parent increases the risk of developing the disease in offspring by 30% [12] and by 60% if both parents are affected [194]. Monogenic mutations that cause T2D are rare. Most often, they have an impact on the leptin-melanocortin axis, thus affecting the functioning of brain structures responsible for regulating appetite and adipocytes.

In patients with type 2 diabetes, genetic signals mainly regulate the development and functioning of B cells [53; 66; 179]. Numerous GWAS have confirmed that the variants significantly affect islet regulatory elements, and a significant proportion of associations are related to dysregulation of β-cell development and insulin secretion rather than impaired insulin action on tissues [53; 179].

A severe degree of insulin resistance and T2D can occur with autosomal dominant inheritance of mutations in certain genes [29], but most cases of T2Dand obesity are considered polygenic, and the predisposition to their development is due to the presence of single nucleotide polymorphisms (SNPs) [192; 180].

Over the past decade, more than 80 significant associations of gene polymorphisms with T2D have been established [69; 84; 223]. Genome wide association studies allow scoring common variants associated with T2D, but collectively they explain only part of the heritability. The role of low-frequency variants in susceptibility to T2D has not been confirmed [69]. The analyses indicate a large number of associations with T2D among rare coding alleles in genes that cause monogenic diabetes. To date, the largest GWAS on T2D is a meta-analysis of more than 2.5 million individuals, including more than 0.4 million cases of T2D [192]. This study identified 1289 distinct association signals with T2D related to 611 genetic loci [236].

The genome of each population has its own intergenic interactions, so other mutations may have a statistically significant impact on the development of diseases, which requires the establishment of population (ethnic) markers for the development of diseases. Whole-genome studies of the Ukrainian population indicate that the genetic diversity of the Ukrainian population is uniquely shaped by evolutionary and demographic forces and cannot be ignored in future genetic and biomedical research. These data will contribute a huge amount of new information, allowing for the discovery of many new, endemic, and medically relevant alleles. The analysis demonstrates unique combinations of genetic components that may have formed this population [147].

Data from studies in the Ukrainian population indicate that the LEPR Q223R polymorphism is associated with an increased risk of developing T2D, regardless of gender. In women, the LEPR Q223R polymorphism is closely associated with the risk of overweight and obesity: the presence of the G allele (GG homozygote and AG heterozygote) was associated with an increase in BMI >25, as well as higher levels of LDL-C and C-peptide. In contrast, in men, an increase in BMI >25 was found mainly in GG homozygotes. The identified gender differences in the association of the LEPR Q223R polymorphism and the development of overweight encourage further study of sex-associated mechanisms of regulation of adipogenesis and lipid metabolism [191]. It was found that in patients with type 2 diabetes and patients with T2Dcombined with obesity, the carriage of the Pro allele can be determined as a protective factor preventing complications in the clinical course of both diseases, whereas the presence of the GPx1 gene Leu mutant allele either in the homo- or heterozygous state is associated with an increased risk of developing both these diseases and concomitant diabetic and cardiovascular complications with a more unfavourable clinical course of both diseases [162].

Obesity, as one of the prerequisites for the development of diabetes, also has its own genetic predictors. Genetic studies in Ukrainian children aged 6-18 years showed that the presence of four linked SNPs of PNPLA3 (rs738409 C/G, rs738408 C/T, rs4823173 G/A, and rs2072906 A/G) of 14 SNPs identified contribute to the development of metabolically unhealthy obesity. This gene encodes the transmembrane protein adiponutrin, which plays an important role in lipid remodelling in the liver [2]. Our studies have shown that the LEPR Q223R polymorphism can be used as a molecular genetic marker of leptin resistance. The Q-allele of the LEPR Q223R polymorphism of the gene contributes to the development of obesity, while the R-allele and R/R genotype of the LEPR gene contribute to a decrease in leptin levels after exercise. The most significant changes in body composition under the influence of a strength training programme were found to occur in women with the LEPR R/R genotype [50]. A study of SNPs in the LCT gene (rs4988234) in Ukrainian children revealed an association of the C/C 13910 genotype with severe forms of abdominal obesity, increased anxiety, and decreased quality of life score resulted from the low physical health component score, which can be used in modelling behavioural interventions and may require possible replacement therapy with exogenous lactase preparations [1]. A genetic study of Ukrainian obese women found that PPARG and PPARGC1A genes polymorphisms are associated with a lower percentage of visceral fat, and are associated with differences in plasma lipoprotein, cholesterol, and triglyceride levels.

However, even the manifestations of a genetically determined metabolic disease such as obesity or diabetes can be reduced through exercise [9]. PPARGC1A gene polymorphism is associated with the effectiveness of exercise in reducing the fat percentage [124]. Aerobic exercise is believed to attenuate epigenetic modifications of genes caused by high-energy diets and reduced physical activity, leading to inhibition or delay in the onset of T2D [49].

Over the past decades, evidence has been accumulating that not only genetic mutations and variations determine the development and susceptibility to disease, but also environmental factors (nutrients, physical activity, stress, and environmental factors) can influence gene activity and thereby predispose to disease development [22; 62]. Since a number of genome-wide studies have shown that SNPs associated with T2Dand glucose (glycaemic) levels explain only a fraction of this disease inheritance, this suggests a significant influence of epigenetic factors [133]. T2D-associated DNA methylation was found in regions related to β-cell-specific transcription factors and decrease in their expression [174].

Evidence is emerging that epigenetic factors may, at least in part, explain not only the beneficial effects of exercise on the prevention and treatment of T2D and other metabolic disorders, but even the beneficial effects on offspring metabolism (e.g., glucose tolerance and glucose clearance) through the transmission from the mother of epigenetic modifications of genes involved in important metabolic pathways [78].

It was found that the nutrition of both parents during the fertilisation period and the mother during pregnancy affects the child's susceptibility to developing these diseases in the future [133; 143].

The influence of epigenetic factors is especially important in the early stages of human development. A mother's lifestyle during pregnancy causes changes in the epigenetic profile of her offspring, which is reflected in gene expression and functional changes. Low birth weight and maternal malnutrition during pregnancy correlate with insulin resistance and T2D in adults [27;177]. Obesity caused by high-fat diets leads to mitochondrial dysfunction in oocytes, which causes insulin resistance in offspring and epigenetic defects transmitted through the maternal line to the 3rd generation [133]. High-energy maternal diets lead to changes in neuronal plasticity in offspring, as well as to the development of hypertension and hyperglycaemia associated with the mechanisms of inflammatory processes in the hypothalamus [57].

It has been established that a wide range of nutrients has an epigenetic effect and improves carbohydrate and fat metabolism in patients with DM[23; 63; 133]. The effectiveness of nutrients on the metabolism of people with diabetes depends on their genetic make-up. In particular, the genetic predisposition to BCAA-related metabolic diseases modifies the effect of the use [221]. The health-enhancing effect of exercise on people with diabetes is explained by the induced epigenetic changes the genome [3;23]. Numerous studies have revealed changes in the epigenetic profile (the number of differentially methylated regions) and gene activity under the influence of health-enhancing exercise programmes [24; 237].

In individuals with T2Dand obesity, physical exercises cause different gene expression profile compared to healthy individuals [187].

Genetics and epigenetics of CVD. Most CVDs and CVD risk factors are of polygenic origin and result from the interaction among environmental factors, lifestyle, and risk alleles of dozens of polymorphisms. Nevertheless, monogenic conditions can lead to severe premature cardiovascular disease and early death, requiring early diagnosis.

The most common monogenic disease leading to premature CVD is familial hypercholesterolaemia (FH). FH has a frequency of approximately 1:200 and is caused mainly by mutations in the LDL receptor (LDLR), apolipoprotein B (APOB), and PCSK-9 genes. The relative frequency of monogenic variants may vary slightly in different populations, but mutations in LDLR are the most common. Although more than 2900 LDLR mutations have been identified, approximately a thousand mutations are thought to cause HF. In contrast to single missense mutations in the APOB gene, pathogenic and presumptively pathogenic mutations in the LDLR gene are predominantly exonic substitutions and missense rearrangements.

Hypertrophic cardiomyopathy (HCM) is the most common familial heart disease with great genetic heterogeneity. Mutations in 11 or more genes encoding cardiac sarcomere proteins (>1400 variants) are responsible for (or associated with) HCM. Genetic testing also allows for a broader spectrum of HCM diseases and the diagnosis of phenocopies of HCM with different natural history and treatment options, but is not a reliable strategy for predicting prognosis [223]. Other monogenic CVD are quite rare compared to HF, such as sitosterolemia or Marfan syndrome, occur with a frequency of less than 1:1000, and the frequencies of many other diseases are so rare that they are not even determined [216].

The discovery of genetic loci associated with complex diseases has outpaced the elucidation of the mechanisms of disease pathogenesis. A genome-wide study of patients with CHD among participants of predominantly European ancestry, identified more than 250 genetic risk loci for CHD [12].

To date, a number of genes have been described, mutations in which cause the development of dilated hypertrophic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy. Among them are mainly genes encoding intercalary disc (ID) proteins, which are involved in maintaining the structural integrity of the myocardium and its functioning, as well as in the functioning of signalling cascades. The studies of Ukrainian researchers have shown that the vast majority of genes whose mutations lead to heart failure encode proteins involved in the development and maintenance of intercellular contacts between cardiomyocytes [17; 18].

Genetic testing is most commonly used to identify the underlying genetic etiology in patients with suspected cardiovascular disease, such as hypertrophic cardiomyopathy or familial hypercholesterolaemia. Genetic testing should be performed in individuals with a good phenotype and in conjunction with a comprehensive family assessment to help interpret and apply the results.

Epigenetic regulation of gene expression affects cardiac function and serves as a link between lifestyle and environmental factors, as well as cardiac health and disease. Epigenetic changes can directly affect cardiac function. Whole-genome DNA methylation profiling in patients with dilated cardiomyopathy indicate differences in the methylation of genes that correlate with heart disease [81].

It is known that there is an inverse relationship between physical activity and CVD incidence or all-cause mortality. The cardioprotective effect of physical activity lies in its ability to change the epigenetic profile of cardiomyocytes, thereby regulating gene activity and changes in epigenetic regulation in other tissues, which reduces the risk of heart disease through exerkines [230]. One of the epigenetic mechanisms that implement the effect of exercise is an increase in the expression of miRNAs [65], some of which are involved in the regulation of cardiovascular disease [47].

Effects of hypoxic stimuli. In recent times, a growing body of evidence suggests that metabolic disorders can be impacted by the implementation of intermittent hypoxic conditioning (IHC) (short-term alternating exposures between hypoxia and normoxia). The induction of hypoxic conditioning is accompanied by substantial changes in gene expression, suggesting that conditioning strategies stimulate a fundamental genomic reprogramming of cells that confers cytoprotection and survival. Human studies also support the beneficial effects of appropriate IHC strategies; e.g., IHC induced beneficial effects on glucose homeostasis in patients with prediabetes reducing fasting glucose and during standard oral glucose tolerance test. The most pronounced positive effects were observed one month after IHC termination.

The responses to hypoxia are mediated by hypoxia-inducible factors (HIFs), which regulate numerous genes involved in various biological processes, including erythrocytosis, angiogenesis, metabolism, survival, and growth. HIF-1α and HIF-2α, as central regulators in cellular response to hypoxia, play pivotal roles in this process. HIF-1α is known to induce inflammation and insulin resistance in obesity. In contrast to HIF-1-α, HIF-2-α appears to exert opposing functions and could be protective against obesity-associated metabolic phenotypes. In Ukraine, interval normobaric training (INT) has been used to treat people with prediabetic carbohydrate disorders who have reduced resistance to hypoxia. The course application of IHT along with an increase in the body's resistance to hypoxia led to the elimination of prediabetic disorders of carbohydrate metabolism. A decrease in fasting plasma glucose concentration was noted one month after IHT. Under the influence of IHT, the levels of total cholesterol, low-density lipoprotein cholesterol and triglycerides, indicators of the cardiovascular stress response to dosed hypoxia decreased, and vasomotor function of the endothelium and the state of microcirculation improved.

2.8. Sleep disturbances as a factor in the development of metabolic and CVD

Epidemiological studies have shown a link between sleep disorders and adverse metabolic outcomes, including obesity, insulin resistance, and T2D in adults, as well as an increased risk of cardiometabolic disease and mortality [40]. Sleep disorders that lead to these diseases include changes in sleep duration, chronic sleep restriction, excessive sleep, changes in sleep architecture, sleep fragmentation, circadian rhythm disorders (shift work), and obstructive sleep apnoea. Labarca G et al. also confirm the impact of sleep apnoea on the risk of developing CVD [109].

There is a relationship between metabolic dysfunction and sleep disorders. Current research suggests that sleep is a potentially modifiable risk factor for cardiometabolic disease and obesity [173]. Obesity, a risk factor for CVD, may be dependent on sleep, but in turn it may increase the risk of some sleep disorders that disrupt sleep, leading to further risk of obesity and increased CVD risk [130].

Wang B, et al. emphasise the importance of integrating sleep management into a lifestyle change programme, especially for people with prediabetes or diabetes, by examining the association between sleep patterns and CVD risk depending on glucose tolerance status in 358,805 participants from the UK without signs of CVD. A sleep score was developed based on five factors: sleep duration, chronotype, insomnia, snoring, and daytime sleepiness. The association between sleep and CVD, including CHD and stroke, was studied according to normal glucose tolerance (NGT), prediabetes and diabetes.

During a mean follow-up period of 12.4 years, 29,663 CVD events were documented. A significant interaction was found between sleep score and glucose tolerance status for CVD (P value for interaction = 0.002). The presence of each of the following factors was associated with an increase in CVD risk of 7% (95% CI 6%-9%) in participants with NGT, 11% (8%-14%) in those with prediabetes, and 13% (9%-17%) in those with diabetes, respectively. Similar patterns of interaction were observed for coronary heart disease and stroke. Among individual sleep factors, sleep duration and insomnia significantly interacted with glucose tolerance status for CVD outcomes (P values <0.05). All five factors of unhealthy sleep accounted for 14.2% (8.7%-19.8%), 19.5% (7.4%-31.0%), and 25.1% (9.7%-39.3%) of cardiovascular disease among participants with NGT, prediabetes, and diabetes, respectively.

Thus, the authors argue that the risk of cardiovascular disease associated with poor sleep patterns was exacerbated by glucose intolerance. These findings emphasise the importance of integrating sleep management into a lifestyle change programme, especially for people with prediabetes or diabetes [218].

Sleep and circadian rhythms modulate or control daily physiological patterns, which is essential for normal metabolic health. Metabolic processes, such as glucose tolerance, change throughout the day and night and at different stages of sleep. During sleep, the brain's glucose utilisation and sympathetic nervous system activity decrease and the tone of the vagus nerve increases. The prevalence of obesity and T2D is increasing worldwide, along with the prevalence of sleep deprivation and sleep disorders. The results of epidemiological and pathophysiological studies conducted in different countries among different socioeconomic groups confirm that sleep disorders increase the risk of developing cardiometabolic disorders, including T2D [168].

There are conflicting data on the impact of sleep on the development of CVD in adolescents.

Wu N et al. determined the relationship between sleep characteristics and cardiovascular risk factors in adolescents with T1D. The authors concluded that all adolescents (conditionally healthy and with type 1 diabetes) have a sleep duration of less than 8 hours. The authors found no significant differences between the two groups in sleep duration, sleep efficiency, sleep onset and sleep latency, and number of awakenings, and concluded that adolescents with and without T1D sleep less than the recommended eight hours per night. The association between sleep efficiency and LDL cholesterol and triglycerides was independent of sleep duration, gender, age, and puberty stage [230].

Moreover, according to Seo YG, sleeping less than 8 hours per day had an impact on the incidence of cardiovascular disease in Korean adolescents with [182].

Reduced sleep duration combined with decreased cardiorespiratory fitness in young people are lifestyle factors that may contribute to CVD [64].

3. Best practices to prevention of DM and CVD

3.1. Analysis of programmes for prevention and correction of the development of cardiovascular disease and diabetes in Ukraine

State programmes to improve public health and combat diseases have been developed and implemented in Ukraine for a long time, since the 1980s [6].

In 2006, the Cabinet of Ministers of Ukraine approved the State Programme for the Prevention and Treatment of Cardiovascular and Cerebrovascular Diseases for 2006-2010 by Resolution №. 761 [148; 149]. The aim of this State Programme was to prevent and reduce the incidence of cardiovascular and cerebrovascular diseases, disability and mortality from their complications, as well as to increase the life expectancy and quality of life of the population [148; 149].

In 2015, Ukraine launched the “Stent for Life” public initiative, which gives patients with acute myocardial infarction a chance to live. The government began procuring high-quality stents and consumables and developing a network of cardiac centres across the country [148]. International and Ukrainian companies became partners in the project.

Ukraine has been fighting diabetes since the declaration of its independence, and the first targeted programme “Diabetes mellitus” for 1998-2001 was introduced in 1998. Subsequently, two more government programmes were developed and adopted for 2002-2007 and 2009-2013. These programmes provided patients with diabetes with free insulin and oral hypoglycaemic drugs [204]. These programmes, despite inadequate funding, were implemented to some extent and yielded positive results [197]. As part of the programme, the Protocols for the provision of medical care in the specialty of Endocrinology were prepared and implemented in 2009, which concentrated modern scientific and industry achievements, recommendations of the American Diabetes Association (ADA) and the International Diabetes Federation (IDF), as well as guidelines used in leading clinics around the world and based on the principles of evidence-based medicine and clinical epidemiology. In 2013, the updated protocols for the treatment of patients with type II diabetes were approved and implemented in clinical practice, primarily for primary and secondary care physicians. Furthermore, thanks to this Programme, the State Register of Diabetes Patients was established in Ukraine, which also includes data on children and adolescents [197].

The Affordable Medicines reimbursement programme was introduced by the Government of Ukraine in April 2017. On April 1, 2019, it was transferred to the National Health Service and became part of the Medical Guarantee Programme. As part of the reimbursement programme, patients with cardiovascular disease, type II diabetes or bronchial asthma can get medicines free of charge or with a small co-payment [139].

In 2021, 2.1 million patients got medicines under the Affordable Medicines Programme using electronic prescriptions. The analysis showed that electronic prescriptions for CVD were provided to 1,767,880 patients, electronic prescriptions for DMto 524,961 patients, and 178,995 patients received electronic prescriptions for insulin-dependent forms of diabetes [90].

The importance of combating CVD for the state is also confirmed by the fact that it is increasing funding to combat them through the Programme of Medical Guarantees. In particular, in 2022, UAH 4.8 billion was allocated for the treatment of priority CVD, including heart attacks and strokes, which is an increase of UAH 1.8 billion compared to 2021. Institutions that have concluded an agreement with the National Health Service for medical care for acute myocardial infarction receive money for the services provided to patients from the National Health Service at an increased rate for each patient treated [215].

The Government has adopted the Procedure for the Implementation of the Programme of Medical Guarantees for 2024. Despite the war and limited resources, the scope of guaranteed medical services for Ukrainians has not been reduced. On the contrary, the Programme of Medical Guarantees is being expanded. In 2024, almost UAH 159 billion will be allocated for the programme, which is UAH 16 billion more than last year. This includes UAH 5.2 billion for the reimbursement of medicines. Moreover, it was noted that the Affordable Medicines reimbursement programme will be developed within the existing areas, such as cardiovascular and cerebrovascular diseases (including primary and secondary prevention of heart attacks and strokes), DMand diabetes insipidus, chronic lower respiratory diseases, mental and behavioural disorders, epilepsy, Parkinson's disease, medicines for post-transplantation patients, and painkillers for palliative patients [131].

Ukraine has shown limited progress towards achieving the diet-related non-communicable disease (NCD) targets. 27.5% of adult (aged 18 years and over) women and 24.5% of adult men are living with obesity. Ukraine's obesity prevalence is higher than the regional average of 25.3% for women but is lower than the regional average of 24.9% for men. At the same time, diabetes is estimated to affect 7.7% of adult women and 8.5% of adult men [75].

It is worth mentioning the government programmes aimed at developing telemedicine. The Cabinet of Ministers of Ukraine approved the Strategy for Telemedicine Development in Ukraine by its Resolution No. 625-r. of July 14, 2023. The gradual introduction of telemedicine in Ukraine took place in Kirovohrad, Rivne, Dnipro, and Poltava regions as part of telemedicine consultations in the areas of CVD, diabetes mellitus, bronchial asthma, and dermatological diseases. Separate local initiatives have also been implemented to introduce telemetry technologies in the emergency medical care and disaster medicine centres, in particular for recording and transmitting electrocardiograms for further analysis and remote consultation by a specialist, regardless of the location of the patient and the healthcare professional. Against the backdrop of the consequences of the COVID-19 pandemic caused by the SARS-CoV-2 coronavirus and the armed aggression of the Russian Federation against Ukraine, priority non-communicable and other diseases (mental disorders, cardiovascular, oncological, pulmonary, metabolic, etc.) not only show no downward trend, but also predictably and inevitably have prerequisites for growth due to the outflow of attention and resources to overcome them. In addition, the issue of rehabilitation and remote monitoring of chronic diseases is becoming more acute. In these circumstances, the use of telemedicine is supported by government and volunteer initiatives involving various countries that provide software and equipment, as well as organise consultations of Ukrainian healthcare professionals and patients with foreign experts [195].

Ukraine in the way of implementation of the european system of health-enhancing physical activity during leisure.

According to the WHO physical inactivity ranks fourth among the factors that cause premature mortality worldwide. In Ukraine, the measures have been taken over the past 20 years to increase the number of people involved in health-enhancing physical activity (HEPA). The concept of humanization of the process of population engagement in HEPA under the conditions of overcoming the consequences of the authoritarian social relations in the field of mass sports, which were typical of the 60-90s of the last century, has been scientifically substantiated. A system of knowledge about the peculiarities of physical recreation of different population groups is being developed on the basis of scientific research. Currently, researchers in Ukraine are in active search for solutions to the challenges of introducing HEPA during leisure.

The main objectives of population engagement in HEPA as one of the priority areas of the national policy to implement the Strategy for the development of physical culture and sports in Ukraine until 2028 adopted in 2020 were determined based on the analysis and generalization of the concepts provided by the International Charter for Physical Education, Physical Activity and Sport, Global action plan WHO on physical activity 2018-2030: more active people for a healthier world, European Sports Charter, best European practices, as well as the results of the studies by Ukrainian researchers. In particular, it is planned to develop a set of indicators and a monitoring mechanism for the level of involvement of the population in physical activity and sports in accordance with a similar collection of Eurobarometer surveys.

The authors headed the working group on program and methodological support of the social project "Active parks – locations of healthy Ukraine" (adopted by the Decree of the President of Ukraine on December 17, 2020 No. 534/2020). The main goal of this project is to introduce HEPA among all populations including people with disabilities. The sets of moderate-intensity exercises on pull-up bars, parallel bars, wall bars, and agility ladder as well as gymnastic exercises without equipment have been developed for outdoor physical activity of untrained people. Each element of the infrastructure is marked with a QR-code with a link to the interactive resource center where participants can access video tutorials of the exercises demonstrated by famous athletes and Ukrainian stars. It is planned to create an on-line platform for a social project to provide consultations and to exchange experiences and ideas between the experts of HEPA, athletes, and participants in active recreation. The recommendations have been implemented in the practice of HEPA of more than 100 city parks in Ukraine through the municipal Sports for All centers for physical health of population. The implementation of the developed action plan resulted in improved level of HEPA, quality of life and life satisfaction, and increased physical and psycho-emotional wellbeing.

Further research will be focused on the peculiarities of the use of HEPA in city parks for the mental and physical recovery of Ukrainians after the end of the Russian Federation's military aggression against Ukraine.

3.2. Primary Prevention of CVD and DM Development

To support countries in their work at the national level, WHO has prepared the Global action plan for the prevention and control of noncommunicable diseases (NCDs) 2013-2030 [226], which includes six main objectives:

1. To raise the priority accorded to the prevention and control of noncommunicable diseases in global, regional and national agendas and internationally agreed development goals, through strengthened international cooperation and advocacy.
2. To strengthen national capacity, leadership, governance, multisectoral action and partnerships to accelerate country response for the prevention and control of noncommunicable diseases.
3. To reduce modifiable risk factors for noncommunicable diseases and underlying social determinants through creation of health-promoting environments.
4. To strengthen and orient health systems to address the prevention and control of noncommunicable diseases and the underlying social determinants through people-centred primary health care and universal health coverage.
5. To promote and support national capacity for high-quality research and development for the prevention and control of noncommunicable diseases.
6. To monitor the trends and determinants of noncommunicable diseases and evaluate progress in their prevention and control.

Primary measures (active identification of risk groups; active lifestyle modification, integrated approach taking into account all risk factors) are more cost-effective than secondary measures, and they can significantly reduce the incidence of cardiovascular disorders. This strategy is practically feasible in low-resource settings, including the use of resource-poor settings, including the use of non-physician healthcare personnel [36].

Researchers promote a personalised multidisciplinary approach to the prevention of CVD in patients with diabetes, taking into account specific recommendations developed for different age groups to optimise results. This strategy is consistent with the principles of evidence-based practice, with the emphasise on the need for public health professionals to adapt recommendations to the individual needs of their clients.

The results of scientific research show that the most effective means of preventing cardiovascular disease and T2Dare: monitoring of blood pressure, glucose level, and lipids, breaking bad habits (cessation of smoking and alcohol consumption), as well as lifestyle modification, including sleep habits, stress (emotions) management, physical activity (PA), and nutrition (diet) [200].

All these can help prevent the development of CVD and diabetes and even slow down the progression of the disease. Most researchers emphasise that a prerequisite for primary and secondary prevention of disease is an integrated approach and continuity of actions that helps to achieve long-term results [224].

3.2.1. Lifestyle modification as a means of CVD and DM prevention

For children and adolescents, the focus is often on lifestyle modification and early management of cardiovascular risk factors. In adults, the focus is on treating existing cardiovascular disease and preventing further complications. For the elderly, the guidelines suggest a more cautious approach, taking into account the general health status, potential side effects of medications, and the goal of maintaining quality of life, which is relating to secondary prevention.

Children and adolescents

Lifestyle modification is extremely important. The cornerstone of the treatment of adolescents with diabetes is an emphasis on lifestyle modification, including diet, physical activity, and weight management. To improve glycaemic control and reduce cardiovascular risk, a healthy diet rich in fruits, vegetables, whole grains, and lean proteins along with regular physical activity is recommended. Studies such as one by Zeitler et al. (2020) emphasise the importance of lifestyle interventions in the management of diabetes and its complications in young people [239].

Adolescents may benefit from educational programmes that emphasise the importance of a healthy lifestyle in preventing cardiovascular disease. Because habits are still being formed, interventions should include education on nutrition, physical activity, and the long-term health impact of lifestyle choices [35].

A systematic review and meta-analysis of school-based interventions confirms the effectiveness of educational programmes aimed at reducing body mass index in adolescents aged 10 to 19 years. Typically, these interventions include multicomponent strategies, including health education, aimed at promoting healthy behaviours related to nutrition, physical activity, and body composition. The evidence suggests that the public health system has the potential to reduce BMI in adolescents towards a healthier range through such interventions [94]

- Family involvement: As adolescents often live with their families, the involvement of parents and caregivers is crucial. Interventions at the family level can create a supportive environment, influence dietary choices, and encourage regular physical activity [110].

According to Kepper MM, et al., health information technology (HIT) has unfortunately not been widely used in outpatient settings to effectively address obesity among young people, especially among disadvantaged populations who face greater barriers to good health. The authors report on the use of PREVENT tool, i.e. the novel health information technology tool for behaviour change to address obesity and prevent chronic disease among adolescents, which facilitates discussion about prevention, provides individualised, evidence-based recommendations for physical activity and food intake, includes an interactive map of community resources to support behaviour change, and automates patient follow-up. Based on the theory of self-determination, the PREVENT tool encourages patient competence and autonomy to motivate behaviour change [103]

Glycaemic control: Achieving and maintaining optimal glycaemic control is essential to minimise the risk of cardiovascular complications. The use of metformin as first-line pharmacotherapy in combination with lifestyle interventions is supported by the ADA's Standards of Care for Diabetes 2023, which emphasises its role in the management of T2D in youth [58].

Management of cardiovascular disease risk factors: Adolescents with T2D often have multiple cardiovascular risk factors, such as hypertension, dyslipidaemia, and obesity. Managing these risk factors through both non-pharmacological interventions (lifestyle modification) and pharmacological treatment (if needed) is crucial. The ADA guidelines recommend regular screening and management of these risk factors to prevent cardiovascular incidents [59].

Psychosocial and behavioural support: Psychosocial and behavioural support is essential for adolescents with T2D to promote adherence to treatment and lifestyle changes. A multidisciplinary approach, including psychological support, can help address behavioural challenges associated with managing a chronic illness in adolescence [178].

Adults

Targeted weight management: Weight management is often the first priority for adults at risk of CVD. Individualised weight loss interventions through a combination of calorie control, dietary modification, and increased physical activity are important [74].

A systematic review and meta-analysis of randomised controlled trials conducted by Madigan CD et al. (2022) showed that behavioural weight management interventions for obese adults delivered in primary care settings are effective in reducing weight and contributing to the prevention of subsequent CV events. The authors emphasise the effectiveness of interventions by different types of healthcare professionals, as well as non-healthcare professionals such as health coaches [32; 122].

Behavioural counselling: Adults may benefit from behavioural counselling to overcome habits that contribute to metabolic syndrome. This may include stress management, smoking cessation, and strategies to improve adherence to lifestyle changes. The US Preventive Services Task Force Recommendation Statement on behavioural counselling interventions to promote healthy eating and physical activity for the prevention of cardiovascular disease in adults describes individualised treatment options to maximise patient outcomes, emphasising the importance of a comprehensive lifestyle change programme and dietary modification. It emphasises the need for personalised obesity management strategies [123].

– Individualised exercise plans: adults may have different fitness levels and preferences. Lifestyle modification should include individualised exercise plans that are prescribed based on a comprehensive fitness assessment and include aerobic exercise, strength training, and flexibility exercises. The key is to encourage regular physical activity.

3.2.2. The role of physical activity in preventing the development of CVD and DM

Experts emphasise that PA is an important element of comprehensive prevention programmes and a key tactic in the fight against obesity due to its numerous benefits such as reducing the risk of coronary heart disease or heart failure and potentially reducing insulin resistance. Due to its low cost, low risk, and non-drug nature of intervention, the European Society of Cardiology recommended in 2015 that exercise be included in cardiac rehabilitation programmes for patients with non-ST-segment elevation acute coronary syndrome [153;172].

Studies examining exercise as a treatment for obesity and metabolic syndrome (MS) often recommend dynamic aerobic exercise, which is known to increase insulin sensitivity [19]. However, the presence of numerous comorbidities and the general health status of obese people can make dynamic exercise difficult, thus making aerobic exercise not universal.

The study by Singh, B. et al. evidences that exercise improves HbA1c levels, which has an impact on reducing mortality rates [186]. Exercise has a different effect on blood glucose levels depending on timing of exercise and meal time, and even on the duration, intensity, and type of exercise. In particular, in patients with T1D, exercise can lead to hypoglycaemia, so blood glucose levels should be monitored immediately before and after exercise. The target range of blood glucose before exercise should be between 7 mmol/l and 12 mmol/L [135].

Some studies substantiate the use of anaerobic strength training, which promotes systemic changes, neutralising metabolic and functional disorders associated with the development of metabolic syndrome (MS). This may include improving tissue sensitivity to insulin and reducing the risk of developing T2D [61].

Aerobic training is particularly effective in significantly reducing weight and improving cardiovascular function, especially in people with primary class 1 obesity. For people with class 2 obesity, physical activities that increase the heart rate to 75% of the baseline resting level are recommended, with intervals of 5 minutes of work and 3 minutes of rest, lasting from 30 to 90 minutes, 3-4 times a week, for 4 months [95].

Aerobic exercise is defined as the use of aerobic metabolism to provide energy for the muscles; it is mainly low- to moderate-intensity physical activity. Aerobic exercise has a positive effect on lipid metabolism, cardiac remodelling, heart failure after myocardial infarction, insulin resistance, and endothelial function. Anaerobic exercise is an activity that uses energy sources without oxygen consumption, such as glycolysis and the phosphagen system. Anaerobic exercise typically refers to high-intensity training, including sprinting and strength training. In several studies, high-intensity exercise is recommended for lowering TG and

LDL cholesterol levels. Similar to aerobic exercise, anaerobic exercise also has a positive effect on body mass index and blood pressure [154]. In some cases, high-intensity training has a more favourable effect on the cardiovascular system and cardiometabolic markers compared to low-intensity training [25]. The benefits of high-intensity intermittent training are that a short time exercise, such as 3-4 sessions per week, can lead to significant changes [99]. However, there is a paradoxical disadvantage of anaerobic training in that high-intensity activity leads to increased mortality and sudden death. It is generally accepted that intense physical activity increases the risk of cardiovascular disease, such as MI, by increasing blood pressure [87]. Finally, intense exercise should be intermittent, especially for a long-term programme. Professional supervision and guidance are essential when performing high-intensity exercise.

Although many studies show a positive correlation between exercise and good health status, a thorough physical assessment is necessary before starting an exercise programme. The intensity, mode, duration, and frequency of exercise can have a significant impact on the outcomes.

Moreover, the intensity of exercise varies from person to person depending on their physical condition [34], comorbidities, and age [219].

The levels of physical activity recommended by WHO to prevent the risk of developing NCDs [225] are as follows:

For children and young people aged 5-17 years, physical activity includes games, competitions, sports, trips, recreational activities, physical education or organized exercise within the family, school, and local community:

Should do at least an average of 60 minutes per day of moderate-to-vigorous intensity, mostly aerobic, physical activity, across the week.

Physical activity of more than 60 minutes per day will have additional health benefits.

Physical activity aimed at the development of the musculoskeletal system should be done at least 3 days a week.

Adults aged 18-64 years:

The exercise intensity recommended to prevent cardiovascular disease for general population by the American Heart Association is 30 minutes 5 times a week for a minimum of 150 minutes per week of moderate exercise or 25 minutes 3 times a week for a minimum of 75 minutes per week. A week of active life. Individuals can choose to do one type of physical activity or a combination of moderate and vigorous activity. They will also benefit if they divide the whole time into several parts of 10-15 minutes per day. For those who want to reduce the risk of heart attack and stroke, 40 minutes of moderate to vigorous aerobic exercise 3 or 4 times a week is recommended [117]. Moderate-intensity exercises are more commonly used among people who have previous exercise experience and enjoy active recreation. Various studies show that the duration of physical exercise, rather than its intensity, is the main factor that leads to the desired outcomes [43].

Adults aged 65 years and older:

Physical activity is seen as an effective way to prevent and counteract age-related changes, particularly in the myocardium and physiological functions [128]. The American College of Sports Medicine and the American Heart Association recommend 30 minutes of moderate-intensity exercise 5 times a week or 20 minutes of vigorous-intensity exercise 3 times a week for older adults [44]. Furthermore, according to the WHO [**Ошибка! Источник ссылки не найден.**], adults in this age group should increase the duration of moderate-intensity exercise to 300 minutes per week or otherwise achieve the same level of activity.

Strength training should be included to strengthen muscle groups and prevent falls in the form of 8-10 exercises with 10-15 repetitions twice a week [128]. Older people are strongly encouraged to attend exercise classes to improve balance and prevent falls [67]. Liu C. J. et al. emphasise the safety of exercise for older people, taking into account contraindications associated with chronic diseases and following safety precautions when exercising with weights [116].

3.2.3 Nutrition as a tool of CVD and DM prevention

Nutrition is the most important behavioral factor in preventing premature CVD death, Metabolic Syndrom and disability, surpassing smoking abstinence and physical activity [97]. As a result, International Guidelines strongly recommend a healthy diet, with particular emphasis on the intake of fruits and vegetables, whole grains, fish, and legumes [14]. In contrast, intake of processed meats and fats should be minimized, aiming at efficacious control of CVD risk factors [14].

Adolescents:

Focus on education and development of healthy habits: Promoting a balanced diet with an emphasis on fruits, vegetables, whole grains, and lean proteins is essential. Limiting the consumption of sugary drinks, processed foods, and excessive salt is particularly important.

Adults:

We suggest that nutrition recommendations for adults of all body sizes should be personalized to meet individual values, preferences and treatment goals to support a dietary approach that is safe, effective, nutritionally adequate, culturally acceptable and affordable for long-term adherence. Adults living with obesity and impaired glucose tolerance (prediabetes) or T2Dmay receive medical nutrition therapy provided by a registered dietitian (when available) to reduce body weight and waist circumference and improve glycemic control and blood pressure. Adults living with obesity can consider any of the multiple medical nutrition therapies to improve health-related outcomes, choosing the dietary patterns and food-based approaches that support their best long-term adherence:

1. Calorie-restricted dietary patterns emphasizing variable macronutrient distribution ranges (lower, moderate, or higher carbohydrate with variable proportions of protein and fat) to achieve similar body weight reduction over 6–12 months
2. Mediterranean dietary pattern to improve glycemic control, HDL-cholesterol and triglycerides, reduce cardiovascular events, reduce risk of type 2

diabetes; and increase reversion of metabolic syndrome with little effect on body weight and waist circumference

3. Vegetarian dietary pattern to improve glycemic control, established blood lipid targets, including LDL-C, and reduce body weight, risk of T2Dand coronary heart disease incidence and mortality

4. Portfolio dietary pattern to improve established blood lipid targets, including LDL-C, apo B, and non-HDL-C, CRP, blood pressure, and estimated 10-year coronary heart disease risk

5. Low-glycemic index dietary pattern to reduce body weight, glycemic control, established blood lipid targets, including LDL-C and blood pressure and the risk of T2Dand coronary heart disease

6. Dietary Approaches to Stop Hypertension (DASH) dietary pattern to reduce body weight and waist circumference; improve blood pressure established lipid targets, including LDL-C, CRP, glycemic control; and reduce the risk of diabetes, cardiovascular disease, coronary heart disease and stroke

7. Nordic dietary pattern to reduce body weight and body weight regain, improve blood pressure and established blood lipid targets, including LDL-C, non-HDL-C and reduce the risk of cardiovascular and all-cause mortality

8. Partial meal replacements (replacing one to two meals/day as part of a calorie-restricted intervention) to reduce body weight, waist circumference, blood pressure and improve glycemic control [7; 153; 193].

Elderly people^

Adjustment of the diet due to aging: Nutrition for older adults includes ensuring adequate intake of nutrients important for bone health (calcium and vitamin D) [199], and maintaining a balanced diet that takes into account any existing medical conditions or mobility limitations. It is also important to pay attention to hydration [60; 171].

In conclusion, it is currently well established that a healthy diet is the cornerstone for CVD primary and secondary prevention. Optimum nutritional strategies promote longevity, reduce the risks of DM(DM), arterial hypertension and stroke, prevent obesity, and thus reduce the risk of CVD. Nutrition should play a central role in prevention of CVD as a non-medicinal agent. More educational strategies should be implemented to emphasize the paramount importance of dietary habits in healthy life and aging [205].

3.2.4. Effects of hypoxic stimuli on glucose homeostasis

In recent times, a growing body of evidence suggests that metabolic disorders can be impacted by the implementation of intermittent hypoxic conditioning (IHC) (short-term alternating exposures between hypoxia and normoxia). The induction of hypoxic conditioning is accompanied by substantial changes in gene expression, suggesting that conditioning strategies stimulate a fundamental genomic reprogramming of cells that confers cytoprotection and survival [190; 4]. Human studies also support the beneficial effects of appropriate IHC strategies; e.g., IHC induced beneficial effects on glucose homeostasis in patients with prediabetes reducing fasting glucose and during standard oral glucose tolerance test. The most pronounced positive effects were observed one month after IHC termination [183].

In Ukraine, interval normobaric training (INT) has been used to treat people with prediabetic carbohydrate disorders who have reduced resistance to hypoxia. The course application of IHT along with an increase in the body's resistance to hypoxia led to the elimination of prediabetic disorders of carbohydrate metabolism. A decrease in fasting plasma glucose concentration was noted one month after IHT. Under the influence of IHT, the levels of total cholesterol, low-density lipoprotein cholesterol and triglycerides, indicators of the cardiovascular stress response to dosed hypoxia decreased, and vasomotor function of the endothelium and the state of microcirculation improved [166]

3.3 Secondary prevention of CVD through rehabilitation interventions

Secondary prevention through comprehensive cardiac rehabilitation is recognised as the most cost-effective intervention to ensure favourable outcomes for a wide range of CVD, reducing cardiovascular mortality, morbidity and disability, and improving quality of life. A comprehensive and up-to-date cardiac rehabilitation programme is mandatory in both inpatient and outpatient settings to ensure the expected outcomes [6].

Comprehensive cardiac rehabilitation (CCR)/secondary prevention should include the following elements [227]:

Assessment of the patient's condition: clinical history: screening for cardiovascular risk factors, comorbidities and disabilities; symptoms: cardiovascular disease (NYHA class for dyspnoea, CCS class for angina, and Fontaine/Rutherford class for obliterative arterial disease of the lower limbs); physical examination: general health, signs of heart failure, cardiac and carotid murmurs, blood pressure control, limbs for arterial pulse and orthopaedic pathology, cerebrovascular events with/without neurological consequences; ECG, cardiac imaging (in particular, left ventricular systolic and diastolic function, evaluation of heart valves), blood test.

Physical activity level: household, occupational, and recreational needs (how many days and minutes per day are spent on average on moderate-intensity or vigorous physical activity); activities appropriate to age, gender, and daily life; readiness to change behaviour, self-confidence, and motivation; barriers to increasing physical activity and social support for making positive changes.

Peak physical performance: testing on a cycle ergometer or treadmill, or 6MWT/ISWT, assessment of frailty.

Education: assessment of literacy level and type of communication required; clear, understandable information about the main goal of the CR programme and the role of each component; information and education about disease perception, empowerment, and self-monitoring; information and motivation for targeted lifestyle modifications.

Expected outcomes: establishing personalised, patient-specific programme objectives.

Optimisation of pharmacological treatment: control and normalisation of glycaemia, HbA1C, total cholesterol, LDL, HDL, triglycerides, uric acid, renal function, peptides; control of hypertension; secondary complications (e.g. excessive dyspnoea, edema, etc.).

Psychosocial rehabilitation, the objective of which is to teach the patient to help themselves in stressful situations and emotional states such as fear and/or depression, to develop the ability to psychologically adapt to the consequences of the disease.

Diagnosing and combating the so-called “risk factors” for the development of CVD through lifestyle modification; In all age groups, creating a favourable environment, taking into account individual preferences, and gradual, sustainable changes are important for successful lifestyle modification. The American Heart Association's 2022 guidelines suggest that the 7 Life`s Simple should be taken into account: healthy eating, weight maintenance/loss, physical activity, smoking cessation, control of BP, HDL, LDL, and blood glucose levels [203].

Recommendations for sleep optimisation and sleep hygiene, treatment of sleep disorders, along with sufficient physical activity and good nutrition, should be included in preventive and therapeutic strategies for maintaining metabolic health.

Achieving a balance between promoting cardiovascular health through physical activity and ensuring the safety of people recovering from ACE or exacerbation of chronic CVD.

Physical therapy / rehabilitation: a gradual and controlled increase in physical activity adapted to the individual capabilities of the person with a special focus on the transition from the inpatient to the outpatient stage:

All patients with acute coronary syndrome (ACS) or post-coronary artery bypass grafting (level of evidence A) before discharge and patients with chronic angina at the first visit to the doctor (level of evidence B) should be referred to a comprehensive outpatient cardiovascular rehabilitation programme. A home-based cardiac rehabilitation programme can be replaced by a supervised programme in a centre for low-risk patients (level of evidence A).

Regardless of the age group, certain principles apply to physical activity for people after ACE with CVD:

– Medical supervision: physical activity plans should be developed in consultation with healthcare professionals, taking into account individual health status and medical history.

– Early mobilisation: early mobilisation is recommended for adults after an acute cardiovascular event (ACE) with CVD. Light exercises such as walking and gentle stretching are usually started in the first days, gradually progressing to moderate-intensity exercises.

– Progression: gradually increasing the intensity and duration of activity is key to avoiding overuse and ensuring the safety of people with CVD recovering from an ACE.

– Education, symptom awareness: post-ACE individuals with CVD should be taught to recognise and respond to symptoms such as chest pain, shortness of breath or dizziness during physical activity.

The approach to physical activity during the first month after a cardiovascular incident or exacerbation of chronic CVD for secondary prevention of cardiovascular events varies across age groups due to differences in fitness levels, health considerations, and potential limitations.

Adults:

A supervised inpatient physical therapy programme may be recommended in the initial stages (the duration of which varies according to individual situation), especially to check individual responses and tolerance, clinical stability, and to identify early signs and symptoms that indicate the need for modification or discontinuation of the programme. Supervision should include a physical examination, monitoring of heart rate, blood pressure, and rhythm before, during, and after exercise. Physical (therapeutic) exercise should be prescribed on an individual basis after a thorough clinical assessment, including risk stratification, behavioural characteristics, personal goals, and exercise preferences. Exercise should be prescribed according to the FITT model (frequency, intensity, time (duration) and type of exercise), with the option of timing (FITT+T) for people with diabetes, taking into account timing of exercise in relation to meal times and a preference for low-intensity strength training [93; 161]. The observation period should be extended in patients with new symptoms, signs, abnormal blood pressure, and increased supraventricular or ventricular ectopy during exercise [165].

In the transition from inpatient to outpatient care, a comprehensive physical rehabilitation programme for people after ACE or exacerbation of chronic CVD, which includes strategic and organisational approaches to combating obesity, arterial hypertension, lipid and carbohydrate metabolism disorders, and is aimed at reducing the risk of possible complications, contributes to more effective recovery of the cardiovascular system, the formation of compensatory mechanisms and improvement of the quality of life of patients, and is safer for patients with severe conditions [19].

According to randomised trials by Colberg SR et al., both aerobic exercise and strength training are shown to improve glycaemic control in patients with type 2 diabetes, and some studies indicate that a combination of strength and aerobic exercise is more effective than using them alone [42]. The most favourable and effective in patients with CVD and DM is interval training (IT), integral exercises with alternating aerobic and anaerobic loads of different intensity, as well as cardio- and strength work with different levels of load, even in older people [52]. Integral interval training includes a cardio (aerobic) part performed at an intensity of 50-70 % of maximum heart rate for 4-6 minutes, followed by strength training for 4-6 minutes. The number of repetitions is from 4 to 8 [6].

There are also a number of studies that report the safety and usefulness of high-intensity interval training in older adults with CHD. The HIIT+R programme included 30 minutes of active exercise (10×3-minute sets). Each session included 1 minute of high-intensity walking on a treadmill with heart rate ranged from 85% to 90% of maximum heart rate (HRmax), followed by low-intensity walking at 60% to 70% of HRmax, and then low- to moderate-intensity resistance training [46].

Mariia Balazh and co-authors show that in the rehabilitation of people with severe functional class, preference should be given to static and dynamic loads, which are gentler and safer than traditional dynamic loads. Summarising the data obtained during the study, it should be noted that patients with FC II showed a more significant improvement in most of the studied indicators than patients with FC III [19].

Frequency: most days (at least 3 days a week, and preferably 6-7 days a week) for aerobic training; 2 times a week for strength training. Intensity: moderate (i.e. 45-59% of peak oxygen consumption, 50-70% of Wpeak (above first ventilatory threshold), 55-69% of HRpeak, 40-59% of heart rate reserve (calculated based on resting heart rate), 4-6 MET or 12/20-14/20 points on the Borg scale) or moderate-to-high intensity for continuous endurance training [6]. Higher exercise intensity for high-intensity interval endurance training according to the chosen protocol. The talk test (i.e., the breathing rate should allow you to talk) can be considered as an additional tool to control intensity when HR cannot be measured. 30-70% of 1RM for upper body exercises and 40-80% of 1RM for lower body exercises, with 12-15 repetitions per set is recommended for resistance/strength training [6].

Time: at least 20-30 min (preferably 45-60 min) per session [6].

Type: aerobic training (walking, jogging, cycling, swimming, rowing, stair climbing, ellipticals, and aerobic dancing), resistance/strength training, flexibility training, balance training, and respiratory muscle training. Coordination exercise and other types of (non-traditional) training may be considered [176].

Organise physical training to ensure energy expenditure of 1000-2000 kcal/week [6].

Adolescents:

Gradual return to activity: A gradual return to physical activity is recommended for adolescents who have had ACE. Supervised exercise programmes provide a structured and controlled environment to ensure safety and appropriate progress.

Encouraging regular physical activity appropriate for their age, such as sport or recreational activity, for at least 60 minutes a day. Encouraging enjoyable and social physical activity is crucial for long-term dietary adherence.

Focus on education and healthy habits related to nutrition, physical activity, tobacco and substance use.

Elderly people:

Individualised approach that takes into account different levels of fitness and comorbidities to improve mobility.

Functional and exercise activities that improve daily activities, such as walking, stair climbing, and balance exercises to reduce the risk of falls and reduce sedentary lifestyle. Regular assessment of tolerance, symptoms, and general health status helps to tailor an exercise regime to their specific needs.

Patients with valvular heart disease are recommended to have CR after heart valve surgery, and they are usually elderly. CR takes place in two phases: from the seventh to the fifteenth day: treatment of complications, respiratory physiotherapy, and assistance with autonomy, if necessary. From day fifteen: rehabilitation to physical exercise after an exercise test with or without VO_2max assessment. CR of patients suffering from heart valve disease has demonstrated its usefulness in reducing left ventricular hypertrophy in patients with aortic valve stenosis. No serious complications were observed in all studies of CR in patients with heart valve disease [73; 213; 212].

Occupational therapy, especially through home modification interventions, plays a crucial role in helping older people with heart failure to safely participate in activities of daily living and prevent falls [111]. This approach emphasises the adaptation of living spaces to improve the use, safety, security, and independence of older people. The literature suggests that multimodal approaches combining physical and occupational therapy are needed to effectively reduce the risk of falls and improve participation in activities of daily living in this population. Further research is recommended to fully explore the impact of such interventions [72].

Expected outcomes: increased participation in household, occupational and recreational activities; improved psychosocial well-being, disability prevention, and independent self-care; improved physical condition; improved prognosis.

4. Ways to self monitoring

4.1. Self monitoring in diabetes mellitus

According to the ADA recommednations (2023), screening for prediabetes and T2Dshould be considered in asymptomatic adults with risk factors (RF) and all individuals 45 years of age and older.

The risk factors are:

- Low physical activity,
- Presence of diabetes in first-degree relatives
- High-risk race/ethnicity
- Women who gave birth to a child weighing more than 4 kg or had gestational diabetes
- Arterial hypertension (≥140/90 mm Hg) or use of antihypertensive therapy
- High-density lipoprotein cholesterol <0.9 mmol/L and/or triglyceride (TG) >2.82 mmol/L (their value is more important than low-density lipoprotein cholesterol)
- Other clinical conditions associated with IR (e.g., obesity, polycystic ovary syndrome)
- History of CVD

Testing for prediabetes and T2Dshould be performed in adults of any age who are overweight/obese (body mass index (BMI) >25 kg/m2) and ≥1 additional diabetes, as well as in women planning pregnancy who are overweight/obese and ≥1 additional diabetes.

If the screening results are within normal limits, it is repeated after ≥3 years (or more often, depending on the initial indicators and FPG). In the presence of prediabetes, testing is performed annually, and women with a history of gestational diabetes are tested for prediabetes every 3 years.

Screening in children for prediabetes and T2Dshould be considered after puberty or age 10 (whichever comes first), in overweight/obese children and adolescents who have ≥1 additional diabetes-related risk factors.

The predisposing factors include:

family history of DM (presence of diabetes in first- or second-line relatives)

high risk race/ethnicity;

signs of insulin resistance or conditions related to it;

mother`s gestational diabetes.

Screening is performed every 3 years [9].

4.2. Self monitoring in CVD

Self-monitoring and monitoring in the primary prevention of CVD involves the assessment of modifiable risk factors. In particular, blood pressure (BP) should be classified as normal, elevated, or hypertension to prevent and treat high BP. In particular, normal blood pressure is systolic blood pressure <120 mm Hg and diastolic blood pressure <80 mm Hg; elevated blood pressure is systolic blood pressure 120-129 mm Hg and diastolic blood pressure <80 mm Hg. After the initial assessment of blood pressure by a specialist, it is advisable to repeat the examination every year for adults with normal blood pressure. In the same aspect, the recommendation to limit sodium intake to <1500 mg/day or at least strive for a 1000 mg/day reduction, as well as to increase dietary potassium intake to at least 3500-5000 mg/day is also emphasized [222].

Population-based studies in the United States show that the optimal level of total cholesterol is about 150 mg/dL (3.8 mmol/L), which corresponds to LDL cholesterol levels of about 100 mg/dL (2.6 mmol/L). The adult population with cholesterol concentrations in this range demonstrates low rates of atherosclerotic cardiovascular disease [80].

At the same time, elevated levels of high-sensitivity C-reactive protein (≥2.0 mg/L) are associated with an increased risk of CVD. In addition, treatment of T2Dis recommended for the primary prevention of cardiovascular disease.

Short sleep duration (<6 hours) and poor quality of sleep are associated with high blood pressure and should be considered in primary prevention. Calculation of body mass index (BMI) is recommended annually or more frequently to identify overweight and obese adults for weight loss [15].

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